



Universidad Centro Occidental Lisandro Alvarado
Postgrado de Cardiología Clínica
Centro Cardiovascular Regional Centro Occidental



Apertura de Ciclo de evidencia científica

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ENFERMEDAD TROMBOEMBÓLICA VENOSA

La **enfermedad tromboembólica venosa (ETV)**, una entidad clínica que comprende:

- la **trombosis venosa profunda (TVP)** de las extremidades,
- el **embolismo pulmonar (EP)**
- el **síndrome Post embolia Pulmonar**

- la **hipertensión pulmonar tromboembólica crónica (HPTEC)**.

Misma
enfermedad

Study outcome events in 906 patients using 2014 ESC model

Intermediate-High Risk Pulmonary Embolism

Rosa Mirambeaux¹, Francisco León¹, Behnood Bikdeli^{2 3 4}, Raquel Morillo¹, Deisy Barrios¹, Edwin Mercedes¹, Lisa Moores⁵, Victor Tapson⁶, Roger D Yusen⁷, David Jiménez^{1 8 9}

- 1,015 normotensive patients with acute PE
- Of these, 97 (9.6%) had intermediate-high risk PE.
- 30-day complicated course in 23 (24%)
- 30-day PE-related mortality in 7 patients (7.2%)

TH Open 2019 Dec 4;3(4):e356-e363.

Death due to PE at 30 days

16/105: **15.2%**
(CI; 8.4-22.1)

13/272: **4.8%**
(CI; 2.2-7.3)

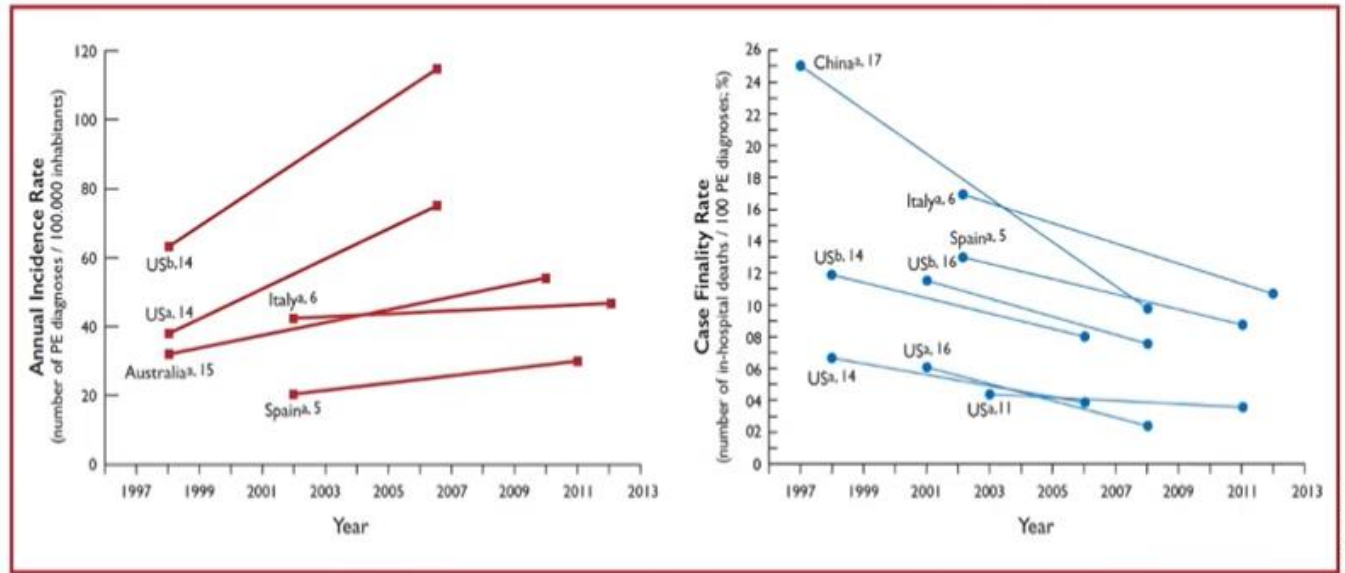
7/333: **2.1%**
(CI; 0.6 -3.6)

1/196: **0.5%**
(CI; 0-1.5)

10x
higher

MAGNITUD DEL PROBLEMA

Algunos datos importantes



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MAGNITUD DEL PROBLEMA

Trends in the Management and Outcomes of Acute Pulmonary Embolism



Analysis From the RIETE Registry

David Jiménez, PhD,* Javier de Miguel-Díez, PhD,† Ricardo Gujarró, MD,‡ Javier Trujillo-Santos, PhD,§ Remedios Otero, PhD,¶ Raquel Barba, PhD,¶ Alfonso Muriel, PhD,¶ Guy Meyer, PhD,** Roger D. Yusen, MD,‡† Manuel Monreal, PhD,‡,|| for the RIETE Investigators

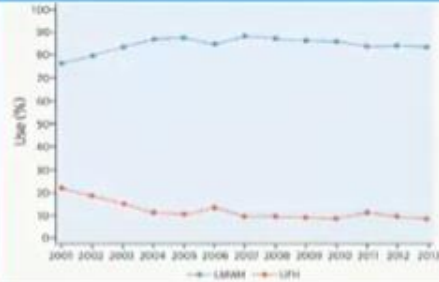
N= 23858

13 años de seguimiento

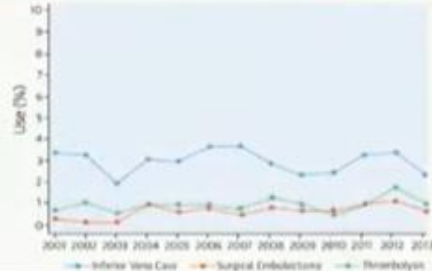
- 25% > 80 años
- 73% Alto o Intermedio-Alto Riesgo (sPESI)

CENTRAL ILLUSTRATION Acute PE Mortality in the RIETE Registry: Significant Reductions in Mortality Over Time

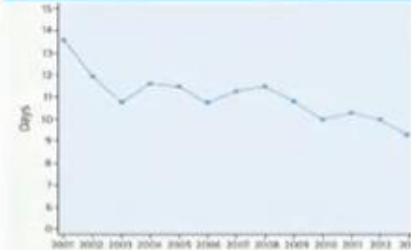
A. Temporal Trends in Anticoagulant Use



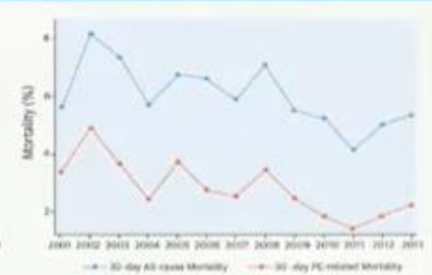
B. Temporal Trends in Use of Other Pharmacological and Interventional Therapies



C. Temporal Trends in Length of Stay



D. Mortality Rates by Calendar Year



Jiménez, D. et al. J Am Coll Cardiol. 2016; 67(21):102-10.

MAGNITUD DEL PROBLEMA

Diagnostic Error in Medicine

Analysis of 583 Physician-Reported Errors

Arch Intern Med. 2009;169(20):1881-1887

**Table 1. Most Frequently Missed Diagnoses
Among 583 Physician-Reported Cases of Diagnostic Error**

Diagnosis	No. (%)
Pulmonary embolism	26 (4.5)
Drug reaction or overdose	26 (4.5)
Lung cancer	23 (3.9)
Colorectal cancer	19 (3.3)
Acute coronary syndrome	18 (3.1)
Breast cancer	18 (3.1)
Stroke, including hemorrhage	15 (2.6)
Congestive heart failure	13 (2.2)
Fracture, various types	13 (2.2)
Abscess, various locations	11 (1.9)
Pneumonia, including type	10 (1.7)
Aortic aneurysm/dissection	9 (1.5)
Appendicitis	9 (1.5)
Depression	9 (1.5)
Diabetes mellitus	8 (1.4)
Tuberculosis	8 (1.4)
Anemia	6 (1.0)
Bacteremia	6 (1.0)
Metastatic cancer	6 (1.0)
Spinal cord compression	6 (1.0)

MAGNITUD DEL PROBLEMA

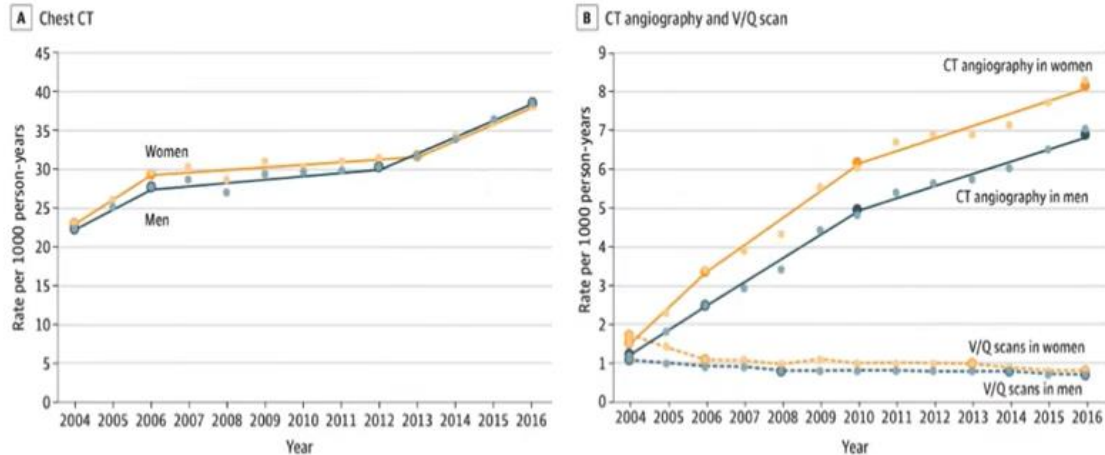
JAMA
Network | Open.

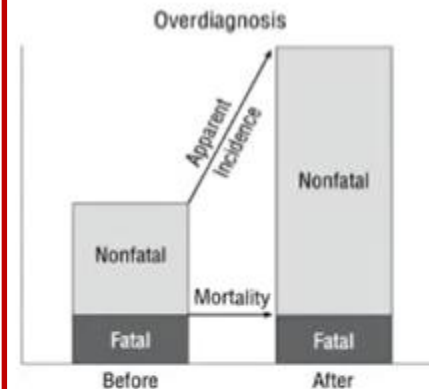
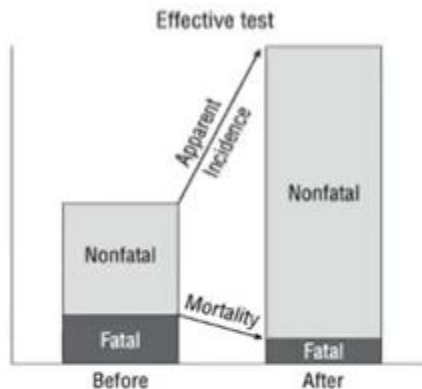
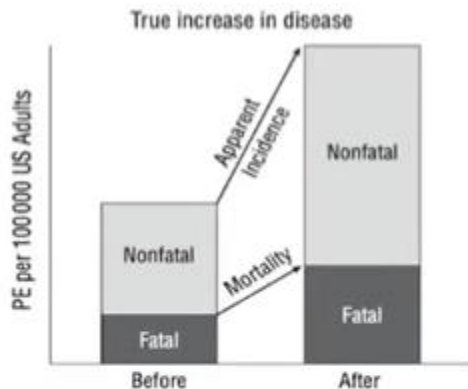


Original Investigation | Imaging
Trends in Imaging for Suspected Pulmonary Embolism
Across US Health Care Systems, 2004 to 2016

Ralph C. Wang, MD, MPH, Shari L. Mittleman, PhD, Emily C. Muller, PhD, Marjorie S. Ryan, PhD, May K. Tsai, MPH, David J. B. Swales, MPH, Robert T. Gatterer, PhD, Alexander K. Rahm, PhD, Nicholas K. Suss, PhD, Shari Robinson, PhD, Rebecca Smith-Bindman, MD

Figure 2. Chest Imaging Rates per 1000 Person-Years by Imaging Test and Sex, With Annual Percentage Changes in Rates Based on Joinpoint Regression Analysis





Scenario

Increase in risk factors results in more pulmonary emboli, with no change in disease severity.

More sensitive test detects more pulmonary emboli, and new cases benefit from treatment → fewer deaths.

More sensitive test detects more pulmonary emboli, and new cases do not benefit from treatment (mild disease).

Apparent incidence

$\frac{\text{Diagnosed PE}}{\text{US population}}$

Increased

Increased

Increased

Mortality

$\frac{\text{Fatal PE}}{\text{US population}}$

Increased

Decreased

No change

Case fatality

$\frac{\text{Fatal PE}}{\text{Diagnosed PE}}$

No change

Decreased

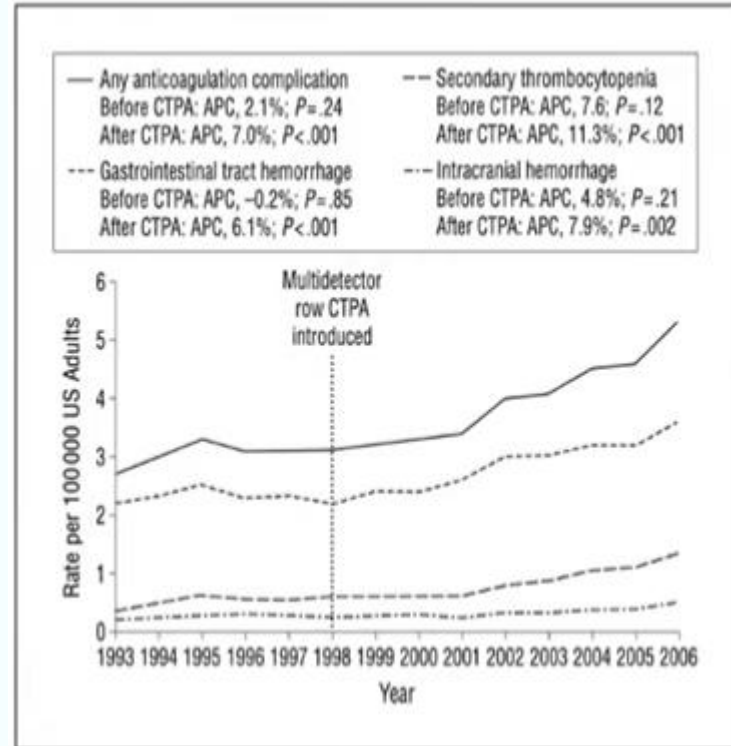
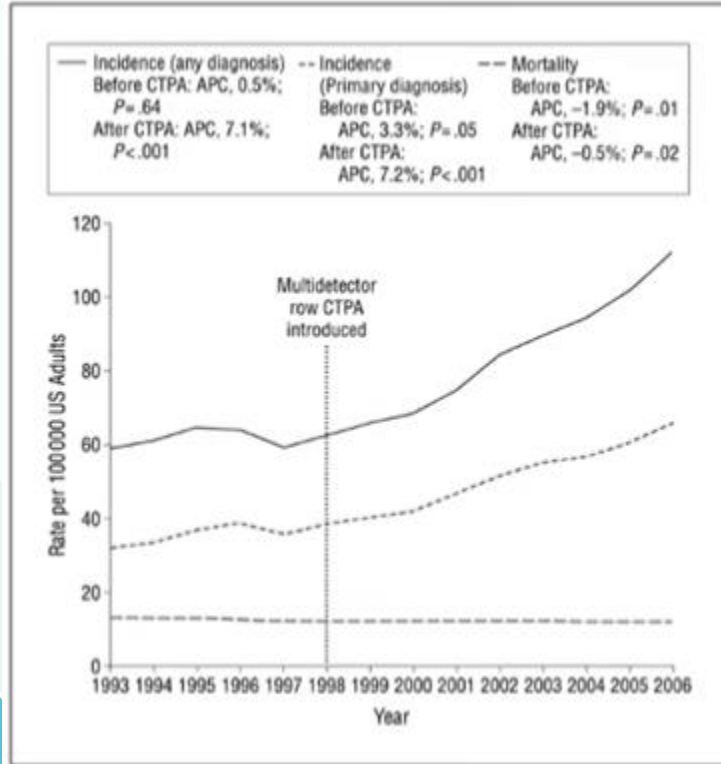
Decreased

LESS IS MORE

Time Trends in Pulmonary Embolism in the United States

Evidence of Overdiagnosis

Rendi Soylesmez Wiener, MD, MPH, Lisa M. Schwartz, MD, MS, Steven Woloshin, MD, MS



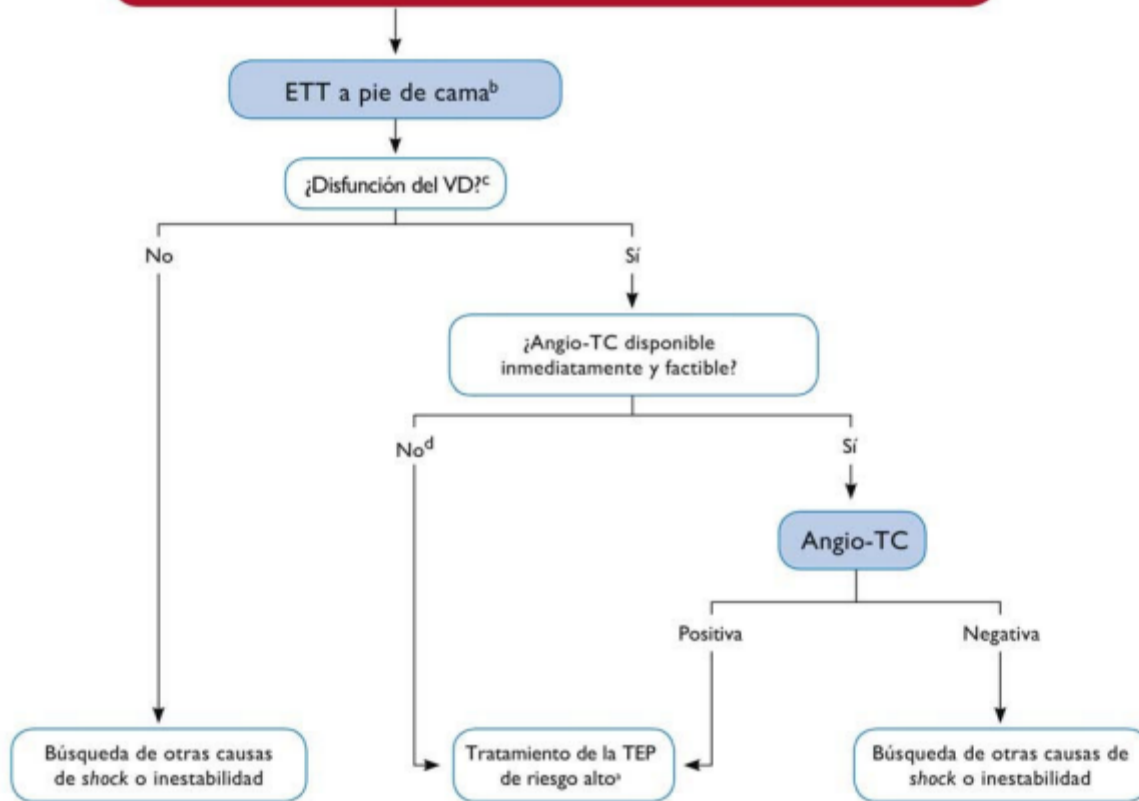
EVALUACIÓN INICIAL

PERT



Pulmonary Embolism Response Team

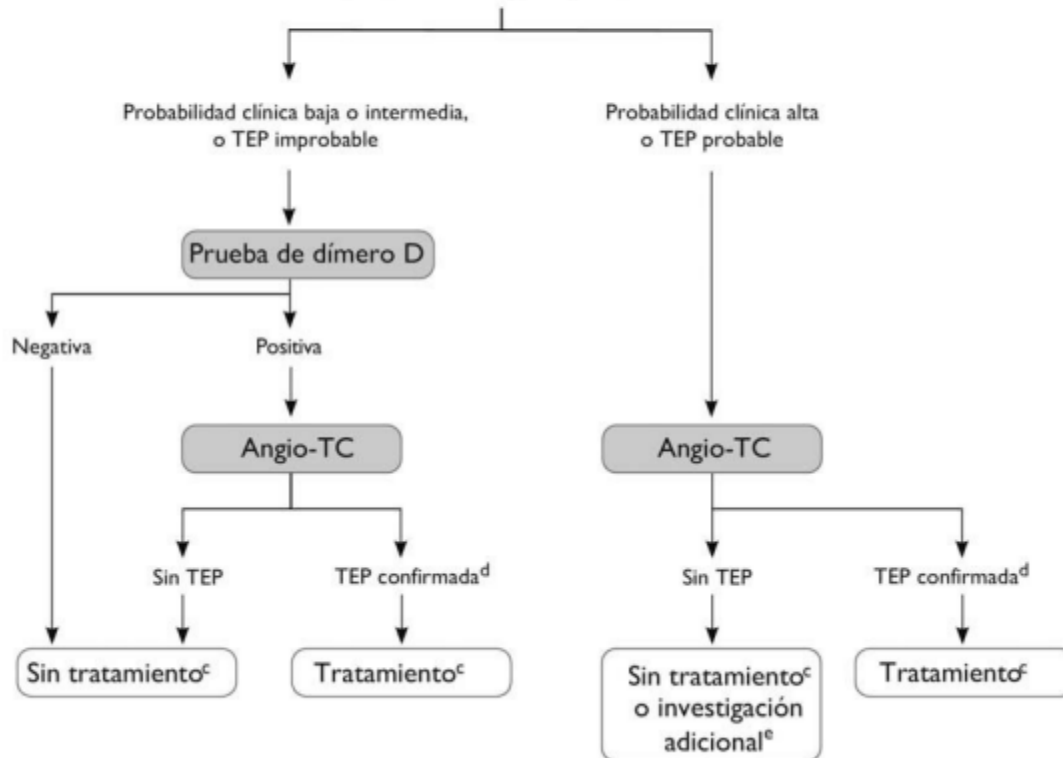
Sospecha de TEP en pacientes con inestabilidad hemodinámica^a



Sospecha de TEP en pacientes sin inestabilidad hemodinámica^a

Evalúe la probabilidad clínica de TEP

Juicio médico o regla de predicción^b



ESCALAS DE PROBABILIDAD PRETEST

Wells criteria¹⁰¹

- Presence of active malignancy: +1
- Haemoptysis: +1
- History of previous DVT or PE: +1.5
- Heart rate >100bpm: +1.5
- Surgery or bed rest ≥3 days in 1 month: +1.5
- Clinical signs and symptoms of DVT: +3
- No presence of an alternative diagnosis as likely as or more likely than PE: +3

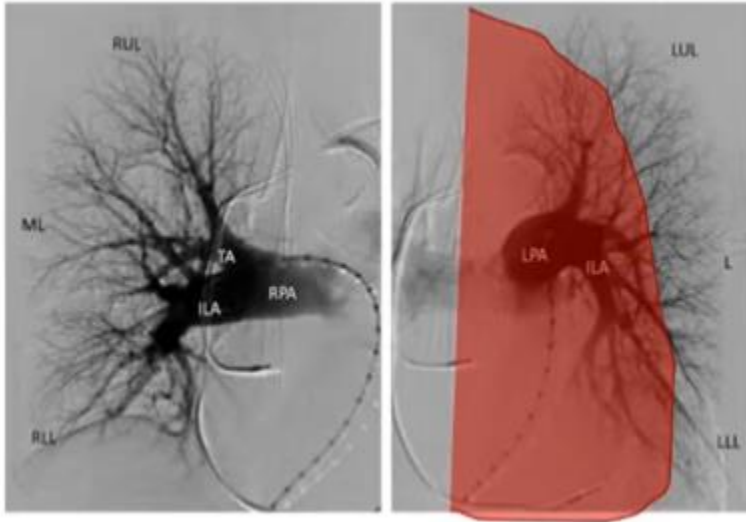
Pretest probability	Points	Prevalence of PE (%; 95% CI)
Low	<2	5.7 (3.7–8.2)
Intermediate	2–6	23.2 (18.3–28.4)
High	>6	49.3 (42.6–56.0)
Unlikely	≤4	8.4 (6.4–10.6)
Likely	>4	34.4 (29.4–39.7)

Regla de probabilidad clínica de Ginebra revisada para la embolia pulmonar

Factor	Puntos de decisión clínica	
	Versión original ⁹¹	Versión simplificada ⁸⁷
TEP o TVP previa	3	1
Frecuencia cardíaca		
75-94 lpm	3	1
≥ 95 lpm	5	2
Cirugía o fractura en el último mes	2	1
Hemoptisis	2	1
Cáncer activo	2	1
Dolor unilateral en extremidades inferiores	3	1
Dolor a la palpación venosa profunda de extremidades inferiores y edema unilateral	4	1
Edad > 65 años	1	1
Probabilidad clínica		
<i>Puntuación en tres niveles</i>		
Baja	0-3	0-1
Intermedia	4-10	2-4
Alta	≥ 11	≥ 5
<i>Puntuación en dos niveles</i>		
TEP improbable	0-5	0-2
TEP probable	> 6	≥ 3

TEP: tromboembolia pulmonar; TVP: trombosis venosa profunda.

MAGNITUD DEL PROBLEMA



Se recomienda asumir el diagnóstico de TEP (sin realizar otras pruebas) si la angio-TC muestra un defecto de llenado **segmentario o más proximal** en pacientes con una probabilidad clínica intermedia o alta¹¹⁵

I

B

Se puede considerar la realización de más pruebas para confirmar la TEP en caso de defectos de llenado subsegmentarios aislados¹¹⁵

IIb

C

2. Estratificación de Riesgo

ESTRATIFICACIÓN DEL RIESGO

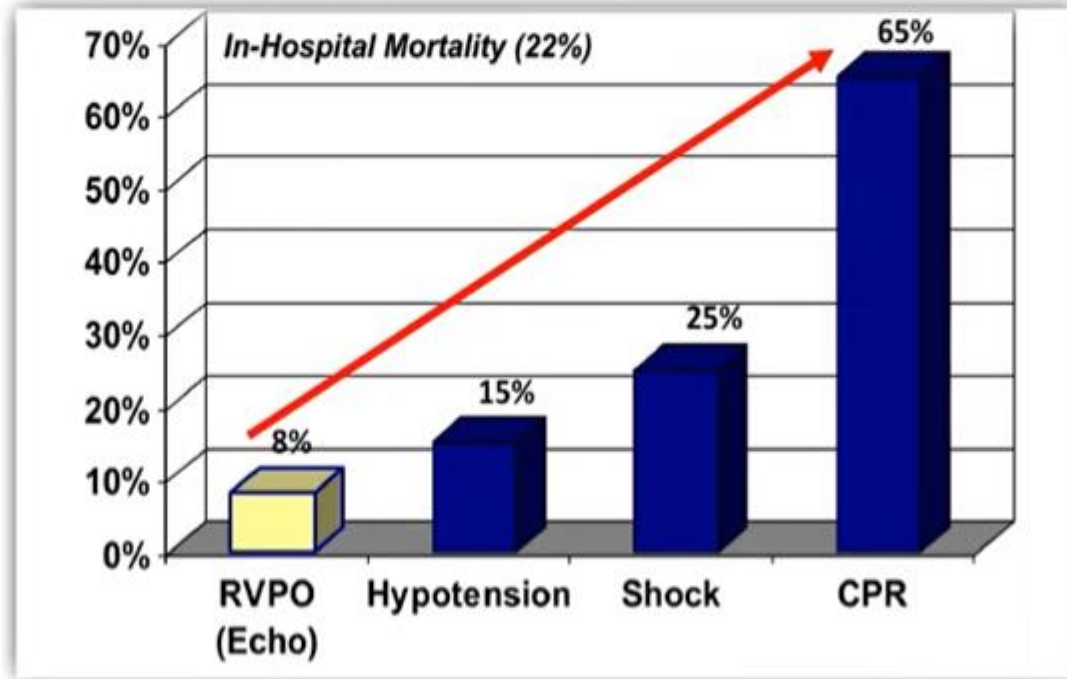
2 Objetivos

- 1. Riesgo de Mortalidad Temprana (30 días) por el TEP
- 2. Establecer el mejor tratamiento

La estratificación es buena en los Extremos y Difícil en el medio

Mortalidad intrahospitalaria del TEP

Management Strategy and Prognosis of Pulmonary Embolism Registry (MAPPET)

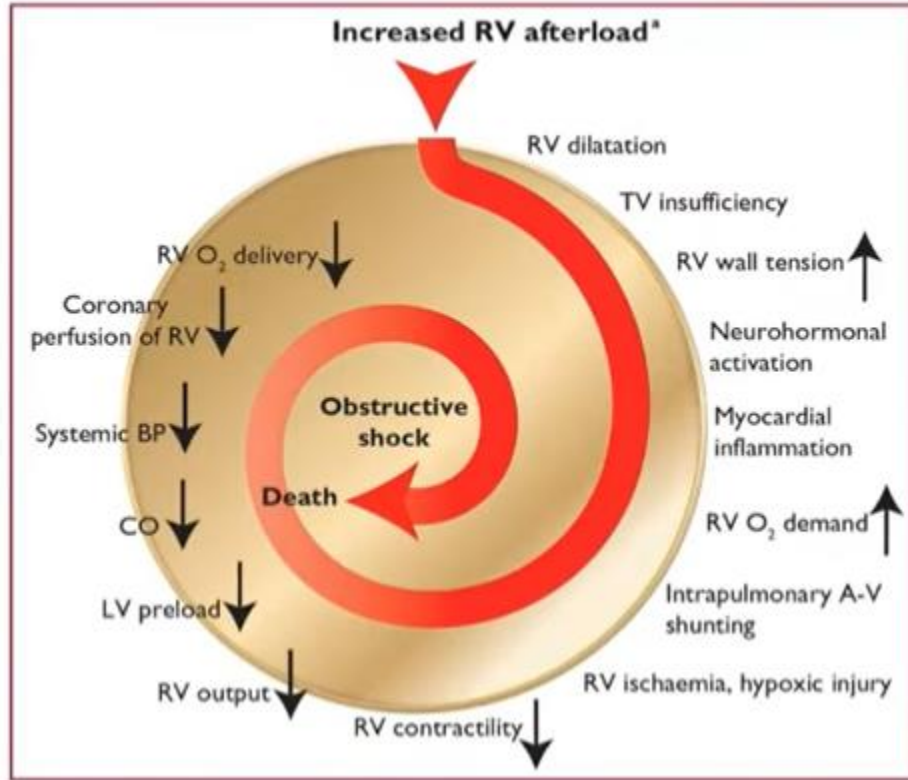


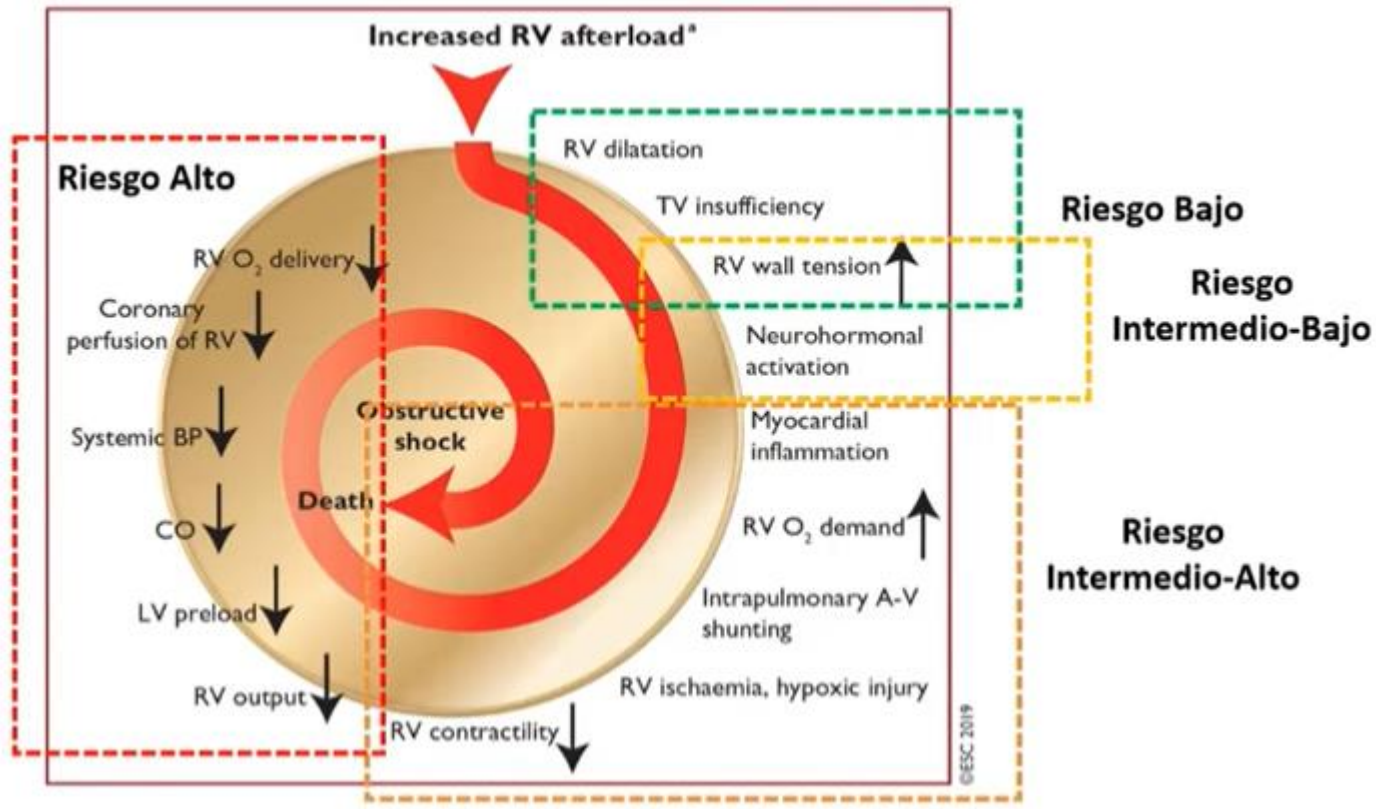


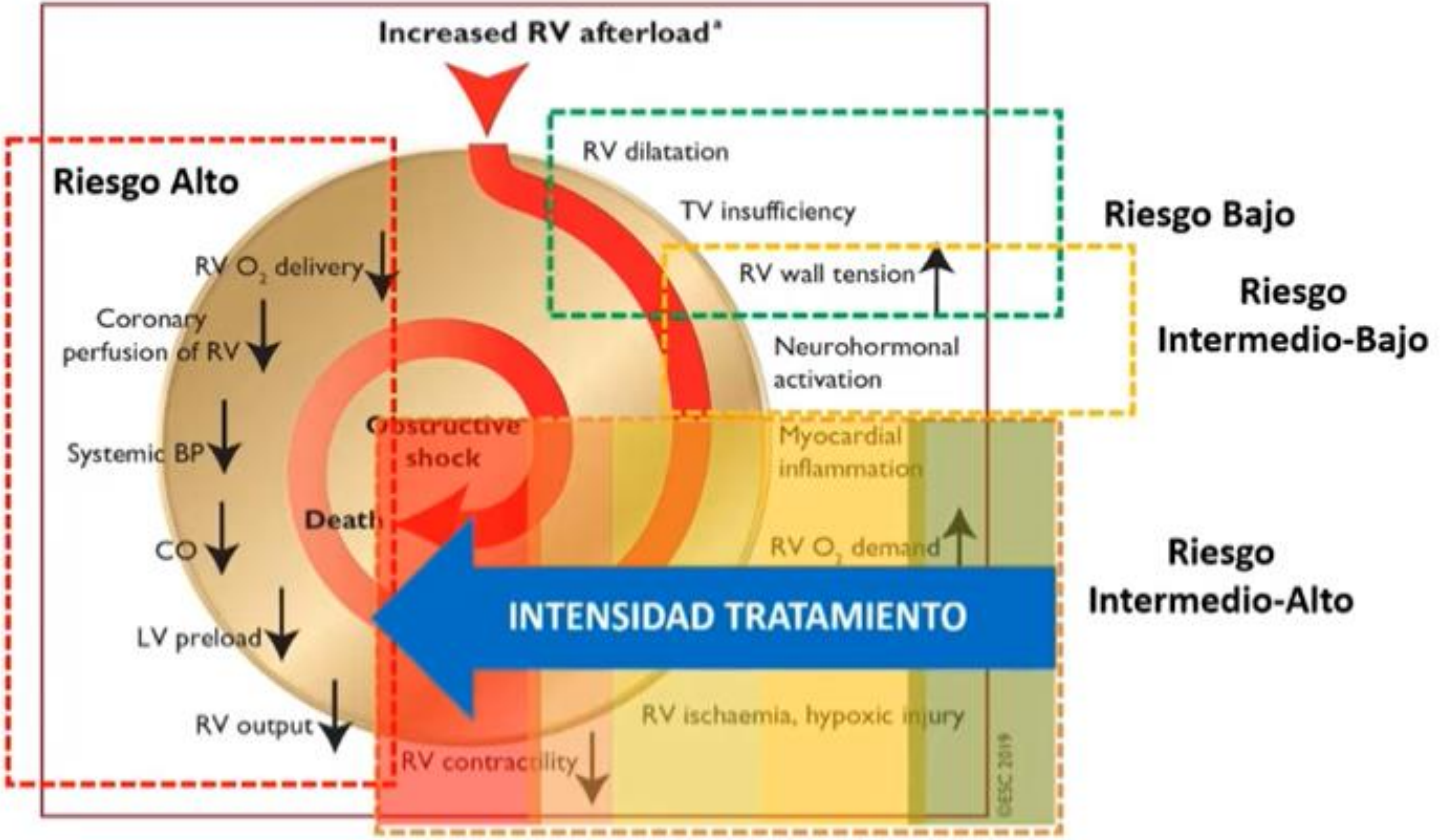
Estratificación Riesgo TEP

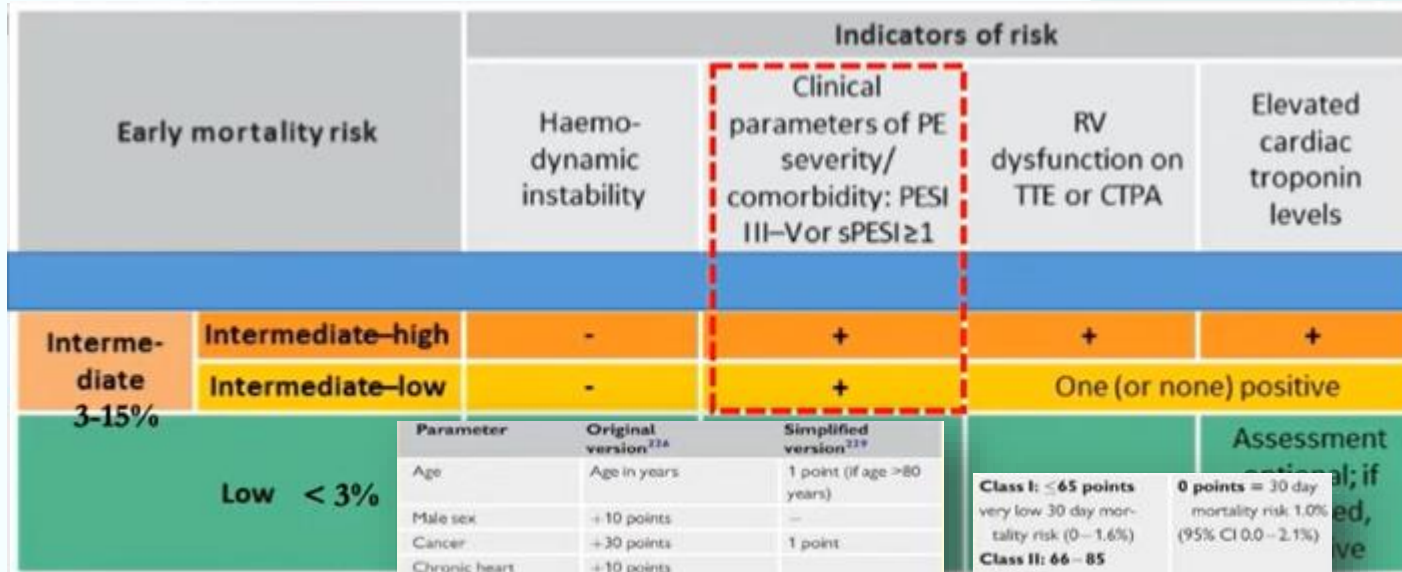
Early mortality risk		Indicators of risk			
		Haemo-dynamic instability	Clinical parameters of PE severity/ comorbidity: PESI III-V or sPESI ≥1	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
5 %	High 15-65%	+	(+)	+	(+)
25 %	Intermediate-high	-	+	+	+
	Intermediate-low	-	+	One (or none) positive	
70 %	Low < 3%	-	-	-	Assessment optional; if assessed, negative

Repercusión VD → principal determinante pronóstico









Parameter	Original version ^{22A}	Simplified version ^{22B}
Age	Age in years	1 point (if age >80 years)
Male sex	+ 10 points	-
Cancer	+ 30 points	1 point
Chronic heart failure	+ 10 points	-
Chronic pulmonary disease	+ 10 points	1 point
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 $< 36^{\circ}\text{C}$	+ 20 points	-
Altered mental status	+ 60 points	-
Arterial oxyhaemoglobin saturation $< 90\%$	+ 20 points	1 point

Class I: ≤ 65 points very low 30 day mortality risk (0–1.6%) (95% CI 0.0–2.1%)	0 points = 30 day mortality risk 1.0% (95% CI 0.0–2.1%)
Class II: 66–85 points low mortality risk (1.7–3.5%)	
Class III: 86–105 points moderate mortality risk (3.2–7.1%)	≥ 1 point(s) = 30 day mortality risk 10.9% (95% CI 8.5–13.2%)
Class IV: 106–125 points high mortality risk (4.0–11.4%)	
Class V: > 125 points very high mortality risk (10.0–24.5%)	

Assessment
... if
... ve

3. ¿Vale el PESI?



ChatGPT aprueba el MIR 2023 con solo un 25% de respuestas incorrectas

Tutores de CTO analizan el examen de esta inteligencia artificial con un muestrario de 20 preguntas



MARTES, 02 DE MAYO DE 2023, A LAS 12:20 . CATEGORIA: [SANIDAD HOY](#)

ChatGPT es capaz de ofrecer un trato más empático que un médico real

La tecnología da respuestas de más calidad ante preguntas de pacientes que un facultativo



ChatGPT

J

VALE EL PESI para evaluar el TEP?



Sí, el índice de gravedad de la embolia pulmonar (PESI) es una escala de evaluación útil para la estratificación del riesgo de mortalidad a corto y largo plazo en pacientes con tromboembolismo pulmonar (TEP).



La escala PESI tiene en cuenta diversos factores de riesgo, como la edad del paciente, la presencia de comorbilidades, la frecuencia cardíaca, la presión arterial sistólica y la presencia de signos clínicos como la disnea y la hipoxemia. Según la puntuación obtenida en la escala PESI, se clasifica al paciente en diferentes categorías de riesgo de mortalidad a corto plazo.

La escala PESI se ha demostrado útil para la toma de decisiones clínicas en pacientes con TEP, ya que permite identificar aquellos pacientes con bajo riesgo de mortalidad y que pueden ser tratados de forma ambulatoria, y aquellos con alto riesgo que requieren tratamiento hospitalario y una evaluación más exhaustiva.

Sin embargo, es importante tener en cuenta que la escala PESI es una herramienta de evaluación y no debe utilizarse de manera aislada para tomar decisiones clínicas. La evaluación clínica integral y el juicio clínico del médico son fundamentales para el diagnóstico y tratamiento adecuados del TEP.

Derivation and Validation of a Prognostic Model for Pulmonary Embolism

Drahomir Aujesky, D. Scott Obrosky, Roslyn A. Stone, Thomas E. Auble, Arnaud Perrier, Jacques Cornuz, Pierre-Marie Roy, and Michael J. Fine

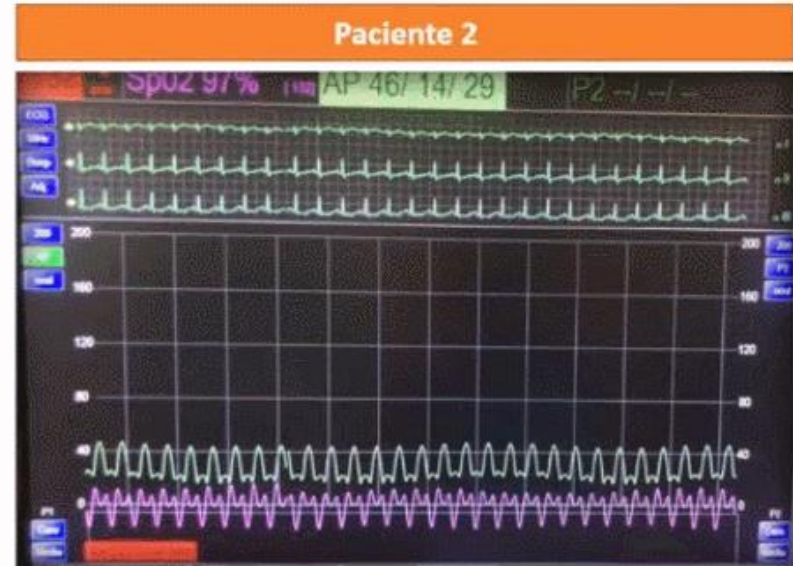
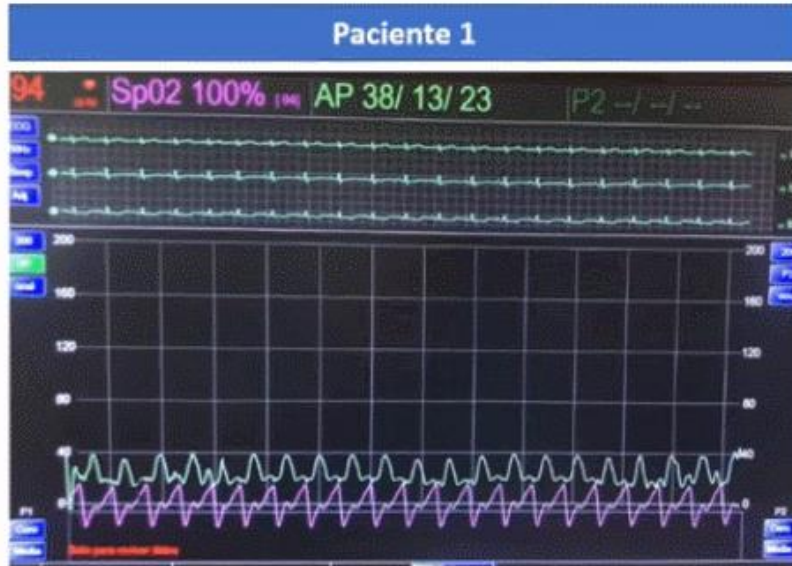


TABLE 4. RISK CLASS–SPECIFIC MEDICAL OUTCOMES IN THE DERIVATION AND VALIDATION SAMPLES

Medical Outcomes	Derivation Sample, % (95% CI) (n = 10,354)	Internal Validation Sample, % (95% CI) (n = 5,177)	External Validation Sample, % (95% CI) (n = 221)	p Value [§]	p Value
30-day mortality					
Class I	1.1 (0.7–1.7)	1.6 (0.9–2.6)	0 (0–6.6)	0.32	0.66
Class II	3.1 (2.5–4.0)	3.5 (2.5–4.7)	1.7 (0–8.9)	0.63	0.72
Class III	6.5 (5.5–7.6)	7.1 (5.7–8.7)	3.2 (0.4–11.2)	0.51	0.43
Class IV	10.4 (9.0–11.9)	11.4 (9.3–13.8)	4.0 (0.1–20.4)	0.44	0.36
Class V	24.5 (22.7–26.4)	23.9 (21.4–26.5)	10.0 (1.2–31.7)	0.69	0.19

- **Permite sobre todo identificar a aquellos pacientes con bajo riesgo de mortalidad a 30 días (Clases I-II)**
- **Es la escala más ampliamente validada en estudios externos**

Pacientes de Intermedio – Alto Riesgo



PESIs 1 + Disfunción del VD + Tnl elevada

Parámetros clínicos asociados a riesgo

- Taquicardia
- Taquipnea
- Saturación de Oxígeno
- Hipotensión Arterial

- **Síncope¹**

- **TVP²**

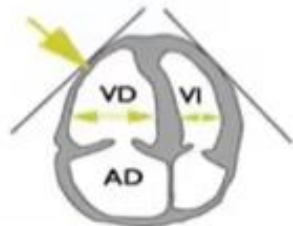
- **ILb₅**

1. *European Heart Journal* (2018) 39, 4186–4195

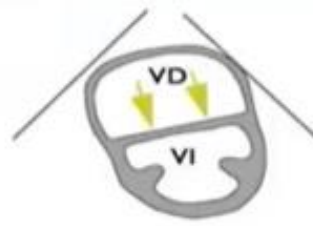
2. *Chest*. 2016;149:192200.



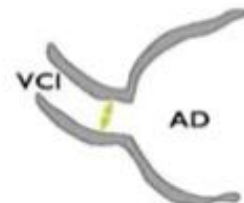
A. Agrandamiento del VD, plano largo del eje paraesternal



B. VD dilatado con un cociente basal VD/VI > 1,0 y signo de McConnell (flecha), plano de 4 cámaras



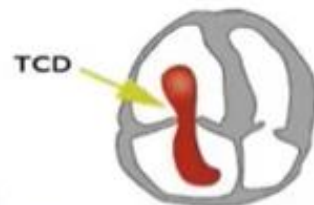
C. Septo intraventricular aplanado (flecha), plano corto del eje paraesternal



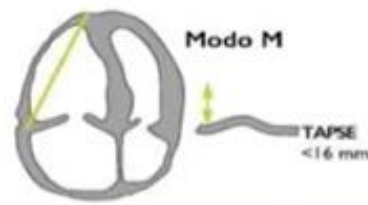
D. Vena cava inferior distendida con colapsabilidad inspiratoria disminuida, plano subcostal



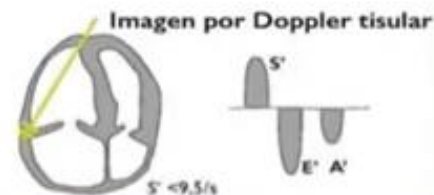
E. Signo 60/60: coexistencia de un tiempo de aceleración de eyección pulmonar < 60 ms y «notch» en mesosístole con gradiente pico sistólico ligeramente elevado (< 60 mmHg) en la válvula tricúspide



F. Trombo móvil en corazón derecho detectado en las cavidades del corazón derecho (flecha)



G. TAPSE disminuido medido en modo M (< 16 mm)



H. Velocidad pico sistólica disminuida del anillo tricúspide (< 9,5 cm/s)

Supplementary Table 3 Prognostic value and cut-off levels of imaging parameters

Parameter	n	Study design	Cut-off value	Study outcome ^a	OR or HR (95% CI)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	NPV (%) (95% CI)	PPV (%) (95% CI)
TTE									
RV dysfunction	1249	Meta-analysis ¹	Various criteria	All-cause mortality	2.4 (1.3–4.3)	74 (61–84)	54 (51–56)	98 (96–99)	8 (6–10)
RV/LV diameter ratio	782 ^b	Prospective cohort ⁴	≥1.0	All-cause mortality	35.7 (3.4–381.0)	21 (10–39)	83 (80–86)	96 (94–97)	6 (2–11)
				PE-related mortality	8.9 (1.1–74.7)	50 (20–80)	83 (80–86)	99 (98–100)	4 (2–9)
TAPSE	782 ^b	Prospective cohort ⁴	≤16 mm	All-cause mortality	2.4 (1.2–4.7)	34 (21–52)	82 (79–85)	96 (95–98)	8 (5–14)
				PE-related mortality	4.4 (1.3–15.3)	50 (24–76)	82 (79–84)	99 (98–100)	3 (1–8)
McConnell sign	411 ^b	Prospective cohort ⁷	Present	PE-related mortality or rescue thrombolysis	3.9 (1.5–10.2)	61 (39–84)	73 (68–78)	97 (91–99)	13 (5–20)
				PE-related mortality or rescue thrombolysis	27.9 (6.2–124.6)	82 (59–100)	86 (81–90)	99 (98–100)	21 (9–33)
Right heart thrombi	15 220	Meta-analysis ⁸	Present	All-cause mortality	3.6 (1.5–8.7)	45 (23–67)	82 (78–86)	97 (95–99)	12 (5–19)
				PE-related mortality	4.8 (2.0–11.3)	26 (20–33)	97 (96–97)	96 (95–96)	17 (14–20)
CTPA									
RV/LV diameter ratio	4395	Meta-analysis ⁹	≥1.0	All-cause mortality	2.5 (1.8–3.5)	—	—	—	—
				PE-related mortality	5.0 (2.7–9.2)	—	—	—	—
RV/LV volume ratio	260	Prospective cohort ¹⁰	>1.2	All-cause mortality	6.5 (1.8–23.8)	85 (64–95)	45 (39–51)	97 (92–99)	11 (7–18)
RA/LA volume ratio	636	Retrospective cohort ¹¹	>1.2	All-cause mortality	2.1 (1.3–3.4)	64 (54–74)	52 (48–56)	91 (87–93)	17 (13–21)
Contrast reflux into the IVC	1649	Meta-analysis ⁹	Present	All-cause mortality	2.2 (1.5–3.2)	—	—	—	—

Validation of the prognostic value and respective cut-off levels of specific imaging parameters in acute pulmonary embolism.

CI = confidence interval; CTPA = computed tomography pulmonary angiography; HR = hazard ratio; IVC = inferior vena cava; LA = left atrium/atrial; LV = left ventricle/ventricular; NPV = negative predictive value; OR = odds ratio; PE = pulmonary embolism; PPV = positive predictive value; RA = right atrium/atrial; RV = right ventricle/ventricular; TAPSE = tricuspid annulus plane systolic excursion; TTE = transthoracic echocardiography.

^aDuring hospital stay or within the first 30 days after PE diagnosis.

^bNormotensive patients with PE.

Parámetros laboratorio asociados a riesgo



Hs-Tpn

Aumento en el 60% de TEP

Aumento de mortalidad

Valores de corte habituales (hs-TpnT > 14)

Valores de corte ajustados a edad

Poco valor por sí solos

Alto valor en combinación con otros parámetros: VD, PESIs.

Alto VPN

Parámetros laboratorio asociados a riesgo

NT-ProBNP
(≥ 600 pg/ml)

Lactato
(≥ 2 mmol/l)²

Cr (TFG)
N-GAL
Cistatina-C
Copeptina

50% de TEP¹

10% Riesgo Mortalidad Precoz¹

23% Riesgo MACE¹

Alto VPN

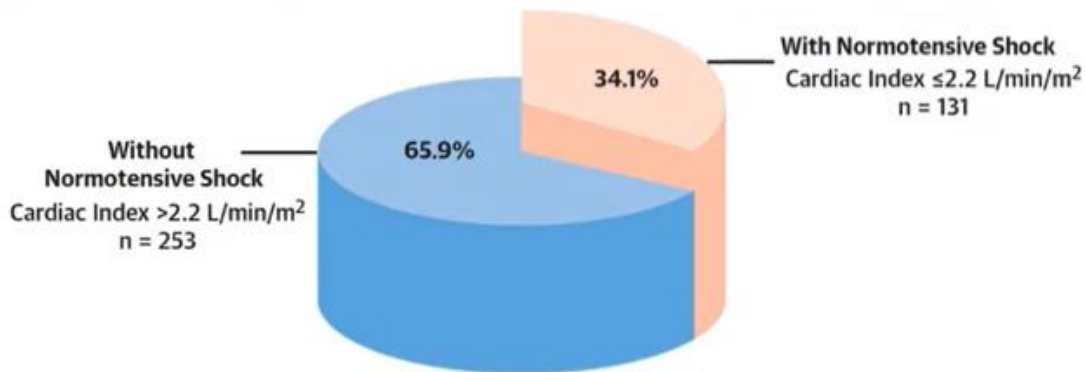
Prevalence and Predictors of Cardiogenic Shock in Intermediate-Risk Pulmonary Embolism



Insights From the FLASH Registry

Sripal Bangalore, MD, MHA,¹ James M. Forowitz, MD,² Daren Beam, MD,³ Wissam A. Jaber, MD,²
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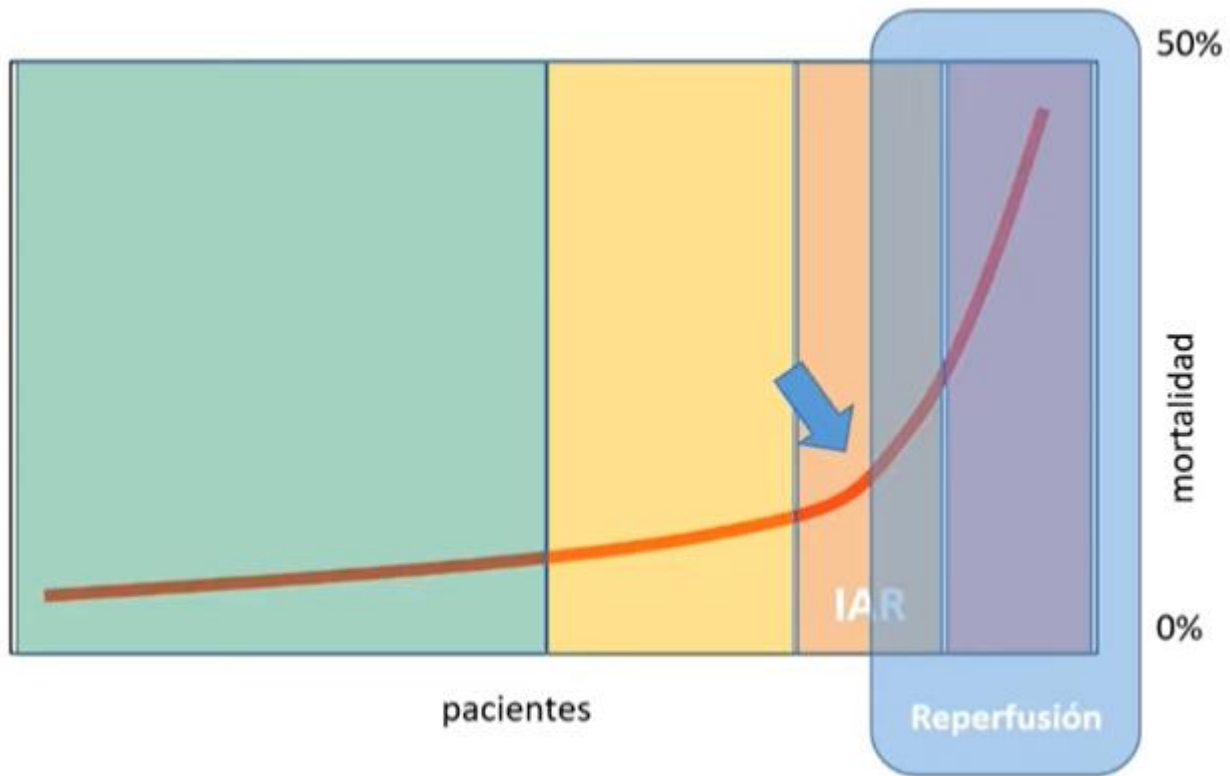
Normotensive Shock in Patients With Intermediate-Risk Pulmonary Embolism From the FLASH Registry



Composite Shock Score

Elevated Troponin + Elevated BNP + Moderate/Severely Reduced RV function + Saddle PE + Concomitant DVT + Tachycardia

Risk Factor Associated With Normotensive Shock
(OR: 5.84; 95% CI: 2.00-17.04)



Reperfusion treatment

Rescue thrombolytic therapy is recommended for patients with haemodynamic deterioration on anticoagulation treatment.²⁸²

As an alternative to rescue thrombolytic therapy, surgical embolectomy^e or percutaneous catheter-directed treatment^e should be considered for patients with haemodynamic deterioration on anticoagulation treatment.

Routine use of primary systemic thrombolysis is not recommended in patients with intermediate- or low-risk PE.^{c,f 179}

¿Qué es deterioro hemodinámico?

¿Debemos esperar o anticipar?

¿Qué es deterioro hemodinámico?

¿Ojo clínico?
NEWS2 +5

Table 5. National Early Warning Score (NEWS) supplementary material.

Physiological parameters	3	2	1	0	1	2	3
Respiration rate (breaths per minute)	≤8		9-11	12-20		21-24	≥25
SpO ₂ (%)	≤91	92-93	94-95	≥96			
Any supplemental oxygen		Yes		No			
Temperature (°C)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	
Systolic BP (mmHg)	≤90	91-100	101-110	111-219			≥220
Heart/pulse rate (beats per minute)	≤40		41-50	51-90	91-110	111-130	≥131
Level of consciousness, AVPU scale				A			V, P or U

Level of consciousness: A: alert; V: responds to voice; P: responds to pain; U: unresponsive. From National Early Warning Score (NEWS): Standardising the assessment of acute-illness severity in the NHS. Report of a working party. Royal College of Physicians, London, 2012²⁴. BP: blood pressure; SpO₂: oxygen saturation

Validation of a Model for Identification of Patients at Intermediate to High Risk for Complications Associated With Acute Symptomatic Pulmonary Embolism

Carolina Fernández, MD; Carlo Bova, MD; Olivier Sanchez, PhD; Paolo Prandoni, PhD; Mareike Lankeit, MD; Stavros Konstantinides, PhD; Simone Vanni, MD; Covadonga Fernández-Golfín, PhD; Roger D. Yusen, MD; and David Jiménez, PhD, FCCP

CHEST

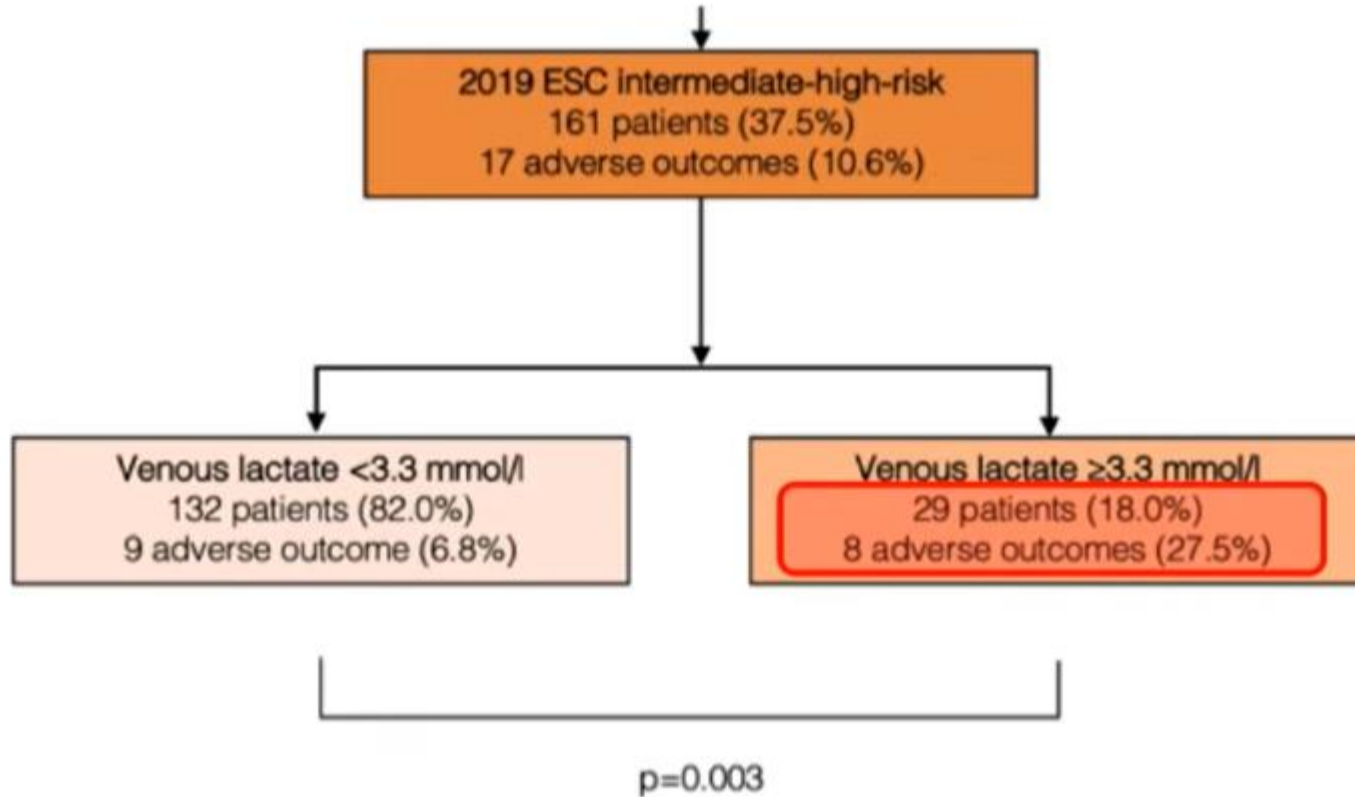
TABLE 1] Bova Score and Staging System for Risk of PE-Related Complications Within 30 Days of Acute Symptomatic PE Diagnosis

Predictor Variable	Points
Systolic BP 90-100 mm Hg	2
Cardiac troponin elevation	2
RV dysfunction (echocardiogram or CT scan)	2
Heart rate \geq 110/min	1

IAR

Normotensive PE patients: 30 day PE related mortality

- Class I (0-2) = 4.4%
- Class II (3-4) = 6.8%
- Class III (>4) = 10.5%



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NEWS2 +5

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- 43% of submassive PE had cardiogenic shock (CI<1.8)
- Bova Score Class III (>4) - 30d 10.5% mortality
- Venous lactate >3.3 mmol/l – 27% adverse outcome

Shock index (HR / SBP) > 1

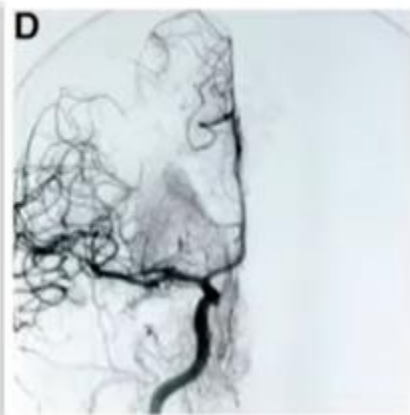
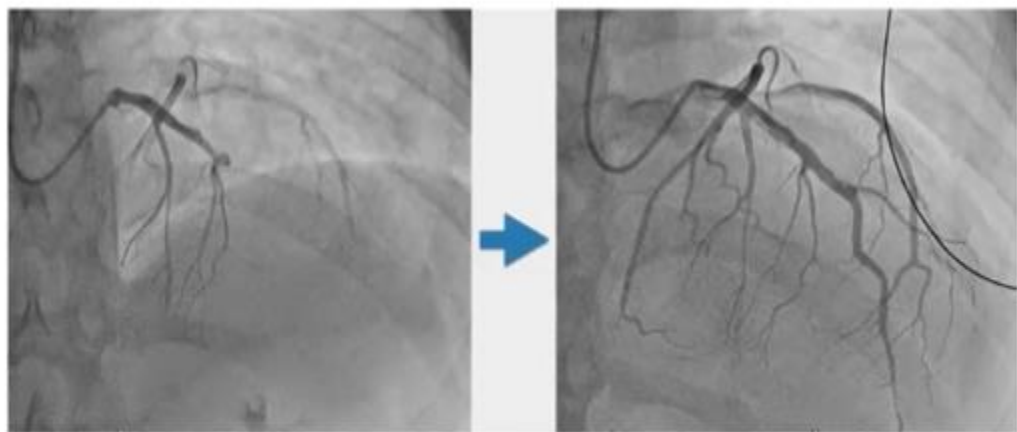
Venous lactate > 3.3 mmol/L

Oliguria o FG <60 ml/min

TVP proximal

PaO₂ / FiO₂ <250







Diagnóstico temprano

Diagnostico

Un tercio de las muertes ocurren repentinamente o a las pocas horas del evento agudo, alrededor del 40% de las muertes se diagnostican post mortem.

- El 7% de las muertes tempranas ocurren en pacientes que fueron diagnosticados y tratados adecuadamente.

Una estrategia de manejo ajustada al riesgo es esencial para los pacientes con diagnóstico de TEP.

Principales estrategias terapéuticas para la EP aguda

- 01 El soporte hemodinámico y respiratorio
- 02 La anticoagulación
- 03 Terapia de reperfusión con:
- 04 Trombólisis sistémica
- 05 Terapia dirigida por catéter.



Variables a considerar



Condición hemodinámica del paciente

Paciente está en shock



Extensión y la proximidad del coágulo



La edad
Condiciones coexistentes

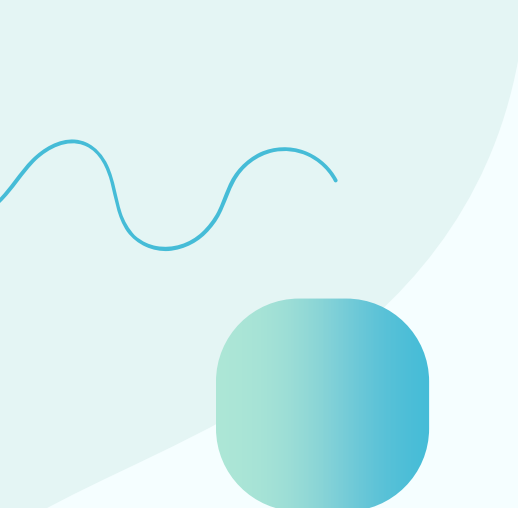


Efectos del coágulo en la función del ventrículo derecho



“Un objetivo principal de la terapia en el manejo de la EP es mejorar la hemodinámica al reducir la tensión en el ventrículo derecho.

Esto conduce a la mejora de los síntomas, la restauración del flujo arterial pulmonar, la disminución del riesgo de EP recurrente y la prevención del desarrollo de hipertensión pulmonar tromboembólica crónica (HPTEC).”



Tratamiento trombolítico.



Dosis de fármaco trombolítico.

- **Estreptoquinasa** 250.000 UI como dosis de carga durante 30 minutos, seguida de 100.000 UI/h durante 12 a 24 horas.
- Régimen acelerado: 1,5 millones de UI en 2 horas.

- **Uroquinasa** 4400 UI/kg como dosis de carga durante 10 minutos, seguida de 4400 UI/kg por hora durante 12 a 24 horas.
- Régimen acelerado 3 millones de UI durante 2 horas.

- **Alteplasa** 100 mg durante 2 horas o 0,6 mg/kg durante 15 minutos (dosis máxima 100 mg).

La evidencia de los efectos beneficiosos de la trombólisis sistémica en pacientes con TEP de riesgo intermedio



Tema lleno de controversia.

El ensayo internacional PEITHO (2012)

Un bolo intravenoso único de tenecteplasa más heparina mostró beneficios en la prevención de la descompensación hemodinámica en comparación con placebo más heparina en pacientes con TEP de riesgo intermedio.

La alteplasa 0,5 mg/kg (máximo 50 mg), administrada en un bolo de 10 mg seguido del resto durante 2 horas, se asoció con una reducción de la hipertensión pulmonar.

Systemic Thrombolysis for Pulmonary Embolism

Evidence, Patient Selection, and Protocols for Management



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Partha Sardar, MD^{c,3}, Chirag Bavishi, MD, MPH^{a,4},
Jay Giri, MD, MPH^d, Saurav Chatterjee, MD^{e,*},⁵

Table 3**Latest recommendations for systemic thrombolysis in patients with acute massive and submassive pulmonary embolism (PE)**

Society	Entity	Recommendations
American College of Chest Physicians, ²⁵ 2016	Massive PE with low bleeding risk	Grade 2B
	Submassive PE	Grade 1B
	Patients with submassive PE who deteriorate (not developed hypotension yet) and low bleeding risk	Grade 2C
American Heart Association, ²⁶ 2011	Massive PE	Class IIa, Level of Evidence B
	Submassive PE with evidence of adverse prognosis and low bleeding risk	Class IIb, Level of Evidence C
	Submassive PE	Class III; Level of Evidence B
European Society of Cardiology, ¹⁵ 2014	Massive PE	Class I; Level of Evidence B
	Submassive PE	Class III, Level of Evidence B

Systemic Thrombolysis for Pulmonary Embolism



Procedures before/ after alteplase

- If possible and indicated, place nasogastric tubes, indwelling bladder catheters, intra-arterial lines, or intravenous lines before administration of systemic alteplase.
- If unable to perform before therapy, delay placement of nasogastric tubes, indwelling bladder catheters, intra-arterial pressure catheters, or intravenous lines for 24 hours if possible.

Alteplase dosing

Massive (or submassive) PE:

- 100-mg IV infusion over 2 h for most patients.
- In patients at high risk of bleeding, relative contraindications (see [Table 1](#)), age >65 y, weight <65 kg, body mass index <25 kg/m², a dose of 50-mg IV infusion over 1 h may be considered (or recommended by the PERT attending).

Cardiac arrest:

- Registered nurse (RN) may administer (physician/advanced practitioner can give if they prefer).
- 50-mg IV over 2–5 min.
- Once alteplase is given for cardiac arrest, high-quality cardiopulmonary resuscitation (CPR) should be continued at least 15 min after the dose to allow drug to circulate. CPR should be continued while alteplase is being administered.
 - If no return of spontaneous circulation 15 min after alteplase bolus: can consider a second 50 mg IV over 2–5 min.
 - If return of spontaneous circulation after alteplase 50-mg bolus: give remaining 50-mg IV infusion over 1 h.

Concomitant anticoagulation

- IV unfractionated heparin (UFH) in full therapeutic doses is the preferred anticoagulant for those receiving alteplase for PE before alteplase infusion.
- While considering/preparing alteplase, initiate UFH treatment with a bolus as endorsed by the Recommended Protocols for Initiation and Maintenance for Heparin Therapy and Prophylaxis for Non-Neonates on the PennMedicine Formulary.
- Once the decision to give alteplase is made, alteplase should be given as soon as possible. Suspend IV UFH treatment immediately before the initiation of alteplase infusion and throughout infusion.
- When the alteplase infusion is complete, check an aPTT immediately and restart UFH without a bolus at the previous infusion rate if aPTT <80 s.
- If a patient received a therapeutic dose of enoxaparin before alteplase, start the UFH infusion 12 h after the last dose of low-molecular weight heparin (LMWH) (24 h if given dalteparin/fondaparinux), provided the patient does not have new renal dysfunction, and did not receive a 1.5-mg/kg enoxaparin dose. If either of the latter two occur, please contact a critical care clinical pharmacy specialist for guidance.
- After 48–72 h of stability, the patient may be transitioned to a LMWH, warfarin, or a novel oral anticoagulant as clinically indicated.

Administration

A dedicated IV line is required; may be given peripherally
100-mg or 50-mg alteplase dose slow infusion (RN):

- Must be given via IV infusion pump.
- Can be found in library under alteplase → pulmonary embolism.
- VTBI entered should be 100 mL (or 50 mL for 50-mg dose).
- Rate of infusion will be 50 mL/h.
- When there is no alteplase left in the vial but drug left in the drip chamber, a 0.9% sodium chloride IV bag (100 mL or 250 mL as available on the unit) should be spiked and attached to the IV tubing where the empty vial was to continue to run at the same rate (50 mL/h) to complete the 2 (or 1 as stated based on dose above) -hour infusion time. No need for further modifications to IV.

Administration (continued)

Infusion pump, when pump is finished infusing, discard the remainder of the sodium chloride bag. This will ensure patient receives the entire dose ordered at correct rate (approximate IV tubing space is approximately 25–28 mL).

50-mg bolus–cardiac arrest dose (RN or physician/advanced practitioner):

- RN may administer (physician/advanced practitioner may give if they prefer) IV over 2–5 min (rate of administration may be prolonged in patients with smaller-gauge IV catheters).
- When RN administers medication, ordering provider must remain at bedside during administration.



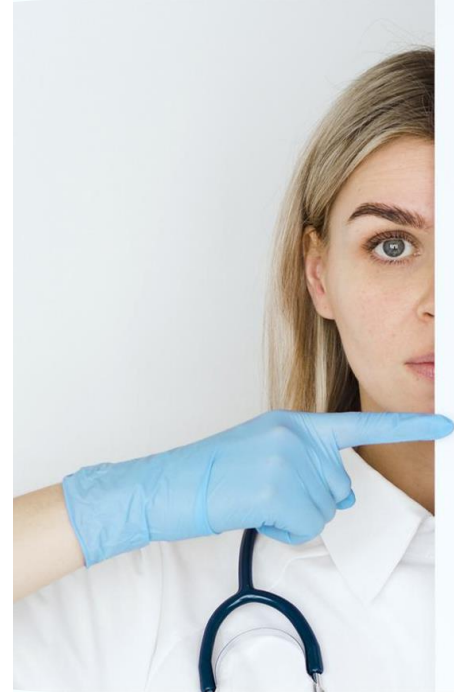
Research **CPD**

Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis

David Planer MD MSc, Stav Yanko PharmD, Ilan Matok PhD, Ora Paltiel MDCM MSc, Rama Zmiron PharmD, Victoria Rotshild PharmD PhD, Offer Amir MD, Gabby Elbaz-Greener MD MHA, Bruria Hirsh Raccach PharmD PhD

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Abstract



La trombólisis percutánea dirigida por catéter (CDT)

Permite la infusión lenta y local de material trombolítico en dosis bajas (alrededor de una cuarta parte de la dosis administrada sistémicamente).

Directamente a las arterias pulmonares, con o sin el uso de fragmentación mecánica o ultrasónica del trombo en situ.



Según la declaración de consenso clínico de la **ESC de 2022**, se debe considerar la CDT en pacientes con EP de alto riesgo cuando la trombólisis ha fallado o está contraindicada.

En pacientes estables en los que ha fracasado el tratamiento anticoagulante, la CDT puede ser una opción viable.



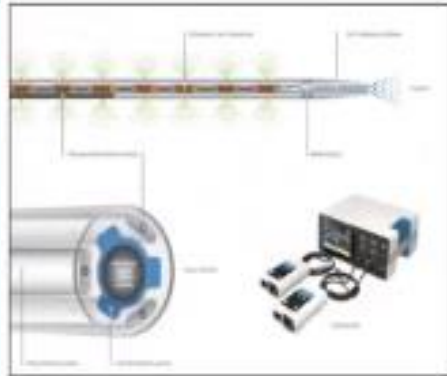
American Society of Hematology 2020 sugirió usar trombólisis sistémica en lugar de CDT en pacientes con EP en los que se considera apropiada la trombólisis.

- La guía CHEST y el informe del panel de expertos adoptaron un enfoque similar.

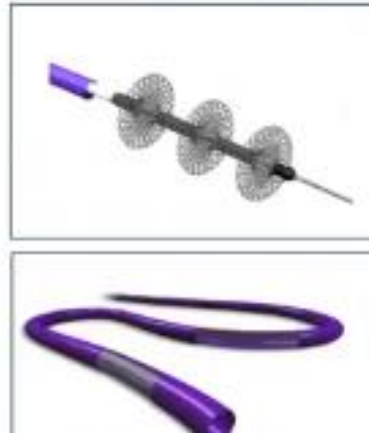


Tratamiento dirigido por catéter para el EP 2014 hasta 2022

**Acoustic pulse
(ultrasound assisted) lysis**



Mechanical thrombectomy



Mechanical thrombus aspiration



EkoSonic™ Endovascular System

EKOSS

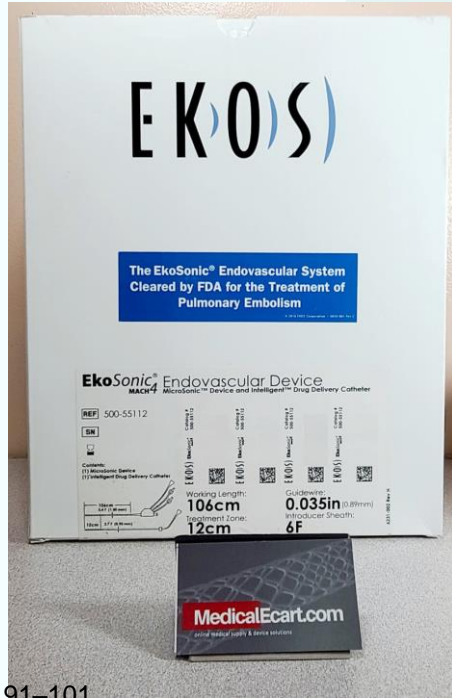
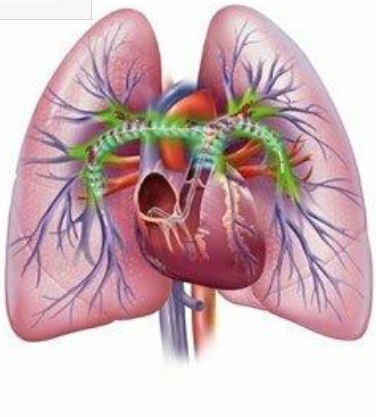
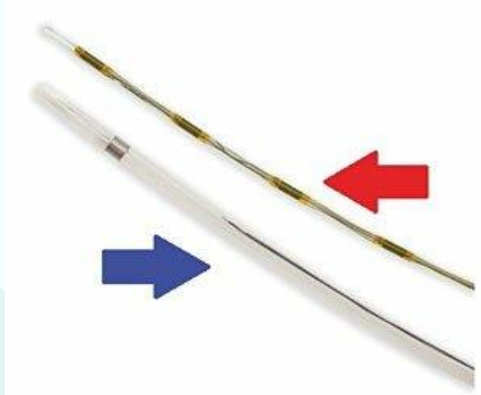


Thermal Coupler

EKOSS

The EkoSonic™ Endovascular System is a minimally invasive endovascular treatment to gently and completely dissolve thrombus and restore blood flow.

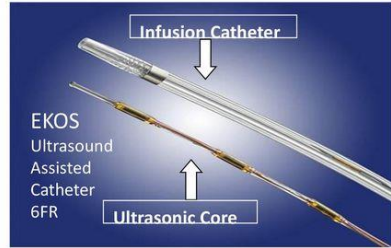
Tratamiento dirigido por catéter



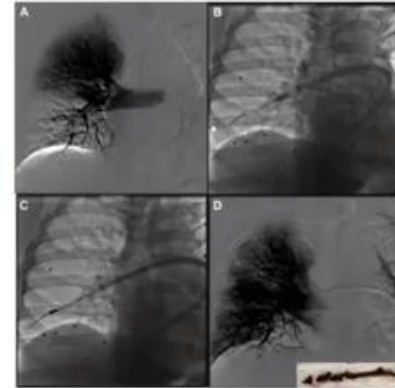
Tratamiento dirigido por catéter

Preferred Catheter(s) for Thrombolysis

4 Fr, 5 Fr
Lengths
0.035" Wire
Platforms



Angiodynamics Uni*Fuse™
Infusion Catheter



Uni-Fuse
INFUSION CATHETER

La trombólisis percutánea dirigida por catéter en ASCARDIO

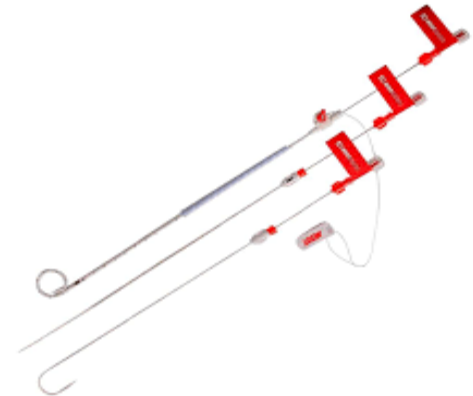
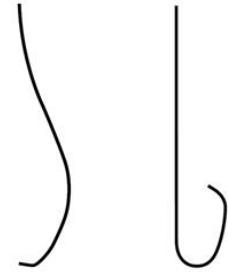
Catéter multipropósito 4Fr o 5 Fr

Otros: Catéter vertebral o JR (Judking right)

Abordaje radial o vena femoral: VCS, VCI aurícula derecha, ventrículo derecho, tronco pulmonar, selectivas ramas o sobre el TP.

Developed in 1960's

Judkins catheter



TEP Masivo



American Heart Association

Thrombolysis in Acute PE	Class	LOE
Massive acute PE and acceptable risk of bleeding complications	IIa	B



Thrombolytic Use in Acute PE	Grade
Acute PE associated with shock with acceptable bleeding risk, we suggest systemically administered thrombolytic therapy	2B



EUROPEAN SOCIETY OF CARDIOLOGY

Recommendations	Class ^a	Level ^b	Ref ^c
PE with shock or hypotension (high-risk)			
It is recommended that intravenous anticoagulation with UFH be initiated without delay in patients with high-risk PE.	I	C	
Thrombolytic therapy is recommended.	I	B	168
Surgical pulmonary embolectomy is recommended for patients in whom thrombolysis is contraindicated or has failed. ^d	I	C	313
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. ^d	IIa	C	

Trombólisis administrada sistemáticamente

TEP Sub Masivo



Thrombolysis in Acute PE	Class	LOE
Submassive acute PE with high risk features (hemodynamic instability, worsening respiratory insufficiency, severe RV dysfunction, or major myocardial necrosis and low bleeding risk	IIb	C



Thrombolytic Use in Acute PE	Grade
Most patients with acute PE not associated with hypotension, we recommend against systemically administered thrombolytics	1B
Select patients with acute PE who deteriorate after starting anticoagulant therapy but are not hypotensive and have low bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy	2C



EUROPEAN SOCIETY OF CARDIOLOGY

Reperfusion treatment			
Routine use of primary systemic thrombolysis is not recommended in patients not suffering from shock or hypotension.	III	B	253
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	253
Thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of haemodynamic decompensation.	IIa	B	252, 253
Surgical pulmonary embolectomy may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high. ⁴	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. ⁴	IIb	B	336

**Risk-adapted
management**



**Assessment of risk
related to acute PE**

**PE treatment (catheter-
directed)**

Pregunta (nuevo ciclo de evidencia)

P (paciente o problema)

I (intervención)

C (comparación)

O (resultado)

En pacientes con tromboembolismo pulmonar agudo de riesgo intermedio, la intervención percutánea guiada por catéter versus **trombolisis sistémica** ¿Reduce mortalidad y complicaciones cardiovascular intrahospitalaria a los 30 días ?

A pulmonary embolism response team's initial 20 month experience treating 87 patients with submassive and massive pulmonary embolism

Akhilesh K Sista¹, Oren A Friedman¹, Eda Dou¹, Brendan Denriv¹, Gulce Askin¹, Jamie Stern¹, Jarlyn Estes¹, Arash Salemi¹, Ronald S Winokur² and James M Horowitz²

Abstract

Pulmonary Embolism Response Teams (PERTs) have emerged to provide rapid multidisciplinary assessment and treatment of PE patients. However, descriptive institutional experience and preliminary outcomes data from such teams are sparse. PERT activations were identified through a retrospective review. Only confirmed submassive or massive PE were included in the data analysis. In addition to baseline variables, the therapeutic intervention, length of stay (LOS), in-hospital mortality, and bleeding rate/episode were recorded. A total of 124 PERT activations occurred over 20 months: 43 in the first 10 months and 81 in the next. 10 of 47 submassive (90.8%) and massive (9.2%) PE patients were included. The median age was 65 (51–75 IQR) years. Catheter-directed thrombolysis (CDT) was administered to 25 patients, systemic thrombolysis (ST) to six, and anticoagulation alone (AC) to 54. The median ICU stay and overall LOS were 6 (3–10 IQR) and 7 (4–14 IQR) days, respectively, with no association with any variables except a brain natriuretic peptide (BNP) >100 ng/mL, (p=0.008). ICU LOS was 20 (14–27 overall LOS). Twelve patients (13.7%) died in the hospital, nine of whom had metastatic or brain cancer, with a median overall LOS of 13 (11–17 IQR) days. There were five major bleeds: one in the ST group, one in the CDT group, and three in the AC group. Overall, (1) PERT activations increased after the first 10 months; (2) BNP >100 ng/mL was associated with a longer LOS; (3) rates of mortality and bleeding did not associate with treatment; and (4) the majority of in-hospital deaths occurred in patients with advanced cancer.

Keywords

pulmonary embolism (PE), PE response team (PERT), massive PE, submassive PE, catheter-directed thrombolysis, hospital length of stay

Journal of the American Heart Association

ORIGINAL RESEARCH

Midterm Prognosis of Patients With Pulmonary Embolism Receiving Catheter-Directed Thrombolysis or Systemic Thrombolysis: A Nationwide Population-Based Study

Donna Shu-Han Lin, MD; Yu-Sheng Lin, MD; Cho-Kai Wu, MD, PhD; Heng-Hau Lin, MD; Jen-Kuang Lee, MD, PhD

BACKGROUND: This study compared the efficacy and safety between catheter-directed thrombolysis (CDT) and systemic thrombolysis for patients with acute pulmonary embolism (PE) with midterm follow-up.

METHODS AND RESULTS: We conducted a prospective open cohort study by using data from the Taiwan National Health Insurance Research Database for 2001 to 2013. Patients who were first admitted for PE and were treated by either systemic thrombolysis or CDT were included and compared. Intense probability of treatment weighting, based on the propensity score, was applied to mitigate treatment imbalance. Systemic thrombolysis-treated patients with intermediate- and high-risk PE were included. The in-hospital mortality rate was significantly lower in the CDT group (52.7% versus 21.4%; odds ratio, 0.49; 95% CI, 0.36–0.67) after inverse probability of treatment weighting. No significant differences between the groups were observed for the safety (bleeding) outcomes. In patients who survived the index PE admission, the 1-year all-cause mortality rate was significantly lower in the CDT group after inverse probability of treatment weighting (52.5% versus 53.2%; hazard ratio [HR], 0.73; 95% CI, 0.56–0.94). Treatment with CDT was also associated with lower risks of recurrent PE (0.3% versus 17.5%; substitution HR, 0.52; 95% CI, 0.41–0.68). The difference remained through the total follow-up.

CONCLUSIONS: Among patients with PE requiring reperfusion therapy, those accepting CDT had lower all-cause mortality and recurrent PE over both short-term and midterm follow-up periods than those receiving systemic thrombolysis. The bleeding risk was similar for both groups. These findings should be cautiously validated in future randomized trials.

Key Words: catheter-directed thrombolysis • intravenous infusion • pulmonary embolism • thrombolytic therapy

Retrospective comparison of ultrasound facilitated catheter-directed thrombolysis and systemically administered half-dose thrombolysis in treatment of pulmonary embolism

Mohsen Sharifi^{1,2,3,4}, Alan Awadsho¹, Bethany Schroeder¹, José Jimenez^{1,2}, Priya Iyer² and Curt Bay²

Abstract

This study retrospectively compared the outcomes of patients who received ultrasound facilitated catheter-directed thrombolysis (UCDT) versus systemically administered half-dose thrombolysis (HDT) in 97 patients with PE. The outcomes assessed changes in baseline pulmonary artery systolic pressure (PASP), right ventricle/left ventricle ratio (RV/LV), cost and duration of hospitalization, death, bleeding and recurrent venous thromboembolism in the short and intermediate term follow-up. Analyses were performed using a covariance adjustment propensity score approach to address baseline differences between groups in variables associated with PASP and RV/LV, covarying baseline scores. The baseline mean ± SE PASP dropped from 49.3 ± 1.1 to 32.5 ± 0.3 mmHg at 36 hours in the HDT group, and from 50.6 ± 1.2 to 35.1 ± 0.4 mmHg in the UCDT group; group × time interaction p -value = 0.007. Corresponding drops in the RV/LV were from a baseline of 1.26 ± 0.05 to 1.07 ± 0.01 in the HDT group and from 1.32 ± 0.05 to 1.14 ± 0.01 in the UCDT group at 36 hours; group × time interaction p -value = 0.269. Statistically significant decreases were noted in PASP and RV/LV for both the HDT and UCDT at 36 hours and follow-up. PASP through follow-up was significantly lower in the HDT than the UCDT group. Likewise, RV/LV was lower in the HDT group. The duration and cost of hospitalization were lower in the HDT group (6.2 ± 1.4 days vs 1.9 ± 0.3 days, p < 0.001; US\$12,000 ± \$3000 vs \$74,000 ± \$4600, p < 0.001). We conclude that both UCDT and HDT lead to rapid reduction of PASP and RV/LV, whereas HDT leads to a lower duration and cost of hospitalization.

Keywords

anticoagulants, embolus, pulmonary embolism (PE), catheter-directed thrombolysis, systemic thrombolysis, thrombus

Research

Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis

David Planer MD MSc, Stacy Yanko PharmD, Ilan Matok PhD, Ora Pattiel MDCM MSc, Rama Zmiro PharmD, Victoria Rotshild PharmD, Omer Amir MD, Gabby Elbaz-Greener MD MHA, Bruria Hirsch Raccach PharmD PhD

■ Cite as: *CMAJ* 2023 June 19;195:E833-43. doi:10.1503/cmaj.229960

Abstract

Background: Thrombolytic options for intermediate- or high-risk pulmonary embolism (PE) include anticoagulation, systemic thrombolysis and catheter-directed thrombolysis (CDT). However, the risk of CDT remains controversial. We sought to compare the efficacy and safety of CDT with other therapeutic options using network meta-analysis.

Methods: We searched PubMed (MEDLINE), Embase, ClinicalTrials.gov and Cochrane Library from inception to Oct. 18, 2022. We included randomized controlled trials and observational studies that compared therapeutic options for PE, including anticoagulation, systemic thrombolysis and CDT among patients with intermediate- or high-risk PE. The efficacy outcome was

in-hospital death. Safety outcomes included major bleeding, intracerebral hemorrhage and minor bleeding.

Results: We included data from 44 studies, representing 28,008 patients. Compared with systemic thrombolysis, CDT was associated with a decreased risk of death [odds ratio (OR) 0.43, 95% confidence interval (CI) 0.32–0.57], intracerebral hemorrhage (OR 0.44, 95% CI 0.29–0.64), major bleeding (OR 0.51, 95% CI 0.33–0.79) and blood transfusion (OR 0.46, 95% CI 0.28–0.77). However, no difference in minor bleeding was observed between the 2 therapeutic options (OR 1.11, 95% CI 0.66–1.87). Compared with anticoagulation, CDT was also associated with decreased risk of death (OR 0.36, 95% CI 0.25–0.52), with no

increased risk of intracerebral hemorrhage (OR 1.33, 95% CI 0.63–2.79) or major bleeding (OR 1.24, 95% CI 0.88–1.75).

Interpretation: With moderate certainty of evidence, the risk of death and major bleeding complications was lower with CDT than with systemic thrombolysis. Compared with anticoagulation, CDT was associated with a probable lower risk of death and a similar risk of intracerebral hemorrhage, with moderate certainty of evidence. Although these findings are largely based on observational data, CDT may be considered as a first-line therapy in patients with intermediate- or high-risk PE. **Protocol registration:** PROSPERO – CRD4202182163

Outcomes of catheter-directed versus systemic thrombolysis for the treatment of pulmonary embolism: A real-world analysis of national administrative claims

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Abstract

Catheter-directed thrombolysis (CDT) and systemic thrombolysis (ST) are used to treat intermediate/high-risk pulmonary embolism (PE) in the absence of comparative safety and effectiveness data. We utilized a large administrative database to perform a comparative safety and effectiveness analysis of catheter-directed versus systemic thrombolysis. From the Optum[®] Clinformatics[®] Data Mart private-payer insurance claims database, we identified 100,744 patients hospitalized with PE between 2004 and 2014. We extracted demographic characteristics, high-risk PE features, components of the Eltixhaus Comorbidity Index, and outcomes including intracranial hemorrhage (ICH), all-cause bleeding, and mortality among all patients receiving CDT and ST. We used propensity score methods to compare outcomes between matched cohorts adjusted for confounders. A total of 1915 patients (1.9%) received either CDT (n = 632) or ST (n = 1283). Patients in the CDT group had fewer high-risk features including less shock (5.4 vs 11.1%; p < 0.001) and cardiac arrest (6.8 vs 11.0%; p = 0.004). In 1:1 propensity-matched groups, ICH rates were 1.9% in both the CDT and ST groups (p = 1.0). All-cause bleeding was higher in the CDT group (1.9 vs 8.7%; p < 0.001), while in-hospital mortality was lower (6.5 vs 10.0%; p = 0.02). Among a national representative cohort of patients with PE at higher risk for mortality, CDT was associated with similar ICH rates, increased all-cause bleeding, and lower short and intermediate-term mortality when compared with ST. The competing risks and benefits of CDT in real-world practice suggest the need for large-scale randomized clinical trials with appropriate comparator arms.

Keywords

pulmonary embolism (PE), thrombolytic therapy, venous thromboembolism (VTE)

Ultrasound-facilitated, catheter-directed thrombolysis vs anticoagulation alone for acute intermediate-high-risk pulmonary embolism: Rationale and design of the HI-PEITHO study

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Abstract

Background Due to the bleeding risk of full-dose systemic thrombolysis and the lack of major trials focusing on the clinical benefits of catheter-directed treatment, heparin anticoagulation remains the standard of care for patients with intermediate-high-risk pulmonary embolism (PE).

Methods and results The Higher-Risk Pulmonary Embolism Thrombolysis (HI-PEITHO) study (ClinicalTrials.gov identifier: NCT04790370) is a multinational multicenter randomized controlled parallel-group comparison trial. Patients with (1) confirmed acute PE; (2) evidence of right ventricular (RV) dysfunction on imaging; (3) a positive cardiac troponin test; and (4) clinical criteria indicating an elevated risk of early death or imminent hemodynamic collapse will be randomized 1:1 to treatment with a standardized protocol of ultrasound-facilitated catheter-directed thrombolysis plus anticoagulation, vs anticoagulation alone. The primary outcome is a composite of PE-related mortality, cardiovascular decompensation or collapse, or non-fatal symptomatic and objectively confirmed PE recurrence, within 7 days of randomization. Further assessments cover, apart from bleeding complications, a broad spectrum of functional and patient-reported outcomes including quality of life indicators, functional status and the utilization of health care resources over a 12-month follow-up period. The trial plans to include 406 patients, but the adaptive design permits a sample size increase depending on the results of the predefined interim analysis. As of May 11, 2022, 27 subjects have been enrolled. The trial is funded by Boston Scientific Corporation and through collaborative research agreements with University of Mainz and The PERT Consortium.

Conclusions Regardless of the outcome, HI-PEITHO will establish the first-line treatment in intermediate-high risk PE patients with imminent hemodynamic collapse. The trial is expected to inform international guidelines and set the standard for evaluation of catheter-directed reperfusion options in the future. (Am Heart J 2022;251:43–53.)



**Gracias por
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