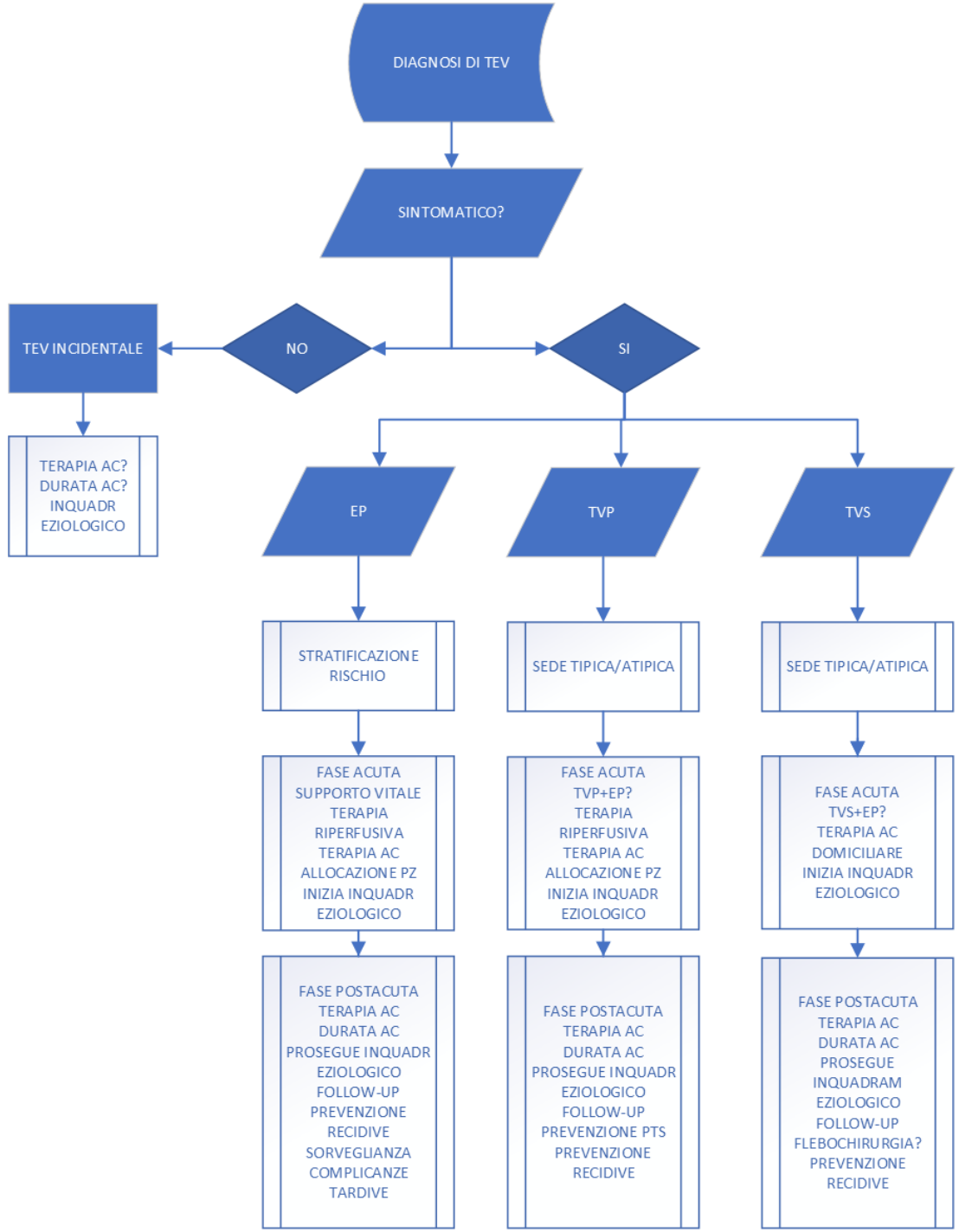
Master in Medicina Vascolare, Malattie trombotiche ed emorragiche

Gestione della Malattia Tromboembolica Venosa

Prof. Raffaele Pesavento

A.A. 2024-25


DIAGNOSI DI TEV
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TERAPIA AC?
DURATA AC?
INQUADR
EZIOLOGICO
EP
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TVS
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RISCHIO
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SEDE TIPICA/ATIPICA
FASE ACUTA
SUPPORTO VITALE
TERAPIA
RIPERFUSIVA
TERAPIA AC
ALLOCAZIONE PZ
INIZIA INQUADR
EZIOLOGICO
FASE ACUTA
TVP+EP?
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FOLLOW-UP
PREVENZIONE
RECIDIVE
SORVEGLIANZA
COMPLICANZE
TARDIVE
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FOLLOW-UP
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PREVENZIONE
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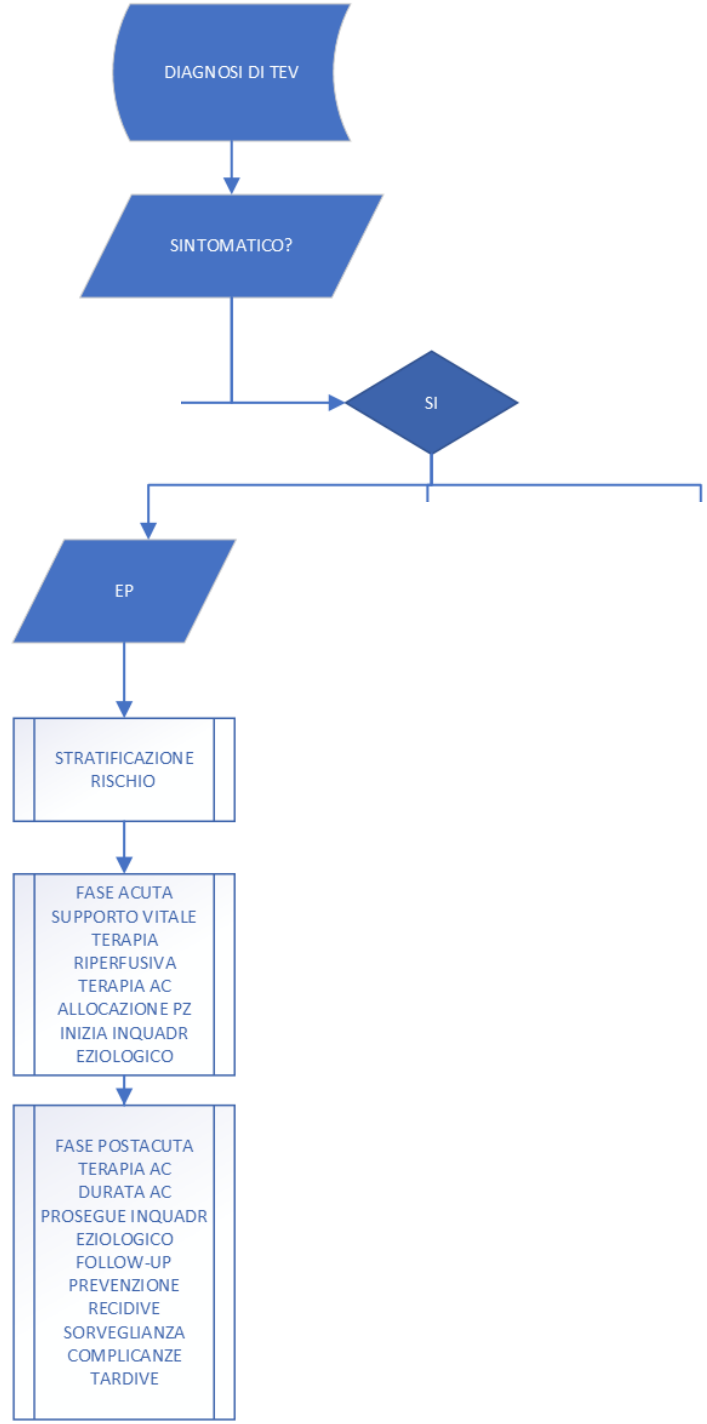
DIAGNOSI DI TEV
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TERAPIA AC
DURATA AC
PROSEGUE INQUADR EZIOLOGICO
FOLLOW-UP
PREVENZIONE RECIDIVE
SORVEGLIANZA COMPLICANZE TARDIVE

Anna 82 anni

Giunge in Pronto Soccorso per dispnea ingravescente da circa 3 giorni. Vive a domicilio dove compie solo brevi spostamenti letto-poltrona.

APR: Miastenia gravis in esiti di resezione di timoma e lobo polmonare superiore sinistro (2016); embolia polmonare segmentaria destra in corso di ricovero per endocardite e riacutizzazione di miastenia (2018); ipertensione arteriosa; dislipidemia; osteoporosi con pregressi crolli vertebrali

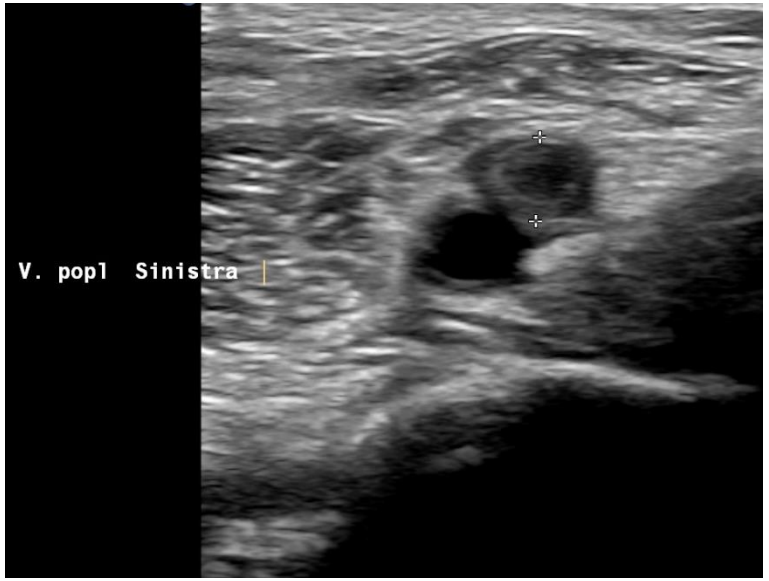
TP domiciliare: Lansoprazolo 30 mg, Bisoprololo 2.5 mg, Mestinon 60 mg x3, Deltacortene 5 mg, Simvastatina 20 mg; Dibase 100000 UI/mese

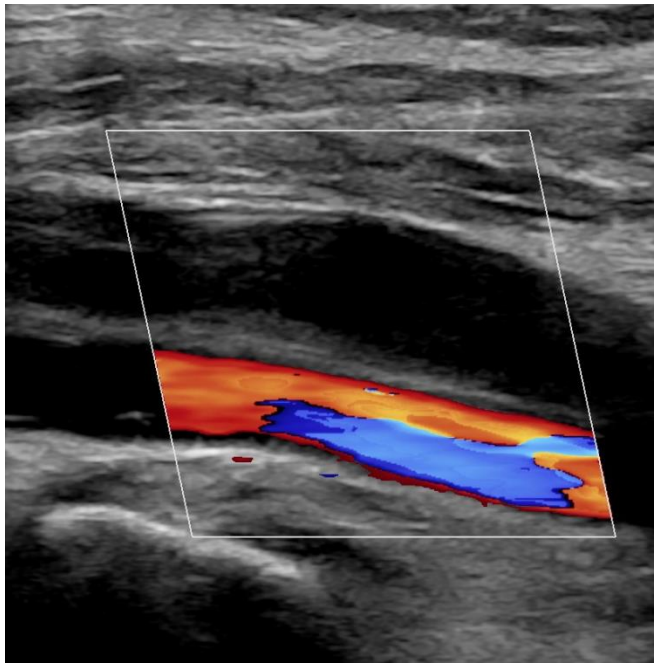
PAO 135/95 mmHg, FC 107 bpm R, SatO2 100% in NC 2 l/min, FR 28 atti/min, TC 36°C, GCS 15

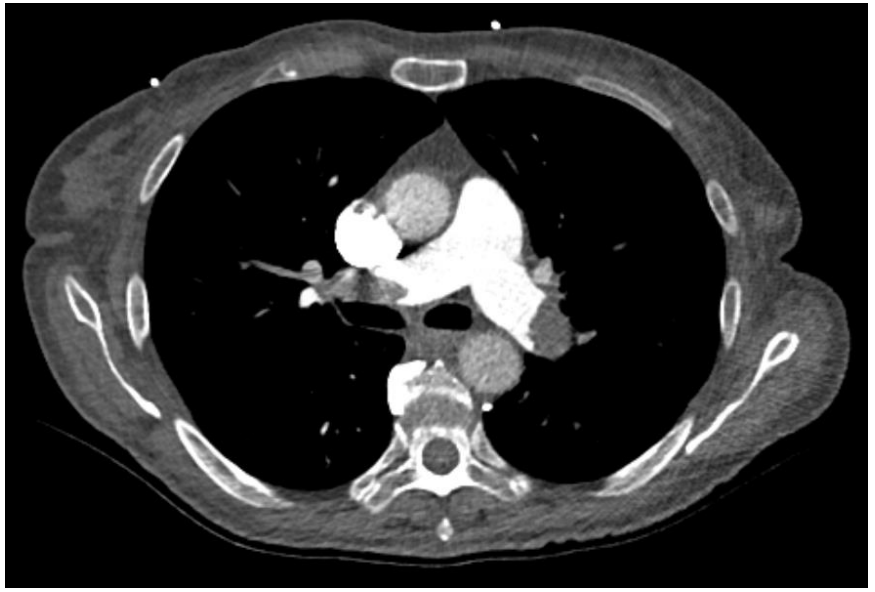
EE: Emocromo, funzionalità epatica e renale nei limiti. Ddimero 11900 (vn <700), TnI 63 (vn <12), BNP 6390 (vn <125)

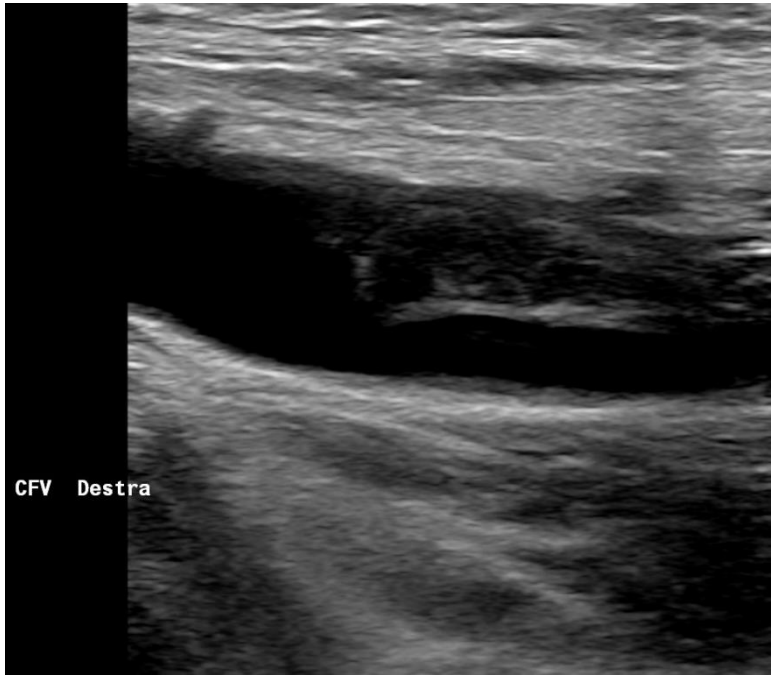
Ecoscopia bedside: Camere cardiache destre dilatate con VCI dilatata ed ipocollassante, CUS positiva in vena poplitea sinistra.

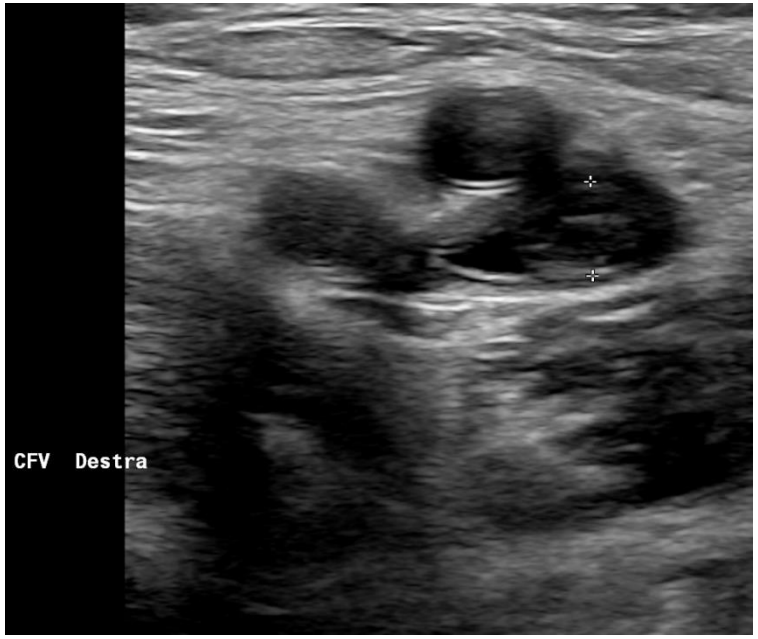
AngioTC: Difetto di riempimento di tipo tromboembolico alle arterie polmonari destra e sinistra, tipo fatto massivo con coinvolgimento delle diramazioni distali.

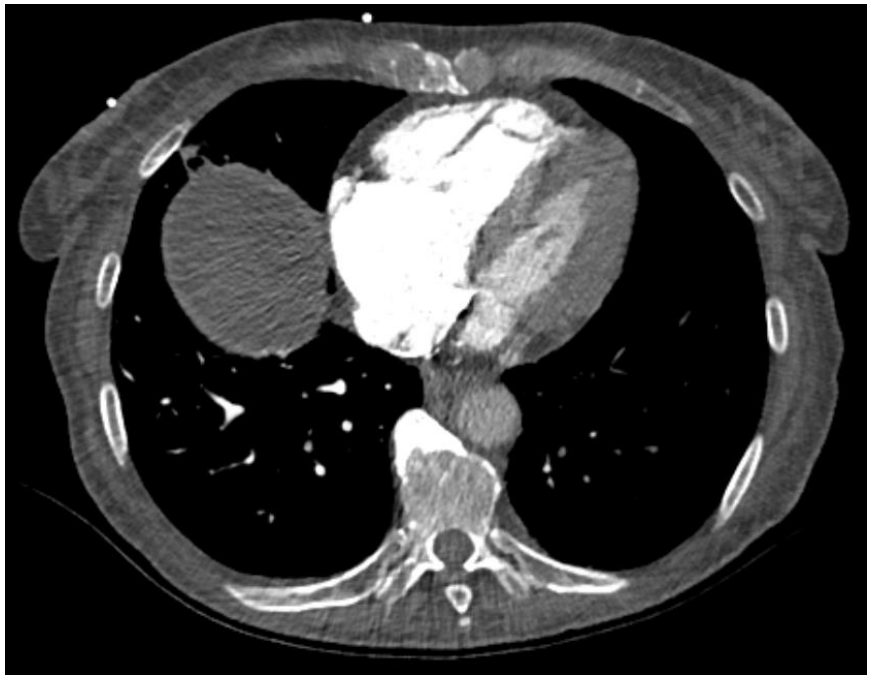

V. popl Sinistra

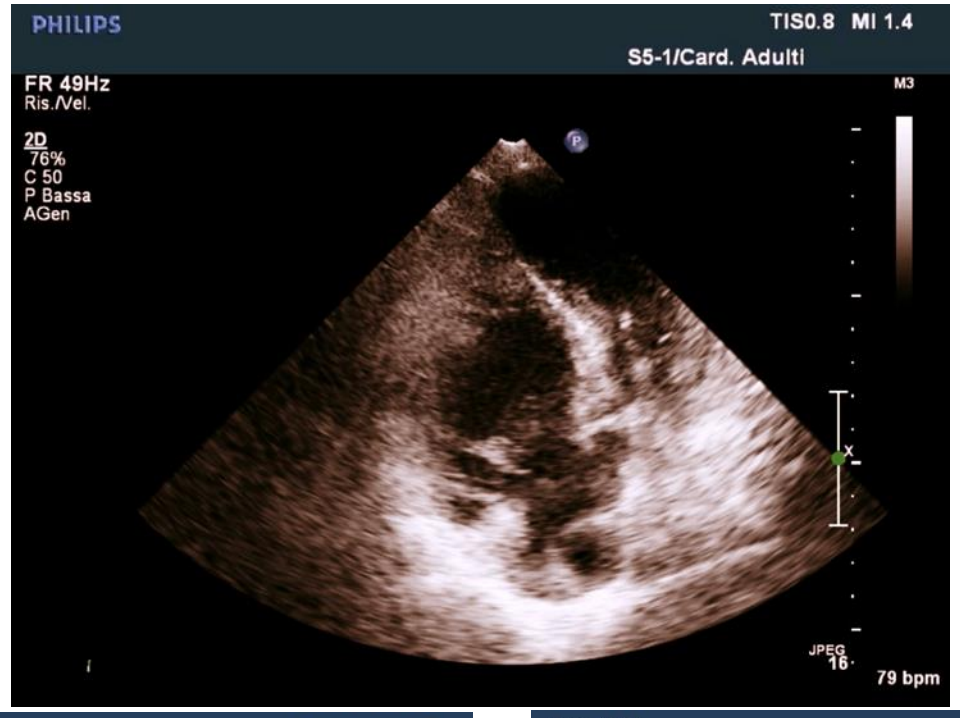




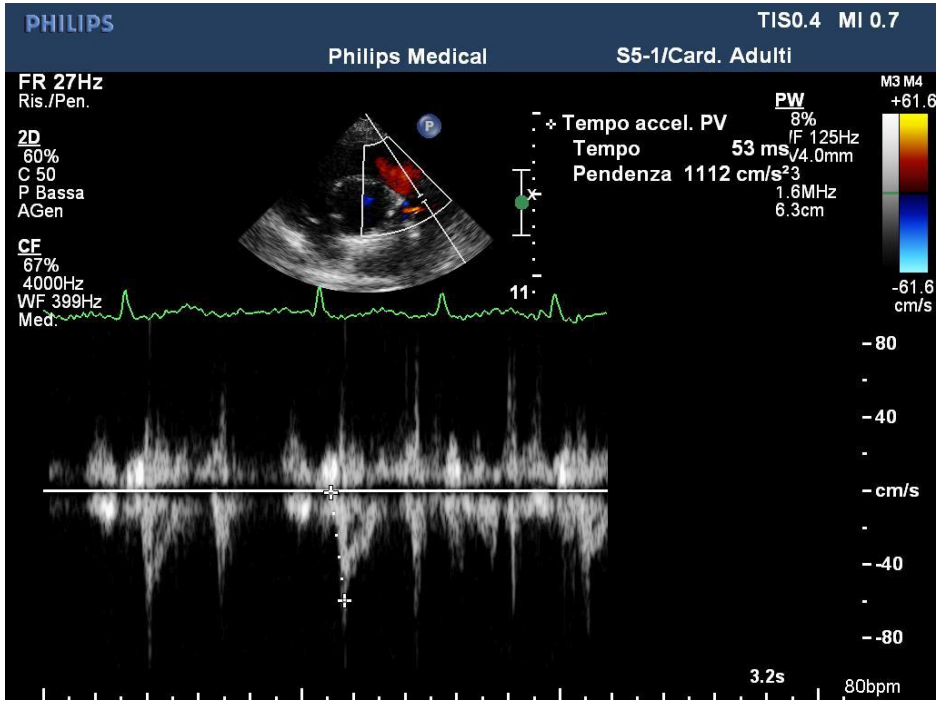

CFV Destra

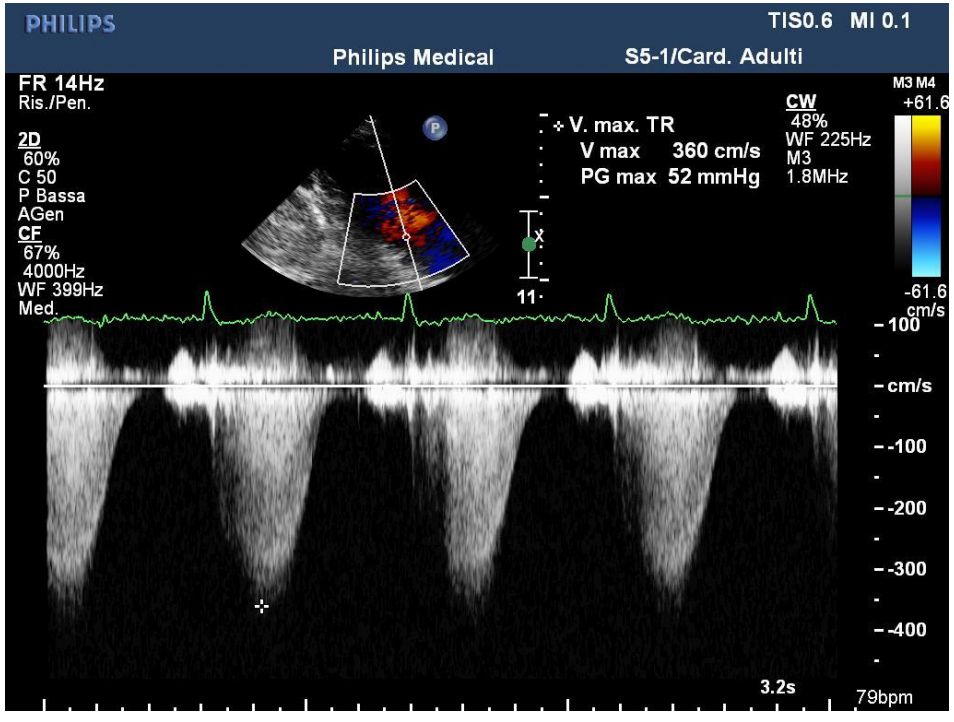

CFV Destra




PHILIPS
TIS0.8 MI 1.4
S5-1/Card. Adulti
FR 49Hz
Ris./Vel.
2D
76%
C 50
P Bassa
AGen
M3
JPEG
16
79 bpm

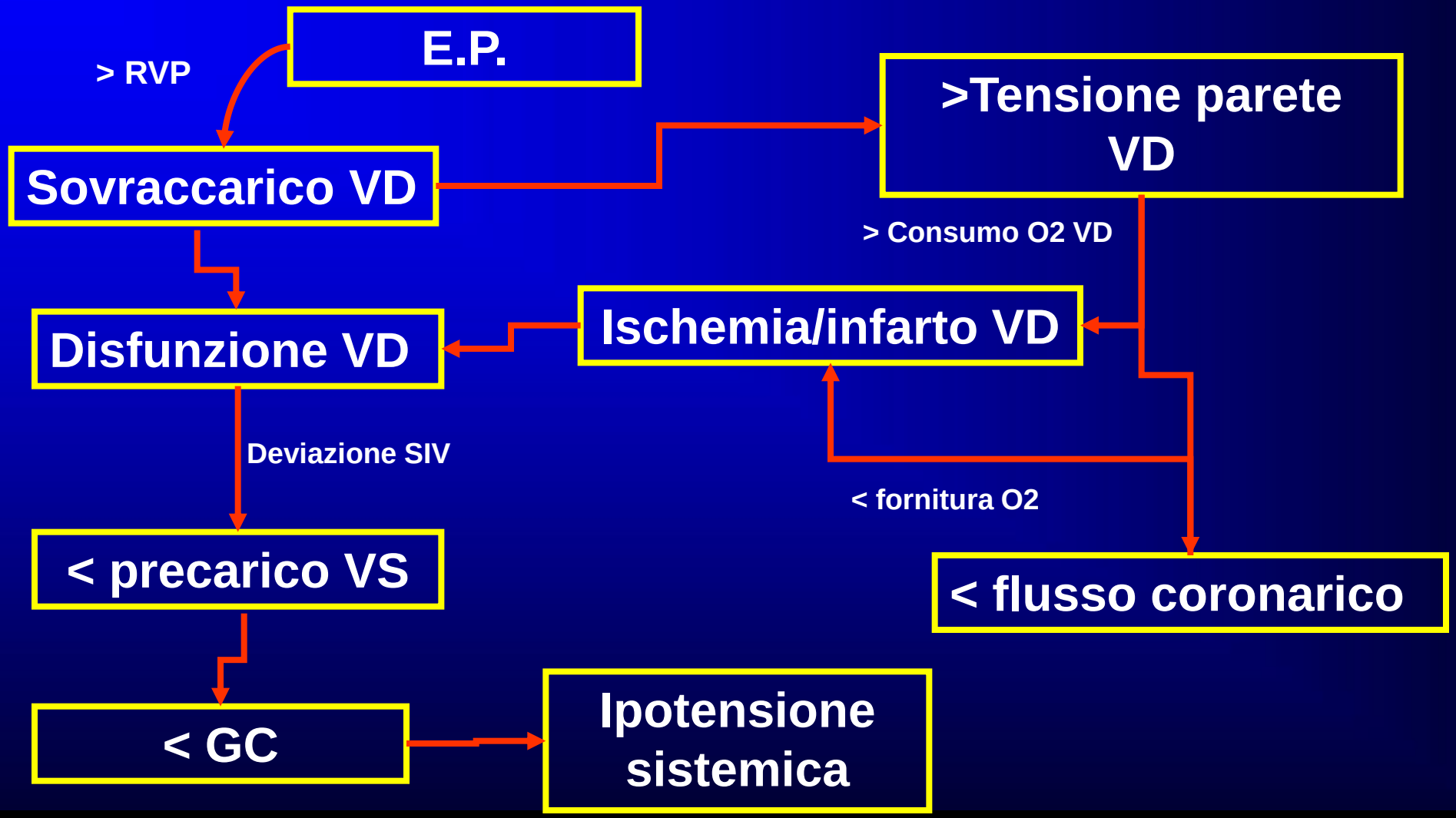
60/60 sign


PHILIPS
TIS0.4 MI 0.7
Philips Medical
S5-1/Card. Adulti
FR 27Hz
Ris./Pen.
2D
60%
C 50
P Bassa
AGen
CF
67%
4000Hz
WF 399Hz
Med.
Tempo accel. PV
Tempo 53 ms
Pendenza 1112 cm/s²
PW
8%
IF 125Hz
V4.0mm
3
1.6MHz
6.3cm
M3 M4
+61.6
-61.6
cm/s
11
80
40
cm/s
-40
-80
3.2s
80bpm


PHILIPS
TIS0.6 MI 0.1
Philips Medical
S5-1/Card. Adulti
FR 14Hz
Ris./Pen.
2D
60%
C 50
P Bassa
AGen
CF
67%
4000Hz
WF 399Hz
Med.
V. max. TR
V max 360 cm/s
PG max 52 mmHg
CW
48%
WF 225Hz
M3
1.8MHz
M3 M4
+61.6
-61.6
cm/s
11
100
cm/s
-100
-200
-300
-400
3.2s
79bpm

EMBOLIA POLMONARE
Fisiopatologia

Cuore polmonare acuto

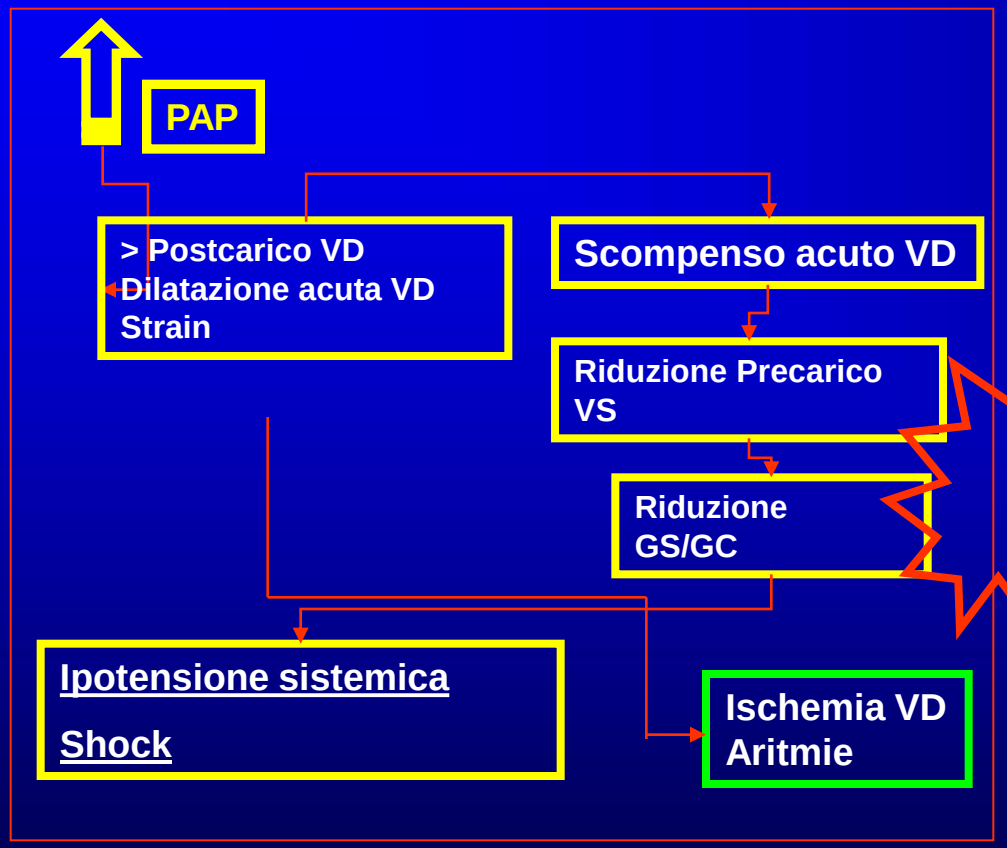


Piazza et al. Circulation 2006

GlaxoSmithKline

EMBOLIA POLMONARE
Fisiopatologia

Cuore polmonare acuto

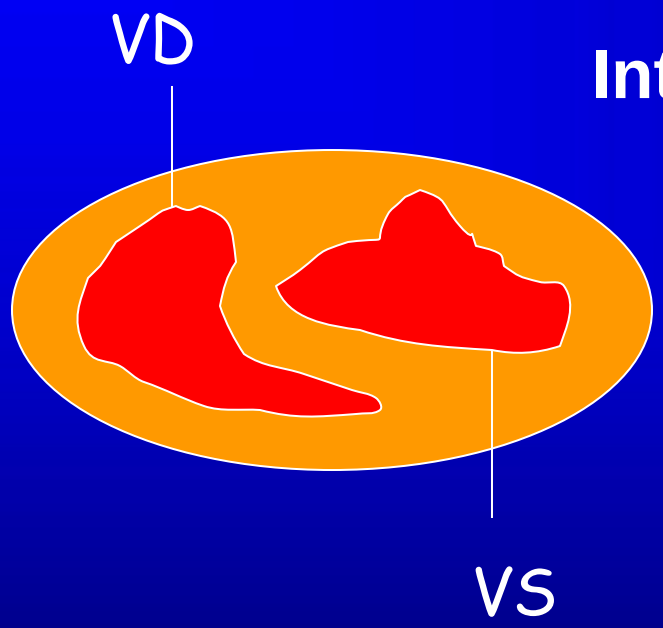


EP Massiva-Submassiva

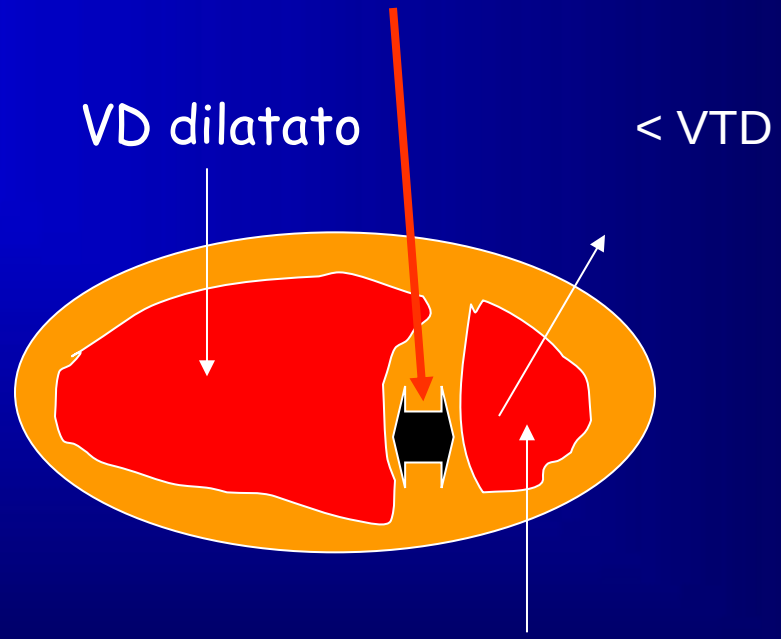
Malattia cardiopolmonare preesistente

EP non massiva – limitata

EMBOLIA POLMONARE
Fisiopatologia



Interdipendenza ventricolare



- Bassa portata
- Ridotta perfusione mm. respiratori

EMBOLIA POLMONARE
Fisiopatologia

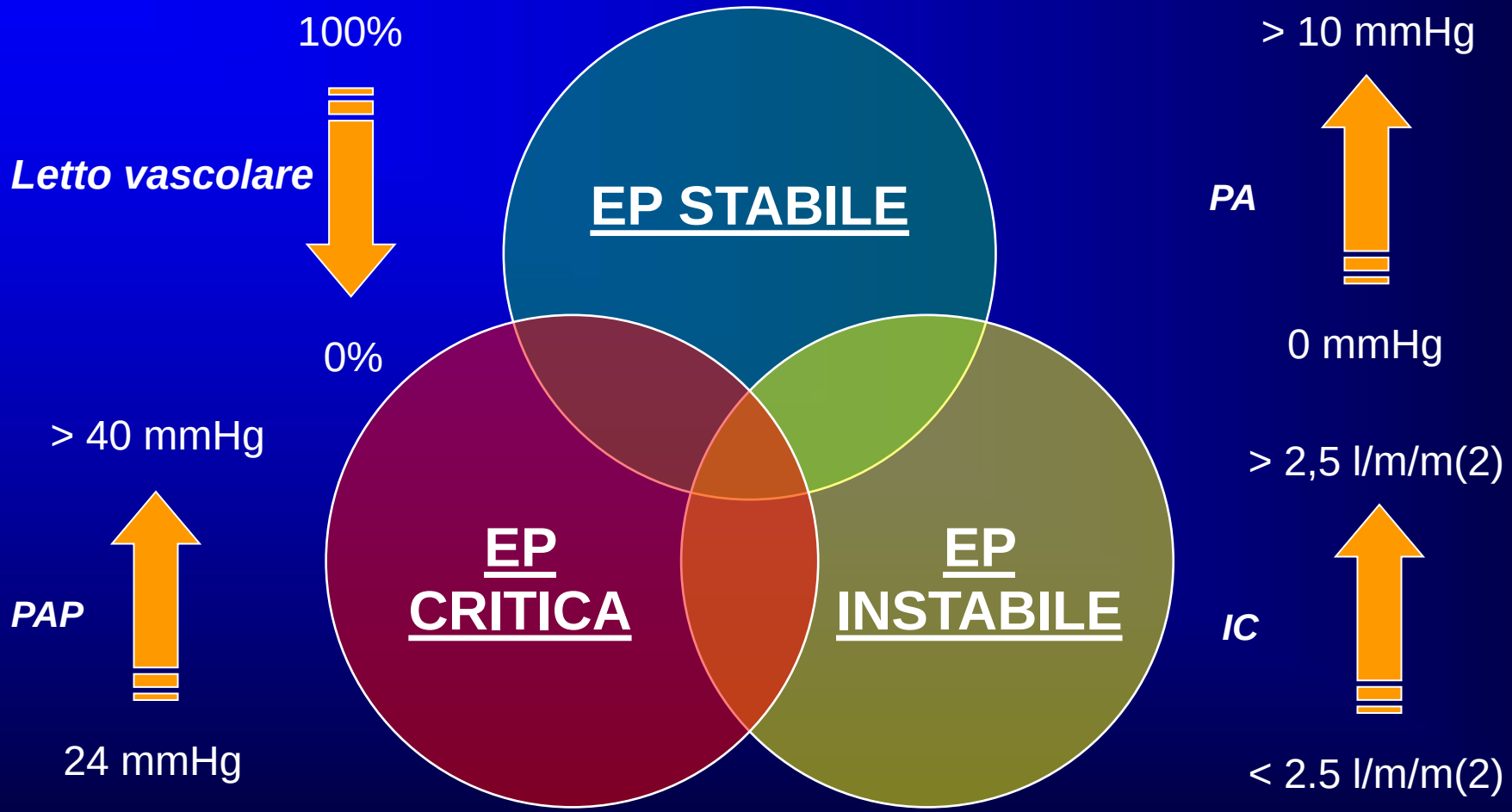
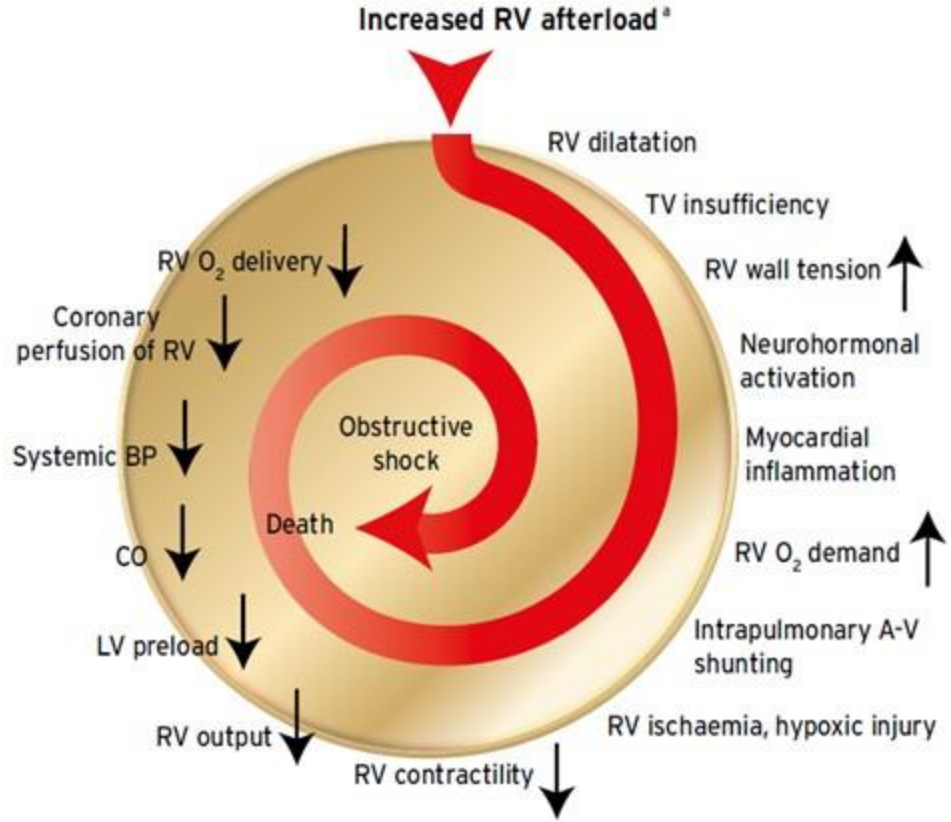


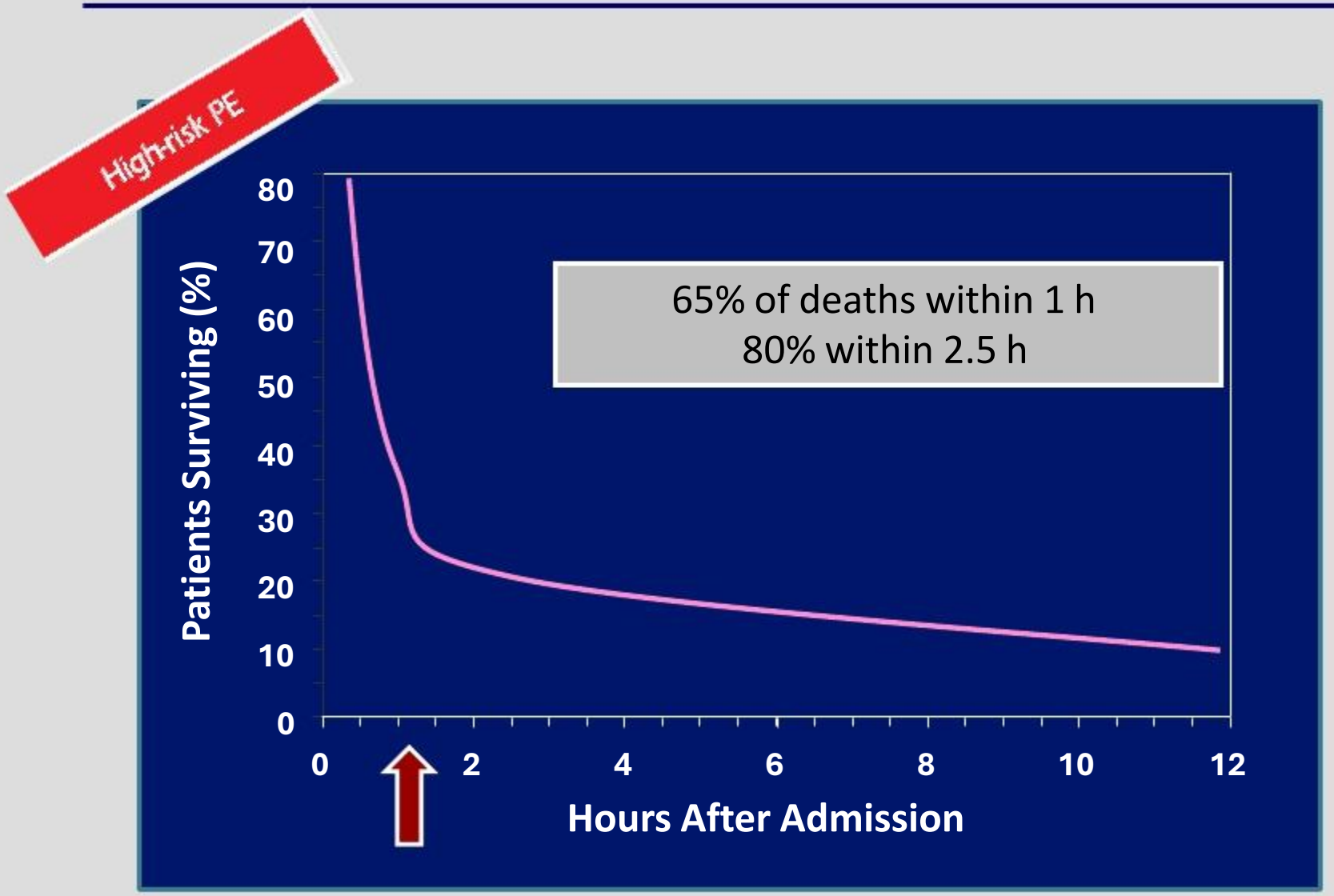
Figure 1 The spiral of haemodynamic collapse in acute PE



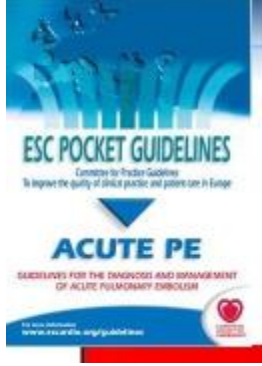
www.escardio.org/guidelines

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

High risk of early death in hemodynamic instability



PD Stein. Chest 1995;108:978-981



Comprehensive Risk Stratification

Severity of PE should be understood as an individual estimate of PE-related early mortality risk, rather than anatomic burden, shape and distribution of intrapulmonary emboli. Therefore current guidelines suggest replacing potentially misleading terms such as "massive, sub-massive, non-massive" with the estimated levels of risk of PE-related early death.

Markers of Right Ventricular Dysfunction

- RV dilatation, hypokinesis or pressure overload on echocardiography
- RV dilatation on spiral computed tomography
- BNP or NT-proBNP elevation
- Elevated right heart pressures at right heart catheterization

Markers of Right Ventricular injury/ischemia

- Troponins

Clinical models predictive of early mortality

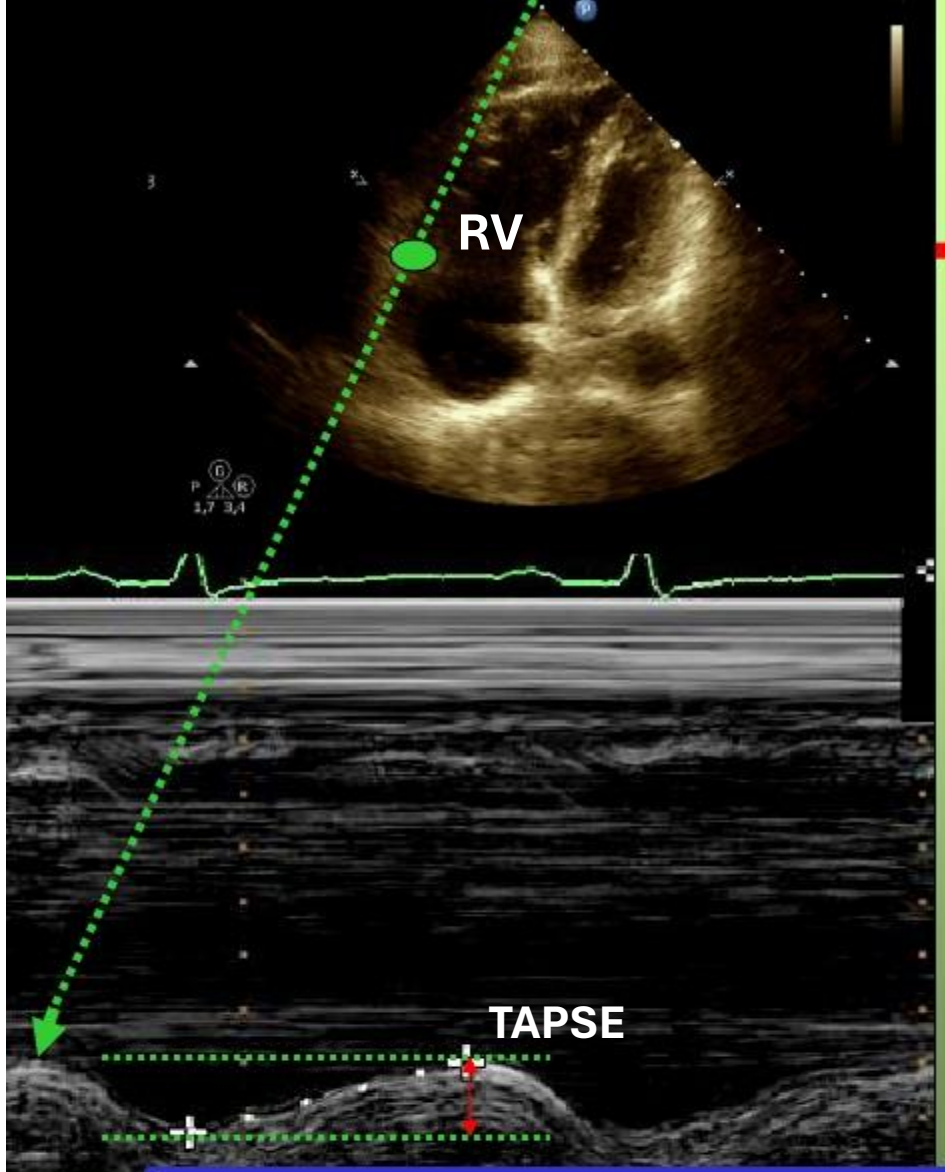
- PESI, sPESI
- BOVA, ……..

Tabella 4. *Reperti ecocardiografici nell'EP*

Definizione	Descrizione/valori
Visualizzazione trombi in transito	
Rapporto diametri VD/VS	> 1.0
Segno di McConnell	Ipocinesia della parete libera del VD con normale cinetica dell'apice ventricolare destro
Segno della D	Setto ventricolare appiattito o sporgente verso il VS
Segno 60/60	Tempo di accelerazione dell'eiezione polmonare nel RVOT ≤ 60 ms, incisura mesosistolica e gradiente VA destro < 60 mmHg o TR Jet < 3.9 m/s valvola tricuspide
Ipocinesia del ventricolo destro	
TAPSE/PAPS	TAPSE/PAPS < 0.4
TAPSE	< 1.7 cm
TDI: Velocità S', E/E', IVA, IVRT, TEI index, Strain imaging	S' < 10 cm/s;
Strain longitudinale parete libera VD	< 20%
VD Tei index	PW Doppler : >0.43 TDI: >0.54
Dilatazione VD	Valutazione qualitativa; Diametro basale > 41 mm, diametro livello medio > 35 mm
Movimento anomalo del setto ventricolare	
Probabilità di ipertensione polmonare	TR jet >2.8 m/s >36mmHg e TR jet < 60 mmHg < 3.9 m/s*
Pressione sistolica VD	
3D: volume, massa, forma	
Frazione di accorciamento VD	< 35%
RVOT VTI	< 9.5 cm
sPAP/Volume sistolico VS	≥1.0 mmHg/ml

* È stata proposta una metodologia di diagnosi per probabilità di ipertensione polmonare per lo studio dei pz. con sospetta ipertensione polmonare che combina il rilievo della velocità di picco del rigurgito tricuspidalico alla presenza di almeno due segni indiretti di ipertensione polmonare (*2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension*). VD: ventricolo destro; VS: ventricolo sinistro; TR: *tricuspid regurgitation*; tricuspide Tei index: tempo isovolumico VD/ tempo di eiezione; RVOT: *right ventricular outflow tract*; PW: *Pulsed-Wave; VCI:* Vena cava inferiore; *IC:* indice di collassabilità; PAT: *pulmonary acceleration time; sPAP: systolic pulmonary pressure; VTI: Velocity time integral*

Pesavento R, da Trattato di Medicina Vascolare, 2024



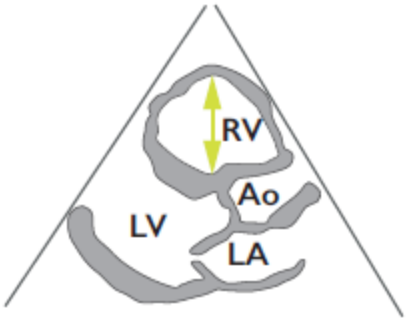
TAPSE – tricuspid annulus plane systolic excursion

n = 16 - 30 mm

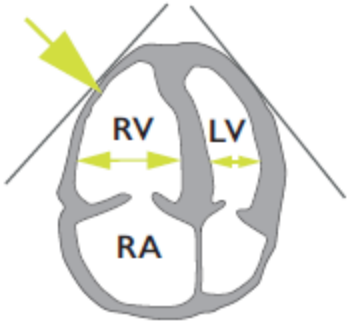
<16 mm
RV dysfunction

…TAPSE should be used routinely as a simple method of estimating RV function, with a lower reference value for impaired RV systolic function of 16 mm….

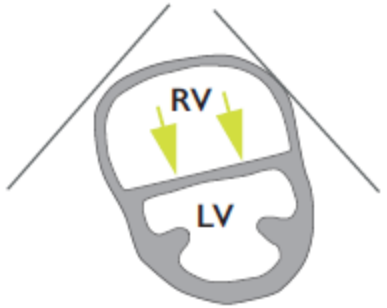
Especially predictive of clinical deterioration and mortality



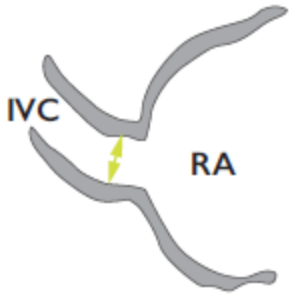
A. Enlarged right ventricle, parasternal long axis view



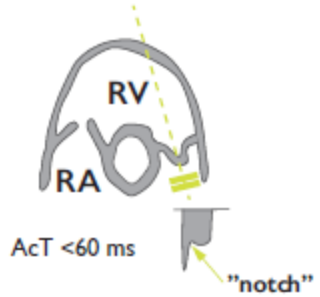
B. Dilated RV with basal RV/LV ratio >1.0, and McConnell sign (arrow), four chamber view

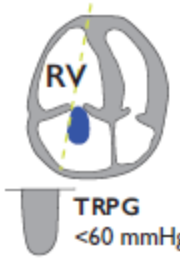


C. Flattened intraventricle septum (arrows) parasternal short axis view

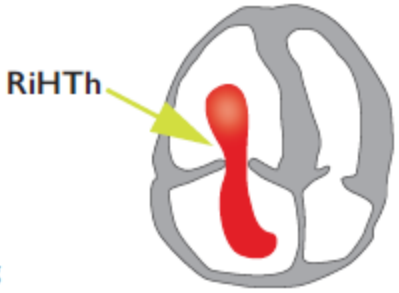


D. Distended inferior vena cava with diminished inspiratory collapsibility, subcostal view

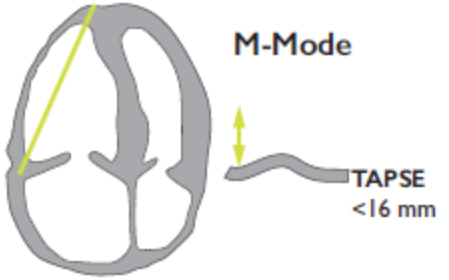




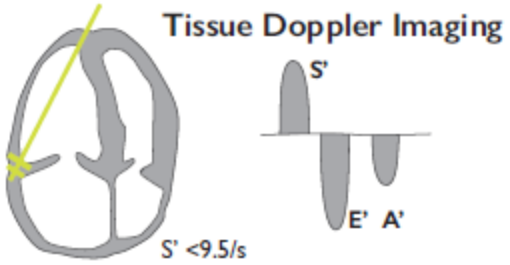
E. 60/60 sign: coexistence of acceleration time of pulmonary ejection <60 ms and midsystolic "notch" with mildy elevated (<60 mmHg) peak systolic gradient at the tricuspic valve



F. Right heart mobile thrombus detected in right heart cavities (arrow)



G. Decreased tricuspid annular plane systolic excursion (TAPSE) measured with M-Mode (<16 mm)



H. Decreased peak systolic (S') velocity of tricuspid annulus (<9.5 cm/s)

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association®
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Circulation 2011, 123:1788-1830:

Management of Massive and Submassive Pulmonary Embolism, Iliofemoral Deep Vein Thrombosis, and Chronic Thromboembolic Pulmonary Hypertension : A Scientific Statement From the American Heart Association

RVD is defined by the presence of at least 1 of:

— RV dilation (apical 4-chamber RV diameter divided by LV diameter >0.9) or RV systolic dysfunction on echocardiography
— RV dilation (4-chamber RV diameter divided by LV diameter >0.9) on CT
— Elevation of BNP (>90 pg/mL)
— Elevation of N-terminal pro-BNP (>500 pg/mL); or
— Electrocardiographic changes (new complete or incomplete right bundle-branch block, anteroseptal ST elevation or depression, or anteroseptal T-wave inversion)

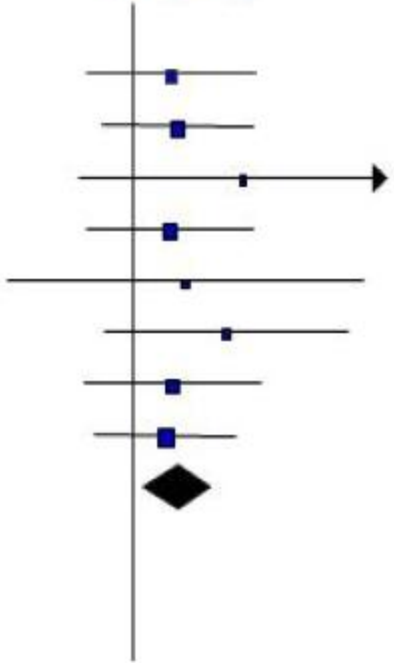
RESEARCH Open Access

The prognostic value of markers of right ventricular dysfunction in pulmonary embolism: a meta-analysis

RVD for short term prognosis

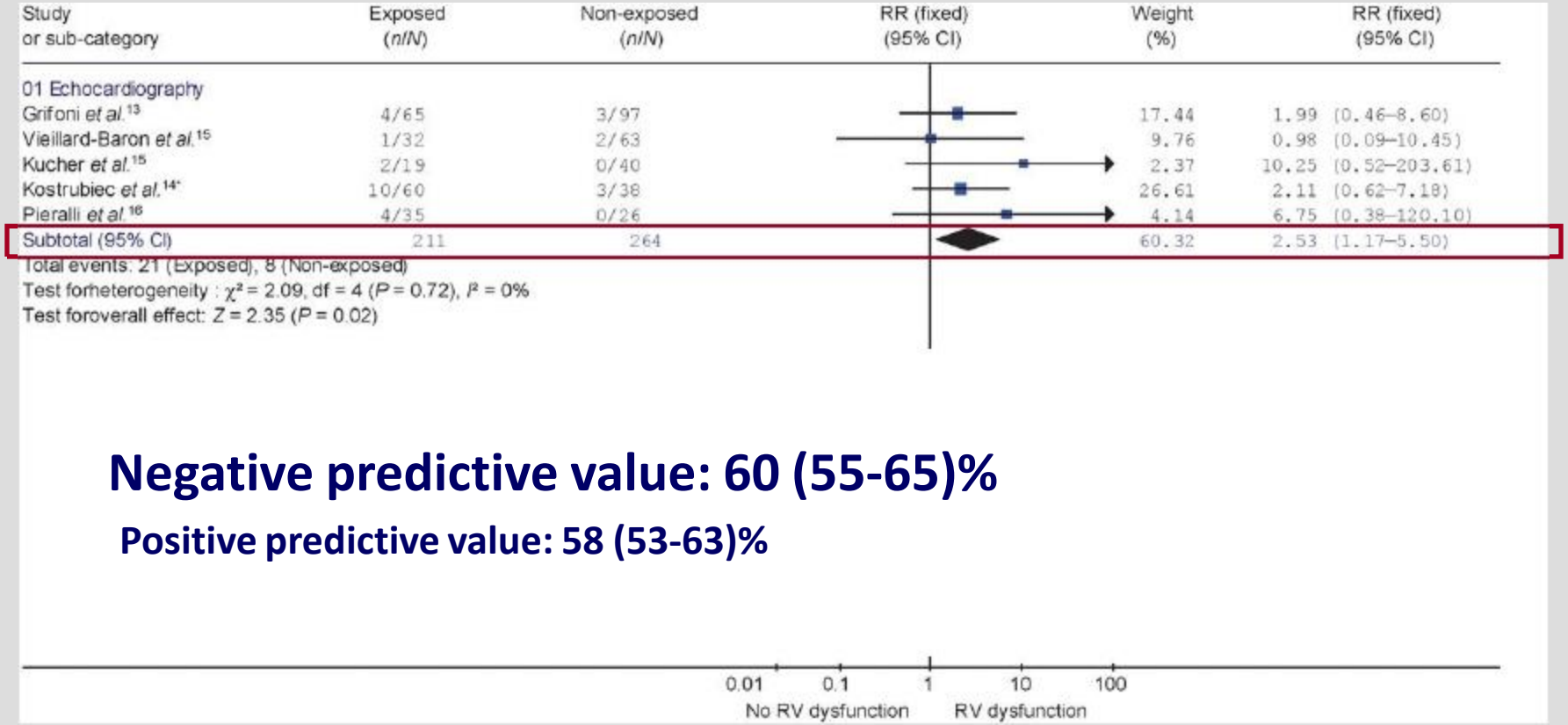
Study	RVD +	RVD -	Weight	OR, random 95% CI
TTE	Deaths, No. / Patients, No.			
Grifoni [7]	4 / 65	3 / 97	15.1%	2.1 [0.4, 9.5]
Kostrubiec [8]	10 / 60	3 / 38	19.2%	2.3 [0.6, 9.1]
Pieralli [9]	4 / 35	0 / 26	4.0%	7.6 [0.4, 147]
Jimenez [10]	4 / 86	3 / 128	15.3%	2.1 [0.4, 9.3]
Logeart [11]	1 / 36	0 / 31	3.4%	2.7 [0.1, 67.7]
Zhu [12]	4 / 198	1 / 270	7.3%	5.5 [0.6, 50]
Gallotta [13]	10 / 65	2 / 25	14.0%	2.1 [0.4, 10.3]
Palmieri [14]	8 / 48	4 / 41	21.6%	1.9 [0.5, 6.7]
Total (95% CI)	**593**	**656**	**100.0%**	**2.36 [1.3, 4.3]**
Total events	45	16		

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.42$, df = 7 (P = 0.98); $I^2 = 0\%$
Test for overall effect: Z = 2.82 (P = 0.005)



Echocardiography in normotensive patients: Value?

Meta-analysis: relative risk of in-hospital death



Negative predictive value: 60 (55-65)%

Positive predictive value: 58 (53-63)%

O Sanchez. Eur Heart J 2008;29:1569-1577

European Heart Journal (2012) 33, 3014–3022
doi:10.1093/eurheartj/ehs258

REVIEW

Clinical update

Pulmonary embolism: risk assessment and management

Stavros Konstantinides[1,2]* and Samuel Z. Goldhaber[3]

…Nevertheless, the prognostic value of cardiac ultrasound in haemodynamically stable patients appears moderate at best, mostly due to the poor standardization of echocardiographic criteria…..

CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Predictive Value of Computed Tomography in Acute Pulmonary Embolism: Systematic Review and Meta-analysis

Felix G. Meinel, MD,[a,b] John W. Nance, Jr, MD,[c] U. Joseph Schoepf, MD,[a,d] Verena S. Hoffmann, PhD,[e] Kolja M. Thierfelder, MD,[b] Philip Costello, MD,[a] Samuel Z. Goldhaber, MD,[f] Fabian Bamberg, MD, MPH[g]

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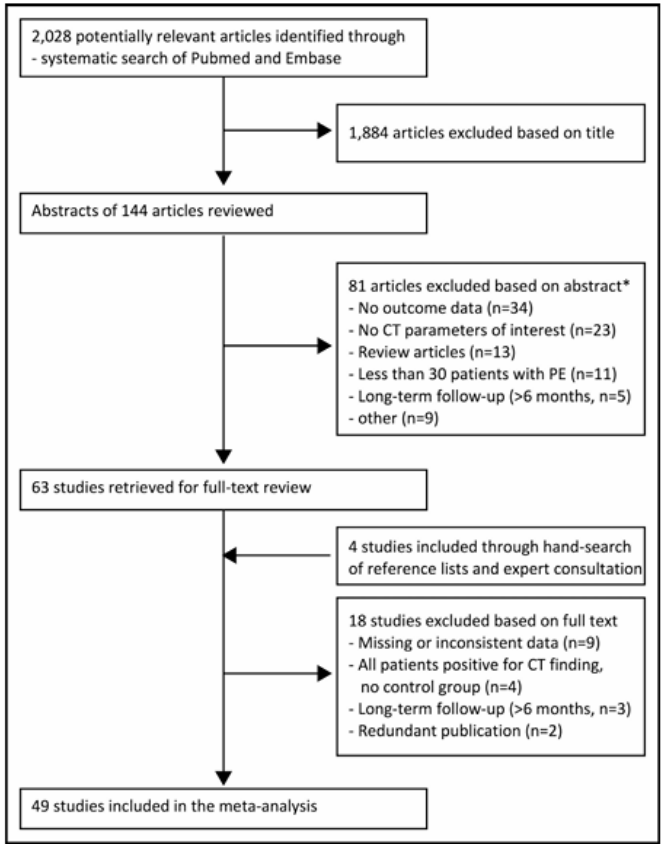
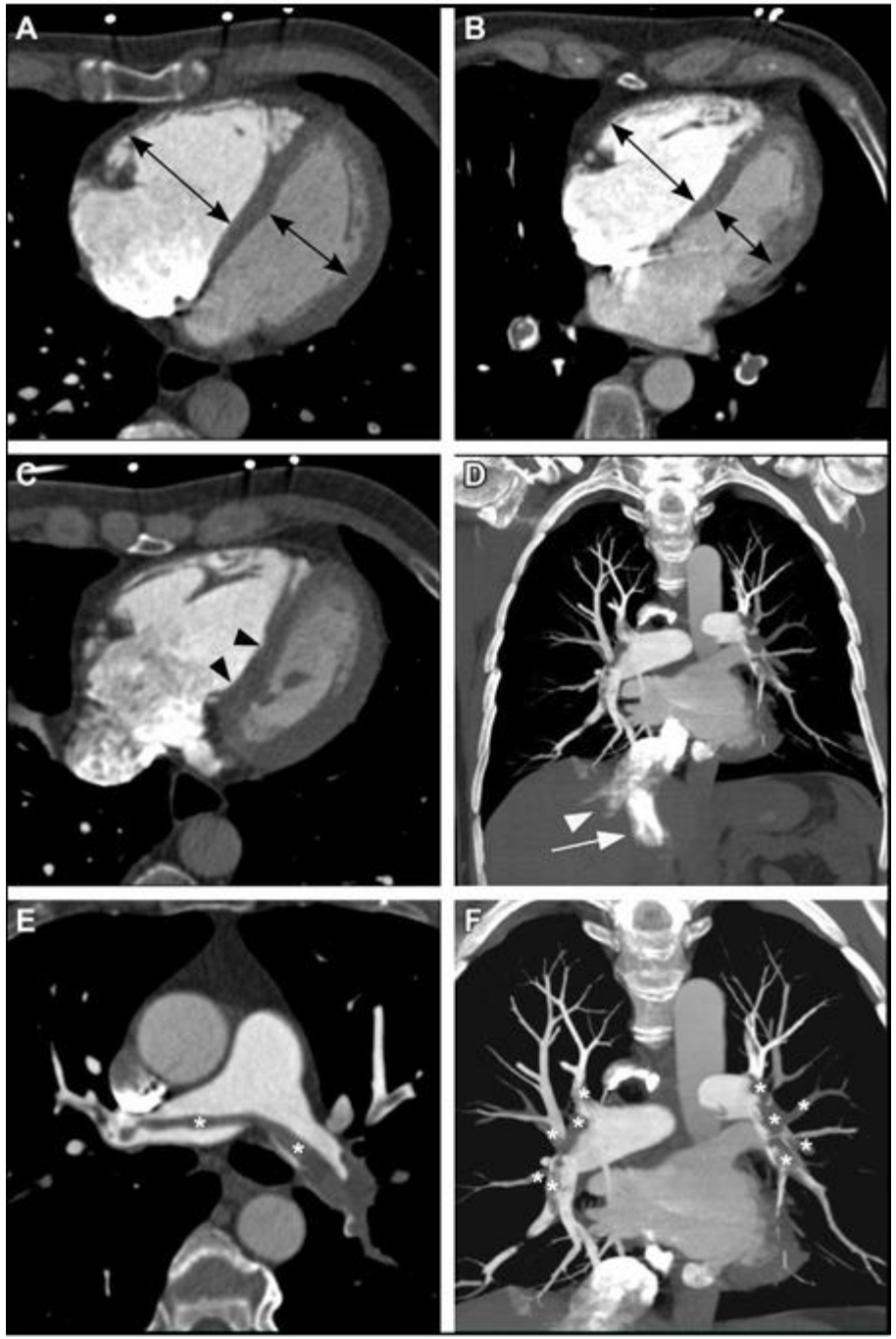
The American Journal of Medicine, Vol 128, No 7, July 2015





CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

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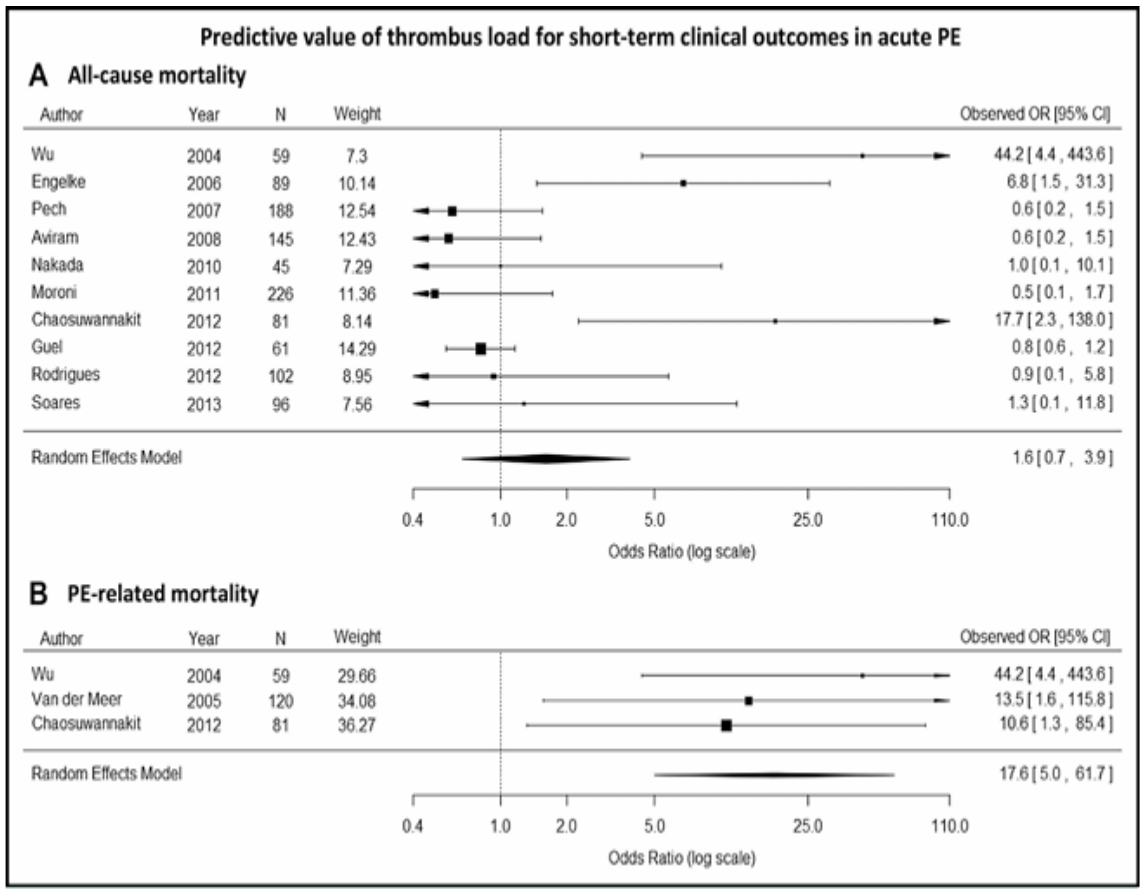
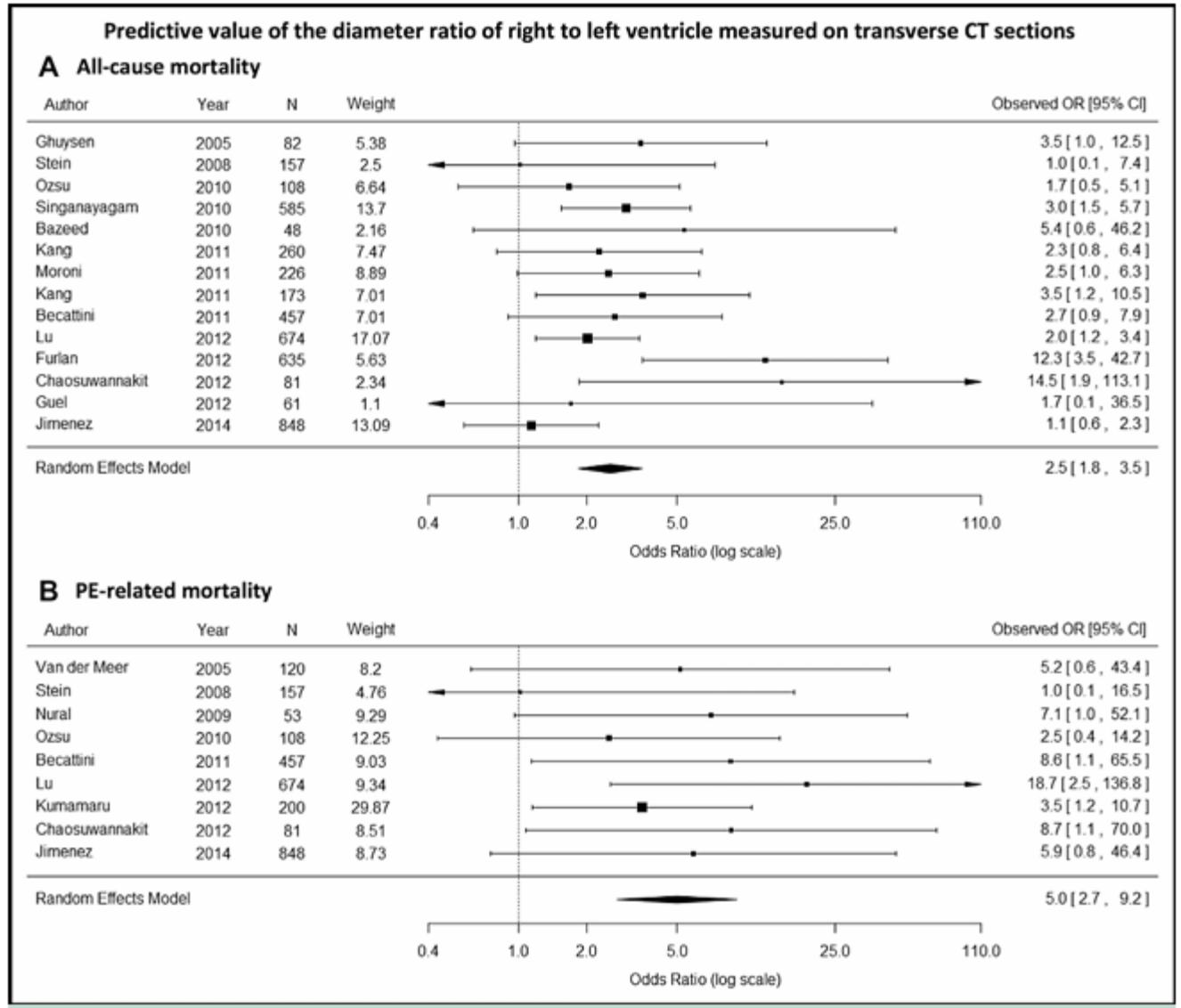
The American Journal of Medicine, Vol 128, No 7, July 2015

Predictive value of thrombus load for short-term clinical outcomes in acute PE



Predictive value of the diameter ratio of right to left ventricle measured on transverse CT sections



Brain-Type Natriuretic Peptide Levels in the Prediction of Adverse Outcome in Patients with Pulmonary Embolism

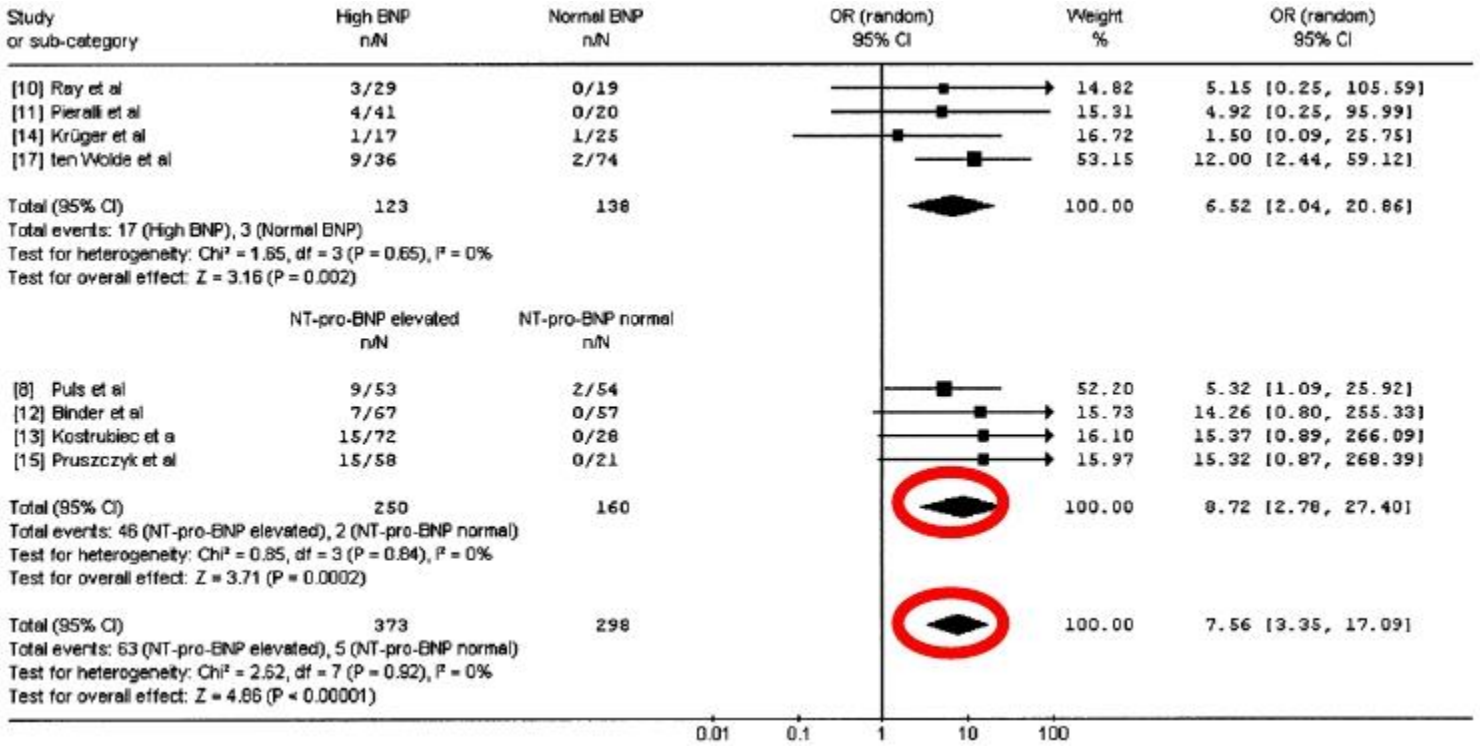
Am J Respir Crit Care Med Vol 178. pp 425–430, 2008

A Systematic Review and Meta-analysis

Frederikus A. Klok[1]*, Inge C. M. Mos[1]*, and Menno V. Huisman[1]

[1] Section of Vascular Medicine, Department of General Internal Medicine–Endocrinology, Leiden University Medical Center, Leiden, The Netherlands

Mortality



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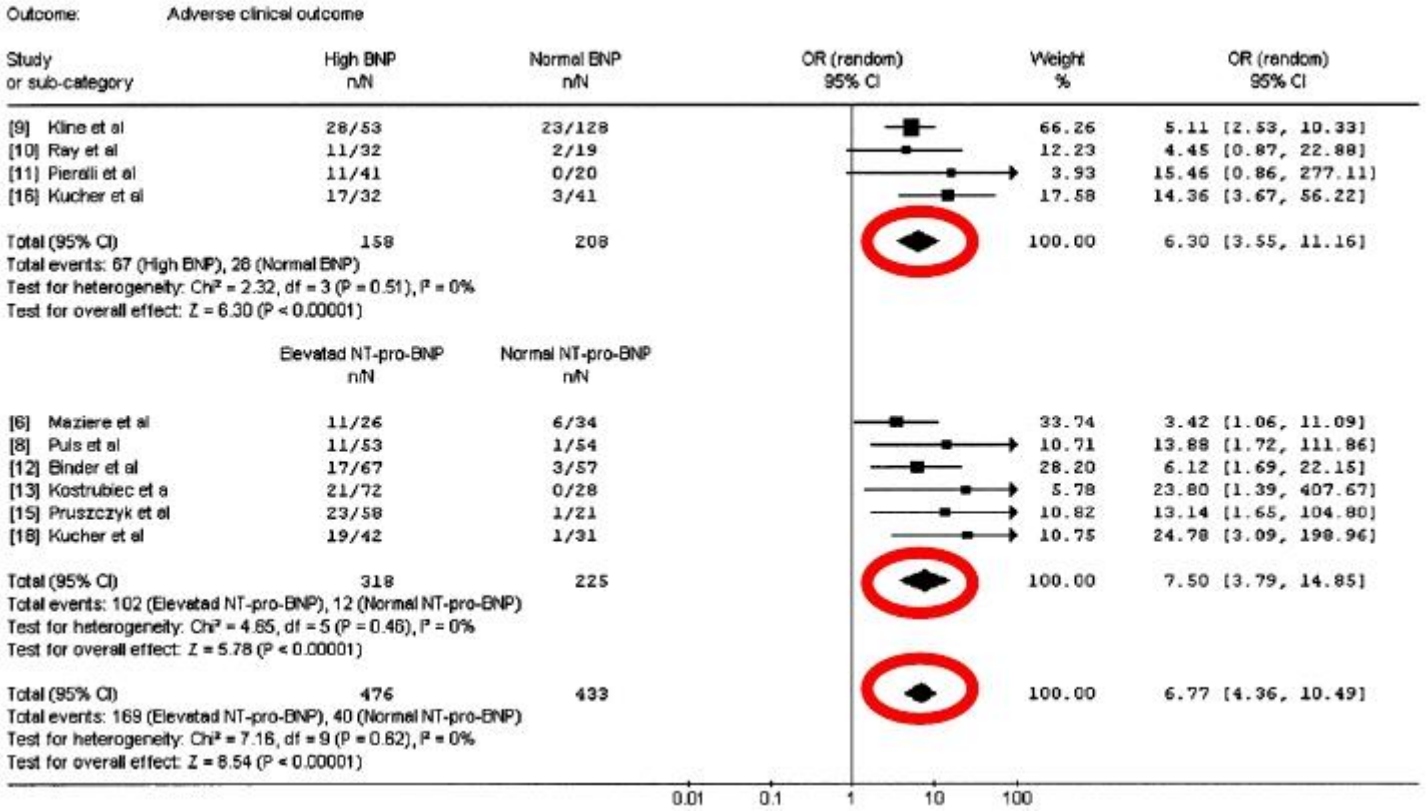
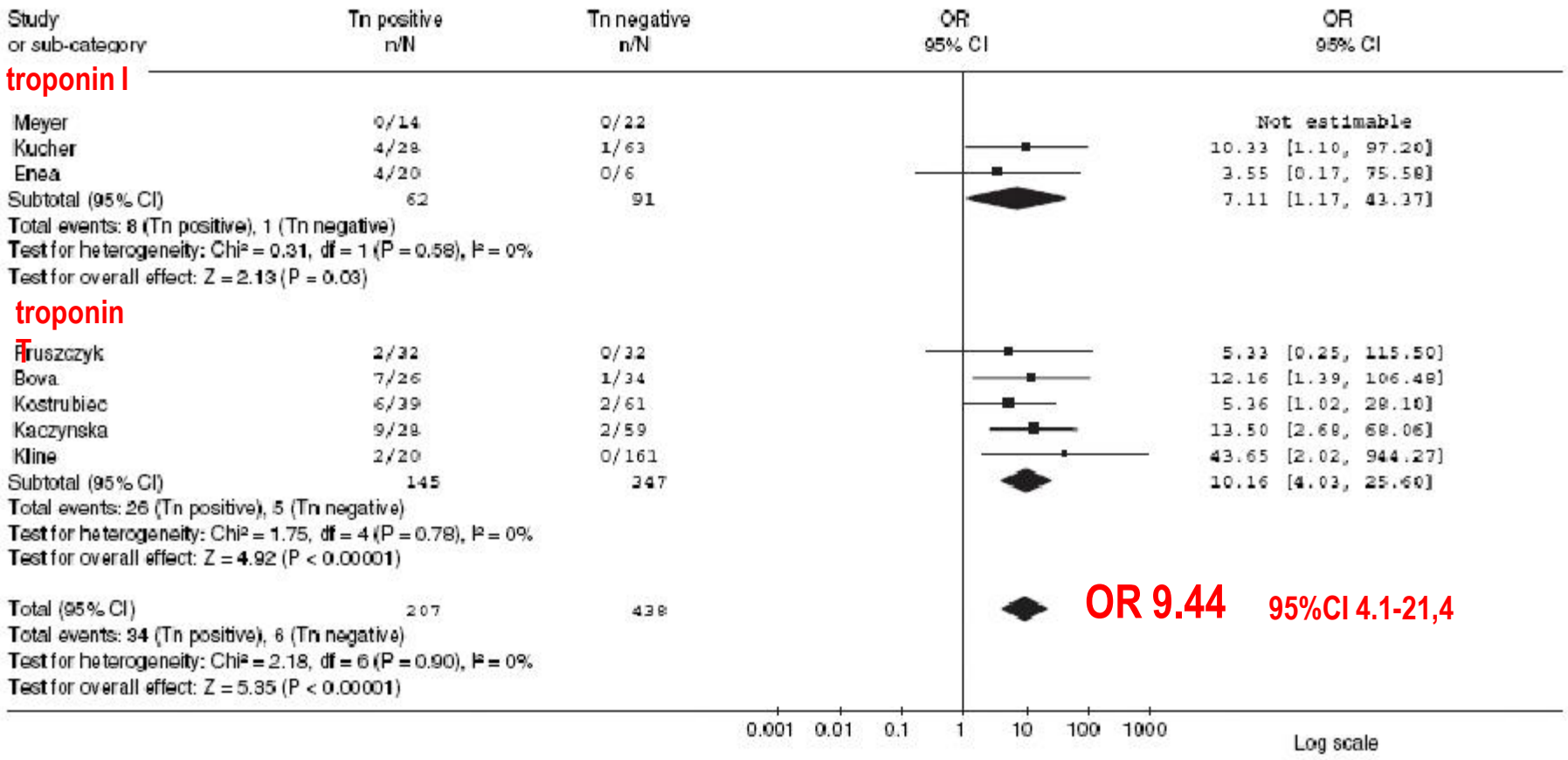


High concentrations of BNP distinguish patients with PE at higher risk of complicated in-hospital course and death from those with low BNP levels. Increased BNP or NT–pro- BNP concentrations alone, however, do not justify more invasive treatment regimens.

Elevated serum troponin I and T forAPE related mortality (n=645).



Becattini C Circulation 2007

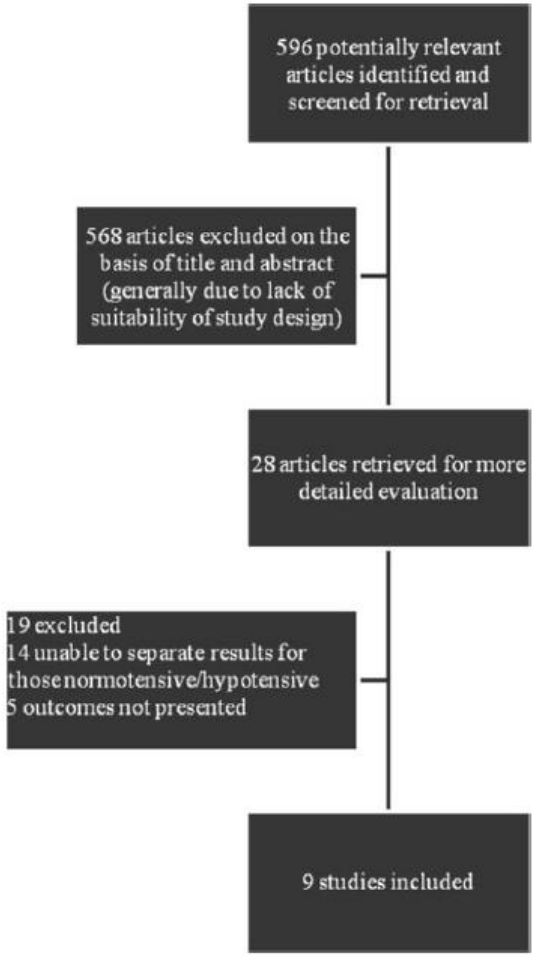
CHEST Original Research
PULMONARY EMBOLISM

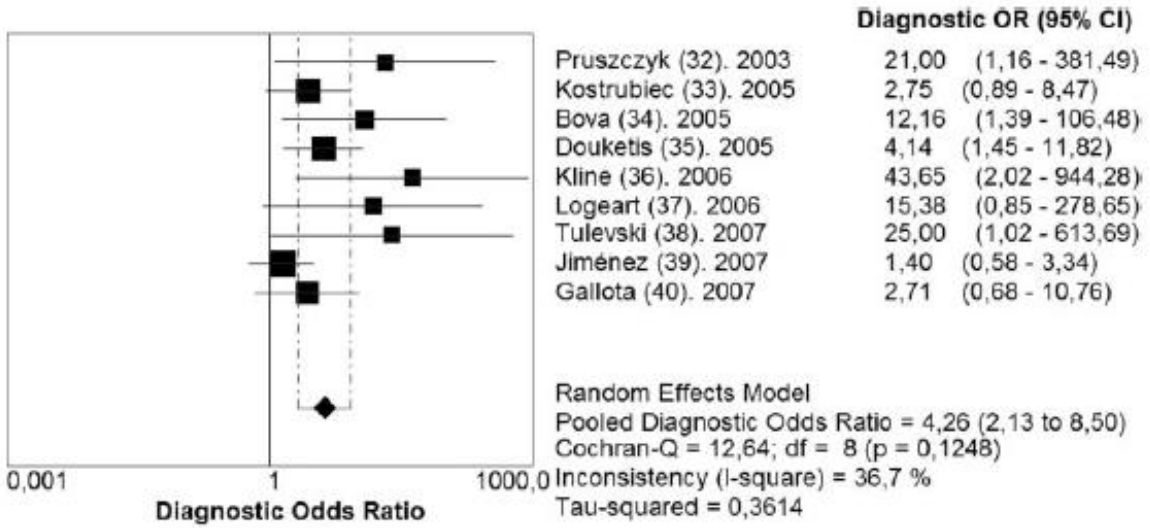
Troponin-Based Risk Stratification of Patients With Acute Nonmassive Pulmonary Embolism

Systematic Review and Metaanalysis

David Jiménez, MD; Fernando Uresandi, MD; Remedios Otero, MD; José Luis Lobo, MD; Manuel Monreal, MD; David Martí, MD; Javier Zamora, MD; Alfonso Muriel, MD; Drahomir Aujesky, MD; and Roger D. Yusen, MD, FCCP

(CHEST 2009; 136:974–982)





Adjusted odds ratio for the Kline, et al, study was not statistically significant.

FIGURE 3. OR of short-term death based on elevated troponin test results in normotensive patients with acute PE: random-effects metaanalysis of nine studies.

Troponins in PE: LOW positive predictive value

Author	Pts(n)	Marker	Ref. value*	Positive (%)	NPV(%)	PPV(%)
Giannitsis, 2000	56	TropT	**0.10**	32	**97**	44
Konstantinides, 2002	106	TropI	**0.07**	41	**98**	14
Konstantinides, 2002	106	TropT	**0.04**	37	**97**	12
Janata,2003	106	TropT	**0.09**	11	**99**	34
Pruszczyk,2003	64	TropT	**0.01**	50	**100**	25

* in ng/mL

N Kucher. Circulation 2003;108:2191

European Heart Journal (2012) 33, 3014–3022
doi:10.1093/eurheartj/ehs258

REVIEW

Clinical update

Pulmonary embolism: risk assessment and management

Stavros Konstantinides[1,2]* and Samuel Z. Goldhaber[3]

Laboratory markers		
Cardiac troponin I, T	Troponin elevation correlated with PE prognosis Sensitive test, high NPV Widely used test	Non-specific test, positive predictive value low (positive test does not justify advanced therapy)
Natriuretic peptides (BNP, NT-proBNP)	BNP/NT-proBNP elevation correlated with PE prognosis High NPV Widely used test	Non-specific test, positive predictive value very low (positive test does not justify advanced therapy) Appropriate cut-off value(s) unclear

Approximately 30-50% of all APE patients troponin positive

The Pulmonary Embolism Severity Index (PESI) and simplified PESI (sPESI)

Demographic characteristics	
Age, per year	Age, in years
Male gender	+ 10
Comorbid illnesses	
Cancer*	+ 30
Heart failure	+ 10
Chronic lung disease	+ 10
Clinical findings	
Pulse ≥ 110 min^{-1}	+ 20
Systolic blood pressure < 100 mmHg	+ 30
Respiratory rate ≥ 30 min^{-1}	+ 20
Temperature < 36 °C	+ 20
Altered mental status†	+ 60
Arterial oxygen saturation < 90%‡	+ 20

Variable	Points[a]
Age > 80 y	1
History of cancer	1
History of chronic cardiopulmonary disease	1
Pulse ≥ 110 beats/min	1
Systolic BP < 100 mm Hg	1
SaO_2 < 90%	1

SaO_2 = arterial oxyhemoglobin saturation.
[a]A total point score for a given patient is obtained by summing the points. The score corresponds with the following risk classes: 0, low risk; ≥ 1, high risk.

Risk class:		mortality
I	≤ 65 points	1,1%
II	66–85 points	3,1%
III	86–105 points	6,5%
IV	106–125 points	10,4%
V	>125 points	24,5%

sPESI

0 points	30-d mortality risk 1.0% (95%CI 0.0-2.1%)
≥ 1 points	10.9% (8.5-13.2%)

Aujesky D et al. Am J Respir Crit CareMed 2005

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association
Learn and Live
(*Circulation*. 2011;123:00-00.)

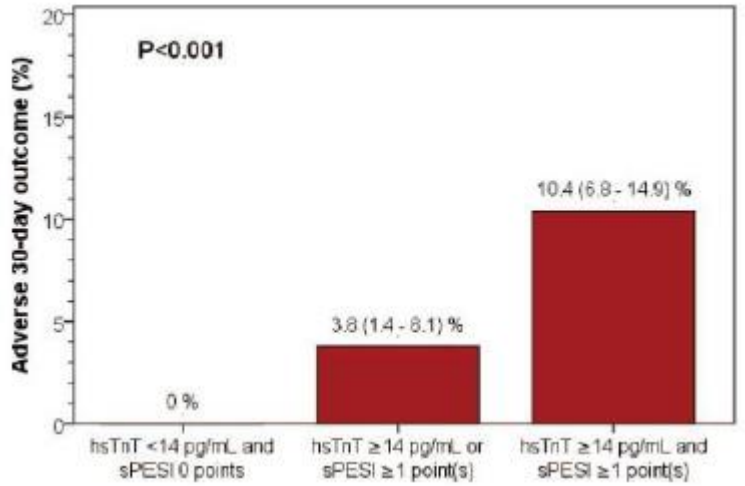
Predictive Value of the High-Sensitivity Troponin T Assay and the Simplified Pulmonary Embolism Severity Index in Hemodynamically Stable Patients With Acute Pulmonary Embolism : A Prospective Validation Study

Mareike Lankeit, David Jiménez, Maciej Kostrubiec, Claudia Dellas, Gerd Hasenfuss, Piotr Pruszczyk and Stavros Konstantinides

526 normotensive patients with acute PE

Table 3. Value of hsTnT and the sPESI, Alone and in Combination, for Predicting an Adverse 30-Day Outcome after Acute Pulmonary Embolism

	Sensitivity	Specificity	PPV	NPV
hsTnT ≥14 pg/mL	0.87	0.42	0.09	0.98
sPESI ≥1 point(s)	0.94	0.40	0.09	0.99
hsTnT ≥14 pg/mL *and* sPESI ≥1 point(s)	1.00	0.26	0.08	1.00



A total of 127 patients (24.1%) low risk by a sPESI of 0 and hsTnT <14 pg/mL; none of them had an adverse 30-day outcome.

The hsTnT assay and the sPESI improve risk stratification of acute PE. Combination of both

modalities may …..identify possible candidates for out-of-hospital treatment

Prognostic Factors for Pulmonary Embolism

The PREP Study, A Prospective Multicenter Cohort Study

Olivier Sanchez[1*], Ludovic Trinquart[2*], Vincent Caille[3], Francis Couturaud[4], Gérard Pacouret[5], Nicolas Meneveau[6], Franck Verschuren[7], Pierre-Marie Roy[8], Florence Parent[9], Marc Righini[10], Arnaud Perrier[10], Christine Lorut[11], Bernard Tardy[12], Marie-Odile Benoit[13], Gilles Chatellier[2], and Guy Meyer[1]

Am J Respir Crit Care Med Vol 181. pp 168–173, 2010

- **Echocardiography, BNP, NTprBNP cTnI 570 consecutive patients with an acute PE.**
- **30-day adverse events: death, secondary cardiogenic shock, or recurrent venous thromboembolism.**

	Complete Case Analysis ($n = 515$)				Multiple Imputation Analysis ($n = 570$)	
Variable	OR (95% CI)	*P* Value	PEV* (%)	Partial PEV* (%)	OR (95% CI)	*P* Value
Altered mental state†	6.8 (2.0–23.3)	<0.01	9.0	3.2	6.8 (2.0–25.5)	<0.01
Cardiogenic shock on admission	2.8 (1.1–7.5)	0.03	11.2	2.7	3.5 (1.4–9.0)	<0.01
Cancer	2.9 (1.2–6.9)	0.02	0.7	0.1	3.1 (1.3–7.2)	<0.01
BNP (↑ of 250 ng/L)	1.3 (1.1–1.6)	<0.01	6.3	2.4	1.3 (1.1–1.6)	<0.01
RV/LV ratio (↑ of 0.1)	1.2 (1.1–1.4)	<0.01	8.7	0.3	1.2 (1.1–1.4)	<0.01

Prognostic Factors for Pulmonary Embolism

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Am J Respir Crit Care Med Vol 181. pp 168–173, 2010

Prognostic Factor	Categories	Points
Altered mental state *		
	No	0
	Yes	10
Cardiogenic shock on admission		
	No	0
	Yes	6
Cancer		
	No	0
	Yes	6
BNP (ng/L)		
	<100	0
	100–249	1
	250–499	2
	500–999	4
	≥1,000	8
RV/LV ratio		
	0.2–0.49	0
	0.5–0.74	3
	0.75–1.00	5
	1.00–1.25	8
	≥1.25	11

<6.5 class I, low risk;

7 – 18.5 class II, intermediate risk;

>18,5 class III, high risk.

complicated outcome

- **Class I 1.8%**
- **class II 11.7%**
- **class III 22.2%**

BNP and echocardiography may be useful determinants of the short-term outcome in PE, together with clinical findings. Patients with PE can be stratified according to the initial risk of adverse outcome, using a simple score based on clinical, echocardiographic, and biochemical variables.

Is RV dysfunction (echo/CT) *plus* myocardial injury (biomarkers) a stronger risk marker ?

Patient group	Complication risk (OR, 95% CI)
Troponin T-negative (<0.04 ng/ml)	-------
Troponin-positive, echo-negative	3.70 (0.76-18.18) *P*=0.107
Troponin-negative, echo-positive	5.56 (0.97-32) *P*=0.055
***Both* troponin- and echo-positive**	**10.00 (2.14-46.80)** ***P*=0.004**

L Binder, S Konstantinides. Circulation 2005;112:1573-1579

CHEST Original Research
PULMONARY VASCULAR DISEASE

A Strategy Combining Imaging and Laboratory Biomarkers in Comparison With a Simplified Clinical Score for Risk Stratification of Patients With Acute Pulmonary Embolism

CHEST 2012; 141(4):916–922

Mareike Lankeit, MD; Vicente Gómez, MD; Carolin Wagner, MD; Drahomir Aujesky, MD; Mónica Recio, MD; Sara Briongos, MD; COL Lisa K. Moores, MD, MC, USA, FCCP; Roger D. Yusen, MD; Stavros Konstantinides, MD; and David Jiménez, PhD; on behalf of the Instituto Ramón y Cajal de Investigación Sanitaria Pulmonary Embolism Study Group*

526 pts with PE

	Study Sample Percent (95% CI)		
	Patients (N = 526)	Death of Any Cause[a] (n = 40)	Nonfatal Recurrence or Major Bleeding[a] (n = 21)
ESC model[1]			
Low risk	39.3 (35.2-43.5)	3.4 (0.9-5.8)	2.4 (0.3-4.5)
Elevated risk	60.7 (56.5-64.8)	10.3 (7.0-13.7)	5.0 (2.6-7.4)
	Patients	Deaths	Nonfatal Adverse Events
sPESI[13]			
Low risk	31.4 (27.4-35.3)	0	1.8 (0-3.9)
High risk	68.6 (64.7-72.6)	11.1 (7.8-14.3)	5.0 (2.7-7.2)

Importantly low-risk patients based on the sPESI had no 30-day mortality compared with 3.4% (95% CI, 0.9-5.8) in low-risk patients by the ESC model.

Both the sPESI and the ESC model successfully predict 30-day mortality after acute symptomatic PE, but exclusion of an adverse early outcome does not appear to require routine imaging procedures or laboratory biomarker testing.

Tools for risk stratification of PE: a critical look

Table I Risk assessment tools in acute pulmonary embolism

	Strengths	Weaknesses
Clinical prediction rules		
PESI	Assessment of clinical severity, comorbidity	Prognostic value for intermediate-risk PE unknown
Geneva risk score	PESI strong for defining low-risk PE, successfully employed in a randomized trial	Clinical scores do not account for RV function, a key prognostic determinant in the early phase
Imaging tests		
Echocardiography	Real-time, bedside assessment of RV size and function, PA systolic pressure	Moderate positive and NPV Poorly standardized parameters and criteria Ultrasound failed to identify candidates for thrombolysis in a randomized trial
CT	Diagnosis of PE and assessment of RV size in one test Findings correlated with PE prognosis	Implications of an enlarged RV on CT for the management of intermediate-risk PE unclear
Laboratory markers		
Cardiac troponin I, T	Troponin elevation correlated with PE prognosis Sensitive test, high NPV Widely used test	Non-specific test, positive predictive value low (positive test does not justify advanced therapy)
Natriuretic peptides (BNP, NT-proBNP)	BNP/NT-proBNP elevation correlated with PE prognosis High NPV Widely used test	Non-specific test, positive predictive value very low (positive test does not justify advanced therapy) Appropriate cut-off value(s) unclear
H-FABP	Early marker of adverse outcome	Not available for routine use at present
GDF-15	'Global' marker of myocardial injury, heart failure, comorbidity	Not available for routine use at present

PESI, Pulmonary Embolism Severity Index; CT, computed tomography; PE, pulmonary embolism; BNP, brain natriuretic peptide; GDF-15, growth differentiation factor-15; H-FABP, heart-type fatty acid-binding protein; NT-proBNP, N-terminal pro-brain natriuretic peptide; PA, pulmonary artery; RV, right ventricular; NPV, negative predictive value.

S Konstantinides and SZ Goldhaber. Eur Heart J 2012

Table 9 Classification of PE based on early mortality risk

ESC European Society of Cardiology

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% of pts	High (death > 15%)	+	(+)	+	(+)
15-20 % of pts Interme-diate (death 3-15%)	Intermediate–high	-	+	+	+
	Intermediate–low	-	+	One (or none) positive	
Low Up to 75 % of pts (death <1%)		-	-	-	Assessment optional; if assessed, negative

CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; TTE = transthoracic echocardiography.

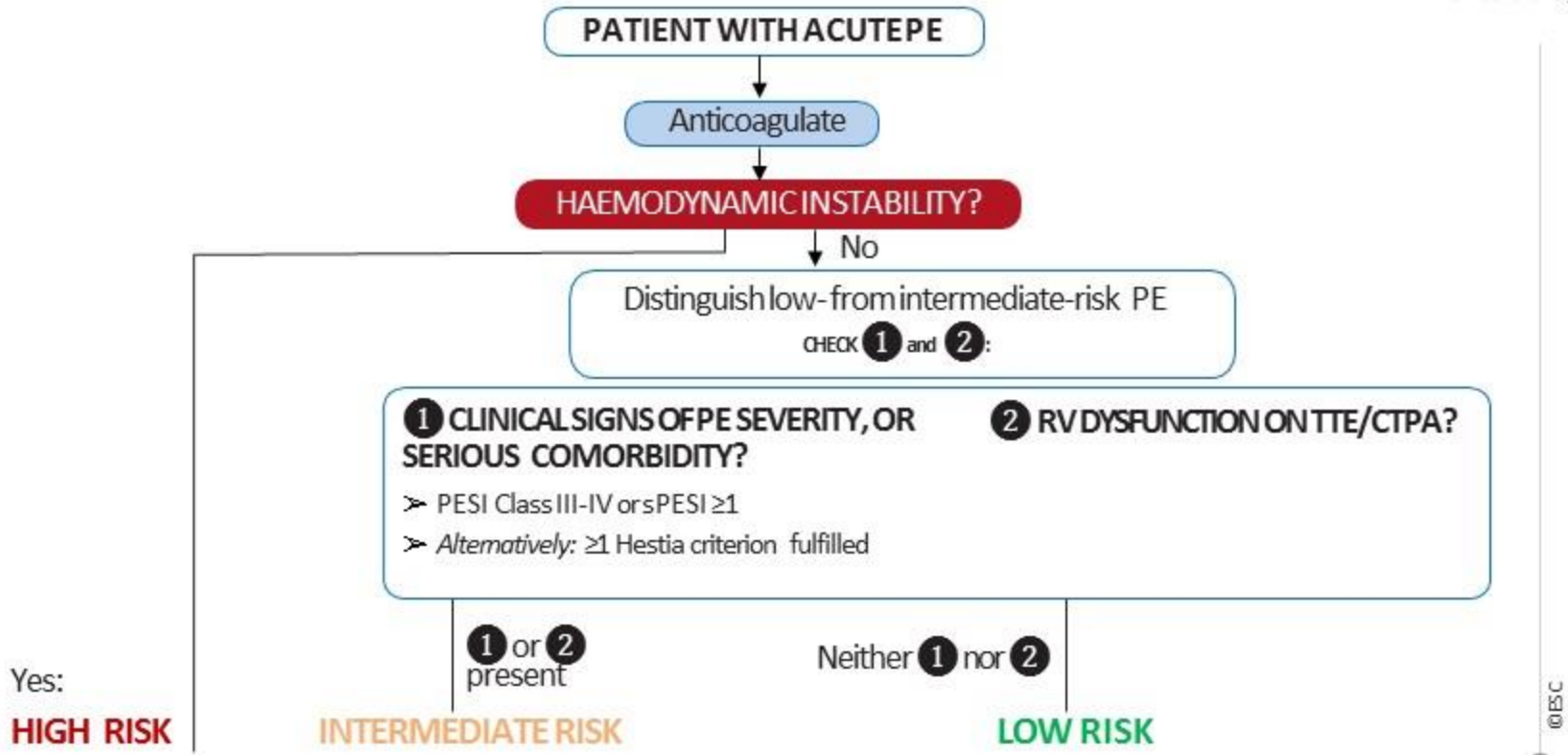
www.escardio.org/guidelines

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 5 Risk-adjusted management strategy for acute PE (1)

ESC European Society of Cardiology



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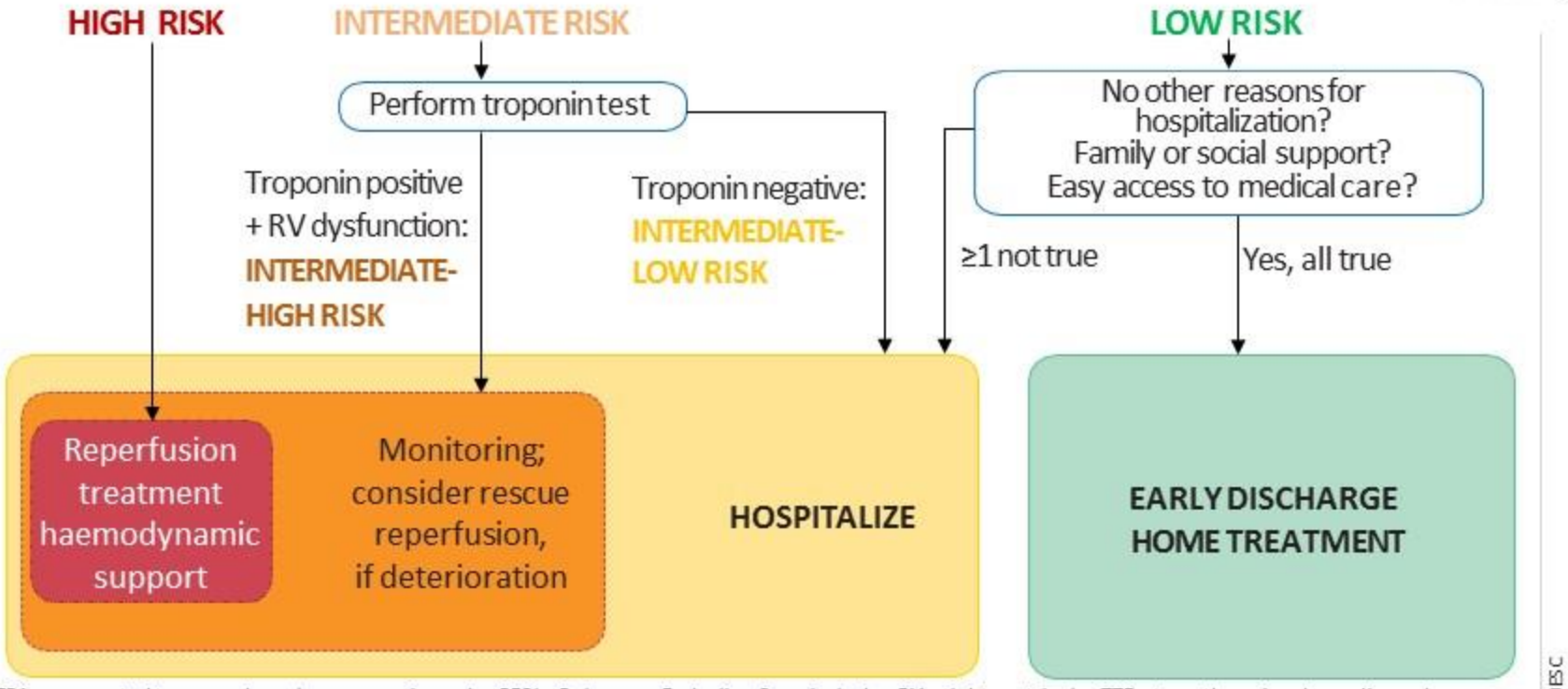
2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 5 Risk-adjusted management strategy for acute PE (2)

ESC European Society of Cardiology

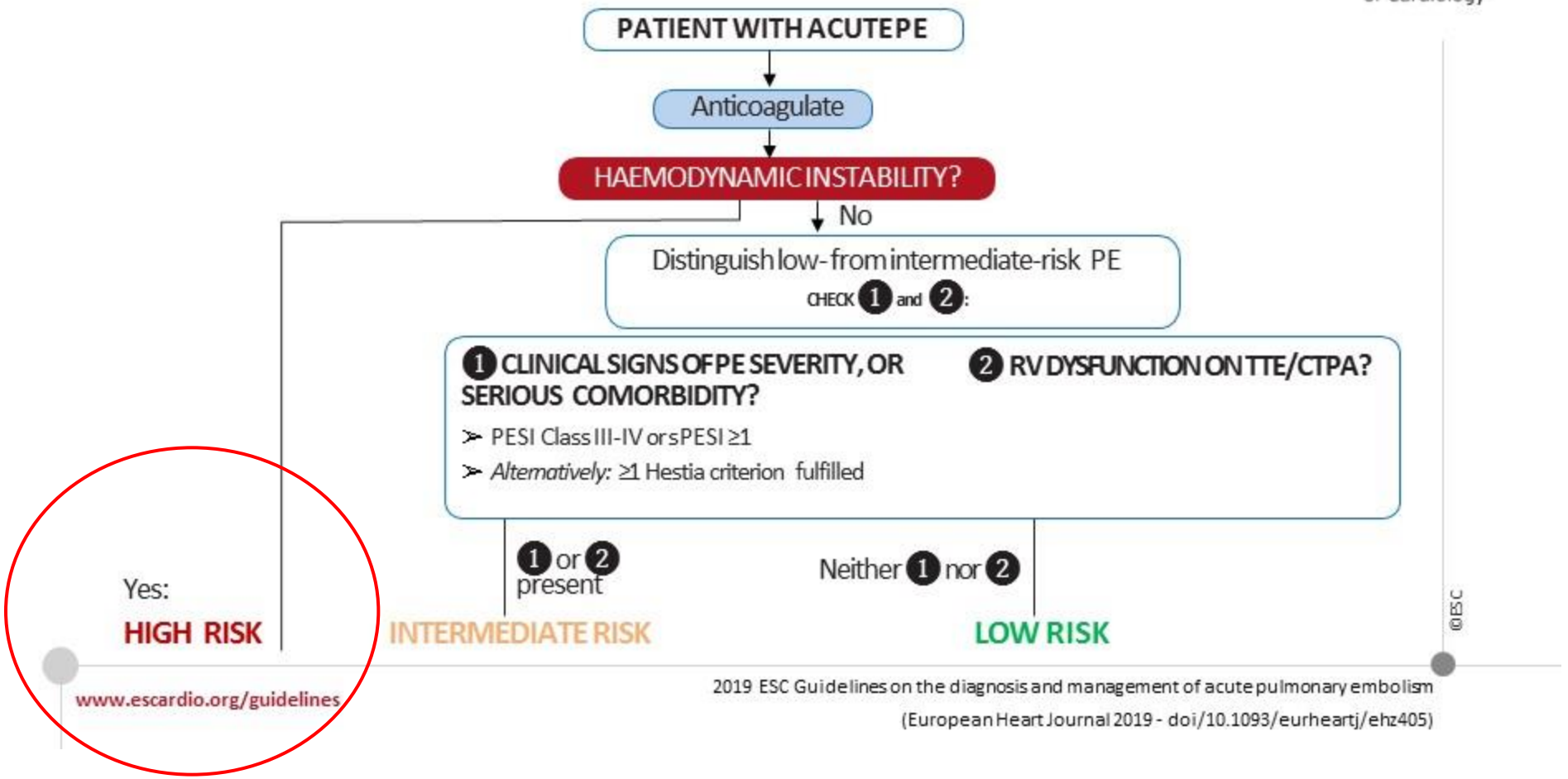


CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; RV = right ventricular; TTE = transthoracic echocardiography.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 5 Risk-adjusted management strategy for acute PE (1)

ESC European Society of Cardiology



www.escardio.org/guidelines

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Tabella 6. *Definizione di instabilità emodinamica*

Shock ostruttivo	PAS < 90 mmHg o necessità di farmaci vasopressori per mantenere valori di PAS ≥ 90 mmHg in assenza di ipovolemia e segni di ipoperfusione d'organo (alterazione stato mentale, tachicardia, oligoanuria, cute fredda marezzata, iperlattacidemia)
Ipotensione	PAS < 90 mmHg o caduta della PAS ≥ 40 mmHg, persistente per almeno 15 minuti e non causata da aritmie, stati ipovolemici, sepsi
Arresto cardiaco	Con necessità di rianimazione cardiopolmonare

PAS: pressione arteriosa sistolica

Pesavento R, Trattato di Medicina Vascolare, Cap 10, Lemma23 Ed 2024

FLOW CHART DECISIONALE PER IL TRATTAMENTO NON FARMACOLOGICO DEL PAZIENTE CON EP AD ALTO RISCHIO

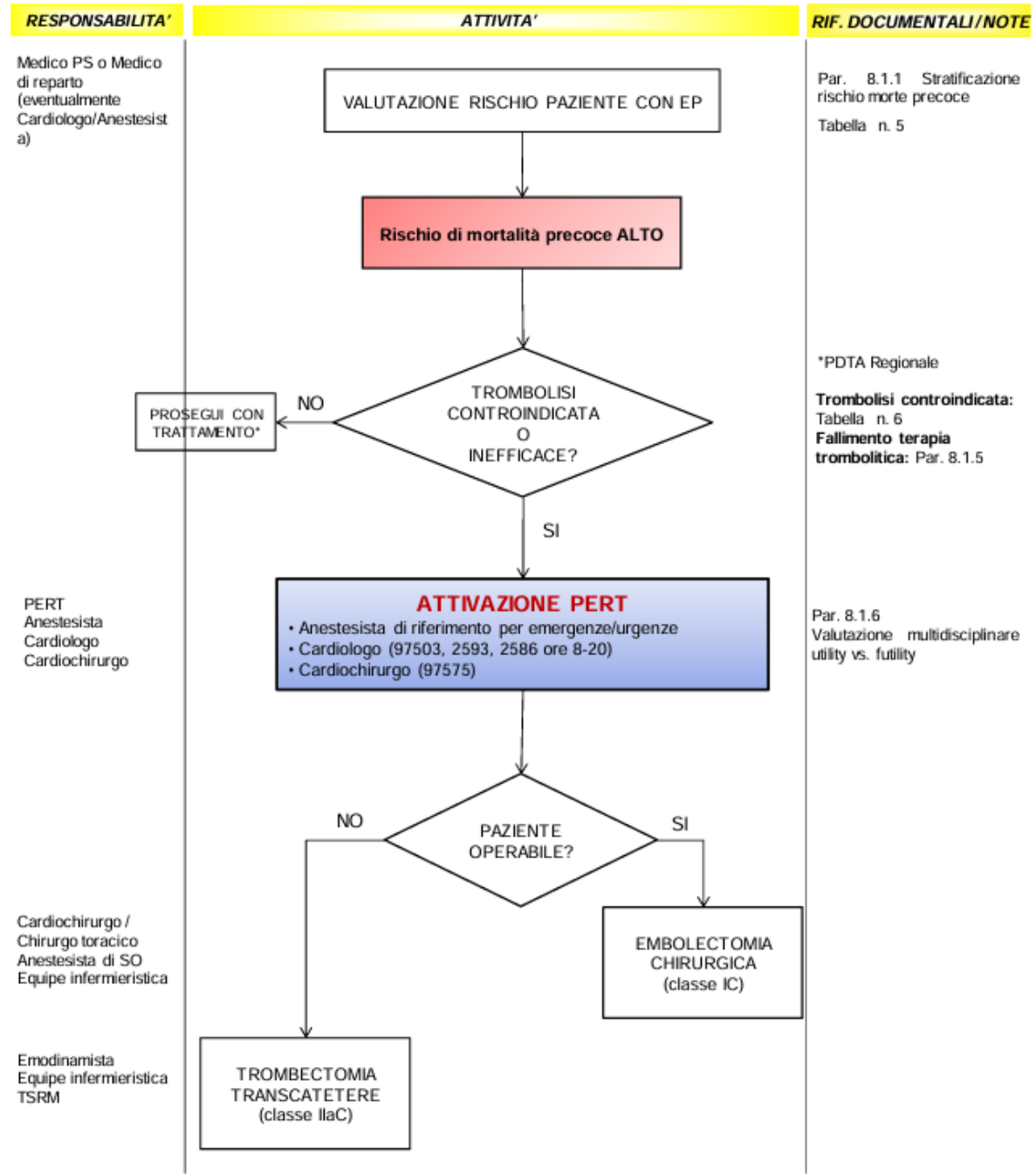
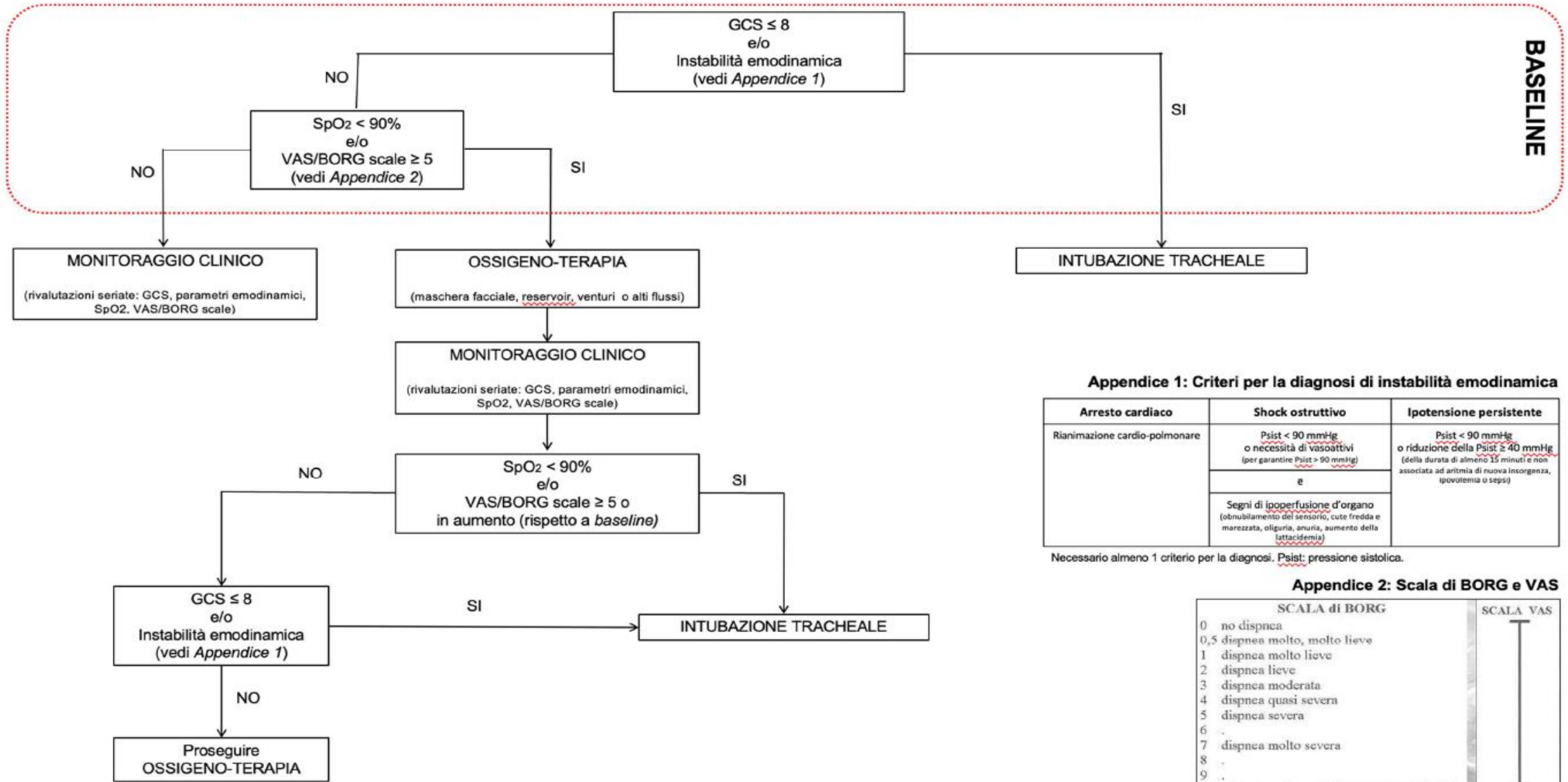


Figura 2. Flow-chart per la gestione dell'insufficienza respiratoria da EP acuta



Appendice 1: Criteri per la diagnosi di instabilità emodinamica

Arresto cardiaco	Shock ostruttivo	Ipotensione persistente
Rianimazione cardio-polmonare	Psist < 90 mmHg o necessità di vasoattivi (per garantire Psist > 90 mmHg)	Psist < 90 mmHg o riduzione della Psist ≥ 40 mmHg (della durata di almeno 15 minuti e non associata ad aritmia di nuova insorgenza, ipovolemia o sepsi)
	e	
	Segni di ipoperfusione d'organo (obnubilamento del sensorio, cute fredda e marezzata, oliguria, anuria, aumento della lattacidemia)	

Necessario almeno 1 criterio per la diagnosi. Psist: pressione sistolica.

Appendice 2: Scala di BORG e VAS

SUPPORTO EMODINAMICO

	Azione	target
NO disfunzione severa VD	Valutare infusione cristalloidi < 500 ml	PAM ≥ 70 mmHG PAS≥90mmHg
Ipotensione/shock/severa disfunzione VD	Noradrenalina 0..01-1 ug/Kg/min	
IC ridotto, PAS >90 mmHg	Associare o da sola Dobutamina 1-20 ug/Kg/min	
Shock cardiogeno refrattario	VA ECMO	

Recommendations for acute-phase treatment of high-risk PE[a] (1)

ESC European Society of Cardiology

Recommendations	Class	Level
It is recommended that anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with high-risk PE.[a]	I	C
Systemic thrombolytic therapy is recommended for high- risk PE.	I	B
Surgical pulmonary embolectomy is recommended for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	I	C

[a] After haemodynamic stabilization of the patient, continue anticoagulation as in intermediate- or low-risk PE.
UFH = unfractionated heparin.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Rationale for thrombolysis in acute PE

Reduce Thrombus Burden (not achievable by AC alone)

- Reverse RV afterload/failure toward prevention of hemodynamic collapse
- Improve pulmonary reperfusion/capillary blood flow/gas exchange
- Restore systemic arterial perfusion pressure
- Decrease the risk of developing chronic pulmonary hypertension (??????)

Piazza G and Goldhaber SZ. Finbrinolysis for acute pulmonary embolism. Vascular Medicine 2010 15(5):419-428

Alteplase Pharmacokinetics

Metabolism – poorly understood but principally hepatic with most occurring with the hepatocytes.

First reading – 60
Second reading – 26 @ 5 minutes later
Third Reading – 12 @ another 5 minutes later

Half-life?

Pharmacokinetics

Rapidly cleared 550-680 mL/minute from plasma giving an initial distribution phase half life ($t_{½\alpha}$) <5 min and in the terminal elimination phase ($t_{½\beta}$) ~40 min.

Thus > 50% of t-PA is cleared from plasma within 5 minutes after discontinuance of an IV infusion and approximately 80% is cleared within 10 minutes.

Risks

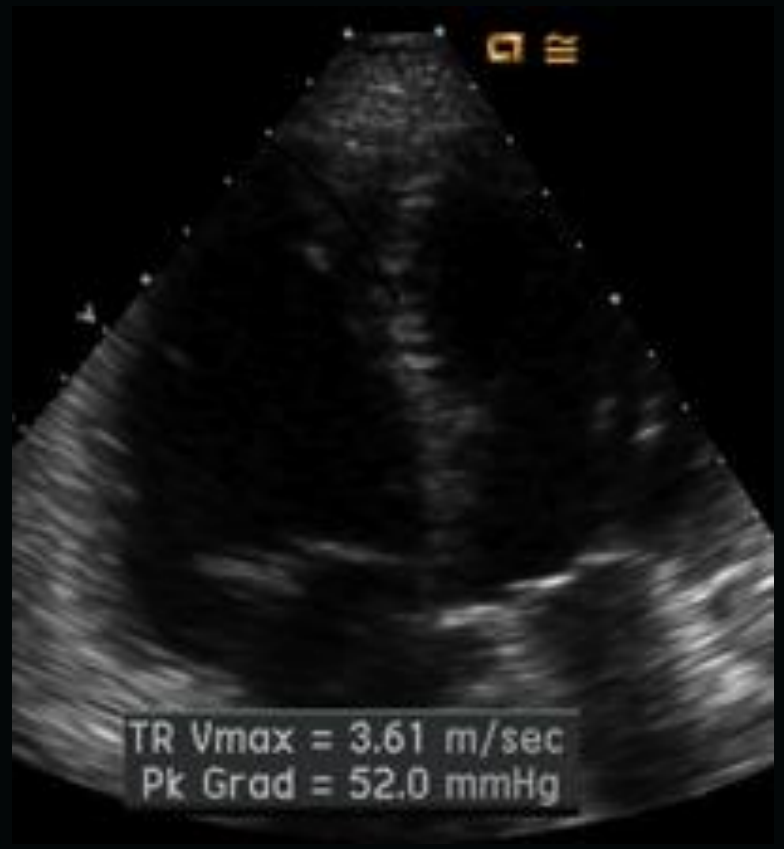
Lysis of normal haemostatic plugs - bleeding

Intracranial haemorrhage, absolute risk is increased 6% in patients of first 10 days, maximal during the first 36 hours after treatment. (*c.f.* 3 month overall risk reduction of 11%)

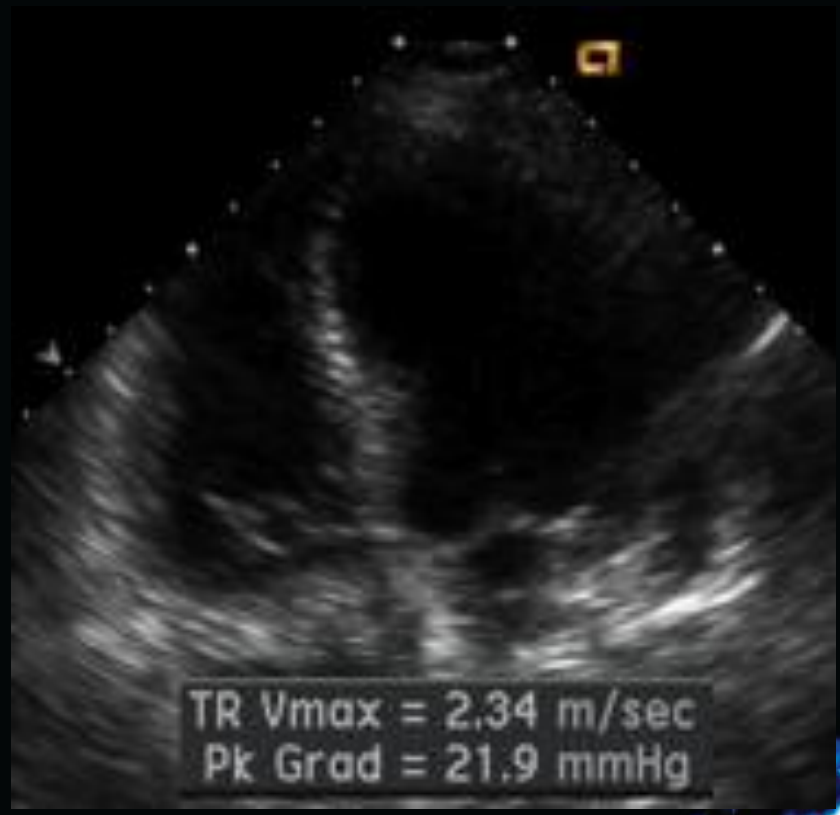
I.V. thrombolysis with tPA

- 100 mg tPA infused over 2 hours (10 mg bolus, 90 mg /2h if conc 1 ml/Kg)
- UHF: either co-administer (only with alteplase; ESC-AHA recomm) or stop and restart when aPTT < 2 ULN then maintain aPTT 50-70 sec.
- Subsequent switch to LMWH –DOAC single-drug approach after careful observation (usually 48-72 h)
  - Persistent clinical stability
  - No (suspected) bleeding
  - No relevant comorbility

Pre and Post tPA
Pulmonary Artery Pressures



Pre Intervention ECHO



Post Intervention ECHO- Day 9

The optimal treatment approach in the unstable patient

- Low quality evidence → lower grade recommendations (ACCP:2B-2C; ESC:IB- IC-IIaC)
- ***Who are the candidates to a reperfusion treatment, provided that the haemorragic risk is tolerable?***
  - Shock/hypotension and confirmed diagnosis (CT, echo, US,)
  - Shock/hypotension, suspected PE and no time for a diagnosis
  - Cardiac arrest and suspected PE (??)
  - Worsening intermediate-high risk PE (rescue treatment –seems rare)
- Relevant fear for hemorragic risk → Many excluded from thrombolysis
- Costs? Not relevant as the patients can die but….always ethical?

JAMA Network™

From: **Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial HemorrhageA Meta-analysis**

JAMA. 2014;311(23):2414-2421. doi:10.1001/jama.2014.5990

Table 2. Absolute Risk Metrics of Outcomes of Major Interest

Outcome of Interest (No. of Studies Reporting)	No. of Events/No. of Patients, Absolute Event Rate (%)		No. Needed to Treat or Harm	*P* Value
	Thrombolytic Group	Anticoagulant Group		
All-cause mortality (16)	23/1061 (2.17)	41/1054 (3.89)	NNT = 59	.01
Major bleeding (16)[a]	98/1061 (9.24)	36/1054 (3.42)	NNH = 18	<.001
ICH (15)	15/1024 (1.46)	2/1019 (0.19)	NNH = 78	.002
Recurrent PE (15)	12/1024 (1.17)	31/1019 (3.04)	NNT = 54	.003
Age >65 y				
All-cause mortality (5)	14/673 (2.08)	24/658 (3.65)	NNT = 64	.07
Major bleeding (5)[a]	87/673 (12.93)	27/658 (4.10)	NNH = 11	<.001
Age ≤65 y				
All-cause mortality (11)	9/388 (2.32)	17/396 (4.29)	NNT = 51	.09
Major bleeding (11)[a]	11/388 (2.84)	9/396 (2.27)	NNH = 176	.89
Intermediate-risk PE				
All-cause mortality (8)	12/866 (1.39)	26/889 (2.92)	NNT = 65	.03
Major bleeding (8)[a]	67/866 (7.74)	20/889 (2.25)	NNH = 18	<.001

Abbreviations: ICH, intracranial hemorrhage; NNH, number needed to harm; NNT, number needed to treat; PE, pulmonary embolism.

[a] Per individual trial criteria with ICH also included for any trials that did not prespecify this.

Epidemiology, patterns of care and mortality for patients with hemodynamically unstable acute symptomatic pulmonary embolism

David Jiménez, Behnood Bikdeli, Deisy Barrios, Andrés Quezada, Jorge del Toro, Gemma Vidal, Isabelle Mahé, Isabelle Quere, Mónica Loring, Roger D. Yusen, Manuel Monreal

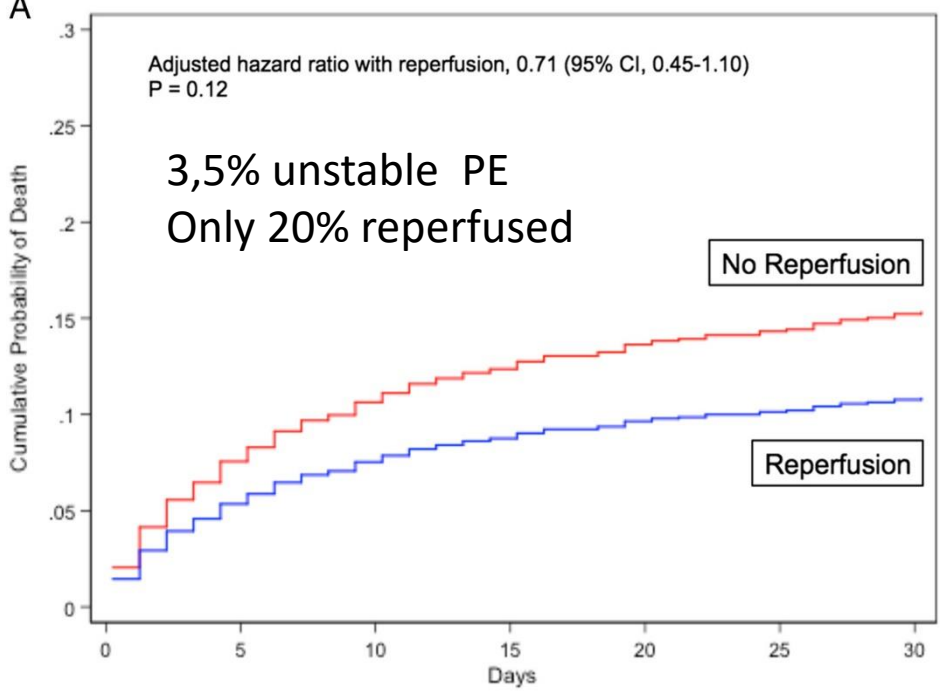
International Journal of Cardiology
Volume 269, Pages 327-333 (October 2018)
DOI: 10.1016/j.ijcard.2018.07.059

Table 3
Clinical events after diagnosis and treatment for patients with acute symptomatic pulmonary embolism.

	All patients $N = 34{,}380$	Unstable PE $N = 1207$	Stable PE $N = 33{,}173$	*P* value
30-day outcomes				
Primary outcome, *n* (%)				
All-cause death	1954 (5.7%)	168 (14%)	1786 (5.4%)	<0.001
PE-related death	998 (2.9%)	113 (9.4%)	885 (2.7%)	<0.001
Secondary outcomes, *n* (%)				
Recurrent PE	201 (0.6%)	3 (0.2%)	198 (0.6%)	0.17
Major bleeding	1274 (3.7%)	75 (6.2%)	1199 (3.6%)	<0.001
7-day outcomes				
Primary outcome, *n* (%)				
All-cause death	815 (2.4%)	110 (9.1%)	705 (2.1%)	<0.001
PE-related death	560 (1.6%)	79 (6.5%)	481 (1.4%)	<0.001
Secondary outcomes, *n* (%)				
Recurrent PE	69 (0.2%)	0 (0%)	69 (0.2%)	0.21
Major bleeding	602 (1.7%)	55 (4.6%)	547 (1.6%)	<0.001

Abbreviations: PE, pulmonary embolism.

A



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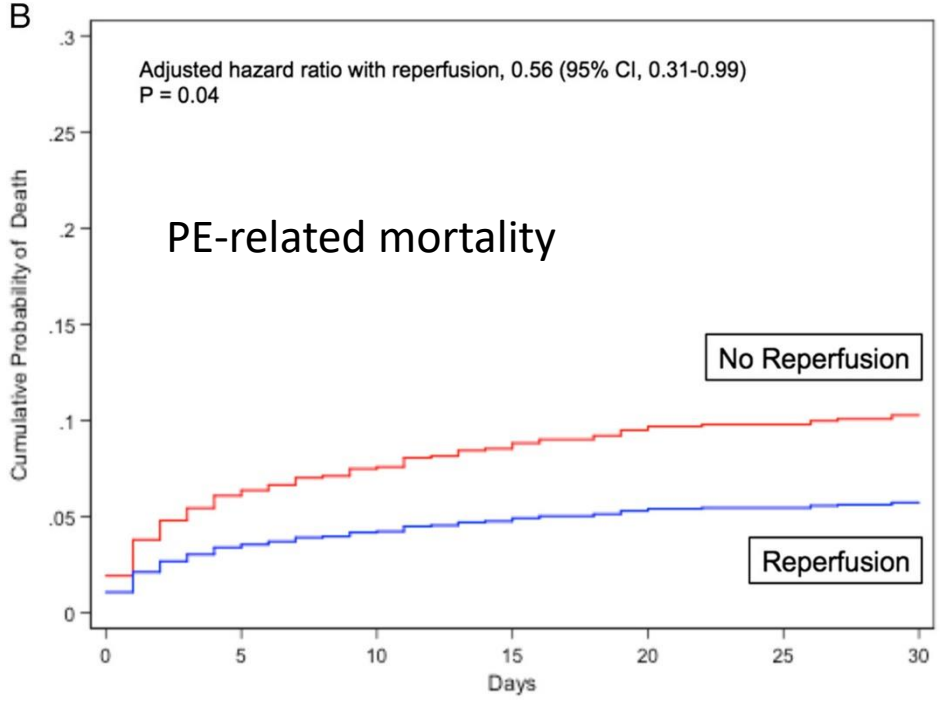


Tabella 6. Controindicazioni assolute e relative alla trombolisi sistemica.

Controindicazioni assolute alla trombolisi sistemica:
- recente chirurgia maggiore - trauma maggiore o al capo nelle precedenti 3 settimane - sanguinamento attivo o diatesi emorragica - storia di stroke emorragico o di origine incerta - stroke ischemico negli ultimi 6 mesi - tumore del sistema nervoso centrale.
Controindicazioni relative:
- attacco ischemico transitorio nei 6 mesi precedenti - terapia anticoagulante orale - gravidanza o prima settimana post-partum - puntura vascolare in siti non comprimibili - manovre di rianimazione polmonare traumatiche - utilizzo di ECMO - epatopatia in stadio avanzato - endocardite infettiva - ulcera peptica attiva - ipertensione refrattaria (sistolica >180 mmHg).

No easy way to stratify the individual expected bleeding risk aft pharmacologic reperfusion (Thrombolytic + heparin!!)

In the «true» ustable PE patient the only absolute CNT should be active uncontrollable bleeding

Reduced Dose Thrombolysis

- Rationale: less is safer
- Higher risk of ICH in the older patients
- Dosages (alteplase)
  - 50 mg in 2 hours
  - 10 mg bolus + 40 mg in 2 hours
  - 0,6 mg/Kg bolus 15 min, max 50 mg

Reduced Dose Bolus Alteplase vs Conventional Alteplase Infusion for Pulmonary Embolism Thrombolysis*

An International Multicenter Randomized Trial

Samuel Z. Goldhaber, MD, FCCP; Giancarlo Agnelli, MD; and Mark N. Levine, MD on behalf of the Bolus Alteplase Pulmonary Embolism Group

(Chest 1994; 106:718-24)

Table 2—*Adverse Events**

Event	Bolus (n=60)	2 h (n=27)	p Value
Death	5†	1	0.66
Death or recurrent PE	6	2	0.99
Nonfatal ICH	0	2	0.09
Major bleeding	2	2	0.58
Other important bleeding	6	4	0.49
Death/ recurrent PE/ major or other important bleeding	10	7	0.38

Reduced major bleeding? P= NS

Reduced ICH? P=NS

However.....

Hemodynamic Effects of Bolus vs 2-h Infusion of Alteplase in Acute Massive Pulmonary Embolism*

A Randomized Controlled Multicenter Trial

Hervé Sors, M.D.; Gérard Pacouret, M.D.; Reza Azarian, M.D.; Guy Meyer, M.D.; Bernard Charbonnier, M.D.; and Gérald Simonneau, M.D.

(Chest 1994; 106:712-17)

Table 2—*Number of Patients (Percent) With Bleeding Complications**

	2-h Group	Bolus Group
Major bleeding	1 (6)	3 (8)
Cerebral hemorrhage	0	0
Hematocrit decrease 15% points	1	3
Important bleeding	2 (12)	0 (0)
Gross hematuria	1	0
Hematocrit decrease > 10% points	1	0
Other bleeding complications	2 (12)	1 (3)
Hemoptysis	1	0
Epistaxis	1	0
Surgical control of bleeding	0	1
Blood transfusion	4 (24)	2 (6)

*No significant differences were found between the treatment groups

Thrombosis Research 133 (2014) 357–363

Contents lists available at ScienceDirect

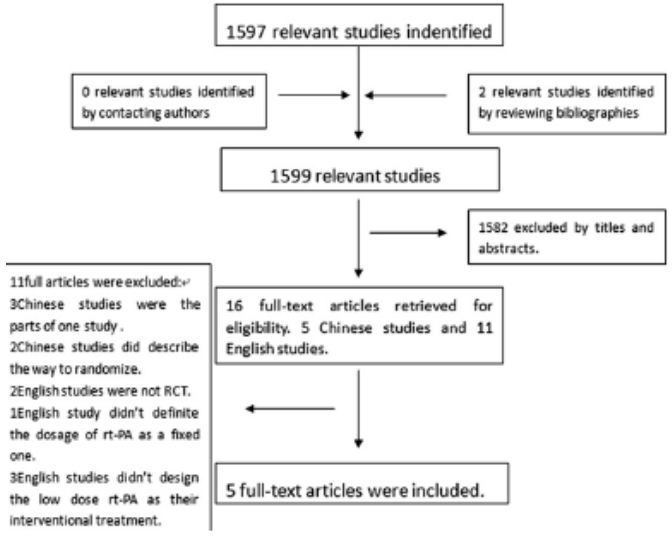
Thrombosis Research

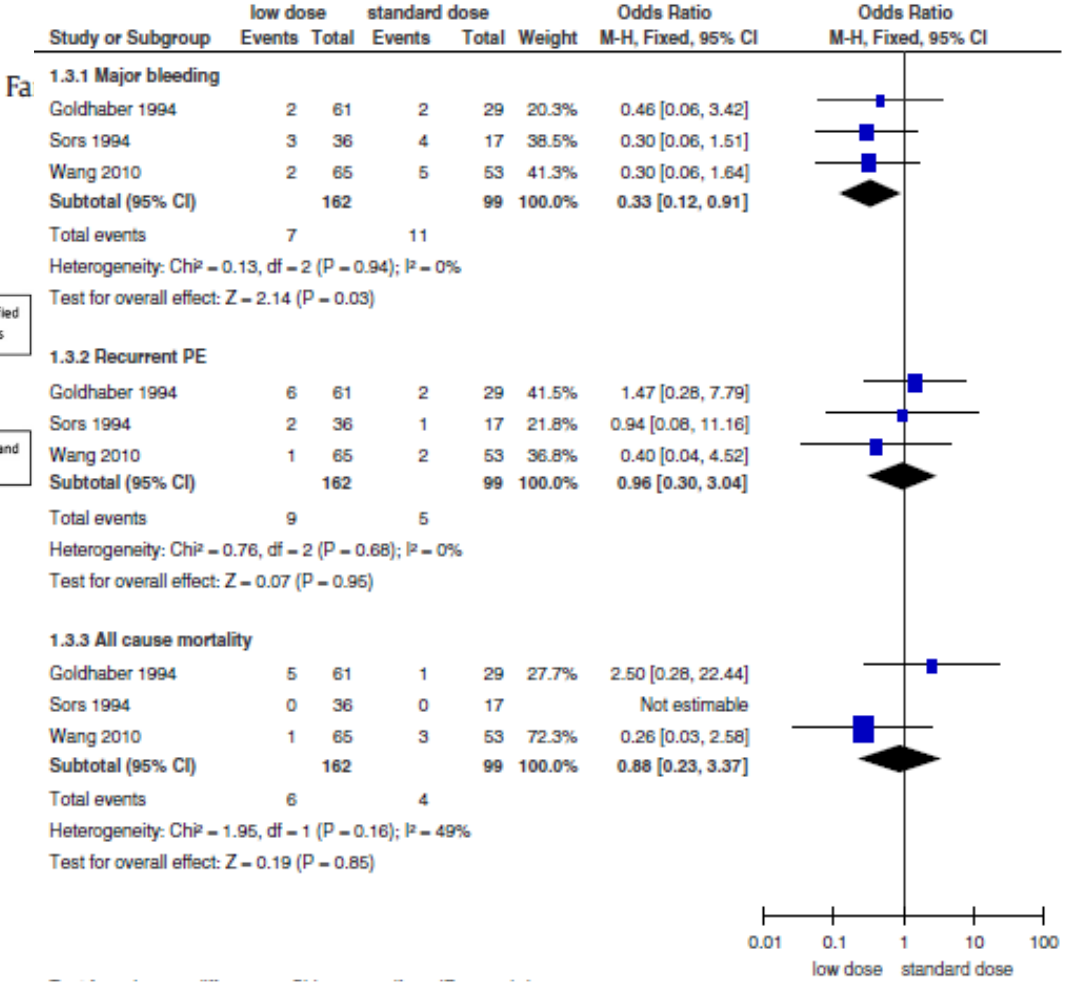
journal homepage: www.elsevier.com/locate/thromres

Regular Article

Lower dosage of recombinant tissue-type plasminogen activator (rt-PA) in the treatment of acute pulmonary embolism: A systematic review and meta-analysis

Zhu Zhang [a], Zhen-guo Zhai [a,*], Li-rong Liang [a], Fa





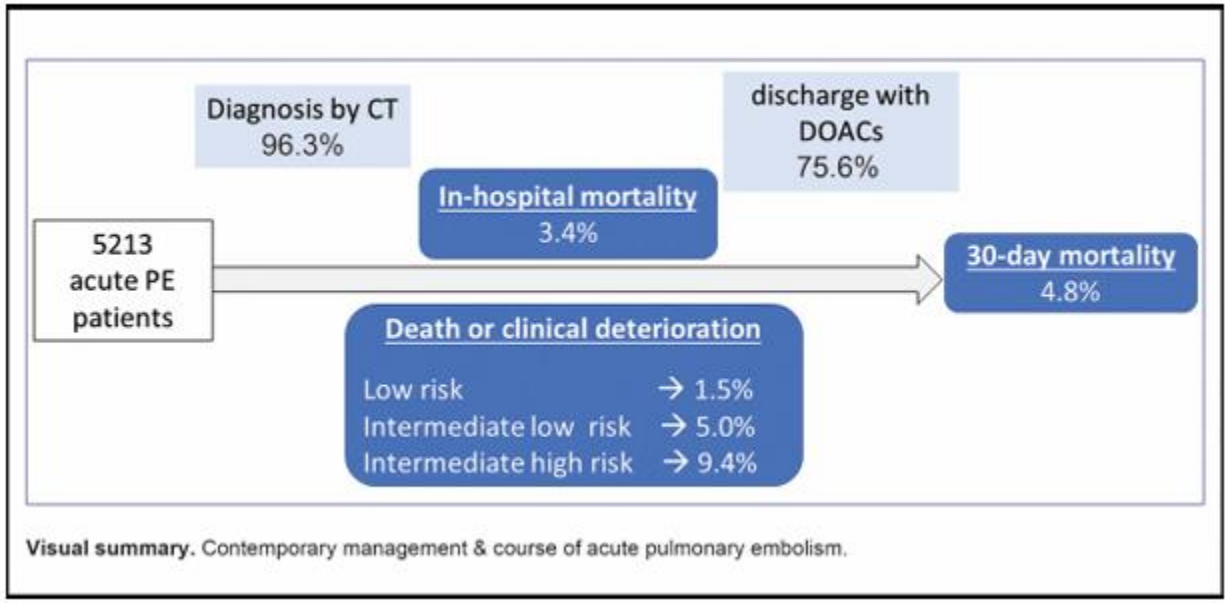
RDT: to whom?

- Elderly
- Weight < 65 Kg
- Pregnant women
- Surgical patients

Heparin Stop and Restart ?

Cath-Directed (or surgical) thrombolysis?

The COPE Study



Visual summary. Contemporary management & course of acute pulmonary embolism.

	In-hospital death				30-day death			
	N (%)	HR	95% CI	*p*	*N* (%)	HR	95% CI	*p*
ESC 2019								
Low risk (sPESI = 0), *n* = 912	*2 (0.2)*	1	–	–	3 (0.3)	1	–	–
Intermediate risk (sPESI ≥ 1), *n* = 4,103	*139 (3.4)*	10.79	2.7–43.6	0.0008	205 (5.0)	15.51	5.0–48.5	< 0.0001
High risk (shock or cardiac arrest), *n* = 177	*36 (20.3)*	54.29	13.0–226.1	< 0.0001	40 (22.6)	83.06	25.7–268.5	< 0.0001
Unknown risk, *n* = 21	*0*	0.0	0.0–.	0.98	0	0.0	0.0–8.9*10^{261}	0.98

Becattini C et al.
Thromb Haemost 2023

The COPE Study

Death in-hospital and at 30 days by anticoagulant treatment strategies and by risk of death.

	In-hospital death			Death at 30 days		
	anticoagulant treatment during hospital-stay		P	anticoagulant treatment during hospital-stay		P
	Not completely oral (n = 4232)	Completely Oral[$] (n = 926)		Not Completely Oral (n = 4232)	Completely Oral[$] (n = 926)	
ESC 2014						
Low risk (sPESI = zero), n = 1687	7/1282 (0.6%)	0/405 (0.0%)	0.21	7/1282 (0.6%)	0/405 (0.0%)	0.21
Intermediate low risk, n = 1838	60/1545 (3.9%)	4/293 (1.4%)	0.03	103/1545 (6.7%)	6/293 (2.1%)	0.002
Intermediate high risk, n = 1206	46/1024 (4.5%)	5/182 (2.8%)	0.28	58/1024 (5.7%)	6/182 (3.3%)	0.19
Intermediate unknown risk, n = 209	12/186 (4.4%)	1/23 (4.3%)	1	18/186 (9.7%)	1/23 (4.4%)	0.70
High risk (shock or cardiac arrest), n = 166	25/155 (16.1%)	1/11 (9.1%)	1	29/155 (18.7%)	1/11 (9.1%)	0.69
Unknown risk, n = 52	0/40 (0.0%)	0/12 (0.0%)	–	0/40 (0.0%)	0/12 (0.0%)	–
ESC 2019						
Low risk (sPESI = zero), n = 901	1/663 (0.2%)	0/238 (0.0%)	1	1/663 (0.2%)	0/238 (0.0%)	1
Intermediate low risk, n = 2320	63/1924 (3.3%)	4/396 (1.0%)	0.01	106/1924 (5.5%)	6/396 (1.5%)	0.0003
Intermediate high risk, n = 1541	49/1289 (3.8%)	5/252 (2.0%)	0.15	61/1289 (4.7%)	6/252 (2.4%)	0.09
Intermediate unknown risk, n = 209	12/186 (6.5%)	1/23 (4.3%)	1	18/186 (9.7%)	1/23 (4.4%)	0.70
High risk (shock or cardiac arrest), n = 166	25/155 (16.1%)	1/11 (9.1%)	1	29/155 (18.7%)	1/11 (9.1%)	0.69
Unknown risk, n = 21	0/15 (0.0%)	0/6 (0.0%)	–	0/15 (0.0%)	0/6 (0.0%)	–

[$] Only oral or after parenteral therapy for <48 h.

Becattini C et al. Vasc Pharmacol 2023

Catheter-directed therapy

Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.[d]	IIa	C
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.	IIa	C

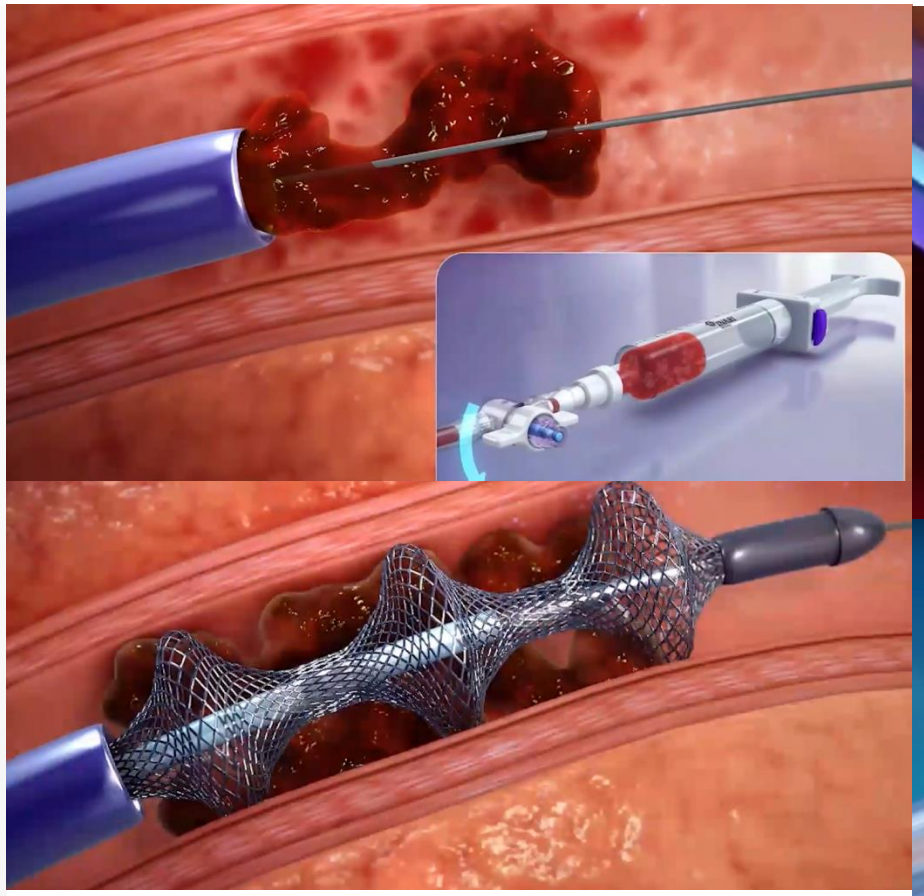
Device	Mechanism of thrombus removal	Technical data#	Source of clinical evidence in pulmonary embolism	Vascular access	CE certificate for PE therapy
Pigtail catheters	Fragmentation and thrombolytic infusion	Diameter 6-8 Fr	Case series	F/J	Not applicable
Indigo system (Penumbra)	Aspiration with mechanical fragmentation	Diameter 8 Fr, 12 Fr Length 115 cm	EXTRACT-PE – single-arm trial[26].	F/J	YES
AngioVac (Angiodynamics)	Large lumen aspiration tube with the system of veno-venous bypass	Diameter 22 Fr	Case series (difficult for PE)	F	NO*
BASHIR endovascular catheter (Thrombolex)	Mechanical fragmentation, aspiration and thrombolytic infusion	Diameter 7 Fr Length 92.5 cm Treatment zone 12.5 cm	Case series	F	NO
FlowTriever System (Inari)	Aspiration with or without mechanical fragmentation	Diameter 16, 20 and 24 Fr Nitinol mesh diameter S 6-10 mm, M 11-14 mm, L 15-18 mm and XL 19-25 mm	FLARE – single-arm trial[25]. FLASH[53]	F	YES
ASPIREX (Straub medical)	Fragmentation and aspiration	Diameter 6 Fr, 8 Fr and 10 Fr Length 85, 110 and 135 cm	Case series	F	YES
AngioJet (Boston Scientific)	Rheolytic thrombectomy with aspiration and possibility for thrombolytic injections	Diameter 6-8 Fr Length 120 cm	Case series	F/J	YES

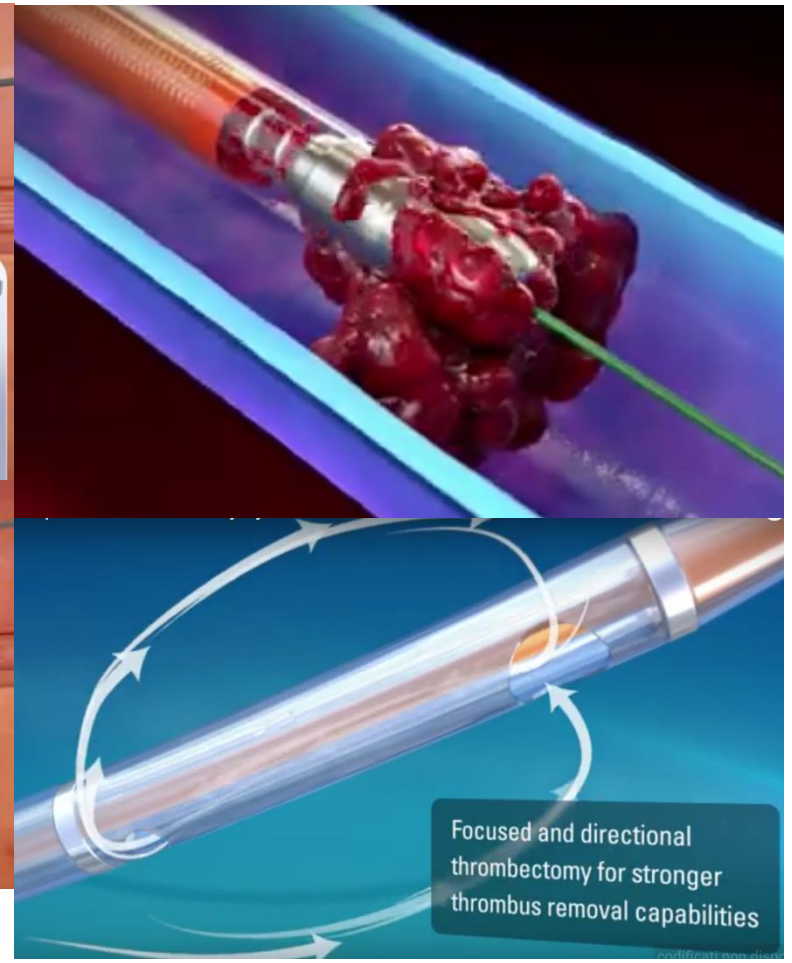
2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

DOI: 10.4244/EIJ-D-22-00246

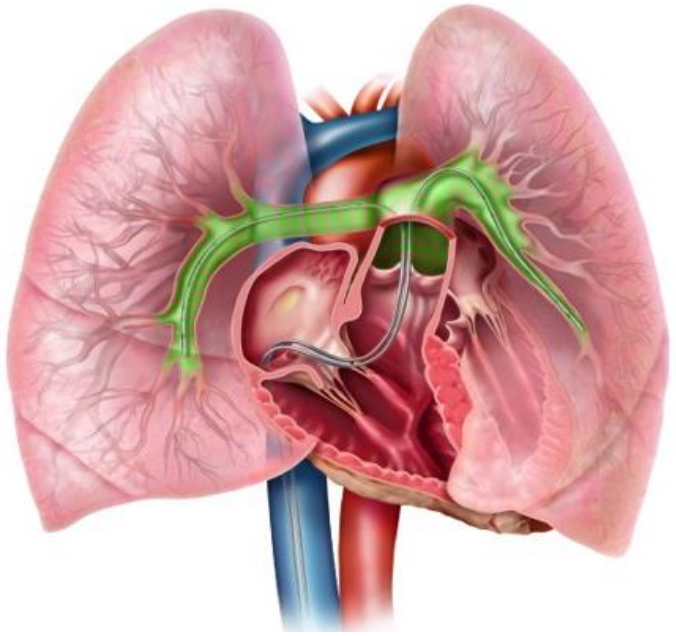
Catheter-directed therapy

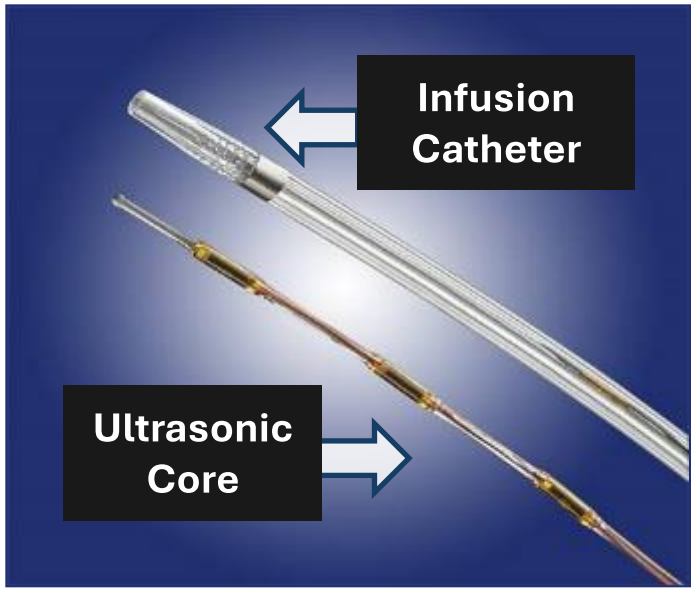


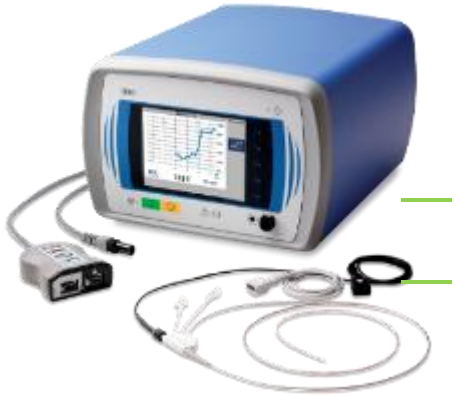


complete removal of thrombus from the pulmonary bed is usually **not required** for haemodynamic stabilisation

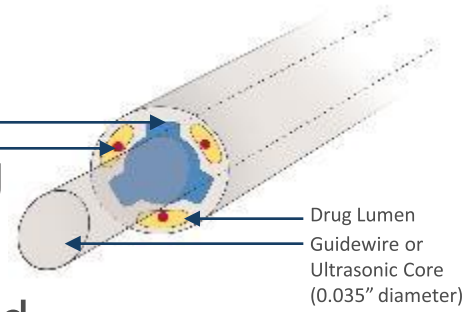
Assisted (US) cath- directed Thrombolysis







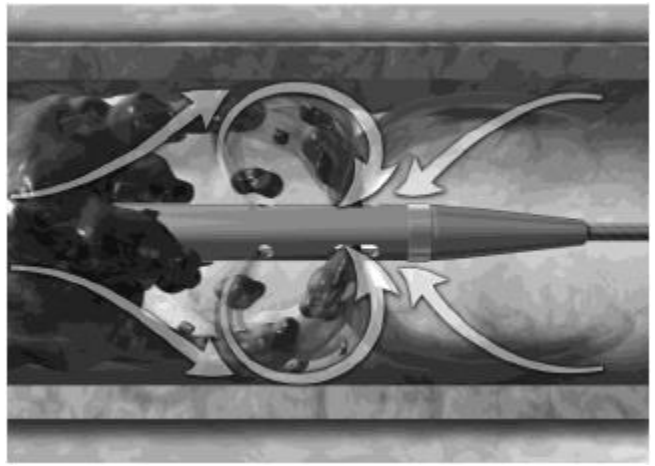
- 5.4 Fr catheter
- 106 an 135 cm working length
- 6, 12, 18, 24, 30, 40 and 50 cm treatment zones

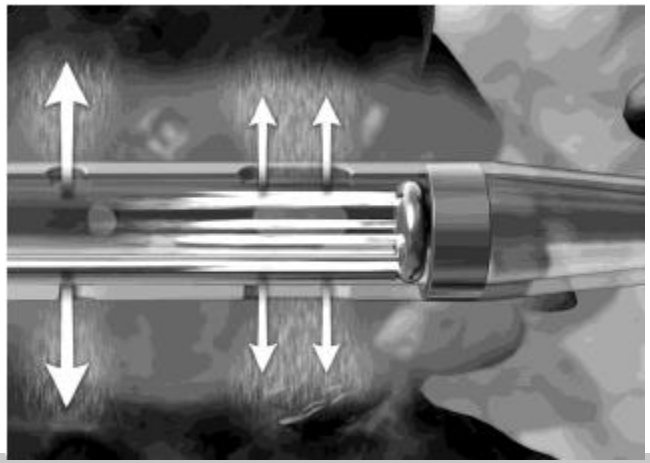


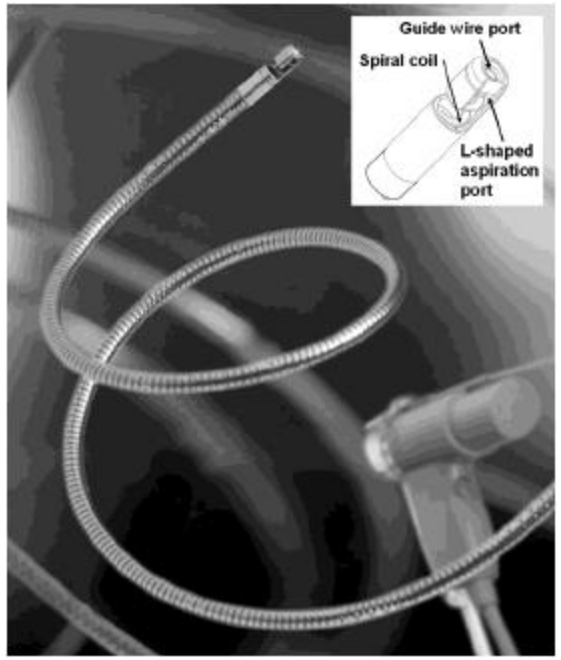
Alternative: Catheter-Based Therapy

N Kucher. In: Management of Pulmonary Embolism. Humana Press 2007

AngioJet Xpeedior, Possis, MN







Aspirex, Straub, CH

Catheter-directed therapy: game changer?

TRIAL	Author	Year	Device	Patient characteristics	Number of subjects	Outcome (efficacy)
ULTIMA[36]	Kucher N	2013	EkoSonic	IHR (n=59, 100%)	59	RV/LV ratio reduced from 1.28±0.19 to 0.99±0.17 at 24 h (p<0.001)
SEATTLE II[37]	Piazza G	2015	EkoSonic	mPE (n=31, 21%); sPE (n=119, 79%)	150	RV/LV ratio reduced from 1.55 to 1.13 at 48 h (p<0.0001), PASP 51.4 reduced to 36.9 mmHg (p<0.0001) at 48 h
OPTALYSE PE[38]	Tapson VF	2018	EkoSonic	IHR (n=101, 100%)	101	RV/LV ratio reduced in all arms
FLARE[25]	Tu T	2019	FlowTriever	IHR (n=106, 100%)	106	RV/LV ratio 1.53 reduced to 1.15 at 48 h
EXTRACT-PE[26]	Sista KA	2021	Indigo Penumbra	sPE (n=119, 100%)	119	Mean RV/LV ratio reduction from baseline to 48 h post-procedure 0.43 (p<0.0001)
SUNSET sPE[51]	Avgerinos DE	2021	USAT (EkoSonic) vs SCDT (Cragg-McNamara or UniFuse)	sPE (n=81, 100%)	81	No significant difference in mean thrombus score reduction between the 2 groups (p=0.76); mean reduction in RV/LV ratio from baseline (1.54±0.30 for USAT, 1.69±0.44 for SCDT) to 48 hours was 0.37±0.34 in the USAT group and 0.59±0.42 in the SCDT group (p=0.01).

PEITHO 7-day rates of major bleeding 8.3% GUSTO criteria / 11.5% ISTH criteria

ULTIMA, SEATTLE II and OPTALYSE 0-10% (meta-analysis 6.7% high risk PE and 1-4% intermediate risk PE).
Only 1 intracranial bleeding in OPTALYSE

DOI: 10.4244/EIJ-D-22-00246

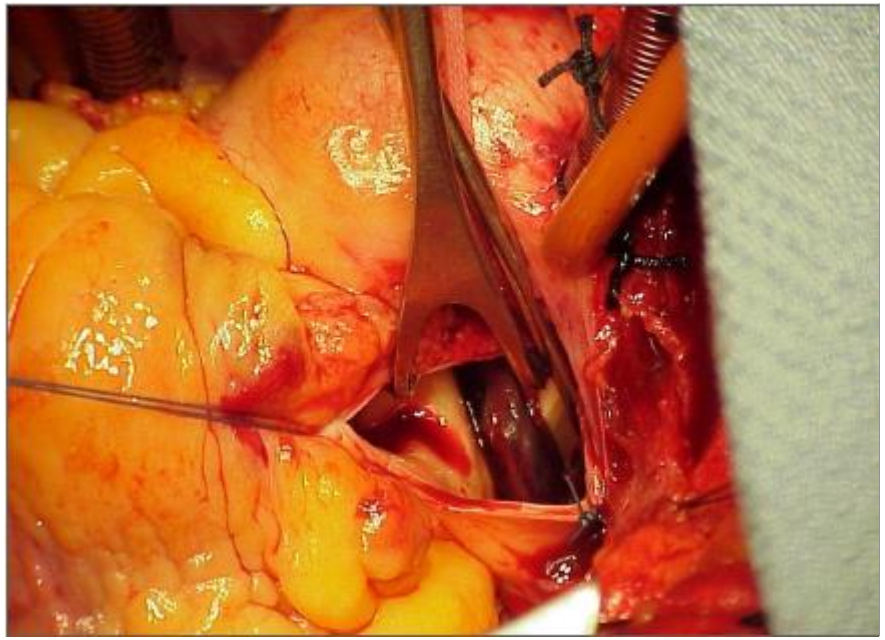
Recommendations for acute-phase treatment of high-risk PE (2)

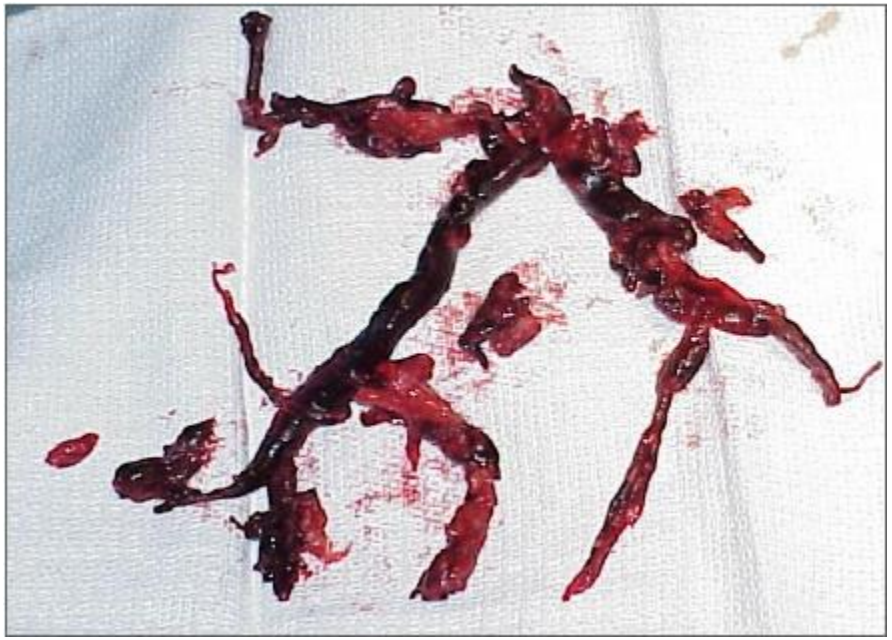
ESC European Society of Cardiology

Recommendations	Class	Level
Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	IIa	C
Norepinephrine and/or dobutamine should be considered in patients with high-risk PE.	IIa	C
ECMO may be considered, in combination with surgical embolectomy or catheter-directed treatment, in patients with PE and refractory circulatory collapse or cardiac arrest.	IIb	C

ECMO = extracorporeal membrane oxygenation.

Alternative: Surgical Embolectomy



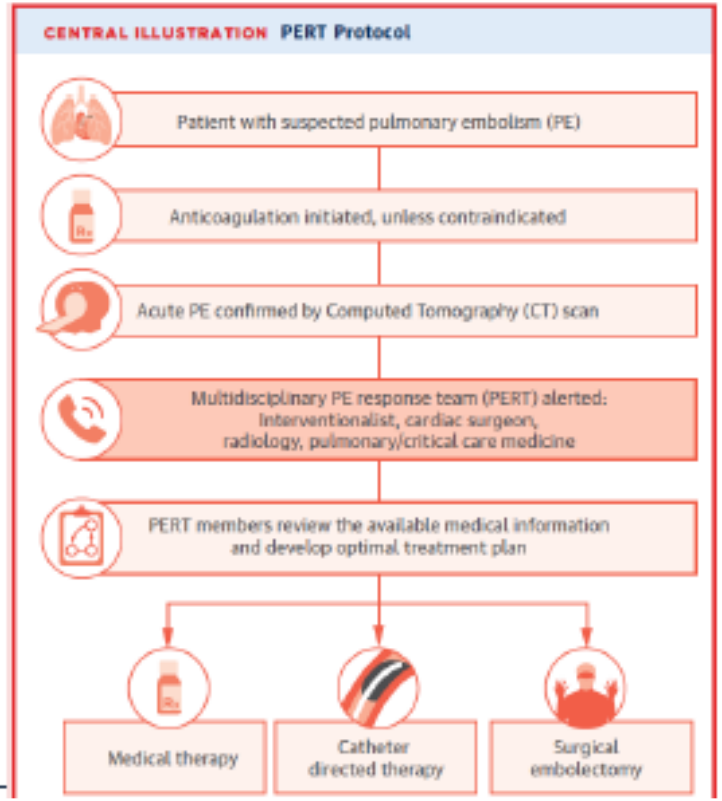


L Aklog. In: Management of Pulmonary Embolism. Humana Press 2007

Acute Pulmonary Embolism

With an Emphasis on an Interventional Approach

Wissam A. Jaber, MD,[a] Pete P. Fong, MD,[b] Giora Weisz, MD,[c] Omar Lattouf, MD,[d] James Jenkins, MD,[e] Kenneth Rosenfield, MD, MHCDS,[f] Tanveer Rab, MD,[a] Stephen Ramee, MD[g]



Evidence shows it works

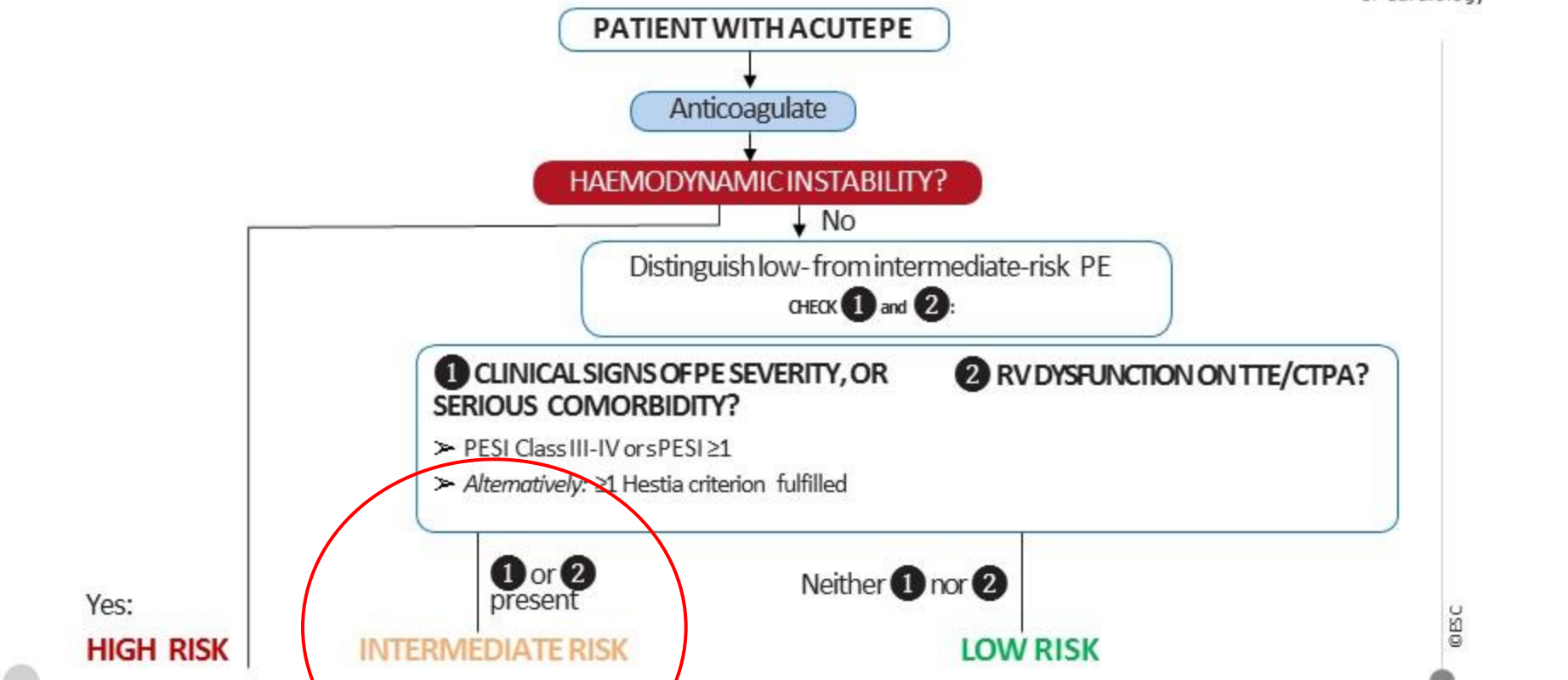
OR 0.88

Jaber, et al. JACC 2016.

In my view the STEMI team should be trained and involved in the management of PE unstable patients

Figure 5 Risk-adjusted management strategy for acute PE (1)

ESC European Society of Cardiology



www.escardio.org/guidelines

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 9 Classification of PE based on early mortality risk

ESC European Society of Cardiology

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
High		+	(+)	+	(+)
Interme-diate	**Intermediate–high**	(death 15%)	+	+	+
	Intermediate–low	(death 3%)	+	One (or none) positive	
Low		-	-	-	Assessment optional; if assessed, negative

©ESC

CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; TTE = transthoracic echocardiography.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

In an attempt to make my thinking about lytics in PE sound less like a brain fart, I decided to read some stuff.

Lyse, damn lyse & thrombolytics

If I have a **MASSIVE PE**

MASSIVE PE if: acute PE with sustained hypotension (SBP < 90 mmHg for at least 15 mins)

TO PREVENT RECURRENT PE OR DEATH:

NNT (tPA) = 10

If I have a **SUBMASSIVE PE**

as per MOFETT

SUBMASSIVE PE if: acute PE without systemic hypotension but with either RV dysfunction or myocardial necrosis

ALL CAUSE MORTALITY:

NNT (tPA) = 65

MAJOR BLEEDING:

NNH (tPA) = 18

If I am **OVER 65**

MAJOR BLEEDING:

NNH (tPA): if >65 = **11**

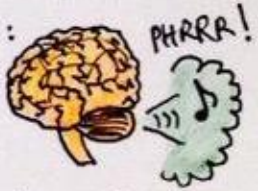
if ≤65 = **175**

and don't get me started on:

Catheter-directed therapy

Surgical embolectomy

ECMO

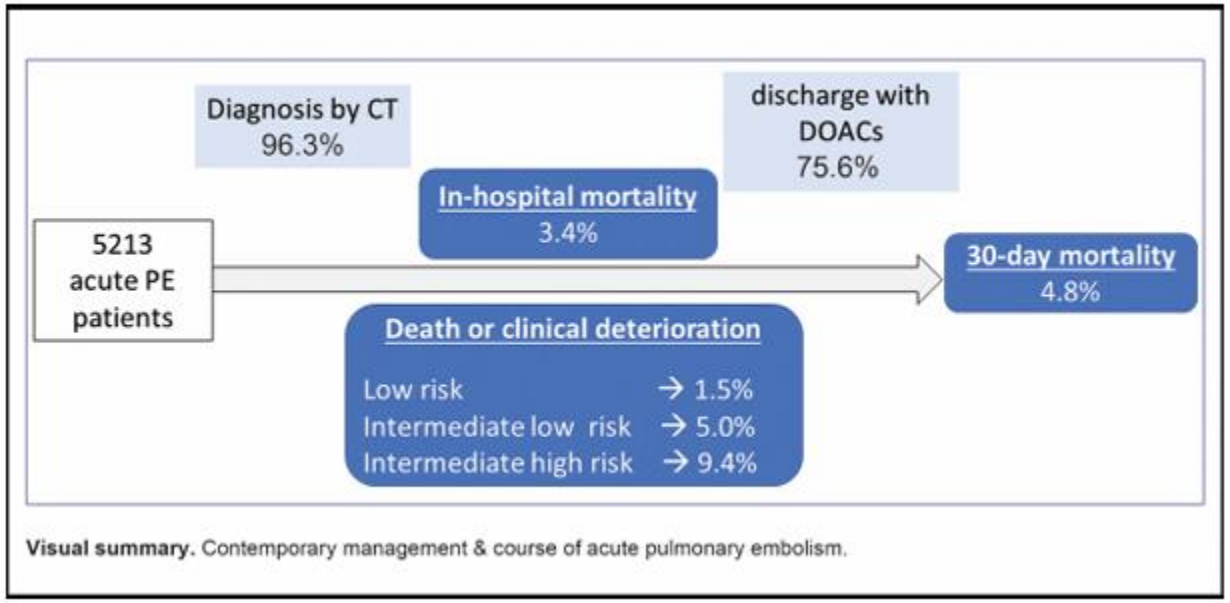


because I will do another brain fart.

REF: THE BOTTOM LINE (www.wessexics.com/The_Bottom_Line and search "Chatterjee")

Quale terapia anticoagulante?

The COPE Study



Visual summary. Contemporary management & course of acute pulmonary embolism.

	In-hospital death				30-day death			
	N (%)	HR	95% CI	*p*	*N* (%)	HR	95% CI	*p*
ESC 2019								
Low risk (sPESI = 0), *n* = 912	*2 (0.2)*	1	–	–	3 (0.3)	1	–	–
Intermediate risk (sPESI ≥ 1), *n* = 4,103	*139 (3.4)*	10.79	2.7–43.6	0.0008	205 (5.0)	15.51	5.0–48.5	< 0.0001
High risk (shock or cardiac arrest), *n* = 177	*36 (20.3)*	54.29	13.0–226.1	< 0.0001	40 (22.6)	83.06	25.7–268.5	< 0.0001
Unknown risk, *n* = 21	*0*	0.0	0.0–.	0.98	0	0.0	0.0–$8.9^{*}10^{261}$	0.98
ESC 2019 with stratification of intermediate-risk patients								
Low risk (sPESI = 0), *n* = 912	2 (0.2)	1	–	–	3 (0.3)	1	–	–
Intermediate low risk, *n* = 2,342	69 (2.9)	9.6	2.4–39.4	0.002	115 (4.9)	15.2	4.8–47.9	< 0.0001
sPESI > 0, no RVD, normal troponin, n = 740	*14 (1.9)*	*6.07*	*1.4–26.7*	*0.0172*	*31 (4.2)*	*12.95*	*4.0–42.4*	*< 0.0001*
sPESI > 0, RVD or increased troponin, n = 1,602	*55 (3.4)*	*11.33*	*2.8–46.5*	*0.0008*	*84 (5.2)*	*16.26*	*5.1–51.4*	*< 0.0001*
Intermediate high risk, *n* = 1,547	*56 (3.6)*	11.23	2.74–46.06	0.0008	*69 (4.5)*	13.84	4.36–43.97	< 0.0001
Intermediate unknown risk, *n* = 214	*14 (6.5)*	19.26	4.37–84.87	< 0.0001	*21 (9.8)*	31.26	9.32–104.79	< 0.0001
High risk (shock or cardiac arrest), *n* = 177	36 (20.3)	54.30	13.04–226.13	< 0.0001	40 (22.6)	83.07	25.70–268.53	< 0.0001
Unknown risk, *n* = 21	0	0.0	0.0–	0.98	0	0.0	0.0–$4.56^{*}10^{262}$	0.98

Becattini C et al.
Thromb Haemost 2023

The COPE Study

Death in-hospital and at 30 days by anticoagulant treatment strategies and by risk of death.

	In-hospital death			Death at 30 days		
	anticoagulant treatment during hospital-stay		P	anticoagulant treatment during hospital-stay		P
	Not completely oral (n = 4232)	Completely Oral[$] (n = 926)		Not Completely Oral (n = 4232)	Completely Oral[$] (n = 926)	
ESC 2014						
Low risk (sPESI = zero), n = 1687	7/1282 (0.6%)	0/405 (0.0%)	0.21	7/1282 (0.6%)	0/405 (0.0%)	0.21
Intermediate low risk, n = 1838	60/1545 (3.9%)	4/293 (1.4%)	0.03	103/1545 (6.7%)	6/293 (2.1%)	0.002
Intermediate high risk, n = 1206	46/1024 (4.5%)	5/182 (2.8%)	0.28	58/1024 (5.7%)	6/182 (3.3%)	0.19
Intermediate unknown risk, n = 209	12/186 (4.4%)	1/23 (4.3%)	1	18/186 (9.7%)	1/23 (4.4%)	0.70
High risk (shock or cardiac arrest), n = 166	25/155 (16.1%)	1/11 (9.1%)	1	29/155 (18.7%)	1/11 (9.1%)	0.69
Unknown risk, n = 52	0/40 (0.0%)	0/12 (0.0%)	–	0/40 (0.0%)	0/12 (0.0%)	–
ESC 2019						
Low risk (sPESI = zero), n = 901	1/663 (0.2%)	0/238 (0.0%)	1	1/663 (0.2%)	0/238 (0.0%)	1
Intermediate low risk, n = 2320	63/1924 (3.3%)	4/396 (1.0%)	0.01	106/1924 (5.5%)	6/396 (1.5%)	0.0003
Intermediate high risk, n = 1541	49/1289 (3.8%)	5/252 (2.0%)	0.15	61/1289 (4.7%)	6/252 (2.4%)	0.09
Intermediate unknown risk, n = 209	12/186 (6.5%)	1/23 (4.3%)	1	18/186 (9.7%)	1/23 (4.4%)	0.70
High risk (shock or cardiac arrest), n = 166	25/155 (16.1%)	1/11 (9.1%)	1	29/155 (18.7%)	1/11 (9.1%)	0.69
Unknown risk, n = 21	0/15 (0.0%)	0/6 (0.0%)	–	0/15 (0.0%)	0/6 (0.0%)	–

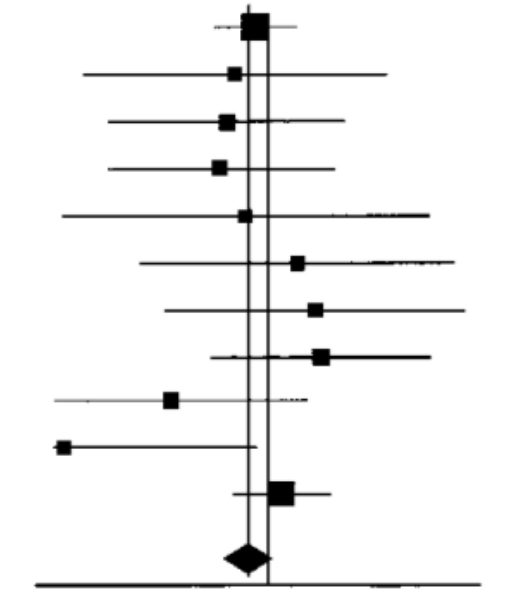
[$] Only oral or after parenteral therapy for <48 h.

Becattini C et al. Vasc Pharmacol 2023

IV Thrombolytic Therapy for Submassive PE

Meta-Analysis

Study	Thrombolysis	Heparin	OR	95% CI
UPET, 1973	10/82	14/78	0.63	0.26 - 1.53
Tibbutt et al, 1974	0/13	1/17	0.41	0.02 - 10.83
Ly et al, 1978	1/14	2/11	0.35	0.03 - 4.42
Dotter et al, 1979	1/15	3/16	0.31	0.03 - 3.36
Marini et al, 1988	0/20	0/10	0.51	0.01 - 27.68
PIOPED, 1990	1/9	0/4	1.59	0.05 - 47.52
Levine et al, 1990	1/33	0/25	2.35	0.09 - 60.24
Dalla-Volta et al, 1992	3/20	1/16	2.65	0.25 - 28.24
Goldhaber et al, 1993	0/46	4/55	0.12	0.01 - 2.35
Jerjes-Sanchez et al, 1995	0/4	4/4	0.01	0.00 - 0.77
Konstantinides et al, 2002	8/118	7/138	1.36	0.48 - 3.87
Total	**25/374**	**36/374**	**0.67**	**0.40 - 1.12**



Recurrent PE or death
Lysis 6.7% vs UFH 9.6%
p=NS

Outcome	Thrombolysis, n/N (%)	Heparin, n/N (%)	OR (95% CI)
Major bleeding	34/374 (9.1)	23/374 (6.1)	1.42 (0.81–2.46)*
Nonmajor bleeding	53/233 (22.7)	22/221 (10.0)	2.63 (1.53–4.54)†
Intracranial hemorrhage	2/374 (0.5)	1/374 (0.3)	1.04 (0.36–3.04)‡

Wan Circulation 2004

Reperfusion Therapy in submassive/intermediate risk PE

- Sharma GV et al (2000). Long-term benefit of thrombolytic therapy in patients with pulmonary embolism. Vasc Med. 5(2):91-5.
- Kline JA et al (2009). Prospective evaluation of right ventricular function and functional status 6 months after acute submassive pulmonary embolism: frequency of persistent or subsequent elevation in estimated pulmonary artery pressure. Chest, 136, pp. 1202–1210
- Fasullo S et al (2011). Six-month echocardiographic study in patients with submassive pulmonary embolism and right ventricle dysfunction: comparison of thrombolysis with heparin. Am J Med Sci. 2011 Jan;341(1):33-9.
- Sharifi M, Bay C, Skrocki L, Rahimi F, Mehdipour M; “MOPETT” Investigators. Moderate Pulmonary Embolism Treated With Thrombolysis (from the "MOPETT" Trial) (2013). Am J Cardiol. Volume 111, Issue 2, 15 January 2013, Pages 273–277

PEITHO study (2014)

1006 normotensive patients
RV dysfunction + TnI o TnT positive

Tenecteplase (30-50 mg) + anticoagulation
VS
placebo + anticoagulation.

Thrombolysis

	Tenecteplase (n = 506)	Placebo (n = 499)	P value
All-cause mortality or haemodynamic collapse within 7 days of randomisation	13 (2.6 %)	28 (5.6 %)	0.015
All-cause mortality within 7 days	6 (1.2 %)	25 (5.0 %)	0.43
Haemodynamic collapse within 7 days	8 (1.6 %)	25 (5.0 %)	0.002
Stroke within 7 days	12 (2.4 %)	1 (0.2 %)	0.003
Major non intracranial bleeding within 7 days	32 (6.3 %)	6 (1.5 %)	<0.001
Minor non intracranial bleeding within 7 days	165 (32.6 %)	43 (8.6 %)	<0.001

Long term data in 2017: no significant difference for mortality, functional outcomes, or echocardiographic metrics to suggest long-term improvement for patients with intermediate-risk PE receiving thrombolytics

<4% of all hospitalised PE patients
<12% of hospitalisations related to intermediate-high-risk or high-risk PE

PEITHO 3 study (ongoing)

EFFICACY: composite all cause of death, hemodynamic decompensation or PE recurrence 30 days

Alteplase 0.6 mg/kg (max 50 mg) in 15 min infusion + anticoagulation
VS
placebo + anticoagulation.

Catheter-directed therapy

Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.[d]	IIa	C
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.	IIa	C

Device	Mechanism of thrombus removal	Technical data#	Source of clinical evidence in pulmonary embolism	Vascular access	CE certificate for PE therapy
Pigtail catheters	Fragmentation and thrombolytic infusion	Diameter 6-8 Fr	Case series	F/J	Not applicable
Indigo system (Penumbra)	Aspiration with mechanical fragmentation	Diameter 8 Fr, 12 Fr Length 115 cm	EXTRACT-PE – single-arm trial[26].	F/J	YES
AngioVac (Angiodynamics)	Large lumen aspiration tube with the system of veno-venous bypass	Diameter 22 Fr	Case series (difficult for PE)	F	NO*
BASHIR endovascular catheter (Thrombolex)	Mechanical fragmentation, aspiration and thrombolytic infusion	Diameter 7 Fr Length 92.5 cm Treatment zone 12.5 cm	Case series	F	NO
FlowTriever System (Inari)	Aspiration with or without mechanical fragmentation	Diameter 16, 20 and 24 Fr Nitinol mesh diameter S 6-10 mm, M 11-14 mm, L 15-18 mm and XL 19-25 mm	FLARE – single-arm trial[25]. FLASH[53]	F	YES
ASPIREX (Straub medical)	Fragmentation and aspiration	Diameter 6 Fr, 8 Fr and 10 Fr Length 85, 110 and 135 cm	Case series	F	YES
AngioJet (Boston Scientific)	Rheolytic thrombectomy with aspiration and possibility for thrombolytic injections	Diameter 6-8 Fr Length 120 cm	Case series	F/J	YES

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

DOI: 10.4244/EIJ-D-22-00246

Catheter-directed therapy: game changer?

TRIAL	Author	Year	Device	Patient characteristics	Number of subjects	Outcome (efficacy)
ULTIMA[36]	Kucher N	2013	EkoSonic	IHR (n=59, 100%)	59	RV/LV ratio reduced from 1.28±0.19 to 0.99±0.17 at 24 h (p<0.001)
SEATTLE II[37]	Piazza G	2015	EkoSonic	mPE (n=31, 21%); sPE (n=119, 79%)	150	RV/LV ratio reduced from 1.55 to 1.13 at 48 h (p<0.0001), PASP 51.4 reduced to 36.9 mmHg (p<0.0001) at 48 h
OPTALYSE PE[38]	Tapson VF	2018	EkoSonic	IHR (n=101, 100%)	101	RV/LV ratio reduced in all arms
FLARE[25]	Tu T	2019	FlowTriever	IHR (n=106, 100%)	106	RV/LV ratio 1.53 reduced to 1.15 at 48 h
EXTRACT-PE[26]	Sista KA	2021	Indigo Penumbra	sPE (n=119, 100%)	119	Mean RV/LV ratio reduction from baseline to 48 h post-procedure 0.43 (p<0.0001)
SUNSET sPE[51]	Avgerinos DE	2021	USAT (EkoSonic) vs SCDT (Cragg-McNamara or UniFuse)	sPE (n=81, 100%)	81	No significant difference in mean thrombus score reduction between the 2 groups (p=0.76); mean reduction in RV/LV ratio from baseline (1.54±0.30 for USAT, 1.69±0.44 for SCDT) to 48 hours was 0.37±0.34 in the USAT group and 0.59±0.42 in the SCDT group (p=0.01).

PEITHO: 7-d rates of MB= 8.3% (GUSTO criteria); 11.5% (ISTH criteria)

ULTIMA, SEATTLE II and OPTALYSE : 7-d rates of MB 0-10%
Meta-analysis: 6.7% high risk PE and 1-4% intermediate risk PE.
Only 1 intracranial bleeding in OPTALYSE

DOI: 10.4244/EIJ-D-22-00246

10.1161/CIRCULATIONAHA.124.072364

Large-bore Mechanical Thrombectomy Versus Catheter-directed Thrombolysis in the Management of Intermediate-risk Pulmonary Embolism: Primary Results of the PEERLESS Randomized Controlled Trial

Running title: *Jaber et al.; The PEERLESS Randomized Controlled Trial*

A

	CDT wins, n	LBMT wins, n	Win Ratio Endpoints	Win ratio [95% CI]	*P* value
Primary Endpoint: 5-component win ratio	10,509	52,693		5.01 [3.68 – 6.97]	<0.001
Secondary Endpoint: 4-component win ratio	5912	7925		1.34 [0.78 – 2.35]	0.30

B

		CDT events, n (%)	LBMT events, n (%)	Odds Ratios for Clinical Outcomes	Odds ratio [95% CI]	*P* value
1	**All-cause mortality**	1 (0.4)	0 (0.0)		2.99 [0.12 – 73.70]	1.00
2	**Intracranial hemorrhage**	1 (0.4)*	2 (0.7)		0.50 [0.04 – 5.51]	0.62
3	**Major bleeding**	19 (6.9)	19 (6.9)		0.99 [0.51 – 1.92]	1.00
4	**Clinical deterioration and/or escalation to bailout therapy**	15 (5.4)	5 (1.8)		3.09 [1.11 – 8.63]	0.04
5a	**Postprocedural ICU admission**	272 (98.6)	114 (41.6)		95.4 [34.6 – 263.6]	<0.001
5b	**If ICU admitted, stay >24 hours**	178 (65.4)	53 (46.5)		2.18 [1.40 – 3.40]	<0.001

10.1161/CIRCULATIONAHA.124.072364

Large-bore Mechanical Thrombectomy Versus Catheter-directed Thrombolysis in the Management of Intermediate-risk Pulmonary Embolism: Primary Results of the PEERLESS Randomized Controlled Trial

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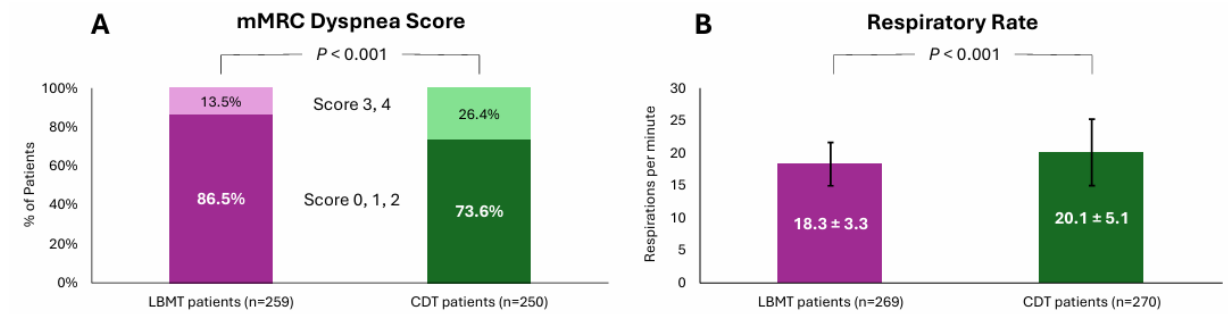
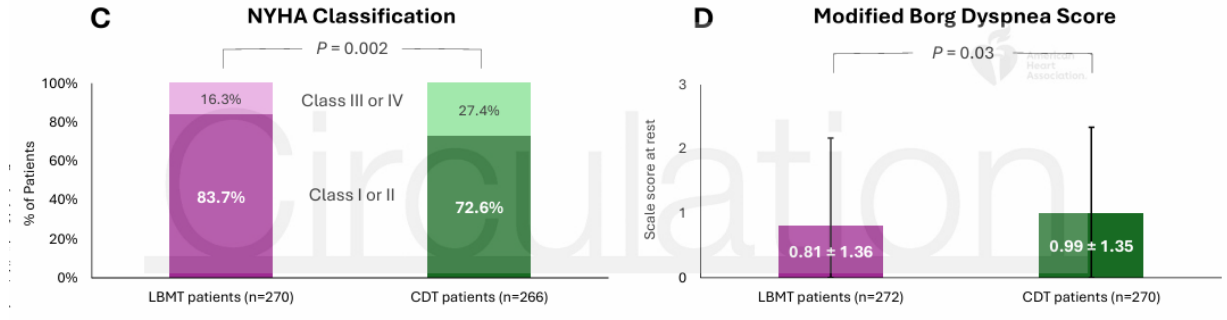
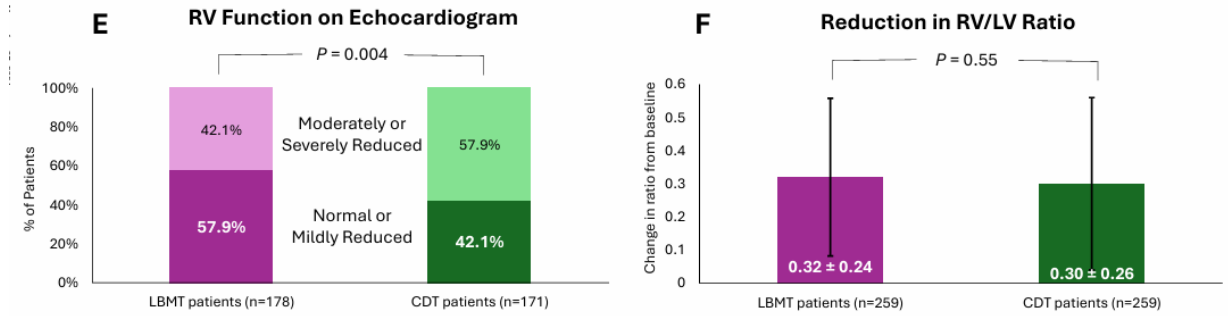
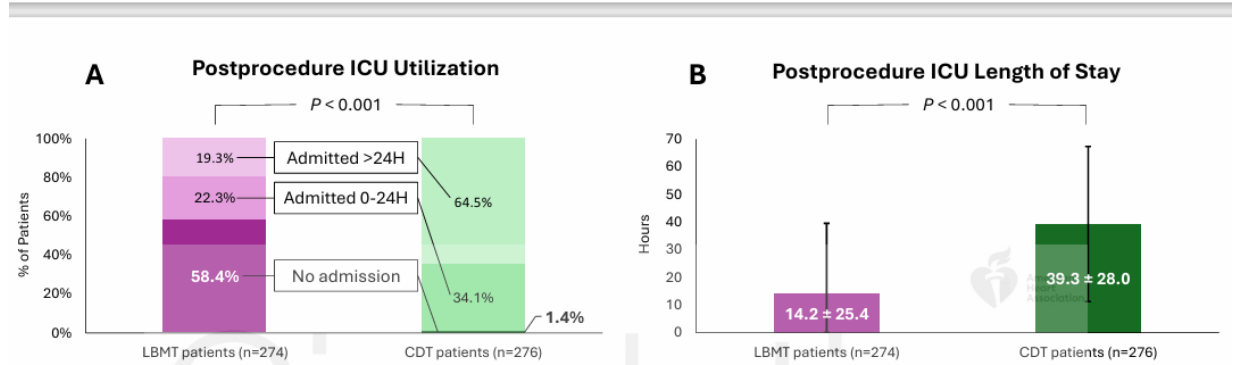








Catheter-directed therapy

ClinicalTrials.gov identifier	Title	Study design	Study device	PE patient category	Intervention	Control	Primary outcome
NCT04790370	Ultrasound-facilitated, Catheter-directed, Thrombolysis in Intermediate-high Risk Pulmonary Embolism (HI-PEITHO)	RCT, 406 patients	EkoSonic TM endovascular system	Intermediate-high risk PE with additional criteria of severity	Ultrasound accelerated catheter-directed thrombolysis	Parenteral anticoagulation	7-day PE mortality, VTE recurrence or cardiorespiratory decompensation

DOI: 10.4244/EIJ-D-22-00246

PE risk stratification: scores

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

Risk strata	
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%)	**≥1point(s)** = 30-day mortality risk 10.9% (95% CI 8.5–13.2%)

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, 2012[24]. BP: blood pressure; SpO_2: oxygen saturation

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 ≥ 110/min	1

Points are assigned for the presence of each variable. The sum of the variable points produces the total point score (Bova risk score; range, 0-7). Bova risk staging increased with point totals: stage I (0-2 points), stage II (3-4 points), or stage III (>4 points). PE = pulmonary embolism; RV = right ventricular.

Pulmonary embolism risk stratification models

ESC-2014 model[a] [10]	**Low risk**	**Intermediate low**		**Intermediate high**
sPESI	0	>0		>0
Echocardiography and troponin	–	Both normal/1 abnormal		Both abnormal
ESC-2019 model[a] [11]	Low risk	Intermediate low		**Intermediate high**
sPESI	0	≥0		≥0
Echocardiography and troponin	Both normal	Both normal or 1 abnormal		Both abnormal
PEITHO model [14]	**Group I**	**Group II**	**Group IIIa**	**Group IIIb**
Echocardiography and troponin	Both normal	1 abnormal	Both abnormal	Both abnormal
Systolic BP ≤ 110 mm Hg, RR > 20 breaths/min−1, cancer or chronic heart failure	–	–	None present	≥1 present
BOVA score [15]	**0 points**	**1 point**	**2 points**	
Systolic BP	>100 mm Hg	–	90-100 mm Hg	
Elevated cardiac troponin	No	–	Yes	
RV dysfunction	No	–	Yes	
Heart rate, beats/min	<110	≥110	–	
Patients are divided into 3 groups: class I if 0 to 2 points, class II if 3 to 4 points, and class III if >4 points.				

Pulmonary embolism risk stratification models

TELOS score [17]	**0 points**	**1 point**	**2 points**	**3 points**
Systolic BP	>100 mm Hg	–	90-100 mm Hg	–
Elevated cardiac troponin	No	–	Yes	–
RV dysfunction	No	–	Yes	–
Heart rate, beats/min	<110	≥110	–	–
Elevated plasma lactate	No	–	–	Yes

Patients are divided into 3 groups: class I if 0 to 2 points, class II if 3 to 5 points, and class III if >5 points.

FAST score [20]	**Points**
Heart rate ≥ 100 bpm	1.5
Syncope at presentation	1.5
Elevated troponin	2

Patients are divided into 2 groups: low risk for adverse in-hospital outcome <3 points and intermediate-high risk for adverse in-hospital outcome ≥3 points.

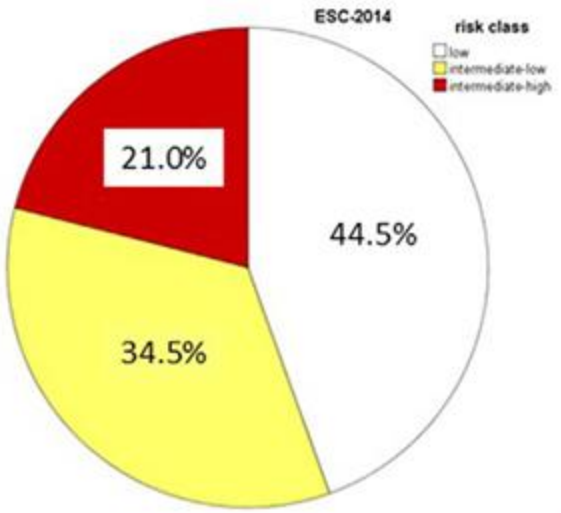
NEWS2 score [18,19]	**3**	**2**	**1**	**0**
Respiratory rate, apm	≤8 or ≥25	21-24	9-11	12-20
Oxygen saturation, %	≤91	92-93	94-95	≥96
Supplemental oxygen		Yes		No
Systolic BP, mm Hg	≤90 or ≥130	91-100	101-110	111-219
Heart rate, bpm	≤40 or ≥131	91-100	41-50	51-90
Level of consciousness	V, P, or U			Awake

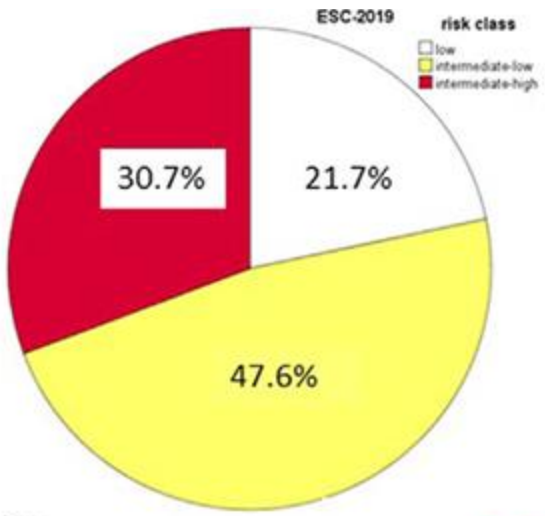
Patients are divided into 3 groups:
i. NEWS2 score < 5 points;
ii. NEWS2 score ≥ 5 and >7 points;
iii. NEWS2 score ≥ 7 points

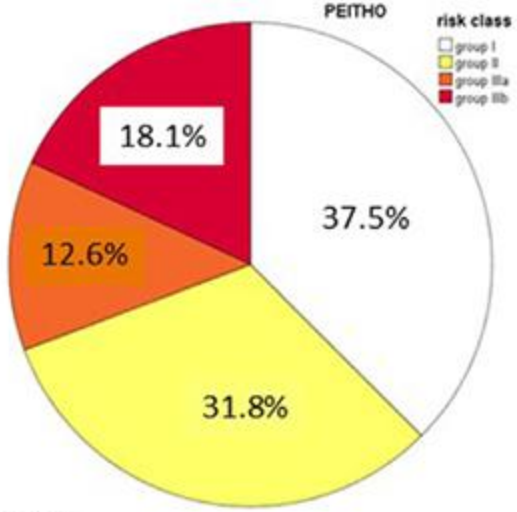
Ma sono davvero utili tutti questi score?

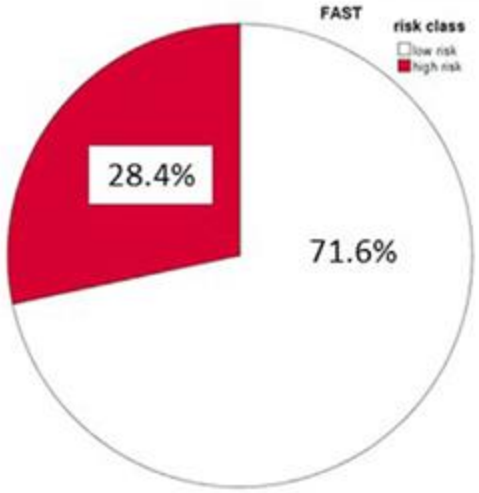
The COPE Study – high risk of death: external validation of different models

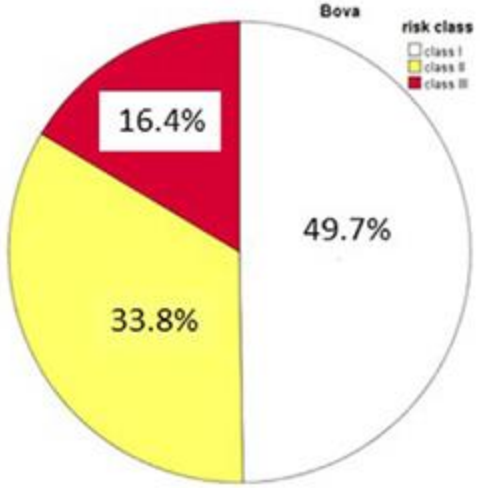
PESI score 102



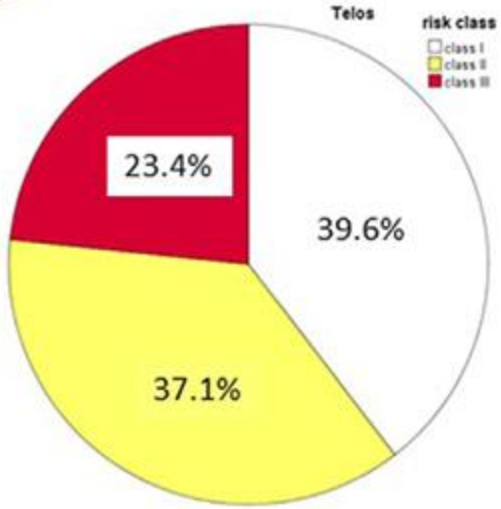


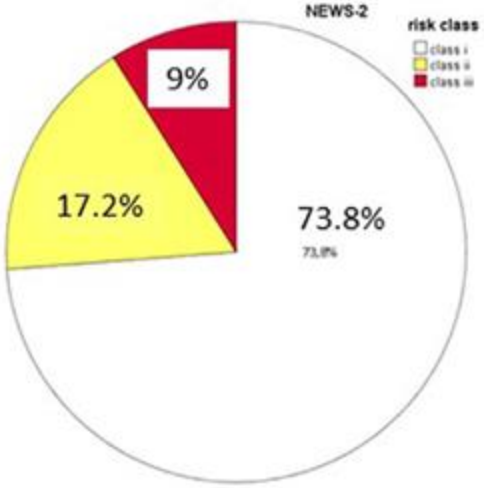






BOVA score 4





NEWS2 score 3

Becattini C et al. J Thromb haemost 2024

The COPE Study – high risk of death: external validation of different models

Multivariable analysis by score or model for study outcome events (N 5036 pts)- Summary

Model	Model components	Predictor of In-hospital death or clinical deterioration
ESC	sPESI ≥ 1	YES
	RVD OR > troponin	YES
	RVD AND > troponin	YES
PEITHO	ALL	YES
FAST	Syncope	NO
Bova	ALL	YES
TELOS	HR ≥ 110 bpm	NO
NEWS2	SBP 101-100 mmHG	NO
	HR 41-50; 91-110;111-130 bpm	NO
	HR ≤ 40 or ≥ 131	NO
	Oxygen sat 94-95%;92-93%;≤91%	NO
	RR 9-11 apm	NO

Modified from Becattini C et al. J Thromb haemost 2024

TABLE 4 Positive and negative predictive values of different scores/models in the primary analysis population ($N = 5036$).

Score/model	Percentage negative predictive value (95% CI)			
	In-hospital death or clinical deterioration	In-hospital death	30-d death	Death due to PE
ESC-2014 (sPESI)	98.7 (98.2-99.2)	99.3 (99.0-99.7)	99.1 (98.7-99.5)	99.6 (99.3-99.9)
ESC-2019 (sPESI)	99.7 (99.3-100)	99.8 (99.5-100)	99.8 (99.5-100)	99.9 (99.7-100)
PEITHO	98.9 (98.3-99.4)	99.1 (98.6-99.6)	98.1 (97.4-98.8)	99.9 (99.7-100)
FAST score	96.9 (96.3-97.4)	97.6 (97.2-98.1)	96.4 (95.4-97.4)	99.2 (98.9-99.5)
Bova	98.5 (98.0-99.0)	98.9 (98.5-99.3)	97.7 (97.1-98.2)	99.7 (99.5-99.9)
TELOS	98.8 (98.3-99.2)	99.2 (98.9-99.6)	98.2 (97.6-98.7)	99.8 (99.6-100)
NEWS2 score	97.7 (97.3-98.2)	98.5 (98.1-98.9)	97.3 (96.8-97.8)	94.9 (92.9-96.9)
Score/model	**Percentage positive predictive value (95% CI)**			
	In-hospital death or clinical deterioration	**In-hospital death**	**30-d death**	**Death due to PE**
ESC-2014 (sPESI)	8.4 (7.0-9.9)	5.9 (4.7-7.2)	7.4 (6.1-8.8)	2.8 (1.9-3.7)
ESC-2019 (sPESI)	6.6 (5.6-7.7)	4.5 (3.6-5.4)	5.6 (4.6-6.7)	2.2 (1.6-2.8)
PEITHO	8.5 (7.1-10.0)	5.9 (4.7-7.2)	7.5 (6.1-8.8)	2.9 (2.0-3.8)
FAST score	6.8 (5.5-8.2)	4.1 (3.0-5.1)	5.6 (4.4-6.9)	2.3 (1.5-3.1)
Bova	9.3 (7.2-11.4)	5.5 (3.9-7.2)	6.9 (5.1-8.8)	3.3 (2.0-4.6)
TELOS	10.4 (8.5-12.3)	7.0 (5.4-8.5)	8.7 (7.0-10.5)	3.7 (2.5-4.8)
NEWS2 score	13.8 (10.7-16.9)	8.7 (6.1-11.2)	10.4 (7.6-13.1)	5.0 (3.1-7.1)

ESC, European Society of Cardiology; NEWS2, National Early Warning Scale 2; PE, pulmonary embolism; sPESI, simplified PE severity index; FAST, fatty acid binding protein, syncope and tachicardia; PEITHO, Pulmonary Embolism Thrombolysis; TELOS, Thrombo-embolism lactate outcome study).

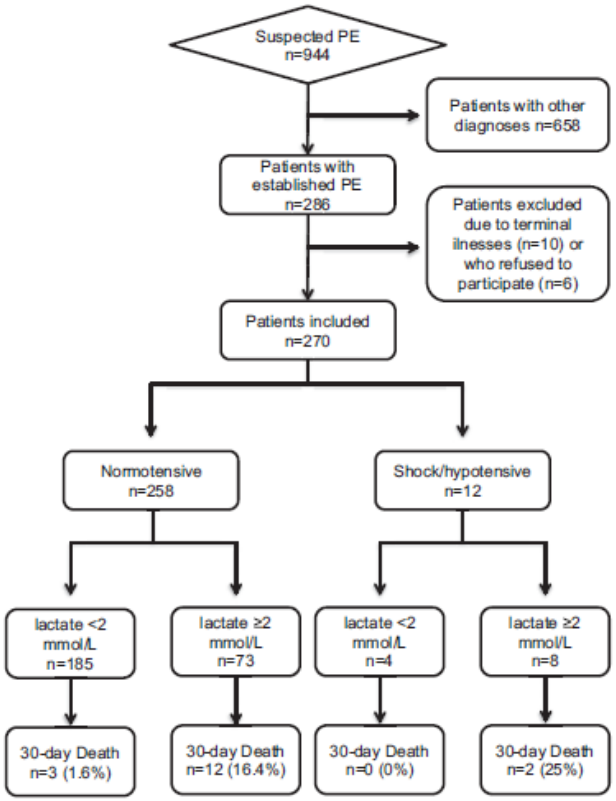
TABLE 5 Performance of different scores/models for study outcome events in the primary population and in the complete-case population.

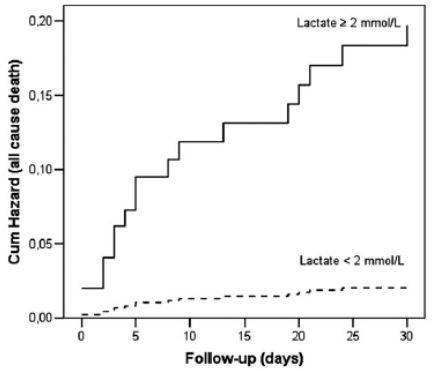
Prognostic model	C-statistic (95% CI)			
	In-hospital death or clinical deterioration	In-hospital death	30-d death	Death due to PE
Primary population (*N* = 5036)				
ESC-2014 (sPESI)	0.700 (0.666-0.734)	0.713 (0.675-0.751)	0.696 (0.665-0.726)	0.721 (0.659-0.784)
ESC-2019 (sPESI)	0.657 (0.624-0.690)	0.652 (0.613-0.692)	0.615 (0.582-0.649)	0.701 (0.645-0.756)
PEITHO	0.692 (0.658-0.726)	0.689 (0.647-0.731)	0.652 (0.616-0.689)	0.749 (0.696-0.803)
FAST score	0.594 (0.553-0.636)	0.563 (0.513-0.613)	0.551 (0.510-0.592)	0.623 (0.549-0.698)
Bova score	0.696 (0.662-0.731)	0.681 (0.639-0.723)	0.626 (0.588-0.664)	0.743 (0.687-0.799)
TELOS score	0.722 (0.688-0.756)	0.723 (0.678-0.762)	0.668 (0.626-0.705)	0.780 (0.730-0.829)
NEWS2 score	0.682 (0.641-0.724)	0.682 (0.634-0.730)	0.637 (0.596-0.678)	0.727 (0.657-0.797)
Complete-case population (*n* = 3544)				
ESC-2014 (sPESI)	0.670 (0.631-0.716)	0.697 (0.644-0.750)	0.674 (0.632-0.715)	0.688 (0.609-0.768)
ESC-2019 (sPESI)	0.636 (0.598-0.674)	0.669 (0.617-0.720)	0.617 (0.571-0.662)	0.696 (0.629-0.763)
PEITHO	0.675 (0.636-0.714)	0.708 (0.654-0.762)	0.682 (0.637-0.727)	0.758 (0.694-0.821)
FAST score	0.581 (0.534-0.627)	0.559 (0.492-0.626)	0.549 (0.494-0.604)	0.633 (0.542-0.725)
Bova score	0.675 (0.637-0.714)	0.702 (0.652-0.751)	0.648 (0.601-0.696)	0.744 (0.685-0.803)
TELOS score	0.711 (0.673-0.749)	0.727 (0.678-0.777)	0.680 (0.633-0.728)	0.788 (0.731-0.845)
NEWS2 score	0.674 (0.631-0.716)	0.684 (0.623-0.744)	0.643 (0.590-0.695)	0.749 (0.672-0.826)
NEWS2 score (*n* = 5009)[a]	0.702 (0.665-0.739)	0.692 (0.646-0.737)	0.637 (0.597-0.678)	0.738 (0.669-0.807)

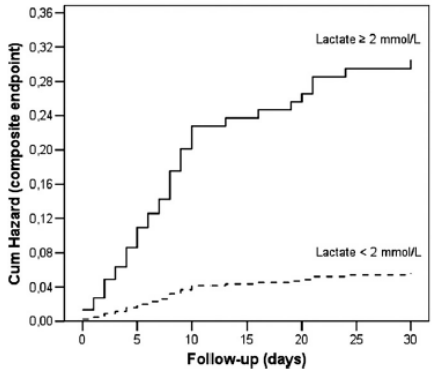
ESC, European Society of Cardiology; NEWS2, National Early Warning Scale 2; PE, pulmonary embolism; sPESI, simplified PE severity index; FAST, fatty acid binding protein, syncope and tachicardia; PEITHO, Pulmonary Embolism Thrombolysis; TELOS, Thrombo-embolism lactate outcome study).

[a] Patients with oxygen saturation available.

Intermediate- risk PE: the role of lactate



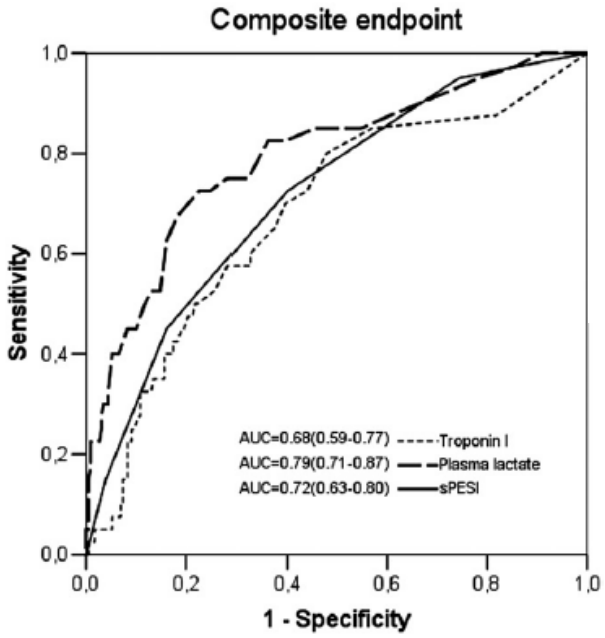


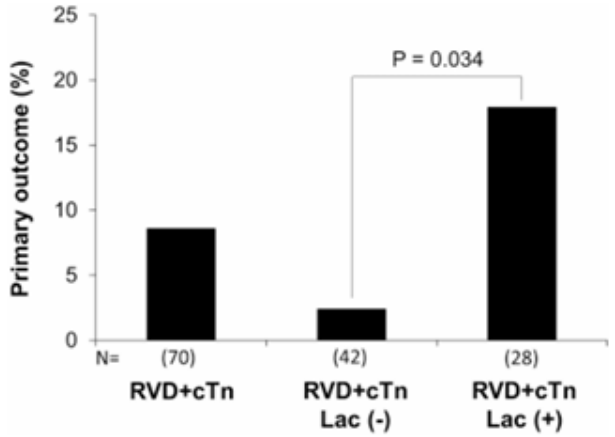


Normotensive pts: 30-d death
PPV 16.4% (95%CI:10.8-19.4)
NPV 98.4% (96.1-99.6)
multiv OR 2.5 (1.1-5.5)

7-d PE complic
Multiv OR 5.3(1.9-14.4)

Pts died: 15% (SE ±4)





RVD+cTN+Lac+ 6.6-fold risk

Vanni S et al. Ann Emerg Med 2013, Thorax 2015

	Total events ($N = 994$)	Bova score ($N = 59$)	TELOS score ($N = 57$)	ESC model ($N = 115$)	Bova + lactate ($N = 112$)
Primary outcome[a]	63 (6.3 %)	11 (18.6 %)	12 (21.1 %)	15 (13 %)	29 (25.9 %)[c]
PE-related death	31 (3.1 %)	6 (10.2 %)	6 (10.5 %)	8 (7 %)	14 (12.5 %)
Hemodynamic collapse[b]	56 (5.6 %)	9 (15.3 %)	9 (15.8 %)	13 (11.3 %)	27 (24.1 %)[c]
All-cause death	32 (3.2 %)	6 (10.2 %)	7 (12.3 %)	9 (7.8 %)	17 (15.1 %)

ESC European Society of Cardiology 2014, *PE* pulmonary embolism, *RV* right ventricle, *TELOS* Thrombo Embolism Lactate Outcome Study

[a] Defined as PE-related mortality or haemodynamic collapse within 7 days from diagnosis; patients may have more than 1 event fulfilling the definition for PE-related complications

[b] See definitions in the "Methods" section

[c] $p < 0.05$ vs ESC model

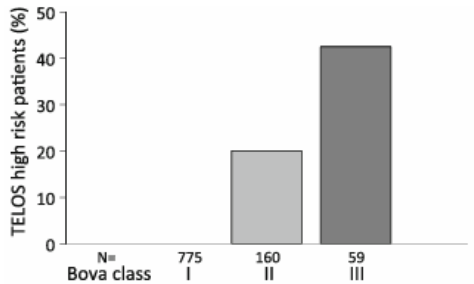


Fig. 1 Distribution of TELOS high risk patients among classes of Bova score

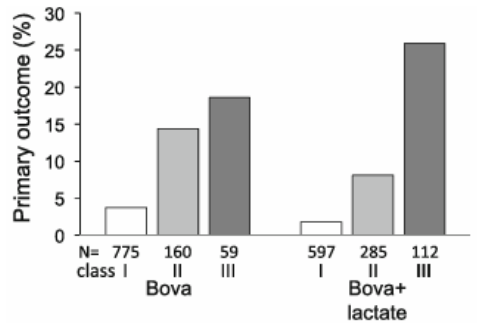
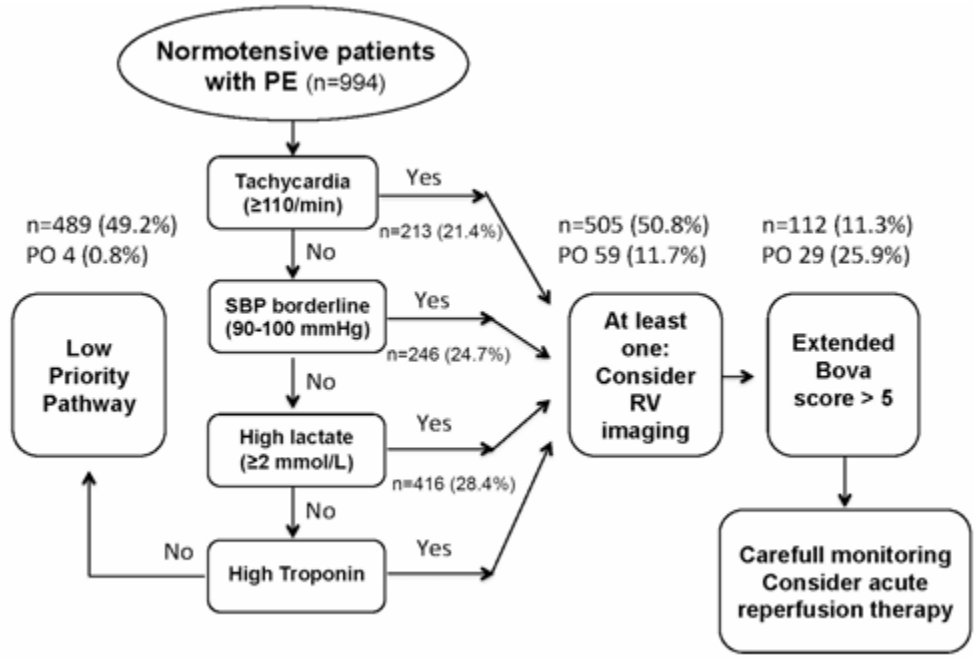
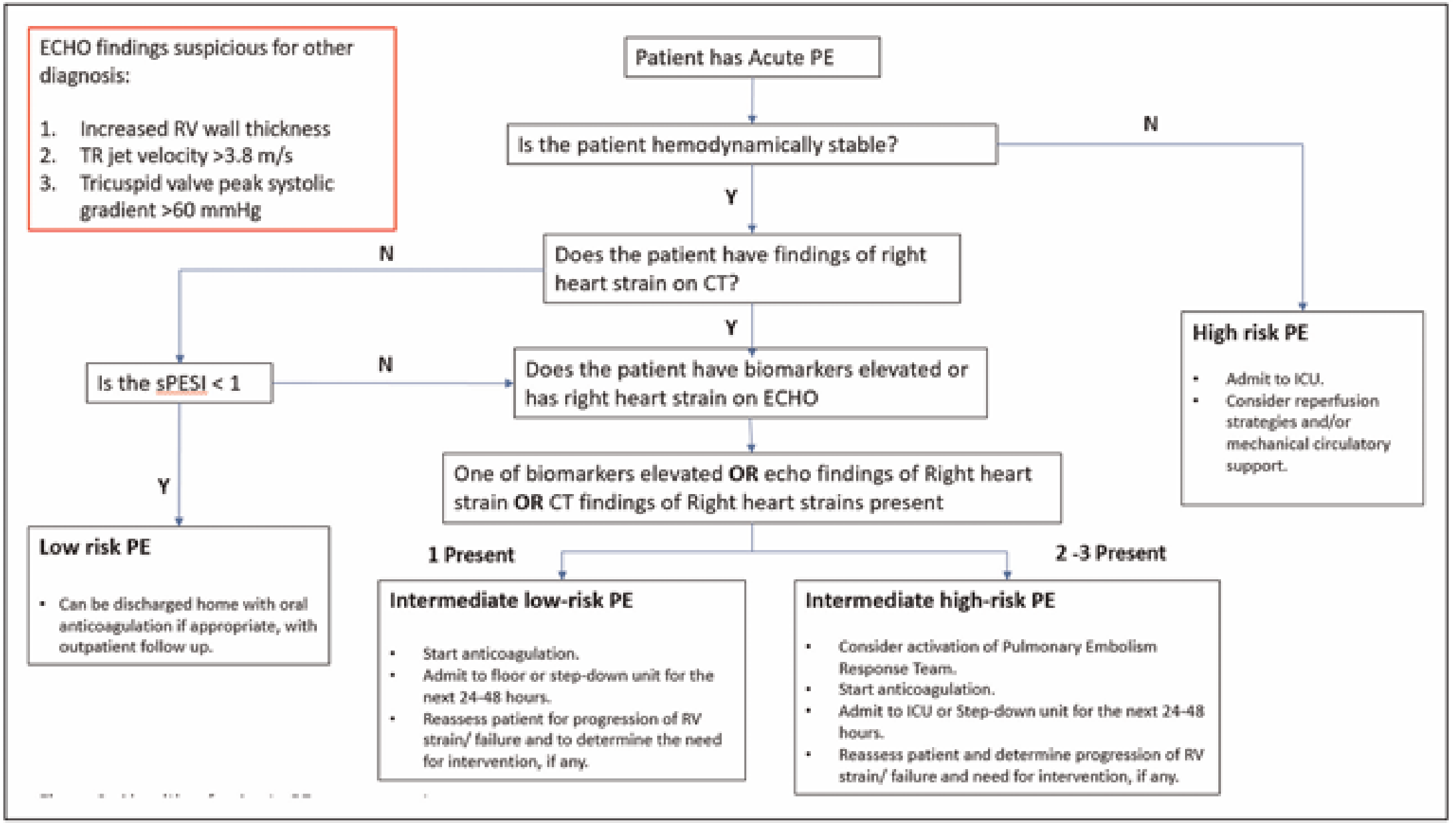


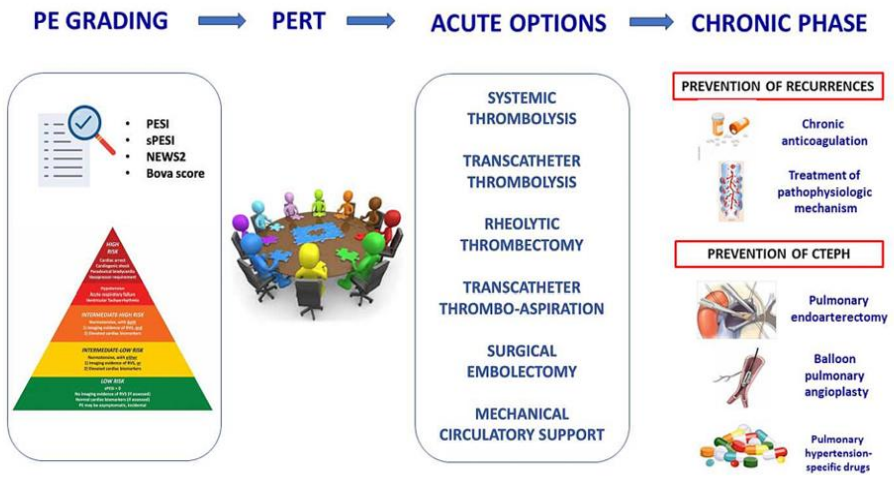
Fig. 2 Incidence of the primary outcome in class *I*, *II* and *III* of Bova and expanded Bova (Bova + lactate) scores

Fig. 3 Proposed prognostic algorithm for bed-side recognition of normotensive patients with PE at high risk of 7-day hemodynamic collapse or death (*PO* primary outcome)



Vanni S et al. Intern Emerg Med 2017


ECHO findings suspicious for other diagnosis:
1. Increased RV wall thickness
2. TR jet velocity >3.8 m/s
3. Tricuspid valve peak systolic gradient >60 mmHg
Patient has Acute PE
Is the patient hemodynamically stable?
N
Y
Does the patient have findings of right heart strain on CT?
N
Y
Is the sPESI < 1
N
Y
Does the patient have biomarkers elevated or has right heart strain on ECHO
High risk PE
• Admit to ICU.
• Consider reperfusion strategies and/or mechanical circulatory support.
Low risk PE
• Can be discharged home with oral anticoagulation if appropriate, with outpatient follow up.
One of biomarkers elevated OR echo findings of Right heart strain OR CT findings of Right heart strains present
1 Present
2 -3 Present
Intermediate low-risk PE
• Start anticoagulation.
• Admit to floor or step-down unit for the next 24-48 hours.
• Reassess patient for progression of RV strain/ failure and to determine the need for intervention, if any.
Intermediate high-risk PE
• Consider activation of Pulmonary Embolism Response Team.
• Start anticoagulation.
• Admit to ICU or Step-down unit for the next 24-48 hours.
• Reassess patient and determine progression of RV strain/ failure and need for intervention, if any.

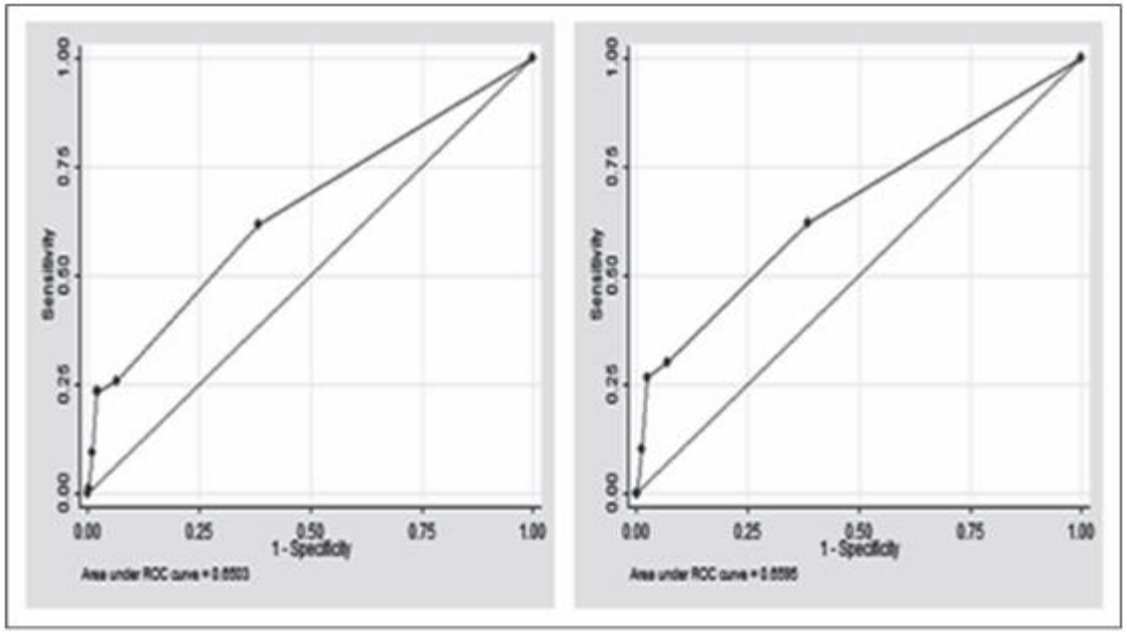


Evaluate
Hemodynamic condition
Age- comorbidities
Effects of the clot on RV function/ischemia
Intracranial bleeding
Bleeding risk
DVT status – risk of early fatal recurrence

PE-CH Score

US-NIS administrative database n 9703 thrombolysed PE pts

Prognostic variable	Odds ratio	Upper 95 % CI	Lower 95 % CI	P-value	Points assigned in PE-CH
Peripheral vascular disease	1.59	2.90	1.12	0.049	1
Prior myocardial infarction	1.80	1.99	1.33	0.046	1
Age>65 (Elderly)	1.99	1.97	2.01	0.007	1
Prior CVA	30.90	36.5	27.21	<0.001	5



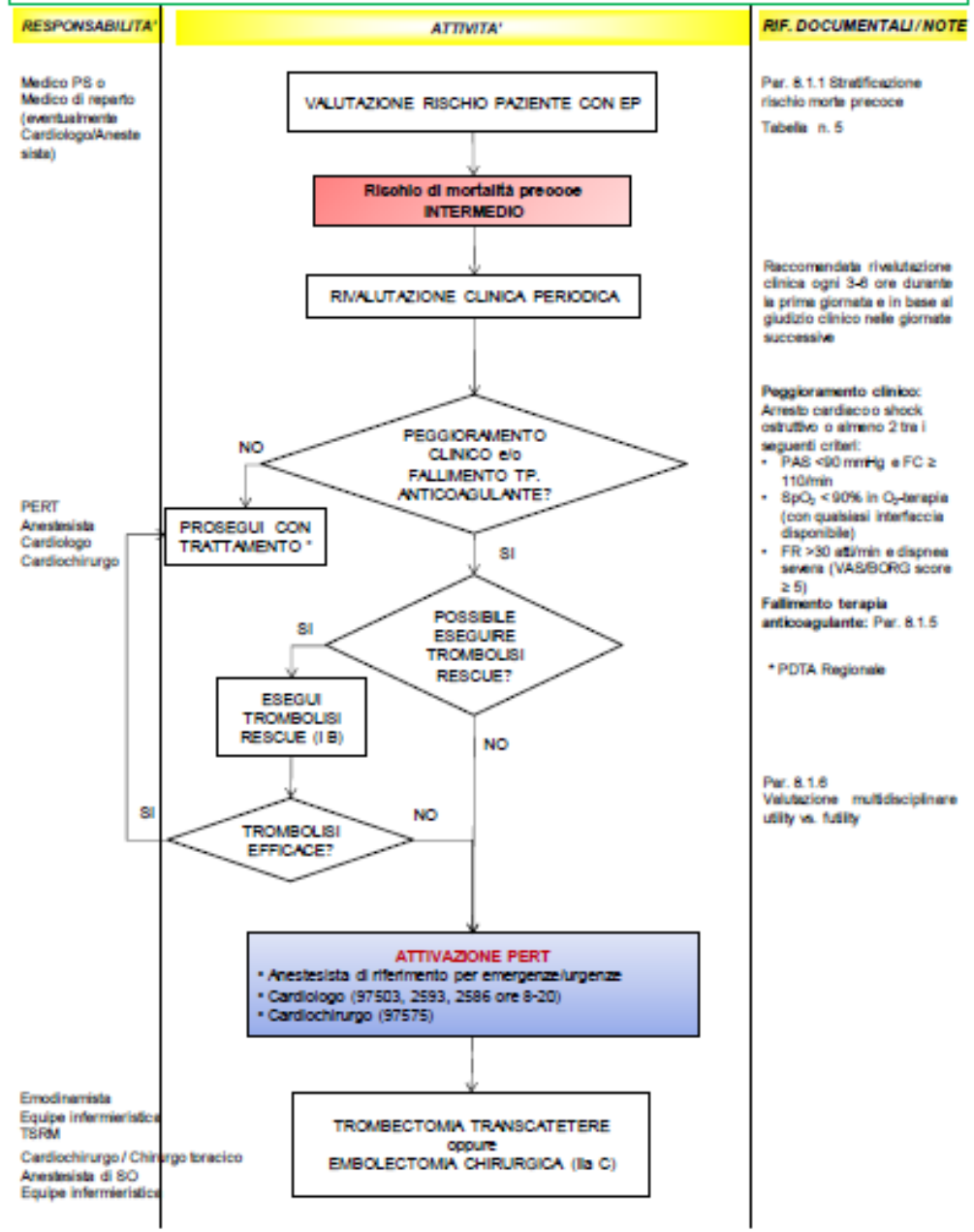
Score	ICH risk
0	1.2%
1	1.9%
2	2.4%
≥ 5	17.8%

Derivation cohort
C-statistic 0.65 (95%CI 0.59-0.71)

Validation cohort
C-statistic 0.66 (95%CI 0.60-0.72)

Andò G et al. Int J Cardiol 2024; Chatterjee S et al. Thromb Haemost 2017

FLOW CHART DECISIONALE PER IL TRATTAMENTO NON FARMACOLOGICO DEL PAZIENTE CON EP A RISCHIO INTERMEDIO



Intermediate-Risk Pulmonary Embolism: only oxygen?

PULMONARY VASCULAR ■

Does Supplemental Oxygen Improve Echocardiographic Parameters in Nonhypoxemic Patients With Intermediate-Risk Pulmonary Embolism?

STUDY DESIGN

Pilot study randomly assigned nonhypoxemic **stable pulmonary embolism with echocardiographic right ventricle (RV) enlargement** to receive anticoagulation for 48 hours with either:

Oxygen Ambient Air

1° outcome

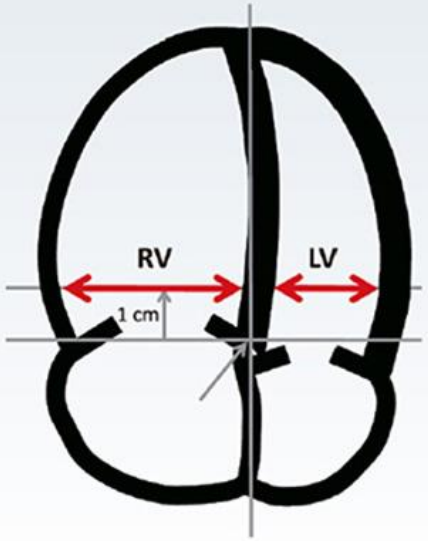
- Normal RV size after 48 hours

2° efficacy outcomes

- Numerical change in RV/left ventricle (LV) diameter ratio at 48 hours and 7 days

RESULTS

Study was prematurely stopped due to COVID-19 pandemic



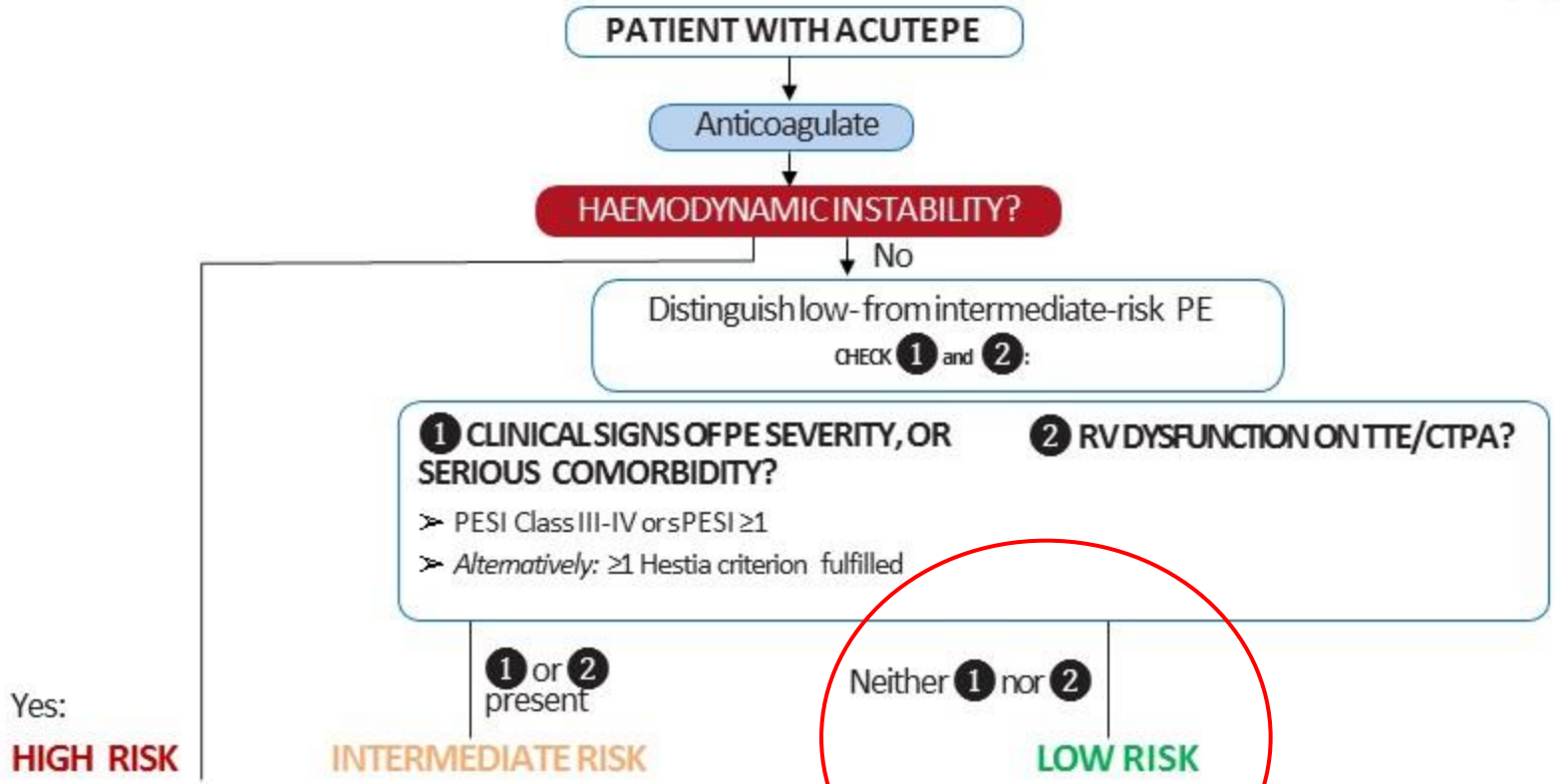
	Oxygen (n=33)	Ambient Air (n=37)
Normalization of RV after 48 hours not significant between the groups ($P = .08$)	14 (42.4%)	8 (21.6%)
Change in RV/LV ratio (baseline to 48 hours) was significant	1.28 to 1.01 $P < .001$	1.21 to 1.08 $P < .01$
Adverse events	None	1 major bleeding 1 death

In analyses limited by a small cohort, supplemental oxygen did not significantly increase the proportion of patients with nonhypoxemic intermediate-risk pulmonary embolism who normalized their RV/LV ratio after 48 hours. Improvement in some ancillary efficacy outcomes was noted.

Barrios D, et al. *CHEST* March 2024 | @journal_CHEST | https://doi.org/10.1016/j.chest.2023.09.007

Figure 5 Risk-adjusted management strategy for acute PE (1)

ESC European Society of Cardiology



www.escardio.org/guidelines

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for early discharge, home treatment

ESC European Society of Cardiology

Recommendations	Class	Level
Carefully selected patients with low-risk PE should be considered for early discharge and continuation of treatment at home, if proper outpatient care and anticoagulant treatment can be provided.	IIa	A

A (negative) clinical judgement should be added

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 1 Hestia rule, pulmonary embolism severity index, and simplified pulmonary embolism severity index

Hestia[9,10]	Answer	PESI[6]	Points	sPESI[7]	Points
Is the patient haemodynamically unstable?[a]	Yes/no	Age	Years	Age > 80 years	1
Is thrombolysis or embolectomy necessary?	Yes/no	Male sex	+10	History of cancer	1
Active bleeding or high risk of bleeding?[b]	Yes/no	History of cancer	+30	Chronic cardiopulmonary disease	1
>24 h of oxygen supply to maintain oxygen saturation > 90%?	Yes/no	History of heart failure	+10	Systolic blood pressure < 100 mmHg	1
Is pulmonary embolism diagnosed during anticoagulant treatment?	Yes/no	History of chronic lung disease	+10	Heart rate ≥ 110 b.p.m.	1
Severe pain needing intravenous pain medication for >24 h?	Yes/no	Heart rate ≥ 110 b.p.m.	+20	Arterial oxygen saturation < 90%	1
Medical or social reason for treatment in the hospital for >24 h (infection, malignancy, no support system)[c]?	Yes/no	Systolic blood pressure < 100 mmHg	+30		
Does the patient have a creatinine clearance of <30 mL/min?[d]	Yes/no	Respiratory rate ≥ 30/min	+20		
Does the patient have severe liver impairment?[e]	Yes/no	Temperature < 36°C/96.8°F	+20		
Is the patient pregnant?	Yes/no	Altered mental status (disorientation, lethargy, stupor, or coma)	+60		
Does the patient have a documented history of heparin-induced thrombocytopenia?	Yes/no	Arterial oxygen saturation < 90%	+20		
If all questions can be answered with 'No', the patient has a negative Hestia rule and is eligible for home treatment		If the PESI Class is I (total score of 0–65) or II (total score of 66–85), a patient is eligible for home treatment		If the sPESI = 0, a patient is eligible for home treatment	

Luijten D et al. Eur Heart J 2024

Study	Design	Comparison	N	Drugs	Discharge	Outcomes	Efficacy % (95%CI)	Safety % (95%CI)	Mortality %	Notes
Aujeski 2011	CRT	PESI class I-II outp vs inpat	344	LMWH-VKA	≤ 24 h	90 d- Recurr. sympt. VTE/ MB	0.6 vs 0	1.8 vs 0	0.6 vs 0.6	
Zondag 2011	Prosp Cohort	Hestia checklist	297	LMWH-VKA	≤ 24 h	id	2.0 (0.8.4.3)	0.7 (0.08-2.4)	1.0 (0.2-2.9)	
Vesta Study 2016	CRT	Hestia alone vs hestia + neg NT-proBNP	550	LMWH-VKA	≤ 24 h	30 d- PE or bleeding mortality/MB	1.1 (0.2-3.2) vs 0 (1-1.3)	1.1 (0.2-3.2) vs 0.4 (0-01-2.0)	1.1 vs 1.5	Low N pts with ↑ NT-pro BNP
		Post-hoc NT-proBNP +					0 (0-10.2) vs 0 (0-14.8)			
HOT-PE Study 2020	Prosp phase 4 trial	RV/LV ratio < 1.0, no free-floating thrombi, Hestia modified	525	Inject. AC Rivarox	≤ 48 h	90 d- Recurr. Sympt VTE or PE-death/MB	0.6 (99.6% CI 2.1)	1.2	0.4	Early stop aft interim analysis
Home-PE study 2021	CRT	Hestia vs sPESI	1975	LMWH-VKA-DOAC	≤ 24 h	30 d- Recurr. VTE + MB + all-cause death	1.33 vs 1.11			No fatal PE

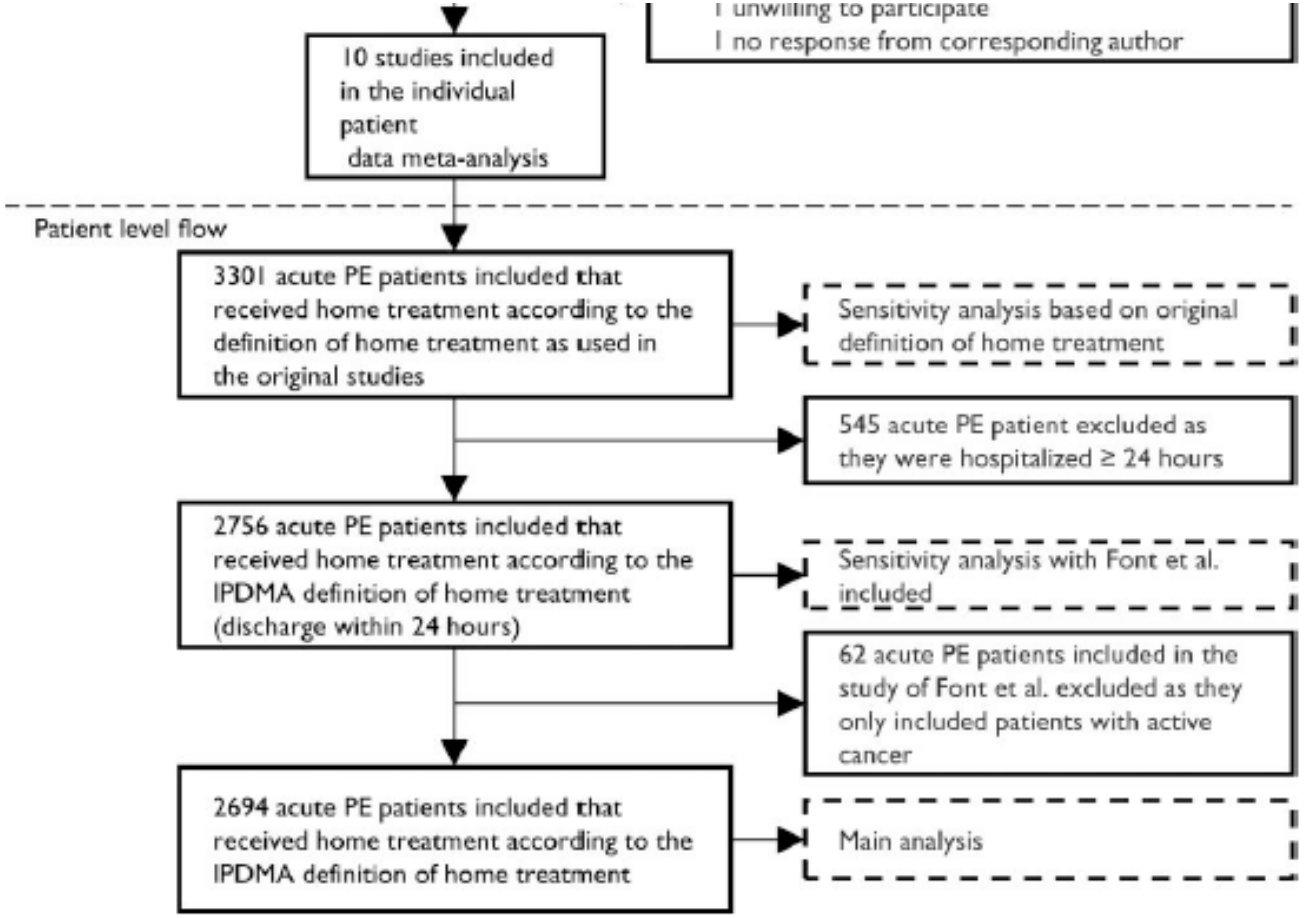
Aujeski et al. Lancet 2011; Zondag W et al. J Thromb Haemost 2011; den Exter et al. Am J Respir Crit Care Med 2016; Barco et al. Eur Heart J 2020;Roy et al. Eur Heart J 2021;

Study	Analysis	Home treatment	CT RV/LV > 1.0 n	CT RV/LV ≤ 1.0 n	Low-risk Pts treated at home with RV %	90 d recurrent VTE % OR(95%CI)	90 d mortality % OR(95%CI)
Hendriks 2020	Post-hoc of Hestia and Vesta studies	Hestia checklist	224	527	30	0.5 vs 1.3 0.33 (0.04-2.7)	2.2 vs 0.9 2.4 (0.68-8.3)
Roy 2021	Home-PE study	Hestia or sPESI	90	616	24.4	0	0

Hendriks Sv et al. A, J Resp Crit Care Med 2020; Roy et al. Eur Heart J 2021

ESC European Society of Cardiology
European Heart Journal (2024) **45**, 2933–2950
https://doi.org/10.1093/eurheartj/ehae378

Safety of treating acute pulmonary embolism at home: an individual patient data meta-analysis



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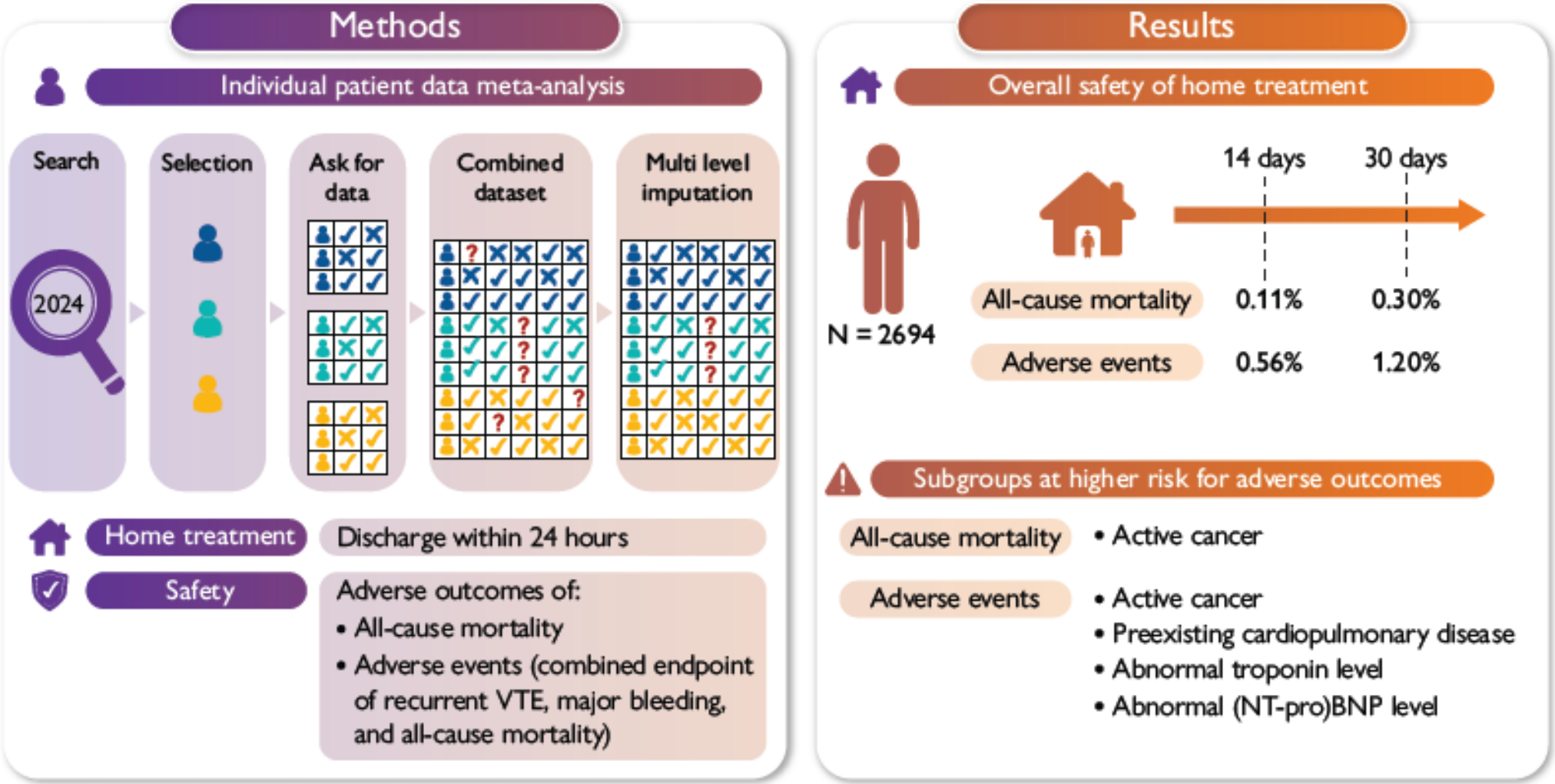
Methods
Individual patient data meta-analysis
Search
2024
Selection
Ask for data
Combined dataset
Multi level imputation
Home treatment
Discharge within 24 hours
Safety
Adverse outcomes of:
• All-cause mortality
• Adverse events (combined endpoint of recurrent VTE, major bleeding, and all-cause mortality)
Results
Overall safety of home treatment
N = 2694
14 days
30 days
All-cause mortality
0.11%
0.30%
Adverse events
0.56%
1.20%
Subgroups at higher risk for adverse outcomes
All-cause mortality
• Active cancer
Adverse events
• Active cancer
• Preexisting cardiopulmonary disease
• Abnormal troponin level
• Abnormal (NT-pro)BNP level

30-days combined endpoint an mortality

	Combined endpoint of VTE, MB, or all-cause morality						All-cause mortality					
	Events (*n*)	Patients (*n*)	%	(95% CI)	RR	(95% PI)	Events (*n*)	Patients (*n*)	%	(95% CI)	RR	(95% PI)
Overall	32	2653	1.2	(0.79–1.6)			8	2660	0.30	(0.09–0.51)		
Age												
18–40*	8	580	1.4	(0.43–2.3)			1	582	0.17	(0.0–0.51)		
41–60	12	1084	1.1	(0.49–1.7)	0.82	(0.45–1.5)	2	1085	0.18	(0.0–0.44)	0.93	(0.47–1.8)
61–80	12	889	1.4	(0.59–2.1)	0.91	(0.61–1.4)	5	893	0.56	(0.07–1.1)	1.3	(0.54–2.9)
>81	0	99	0.0	(0.0–0.0)	0.49	(0.31–0.77)	0	99	0.0	(0.0–0.0)	0.84	(0.62–1.1)
Sex												
Female	18	1260	1.4	(0.77–2.1)	1.4[g]	(0.57–3.4)	6	1264	0.47	(0.09–0.85)	1.7	(0.98–2.9)
Male*	14	1393	1.0	(0.49–1.5)			2	1396	0.14	(0.0–0.34)		
Symptoms												
Incidental	0	15	0.0	(0.0–0)	1	(0.0–986)	0	15	0.0	(0.0–0)	1.0	(0.0–986)
Symptomatic*	20	1640	1.2	(0.69–1.8)			6	1640	0.37	(0.08–0.66)		

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30-days combined endpoint an mortality

	Combined endpoint of VTE, MB, or all-cause morality						All-cause mortality					
	Events (*n*)	Patients (*n*)	%	(95% CI)	RR	(95% PI)	Events (*n*)	Patients (*n*)	%	(95% CI)	RR	(95% PI)
Treatment												
LMWH or VKA	14	1007	1.4	(0.67–2.1)	1.4	(0.72–2.9)	6	1011	0.59	(0.12–1.1)	2.6	(0.91–7.5)
DOAC*	17	1530	1.1	(0.58–1.6)			1	1533	0.07	(0.0–0.2)		
Cancer[a]												
Yes	5	211	2.4	(0.31–4.4)	2.7	(1.4–5.2)	4	215	1.9	(0.06–3.7)	4.9	(2.7–9.1)
No*	27	2442	1.1	(0.7–1.5)			4	2445	0.16	(0.0–0.32)		
Previous VTE												
Yes	13	829	1.6	(0.73–2.4)	1.3	(0.65–2.6)	3	831	0.36	(0.0–0.77)	1.8	(0.57–5.7)
No*	18	1708	1.1	(0.57–1.5)			4	1713	0.23	(0.0–0.46)		
Decreased kidney function[b]												
Yes	1	202	0.49	(0.0–1.5)	0.35	(0.14–0.88)	0	203	0.18	(0.0–0.76)	0.66	(0.39–1.1)
No*	31	2451	1.3	(0.82–1.7)			8	2457	0.31	(0.09–0.53)		
Pre-existing cardiopulmonary disease[c]												
Yes	8	476	1.8	(0.57–2.9)	1.9	(0.9–3.8)	2	478	0.34	(0.0–0.86)	1.8[i]	(0.36–9.5)
No*	24	2177	1.1	(0.65–1.5)			6	2182	0.29	(0.06–0.52)		

14-days

Pre-existing cardiopulmonary disease[c]												
Yes	6	479	1.30	(0.29–2.3)	3.5	(1.5–7.9)	1	480	0.28	(0.0–0.75)	2. 70[g]	(0.68–11)
No*	9	2181	0.40	(0.13–0.67)			2	2184	0.08	(0.0–0.2)		

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30-days combined endpoint an mortality

	Combined endpoint of VTE, MB, or all-cause morality						All-cause mortality					
	Events (*n*)	Patients (*n*)	%	(95% CI)	RR	(95% PI)	Events (*n*)	Patients (*n*)	%	(95% CI)	RR	(95% PI)
Abnormal troponin[d]												
Yes	6	248	2.6	(0.59–4.5)	2.9	(1.5–5.7)	1	249	0.6	(0.0–1.6)	2.2	(0.59–8.1)
No*	19	1941	1.0	(0.53–1.4)			5	1947	0.23	(0.02–0.44)		
Abnormal (NT-pro)BNP[e]												
Yes	6	208	2.7	(0.47–4.9)	3.3	(1.6–7.1)	1	210	0.4	(0.0–1.3)	0.84	(0.52–1.4)
No*	19	2149	0.91	(0.51–1.3)			5	2154	0.24	(0.03–0.45)		
Signs of RV overload[f]												
Yes	9	325	2.7	(0.96–4.5)	2.0[h]	(0.68–6)	2	327	0.55	(0.0–1.4)	0.70	(0.4–1.2)
No*	8	905	0.9	(0.29–1.5)			3	909	0.35	(0.0–0.74)		

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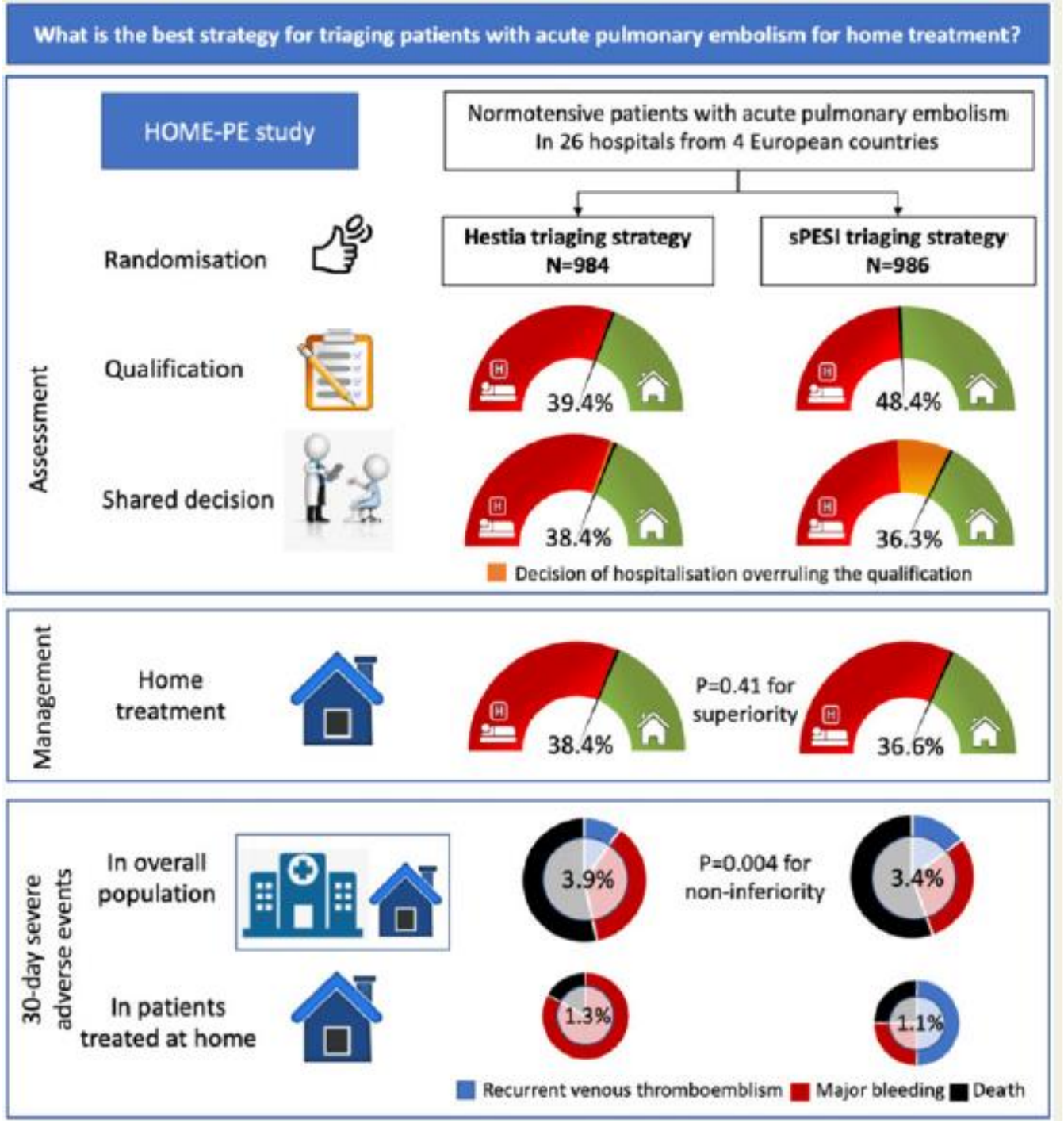


High value of clinical Judgement and individualized Treatment added to explicit models of risk stratification

JAMA Network Open.

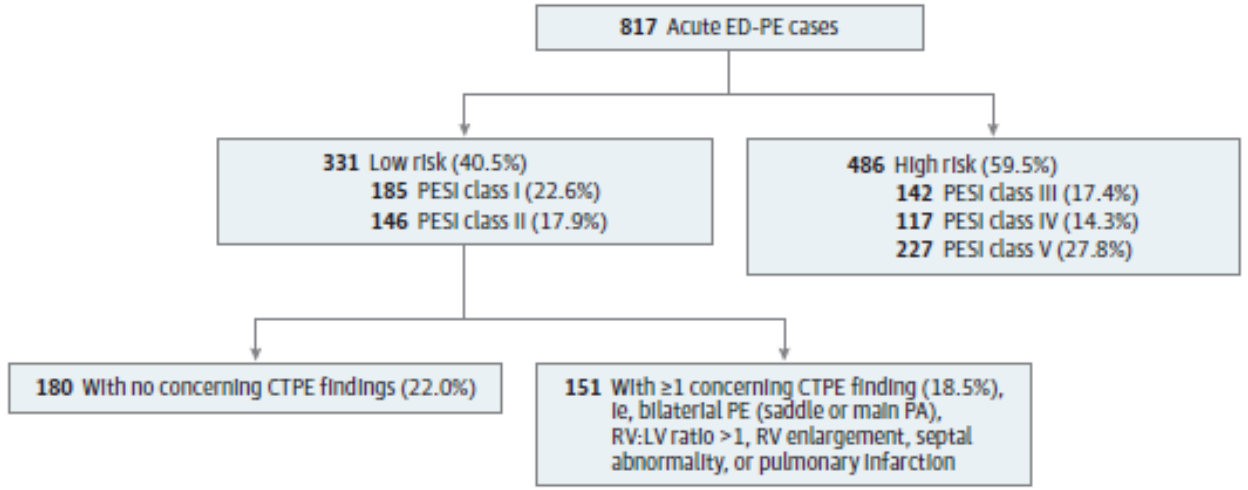
Original Investigation | Emergency Medicine

Adverse Clinical Outcomes Among Patients With Acute Low-risk Pulmonary Embolism and Concerning Computed Tomography Imaging Findings

Connor O'Hare, MD; Kelsey A. Grace, MD; William J. Schaeffer, DO; S. Nabeel Hyder, MD; Michael Stover, BS; Amber L. Liles, MD, MPH; Minhaj S. Khaja, MD, MBA; James A. Cranford, PhD; Keith E. Kocher, MD, MPH; Geoffrey D. Barnes, MD, MSc; Colin F. Greineder, MD, PhD

JAMA Network Open. 2023;

Figure 1. Risk Stratification of Acute Pulmonary Embolisms Diagnosed in the Emergency Department (ED-PEs)



Characteristic	Acute ED-PEs			Low-risk PEs		
	Low-risk PEs (n = 331)	High-risk PEs (n = 486)	*P* value	No concerning CTPE findings (n = 180)	≥1 Concerning CTPE findings (n = 151)	*P* value
CTPE findings						
Laterality, No. (%)						
Bilateral	181 (54.7)	250 (51.4)	.36	67 (37.2)	114 (75.5)	<.001
Unilateral	150 (45.3)	236 (48.6)	.36	113 (62.8)	37 (24.5)	<.001
Largest artery involved, No. (%)						
Saddle	7 (2.1)	20 (4.1)	.12	0	7 (4.6)	.004
Main	51 (15.4)	100 (20.6)	.06	2 (1.1)	49 (32.5)	<.001
Lobar	74 (22.4)	107 (22.0)	.91	35 (19.4)	39 (25.8)	.16
Segmental	145 (43.8)	191 (39.3)	.20	99 (55)	46 (30.5)	<.001
Subsegmental	54 (16.3)	250 (51.4)	.37	44 (24.4)	10 (6.6)	<.001

Figure 2. Clinical Outcomes and Findings on Pulmonary Embolism–Protocol Computed Tomography (CTPE)

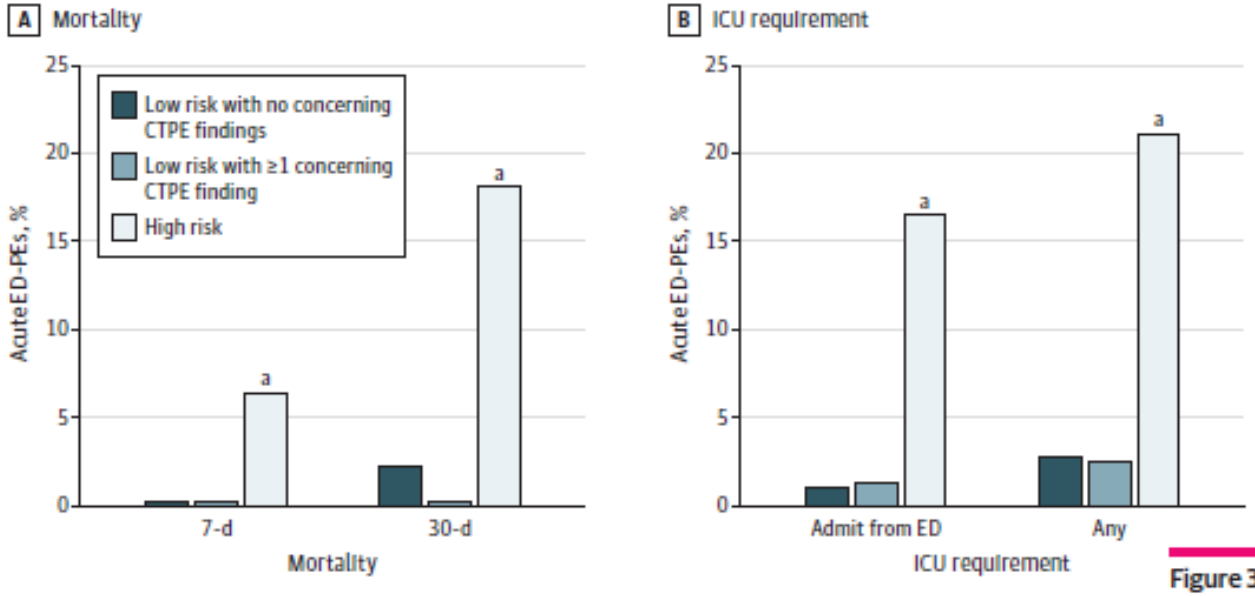
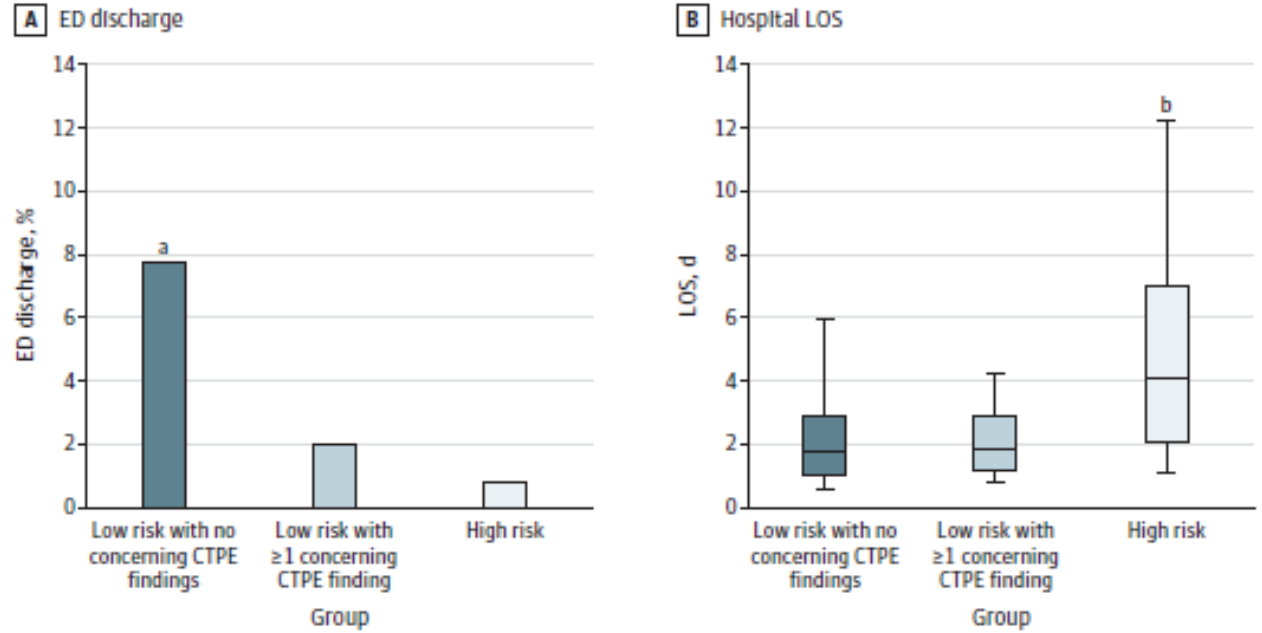


Figure 3. Hospitalization and Findings on Pulmonary Embolism–Protocol Computed Tomography (CTPE)



Trends in Discharge Rates for Acute Pulmonary Embolism in U.S. Emergency Departments

Nathan W. Watson, BS; Brett J. Carroll, MD; Anna Krawisz, MD; Alec Schmaier, MD, PhD; and Eric A. Secemsky, MD, MSc

Ann Intern Med. 2024;

Figure 1. Patient flow diagram for cohort formation, 2012–2020.

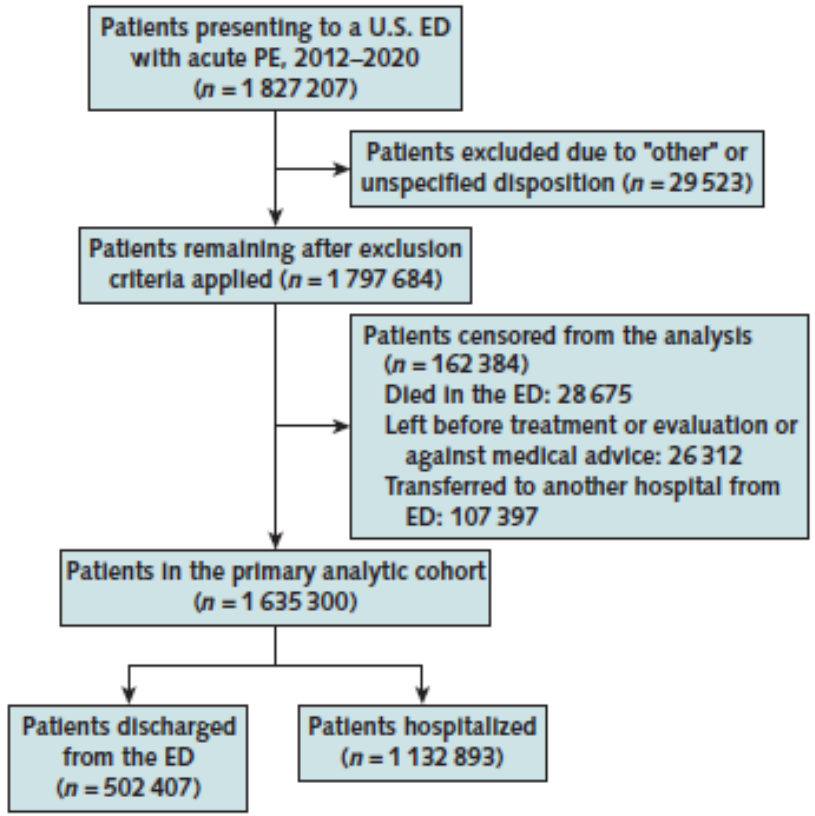
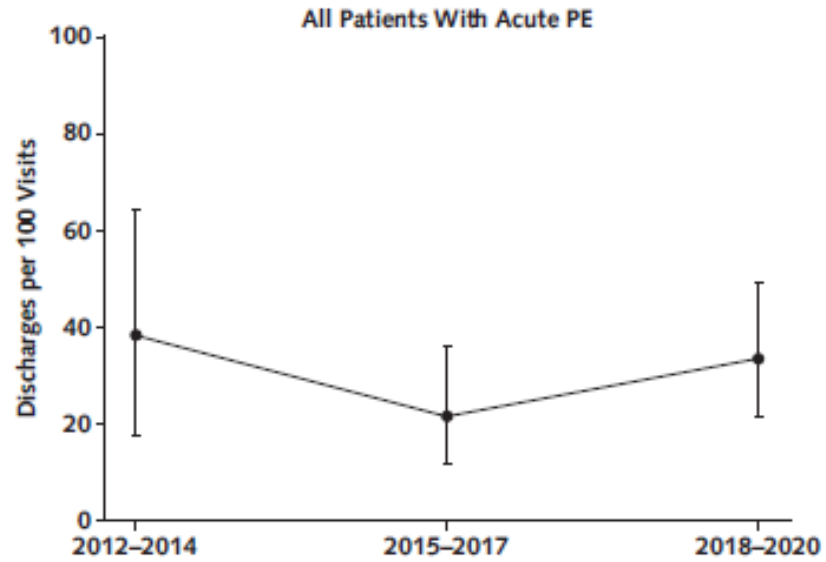
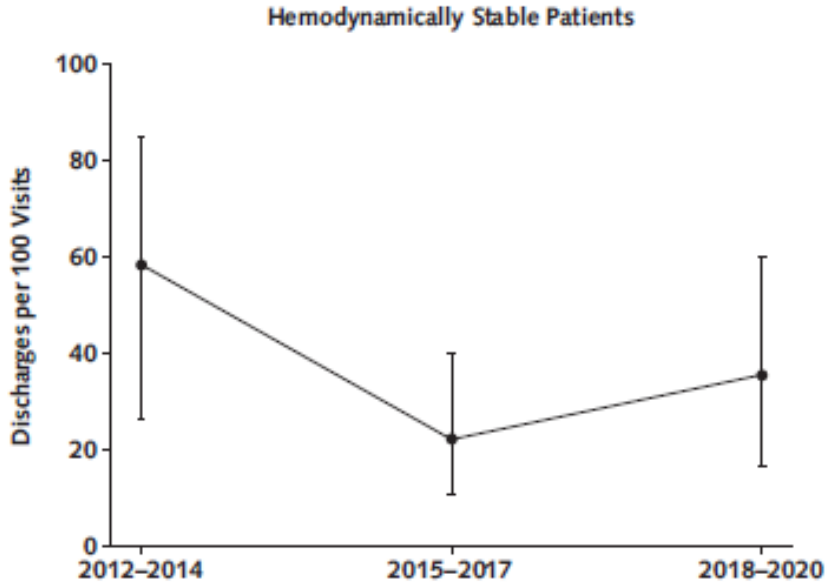
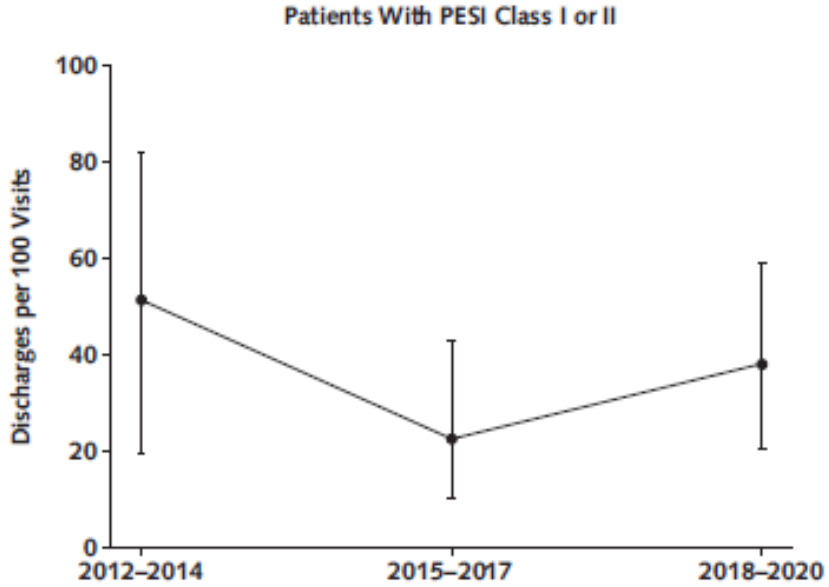


Figure 2. National temporal trends in ED discharge rates for all patients with acute PE.




Hemodynamically Stable Patients
Discharges per 100 Visits
100
80
60
40
20
0
2012–2014
2015–2017
2018–2020


Patients With PESI Class I or II
Discharges per 100 Visits
100
80
60
40
20
0
2012–2014
2015–2017
2018–2020

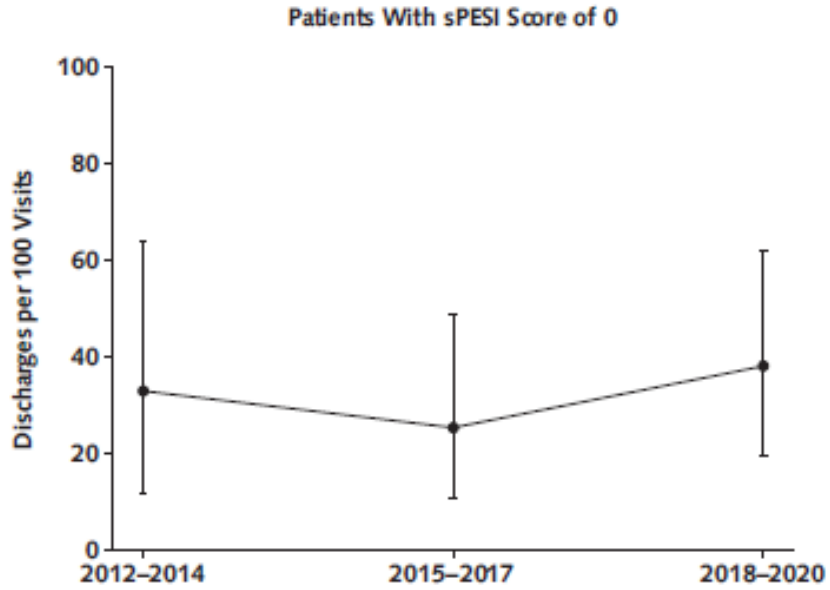

Patients With sPESI Score of 0
Discharges per 100 Visits
100
80
60
40
20
0
2012–2014
2015–2017
2018–2020

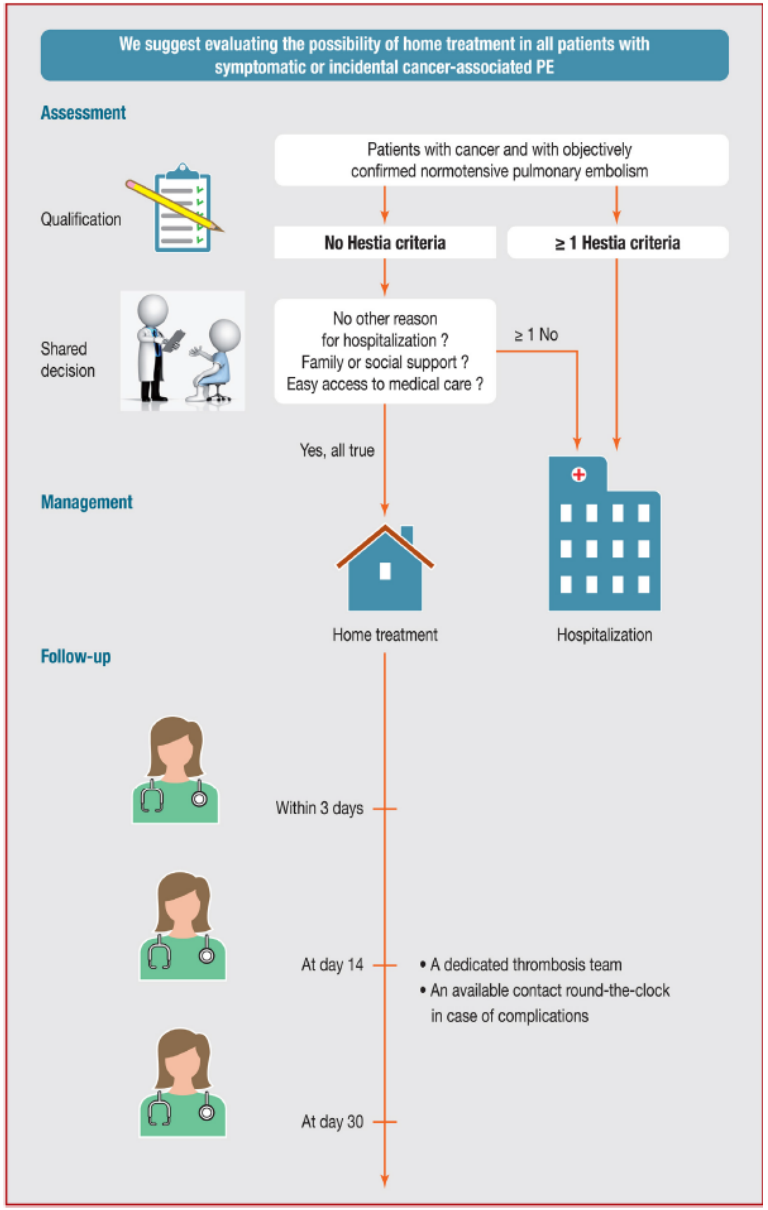
Table 2. Univariable and Multivariable Regression Analysis for Predictors of Discharge Among All Patients With Acute PE in the ED

Variable	Admitted (n = 1 132 893)	Discharged (n = 502 407)	Unadjusted Risk Ratio (95% CI)	Adjusted Risk Ratio (95% CI)*
Year	-	-	0.99 (0.86-1.15)	1.01 (0.89-1.14)
Demographic characteristics				
Mean age (±SE), *y*	59.4 ± 2.31	54.0 ± 4.89	0.99 (0.97-1.00)	0.99 (0.98-1.00)
Male sex, *n (%)*	496 661 (43.8)	143 431 (28.5)	0.62 (0.36-1.06)	0.65 (0.39-1.10)
Race, *n (%)*				
White	825 856 (72.9)	382 327 (76.1)	1.12 (0.59-2.14)	1.24 (0.63-2.43)
Black	273 607 (24.2)	113 689 (22.6)	0.94 (0.46-1.90)	0.85 (0.40-1.81)
Other	33 431 (3.0)	6391 (1.3)	0.51 (0.06-4.04)	0.48 (0.06-3.37)
Hispanic or Latino ethnicity, *n (%)*	116 422 (10.3)	33 766 (6.7)	0.71 (0.24-2.07)	0.70 (0.24-2.04)
Comorbidities, *n (%)*				
Cancer	107 477 (9.5)	71 346 (14.2)	1.63 (0.88-3.01)	1.62 (0.88-3.01)
Dementia	44 677 (3.9)	0 (0.0)	-	-
Cerebrovascular disease	81 906 (7.2)	7662 (1.5)	0.26 (0.03-1.82)	0.31 (0.04-2.20)
COPD	220 236 (19.4)	129 755 (25.8)	1.27 (0.65-2.50)	1.23 (0.71-2.13)
Congestive heart failure	141 833 (12.5)	57 897 (11.5)	0.93 (0.48-1.79)	1.05 (0.53-2.06)
Diabetes mellitus	193 964 (17.1)	117 088 (23.3)	1.29 (0.66-2.52)	1.65 (0.77-3.55)
History of VTE	257 236 (22.7)	188 025 (37.4)	1.59 (0.86-2.94)	1.55 (0.87-2.74)
History of HIV	2812 (0.2)	0 (0.0)	-	-
End-stage renal disease	27 459 (2.4)	0 (0.0)	-	-
Chronic kidney disease	125 231 (11.8)	11 383 (2.4)	0.25 (0.04-1.35)	0.26 (0.04-1.58)
Coronary artery disease	170 925 (16.1)	40 951 (8.6)	0.58 (0.26-1.31)	0.75 (0.29-1.95)
Alcohol use disorder	28 658 (2.7)	1221 (0.3)	0.12 (0.01-1.23)	0.18 (0.01-1.96)
Asthma	159 345 (15.0)	75 581 (15.9)	1.04 (0.52-2.06)	0.90 (0.47-1.71)
Osteoporosis	41 398 (3.9)	28 644 (6.0)	1.34 (0.28-6.38)	1.20 (0.23-6.14)
Depression	109 497 (10.3)	55 095 (11.6)	1.09 (0.51-2.30)	1.15 (0.56-2.35)
Hyperlipidemia	196 562 (18.6)	74 919 (15.8)	0.87 (0.38-1.95)	0.96 (0.40-2.30)
Hypertension	435 482 (41.1)	202 888 (42.7)	1.04 (0.58-1.86)	1.27 (0.73-2.20)
Obesity	243 026 (23.0)	52 705 (11.1)	0.52 (0.15-1.70)	0.5 (0.15-1.61)
Obstructive sleep apnea	60 746 (5.7)	0 (0.0)	-	-
Geographic region, *n (%)*				
Northeast	243 535 (21.5)	124 371 (24.8)	1.13 (0.62-2.04)	1.94 (0.59-6.35)
Midwest	262 349 (23.2)	78 352 (15.6)	0.70 (0.30-1.60)	0.72 (0.31-1.66)
South	398 139 (35.1)	143 122 (28.5)	0.80 (0.43-1.49)	0.84 (0.44-1.58)
West	228 869 (20.2)	156 563 (31.2)	1.46 (0.73-2.92)	1.59 (0.59-4.25)
Teaching hospital, *n (%)*	172 659 (15.2)	110 553 (22.0)	1.34 (0.68-2.66)	1.47 (0.72-3.01)
Primary payment, *n (%)*				
Private insurance	254 224 (24.8)	178 567 (36.4)	1.30 (0.78-2.18)	1.19 (0.75-1.91)
Medicare	507 699 (49.5)	208 887 (42.5)	0.91 (0.50-1.65)	1.27 (0.64-2.52)
Medicaid/other state program	173 792 (16.9)	87 878 (17.9)	0.99 (0.55-1.76)	0.94 (0.50-1.79)
Other	90 681 (8.8)	15 592 (3.2)	0.43 (0.09-1.90)	0.50 (0.13-1.87)
Rural location, *n (%)*	73 789 (6.8)	38 856 (8.0)	1.12 (0.31-4.05)	1.05 (0.28-3.87)
Hemodynamically stable, *n (%)*†	599 540 (59.6)	319 751 (66.0)	1.20 (0.66-2.17)	1.15 (0.65-2.04)
PESI class I or II, *n (%)*	583 457 (59.5)	327 441 (68.1)	1.28 (0.73-2.25)	0.96 (0.43-2.13)
sPESI score of 0, *n (%)*	490 788 (43.3)	242 989 (48.4)	1.15 (0.64-2.06)	1.06 (0.58-1.93)

USE OF ORAL ANTICOAGULANTS AT DISCHARGE WAS MORE FREQUENT AT TEACHING INSTITUTIONS AND AMONG PTS WITH PRIVATE INSURANCE

Altogether, these findings suggest that outpatient management of acute PE remains underutilized despite clinical evidence and guideline recommendations. Further investigation of the root causes of ED triage decisions and dedicated interventions to improve appropriate use of outpatient management are warranted.

Home treatment of PE cancer PTS: the INNOVTE CAT Working Group



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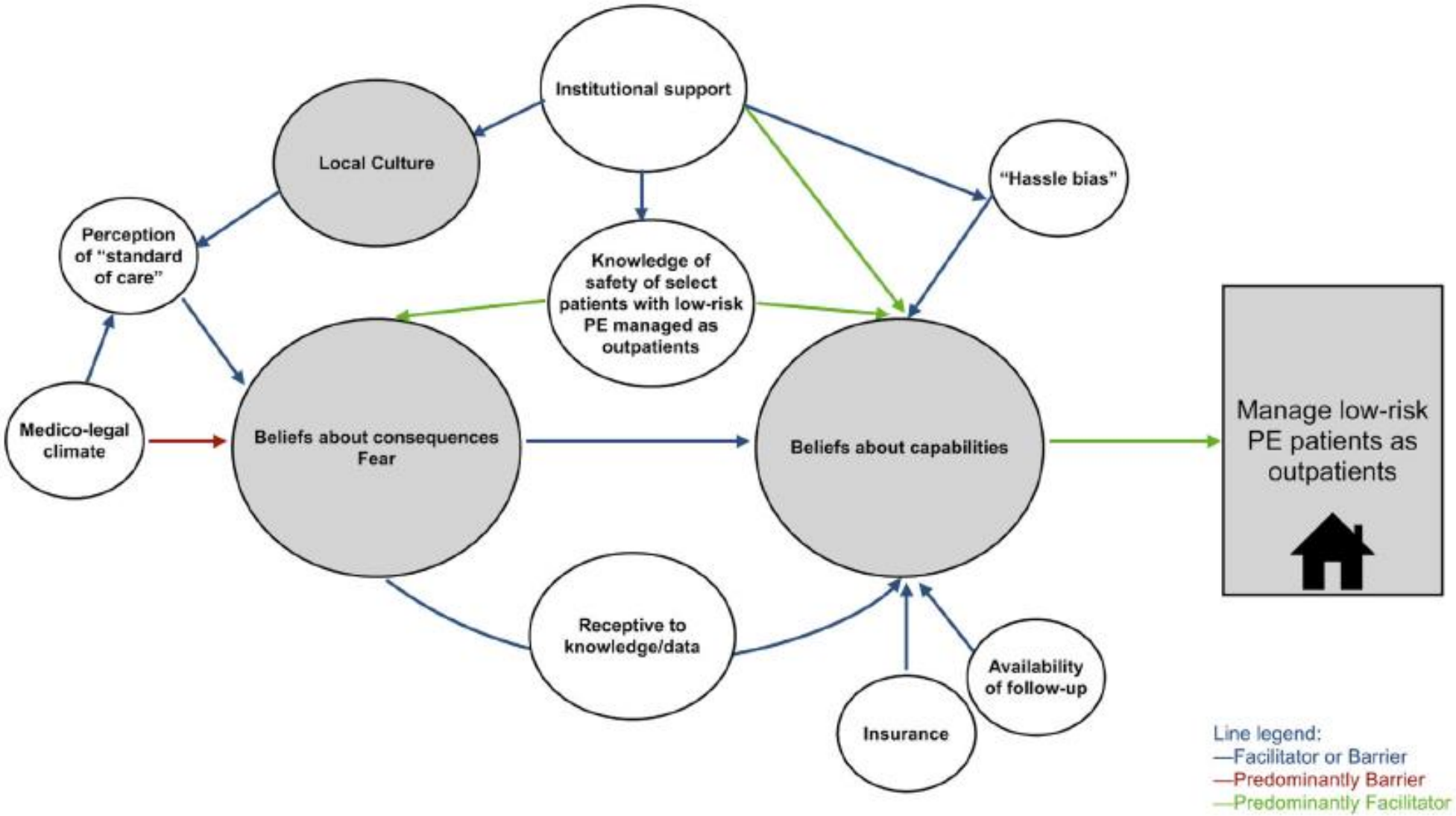
Barriers and facilitators to the outpatient management of PE



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Development and Validation of a Natural Language Processing Model to Identify Low-Risk Pulmonary Embolism in Real Time to Facilitate Safe Outpatient Management

Krunal D. Amin, MD*; Elizabeth Hope Weissler, MD; William Ratliff, MBA; Alexander E. Sullivan, MD; Tara A. Holder, MD; Cathleen Bury, MD; Samuel Francis, MD; Brent Jason Theiling, MD, MS; Bradley Hintze, BS; Michael Gao, BS; Marshall Nichols, MS; Suresh Balu, MBA; William Schuyler Jones, MD; Mark Sendak, MD, MPP

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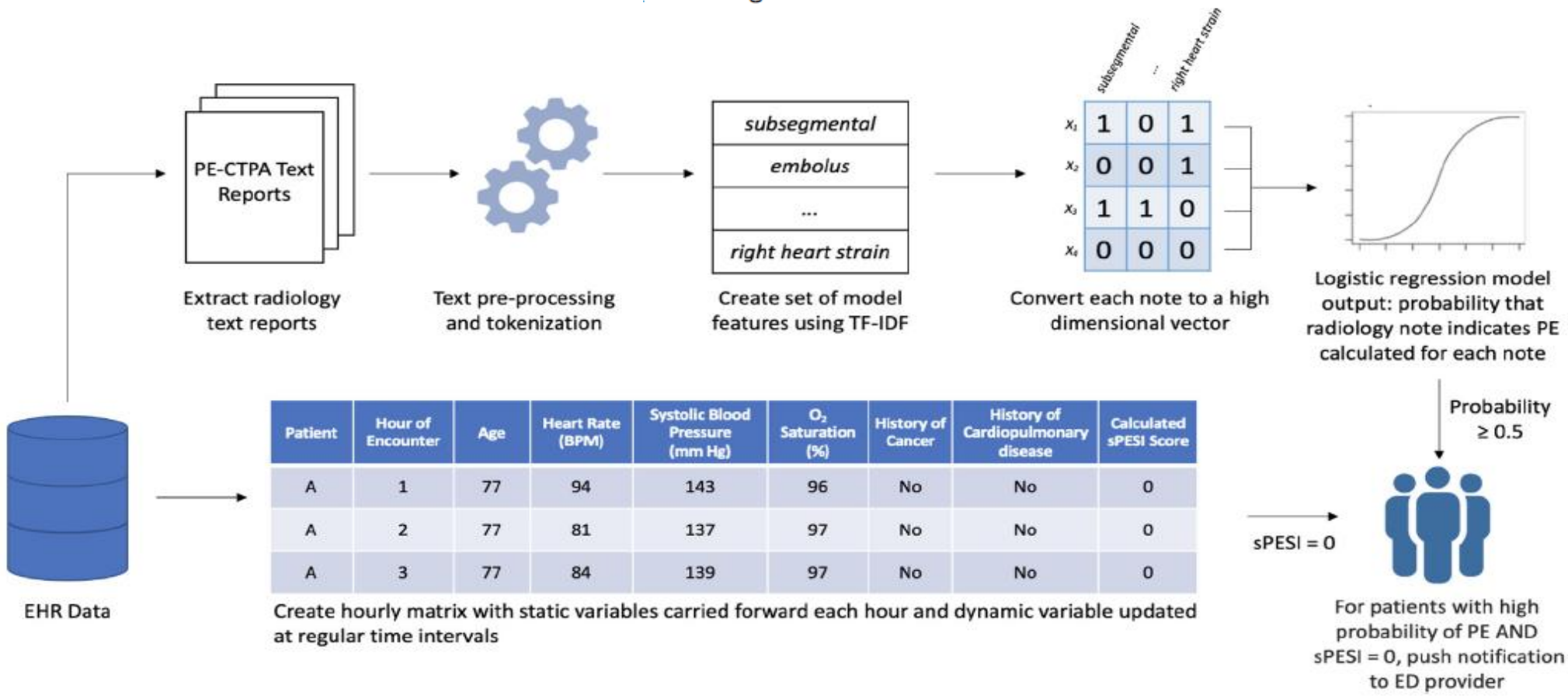

Patient	Hour of Encounter	Age	Heart Rate (BPM)	Systolic Blood Pressure (mm Hg)	O_2 Saturation (%)	History of Cancer	History of Cardiopulmonary disease	Calculated sPESI Score
A	1	77	94	143	96	No	No	0
A	2	77	81	137	97	No	No	0
A	3	77	84	139	97	No	No	0

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Table 2. Prediction accuracy by cohort and sPESI Score for internal validation and temporal validation cohorts classified by low-risk PE (sPESI=0) and high-risk PE (sPESI≥1)*.

Cohort	AUROC	AUPRC	Sensitivity	Specificity	PPV	NPV	F1-Score
Internal Validation (n=3,109)	0.99 (0.98-1.00)	0.97 (0.96-0.99)	0.87 (0.84-0.90)	0.99 (0.99-1.00)	0.96 (0.94-0.98)	0.98 (0.98-0.99)	0.91 (0.89-0.94)
Low-risk PE (sPESI=0; n=77)	0.98 (0.97-1.00)	0.97 (0.93-0.99)	0.85 (0.77-0.94)	0.99 (0.99-1.00)	0.97 (0.91-1.00)	0.99 (0.98-0.99)	0.91 (0.86-0.95)
High-risk PE (sPESI≥1; n=257)	0.99 (0.98-1.00)	0.98 (0.97-0.99)	0.88 (0.85-0.92)	0.99 (0.99-1.00)	0.96 (0.94-0.99)	0.98 (0.98-0.99)	0.92 (0.90-0.94)
Temporal Validation (n=1,819)	0.99 (0.99-1.00)	0.98 (0.96-0.99)	0.86 (0.81-0.91)	0.99 (0.99-1.00)	0.93 (0.89-0.96)	0.99 (0.98-0.99)	0.90 (0.86-0.93)
Low-risk PE (sPESI=0; n=33)	0.99 (0.98-1.00)	0.97 (0.93-0.99)	0.80 (0.71-0.89)	0.99 (0.99-1.00)	0.95 (0.89-0.99)	0.98 (0.97-0.99)	0.87 (0.85-0.92)
High-risk PE (sPESI≥1; n=135)	0.99 (0.99-1.00)	0.98 (0.97-0.99)	0.88 (0.83-0.95)	0.99 (0.99-1.00)	0.92 (0.89-0.97)	0.99 (0.98-0.99)	0.90 (0.87-0.94)

Methods

Design

- Retrospective cohort study
- Acute PE patients aged 70 years or older
- Diagnosed at the emergency department of LUMC or within <48 hours of hospitalization between 2015-2022

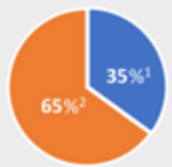
Objectives

- Performance of risk stratification with a focus on:
  - Home treatment
  - Reperfusion treatment
- Mortality based on
  - ESC risk classification
  - Acute Presenting Older Patient (APOP) score

N=242

Results

Home treatment/hospitalization (n=230)



All patients with negative Hestia criteria received home treatment (n=59)

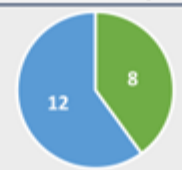
Outcomes within 14-days:
- 0 deaths
- 0 recurrent VTE's
- 1 major bleeding (day 7; hematuria from RCC)

[1] 81 patients [2] 149 patients; 9 PEs diagnosed shortly after hospitalization and 3 patients transferred from our emergency department to another hospital were excluded from this sub-analysis

Reperfusion treatment

20 high risk patients based on the ESC classification evaluated for reperfusion treatment:

14-day mortality: 42%



14-day mortality: 63%

Received reperfusion treatment
Received no reperfusion treatment

Mortality

APOP score	≥45%	<45%
14-day mortality:	28%	3.2%

HR 10.2 (95%CI 2.6-39)

ESC-guideline	Low-risk PE	Int-risk PE	High-risk PE
14-day mortality:	0%	7.8%	51%

As the APOP score was introduced in 2018, it was available in only 121 patients

Conclusion

Home treatment of older PE patients selected with a negative Hestia criterium was safe in our cohort.
Mortality in the high-risk group was high also for patients receiving reperfusion treatment.
The ESC risk-classification and APOP score identified patients at higher mortality, suggesting their potential utility in clinical decision-making.