Spreading knowledge – improving outcomes

Pulmonary Embolism

Management Challenges

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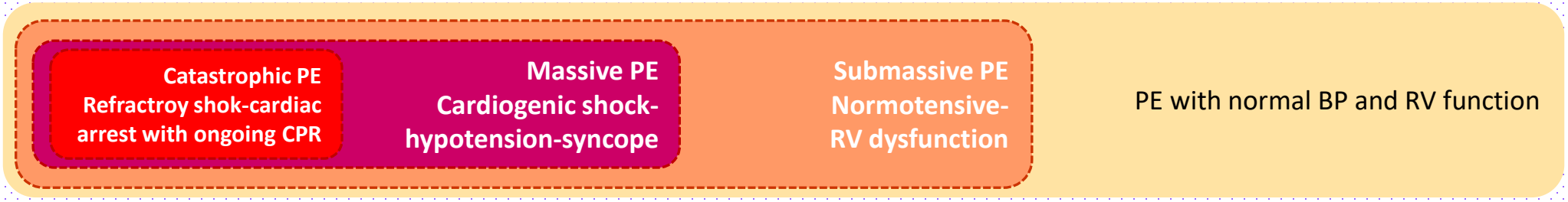
Outline

- Spectrum & definitions
- Trends & outcomes
- Risk stratifications
- Subsegmental PE: should anticoagulation be given?
- Low risk: is outpatient treatment safe?
- Intermediate low: anticoagulation alone
- Intermediate high: thrombolytic therapy and CDT!
- High risk: systemic thrombolytic vs CDT

Spectrum of Pulmonary Embolism



30-day mortality*

57.1%

Patients with shock or hypotension (systolic blood pressure <90 mmHg or decrease in systolic blood pressure of ≥40 mmHg from baseline) for 15 minutes and RV dysfunction

6.7%

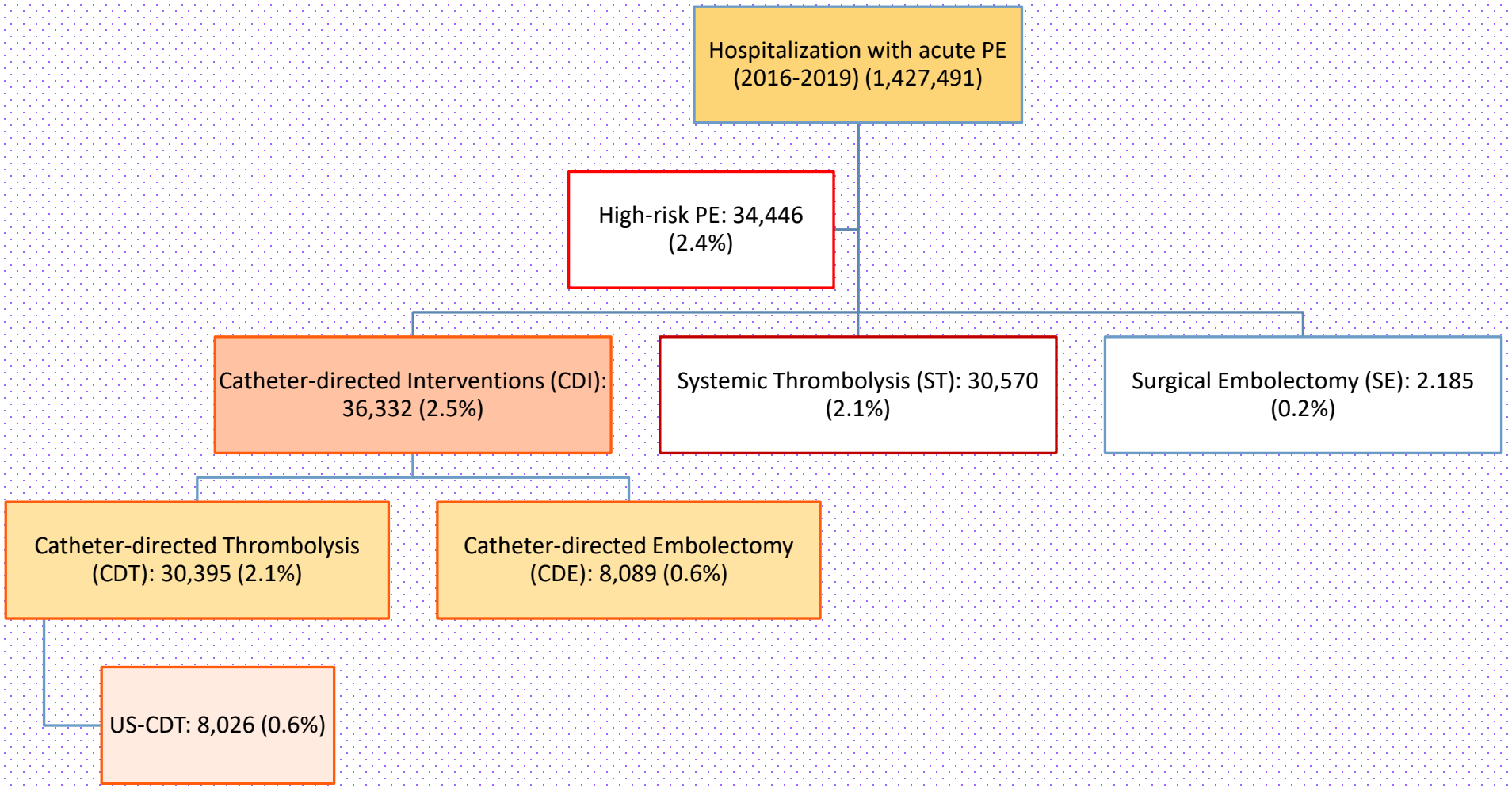
Patients without shock or hypotension but with signs of RV dysfunction and/or positive cardiac biomarkers or sPESI ≥1.

3.5%

Patients without shock/hypotension and no signs of RV dysfunction or with sPESI <1

*Gupta R, Ammari Z, Dasa O, et al. Long-term mortality after massive, submassive, and low-risk pulmonary embolism. Vascular Medicine

Contemporary National Trends and Outcomes of Pulmonary Embolism in the United States



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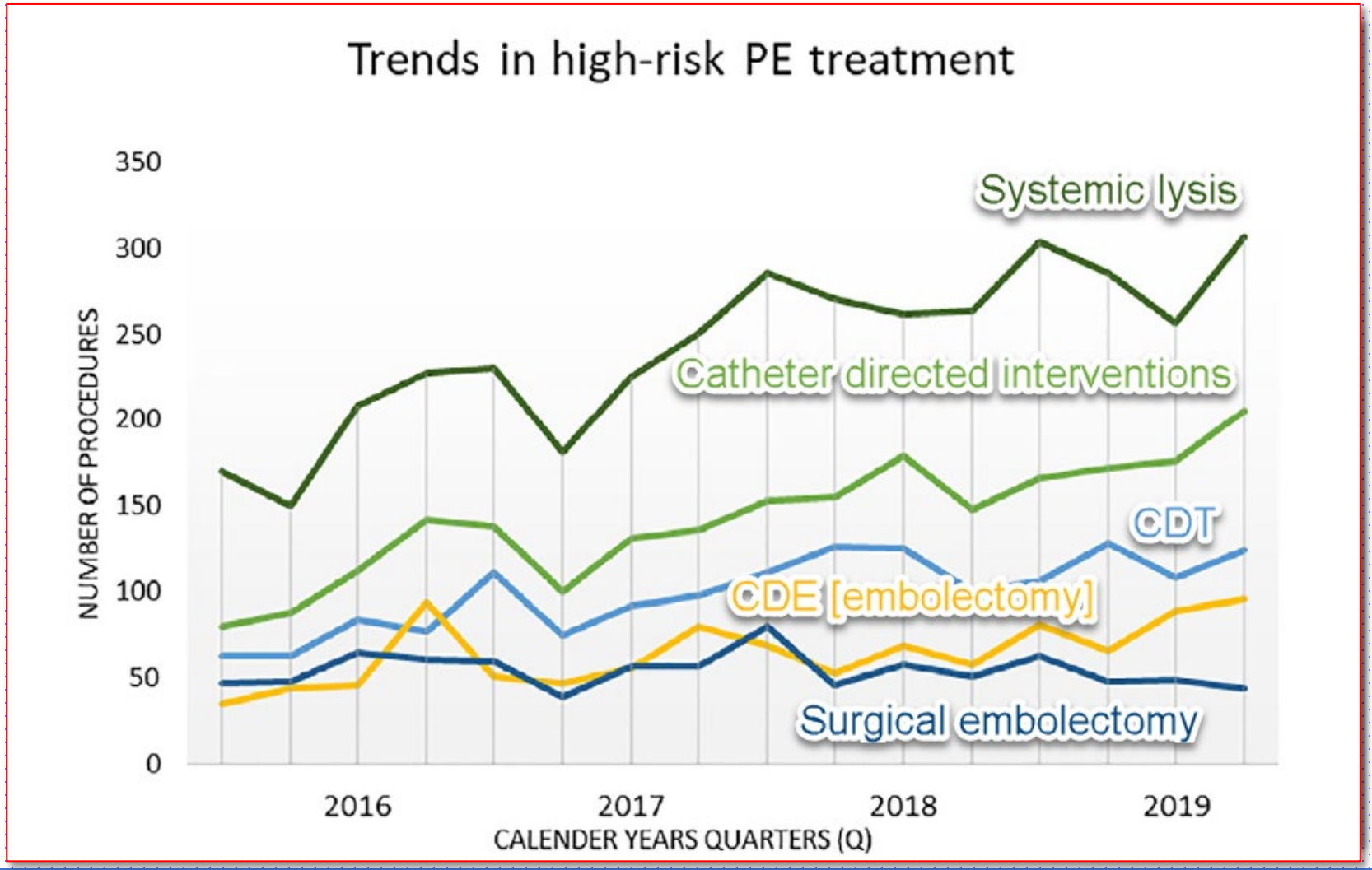

Outcome by Treatment Method

Outcomes stratified by treatment method

Variable	In-Hospital Mortality	ICH	Non-ICH
Anticoagulation alone (n=1,269,394)	78,940 (6.2%)	9,491 (0.7%)	154,289 (12.2%)
IVC filter (n=103,411)	7,100 (6.9%)	5,507 (5.3%)	28,362 (27.4%)
Systemic thrombolysis (n=30,570)	5,033 (16.5%)	556 (1.8%)	4,181 (13.7%)
Catheter-directed thrombolysis (n=30,395)	1,415 (4.7%)	185 (0.6%)	3,090 (10.2%)
Catheter-directed embolectomy (n=8,089)	898 (11.1%)	234 (2.9%)	1,209 (14.9%)
Surgical embolectomy (n=2,185)	279 (12.8%)	66 (6%)	425 (19.5%)

ICH = intracranial hemorrhage; IVC = inferior vena cava.

Original and Simplified Pulmonary Embolism Severity Index (PESI)

	Original PESI	Simplified PESI
Age	Age in years	1 (>80 ys)
Male sex	+10	
History of cancer	+30	1
History of heart failure	+10	1
History of chronic lung disease	+10	
Pulse ≥110 beats/min	+20	1
Systolic blood pressure <100 mm Hg	+30	1
Respiratory rate ≥30 breaths/min	+20	
Temperature <36◦C	+20	
Altered mental status	+60	
Arterial oxyhemoglobin saturation <90%	+20	1
	Class I: ≤65 points: very low 30 day mortality risk (0–1.6%) **Class II: 66–85 points:** low mortality risk (1.7–3.5%)	**0 points** = 30 day mortality risk 1.0% (95% CI 0.0–2.1%)
	Class III: 86–105 points: moderate mortality risk (3.2–7.1%) **Class IV: 106–125 points:** high mortality risk (4.0–11.4%) **Class V: >125 points:** very high mortality risk (10.0–24.5%)	**≥1 point(s)** = 30 day mortality risk 10.9% (95% CI 8.5–13.2%)

Heart Rate and Mortality in Patients With Acute Symptomatic Pulmonary Embolism

*Ana Jaureguízar, MD; David Jiménez, MD, PhD; Behnood Bikdeli, MD; Pedro Ruiz-Artacho, MD, PhD; Alfonso Muriel, PhD; Victor Tapson, MD; Raquel López-Reyes, MD, PhD; Beatriz Valero, MD; Gili Kenet, MD; Manuel Monreal, MD, PhD; and the Registro Informatizado de la Enfermedad TromboEmbólica Investigators**

Design	Goal	Enrollment
RIETE registry 2001-2021	Examine the relationship between admission HR, and short-term mortality	N= 44,331 normotensive symptomatic PE patients

Primary Endpoint: 30 day, all cause and PE specific mortality

Characteristic	Admission HR, beats/min						
	< 60	60–< 80	80–< 100	100–< 110	110–< 120	120–< 140	≥ 140
No. (%) of patients	1,060 (2.4)	10,627 (24)	16,997 (38)	6,975 (16)	4,219 (9.5)	3,625 (8.2)	828 (1.9)
30-d all-cause mortality							
No. of deaths	26	305	752	474	305	302	88
Mortality, %	2.5	2.9	4.4	6.8	7.2	8.3	10.6
30-d all-cause mortality							
Model 1, unadjusted	0.54 (0.37-0.81), P < .01	0.64 (0.56-0.73), P < .001	1 [reference]	1.58 (1.40-1.77), P < .001	1.68 (1.47-1.93), P < .001	1.96 (1.71-2.26), P < .001	2.57 (2.04-3.24), P < .001
Model 2, adjusted for age and sex	0.48 (0.33-0.72), P < .001	0.61 (0.53-0.70), P < .001	1 [reference]	1.62 (1.44-1.83), P < .001	1.81 (1.58-2.08), P < .001	2.21 (1.92-2.54), P < .001	2.64 (2.08-3.34), P < .001
Model 3, adjusted for all covariates†	0.52 (0.35-0.78), P < .01	0.64 (0.56-0.74), P < .001	1 [reference]	1.51 (1.33-1.71), P < .001	1.65 (1.43-1.91), P < .001	1.85 (1.59-2.15), P < .001	2.39 (1.86-3.06), P < .001

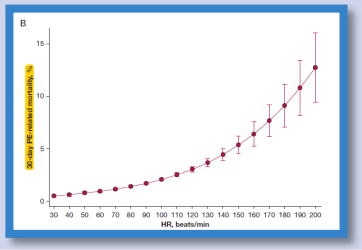

TABLE 3 Test Characteristics of the sPESI and Bova Score According to Different HR Cutoffs*

Variable	sPESI		
	HR ≥ 110 beats/min	HR ≥ 100 beats/min	HR ≥ 80 beats/min
Low-risk prevalence	34.7 (34.3-35.1)	28.7 (28.3-29.1)	12.0 (11.7-12.3)
Sensitivity	93.4 (92.3-94.4)	95.3 (94.4-96.2)	98.8 (98.2-99.2)
Specificity	36.2 (35.7-36.7)	30.0 (29.5-30.4)	11.2 (10.9-11.5)
Positive predictive value	7.3 (7.0-7.6)	6.8 (6.5-7.1)	5.0 (4.8-5.2)
Negative predictive value	99.0 (98.9-99.2)	99.2 (99.0-99.3)	99.5 (99.3-99.7)
Positive likelihood ratio	1.46 (1.45-1.48)	1.36 (1.35-1.38)	1.11 (1.11-1.12)
Negative likelihood ratio	0.18 (0.16-0.21)	0.16 (0.13-0.19)	0.11 (0.07-0.16)

Patients in the higher strata of HR levels had a higher rates of 30-day all-cause and PE-related death

CHEST 2022; 161(2):524-534

Heart Rate and Mortality in Patients With Acute Symptomatic Pulmonary Embolism

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Design

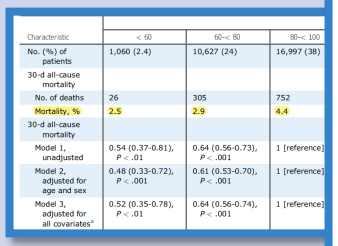
RIETE registry 2001-2021

nrollment

31 normotensive matic PE patients

Primary

ortality



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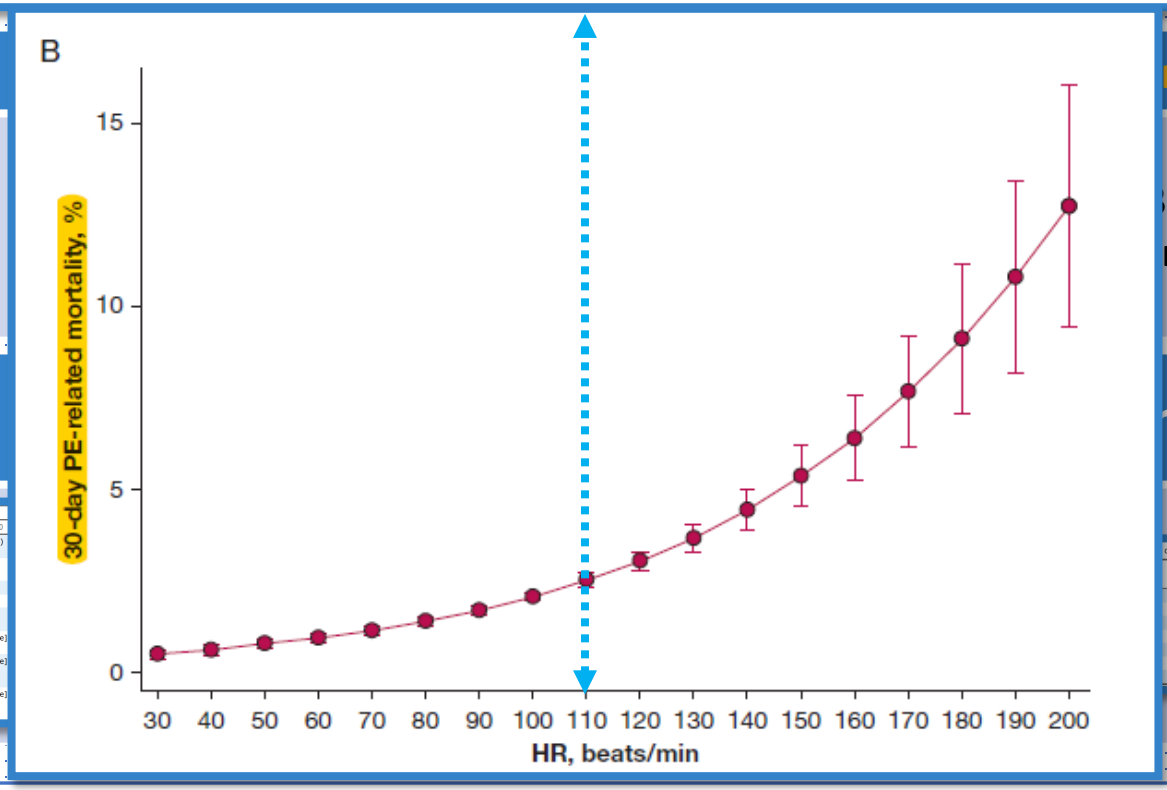

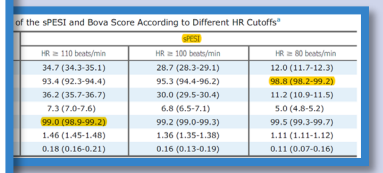

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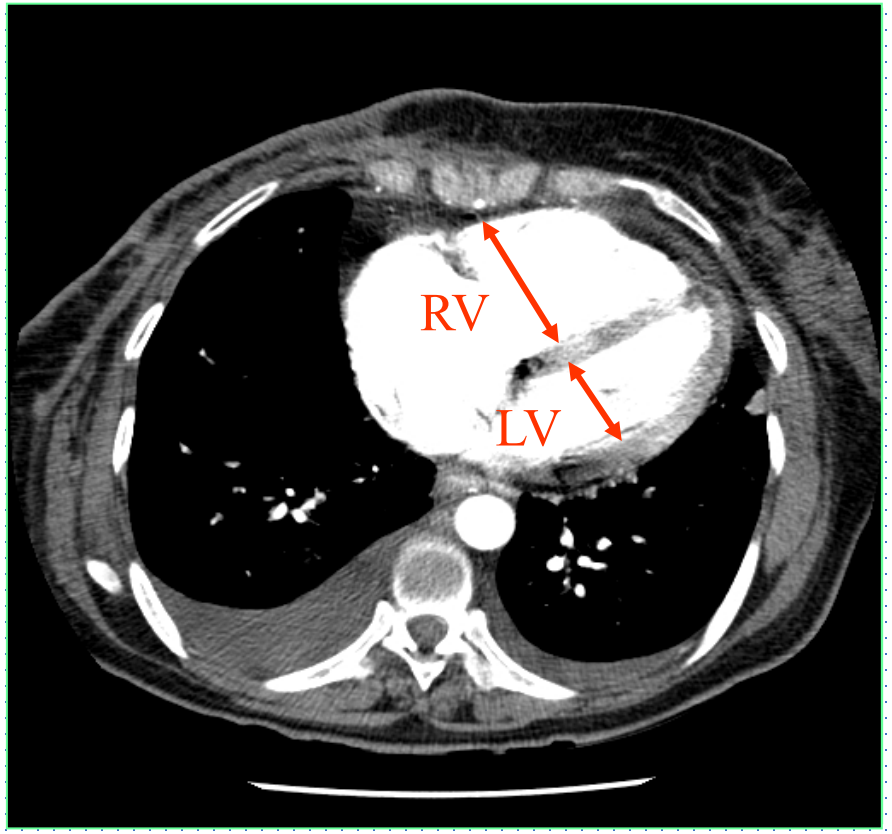
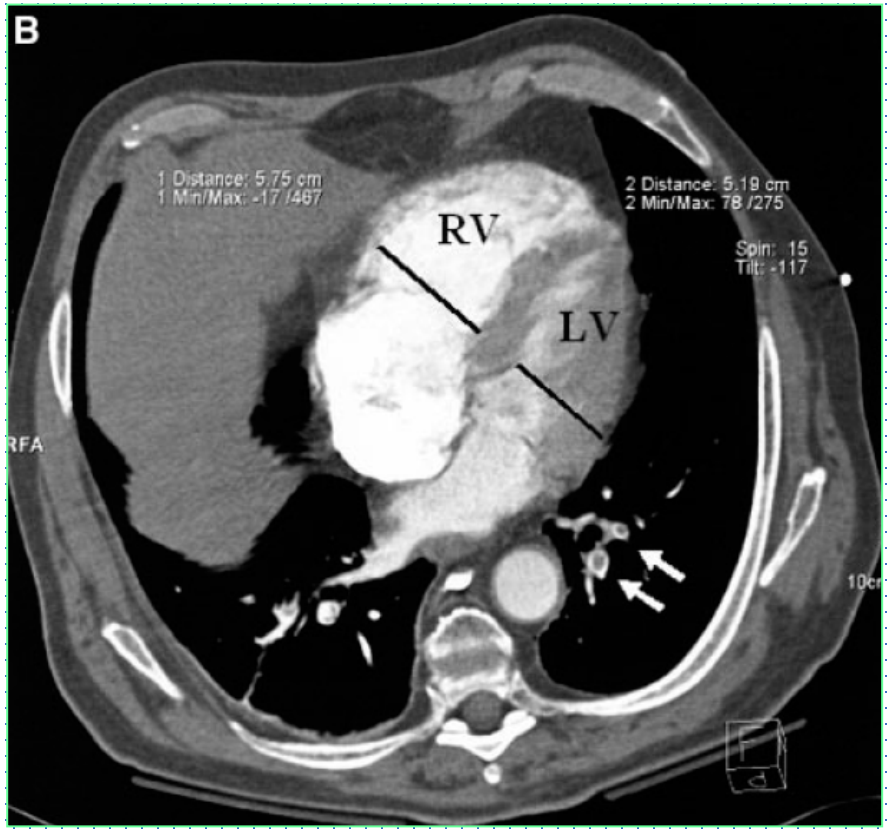
Right Ventricular Enlargement on Chest Computed Tomography

A Predictor of Early Death in Acute Pulmonary Embolism





RVD/LVD > 0.9 for predicting 30-day death:
Hazard ratio, **5.17** (1.63-16.35) *P*= 0.005

U. Joseph Schoepf et al. Circulation. 2004;110:3276-3280

CHEST

Original Research

PULMONARY EMBOLISM

Prognostic Value of Echocardiographic Right/Left Ventricular End-Diastolic Diameter Ratio in Patients With Acute Pulmonary Embolism*

Results From a Monocenter Registry of 1,416 Patients

Benoît Frémont, MD; Gérard Pacouret, MD; David Jacobi, MD; Raphaël Puglisi, MD; Bernard Charbonnier, MD; and Axel de Labriolle, MD

Sensitivity and specificity of RV/LV ratio > 0.9 for predicting hospital mortality were 72% and 58% in 1416 patients with PE

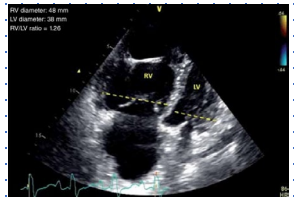


Table 3—*Multivariate Analysis for Risk Factors of In-hospital Mortality in the Study Population*

Variables	OR	95% CI	p Value
RV/LV ratio ≥ 0.9	2.66	1.68–5.99	0.01*
History of left-heart failure	8.99	3.06–26.33	< 0.0001*
Systolic arterial pressure < 90 mm Hg	10.73	3.50–32.81	< 0.0001*
Thrombolysis	1.33	0.58–3.05	0.49

*Statistically significant.

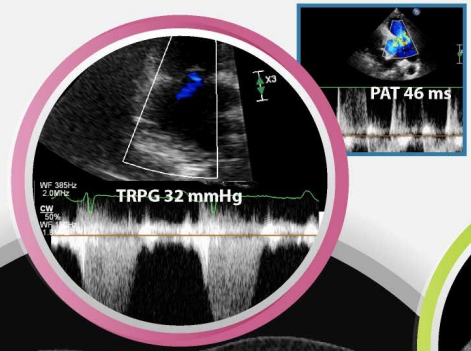
Zeng WJ, Sun YJ, Xiong CM, Gu Q, He JG. Chin Med J (Engl). 2011 Jun;124(11):1672-7. PMID: 21740775.

Right Ventricular Strain in Acute Pulmonary Embolism

60/60 Sign

Right ventricular systolic pressure (RVSP) less than 60 mmHg (using tricuspid regurgitation pressure gradient (TRPG) and CVP) and a pulmonary acceleration time (PAT) less than 60 msec

(continuous wave doppler for TRPG)

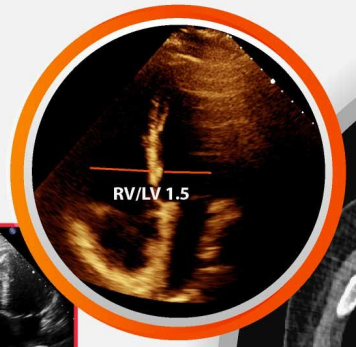


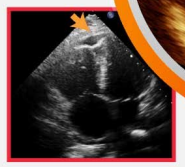
Pulse wave doppler

RV/LV > 0.9

Dilated RV with end-diastolic basal RV/LV >1, and McConnel sign

(RV focused apical 4 chamber view)

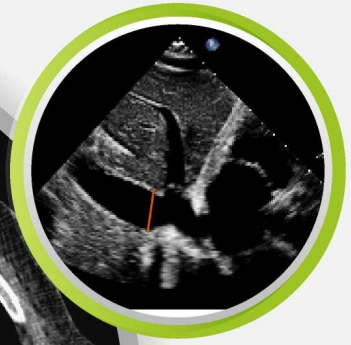




Distended IVC

Distended inferior vena cava with diminished inspiratory collapsibility/distensibility

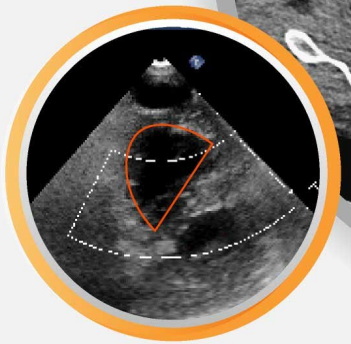
(subcostal view)



D Sign

Flattened interventricular septum due to increased RV pressure and seen in both diastole and systole

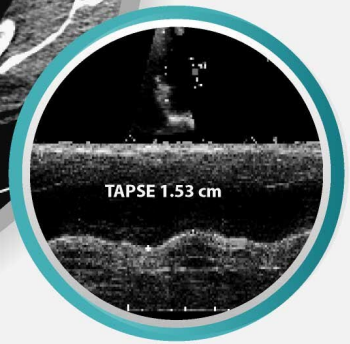
(parasternal short axis)



TAPSE <16 mm

Decreased tricuspid annular plane systolic excursion.

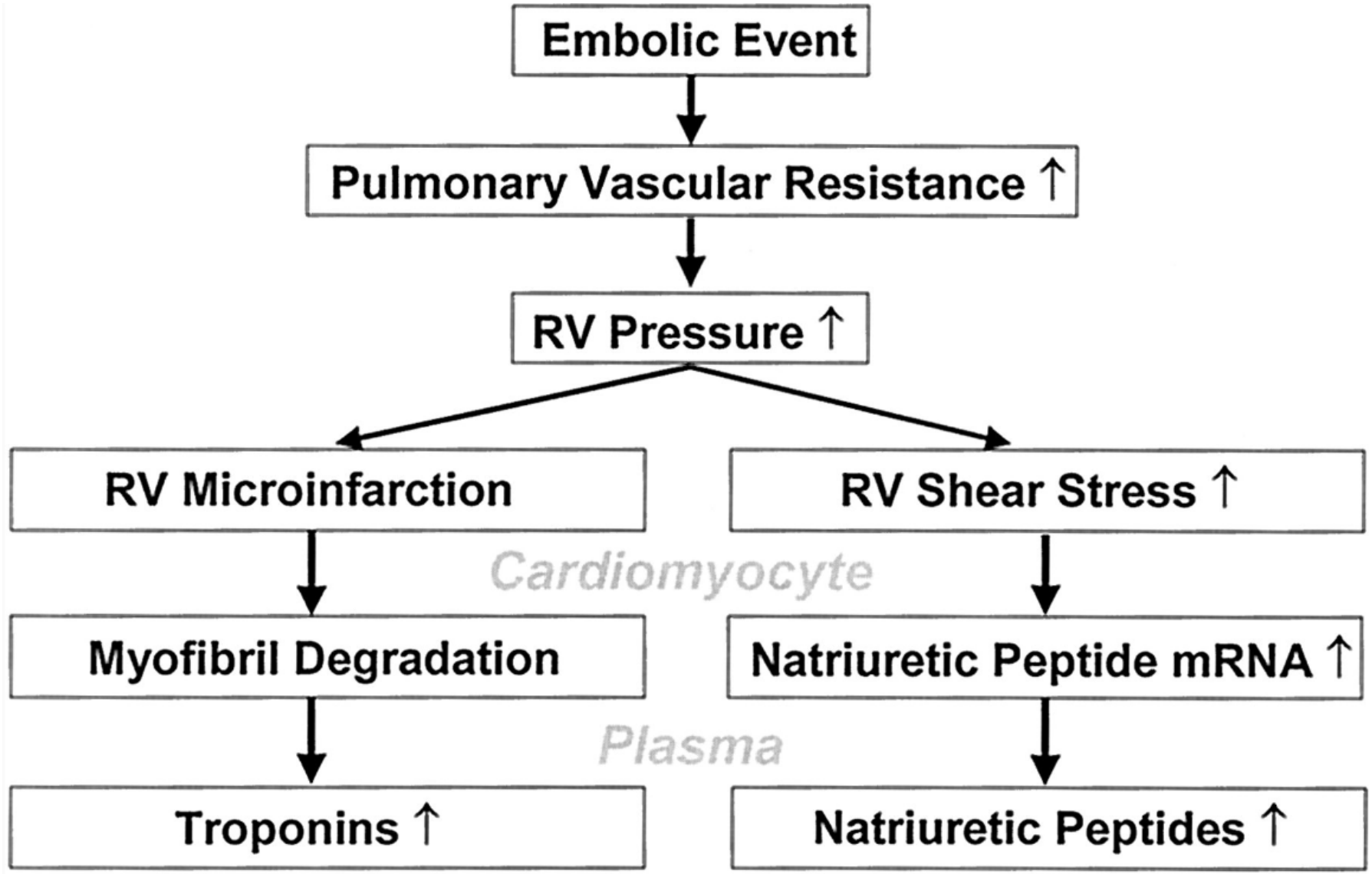
(M-mode)



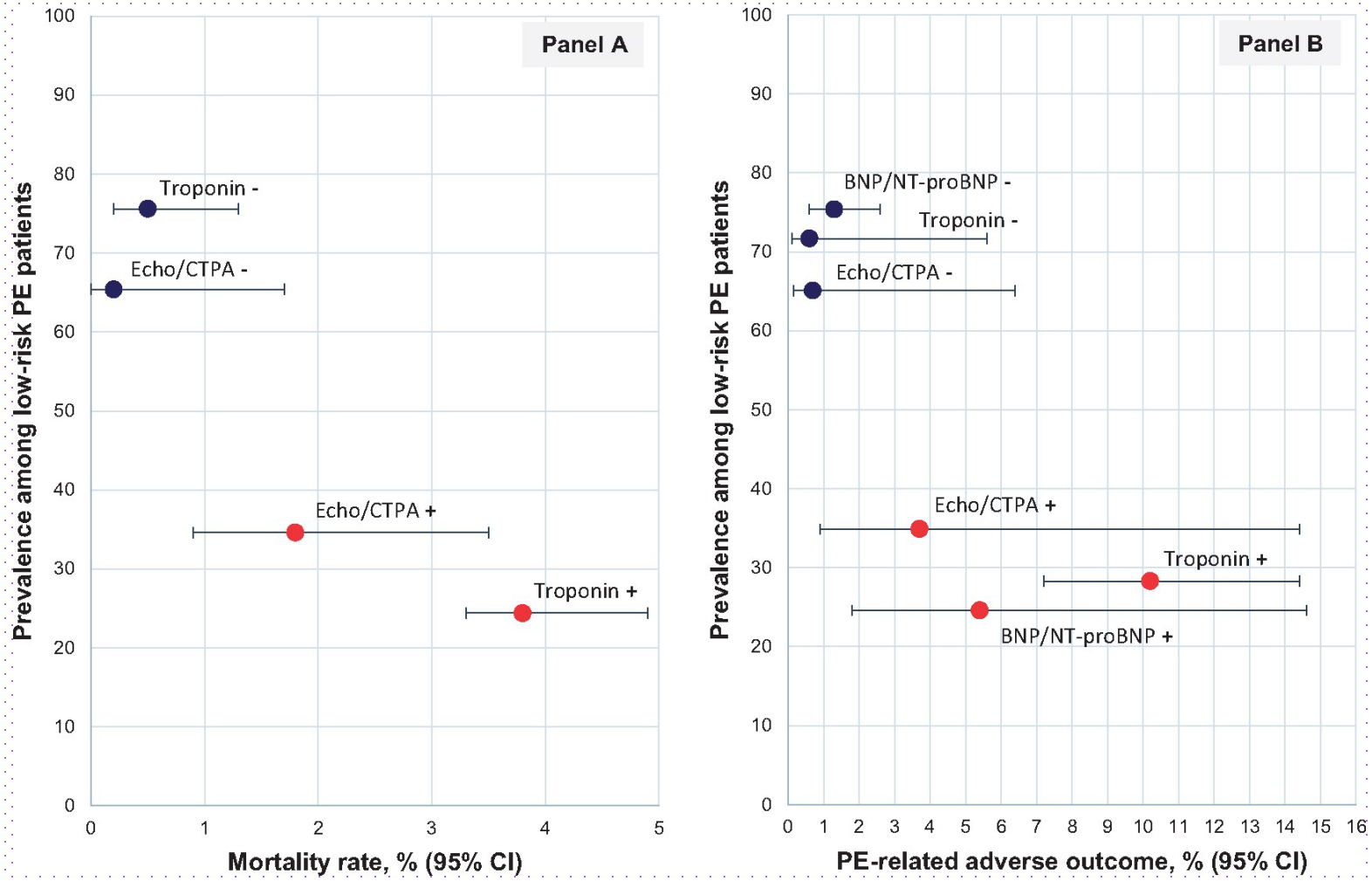
Vel S' <9.5 cm/s

Decreased peak systolic velocity of tricuspid annulus

(pulse wave Tissue Doppler imaging: TDI)


Embolic Event
Pulmonary Vascular Resistance ↑
RV Pressure ↑
RV Microinfarction
RV Shear Stress ↑
Cardiomyocyte
Myofibril Degradation
Natriuretic Peptide mRNA ↑
Plasma
Troponins ↑
Natriuretic Peptides ↑

Prognostic value of right ventricular dysfunction or elevated cardiac biomarkers in patients with low-risk pulmonary embolism: a systematic review and meta-analysis



PESI Classes I or II, PESI < 86 points, or sPESI = 0) or Hestia (all criteria absent)

Early death, hemodynamic collapse, and/or recurrent venous thromboembolism.

Barco S, Mahmoudpour SH, Planquette B, Sanchez O, Konstantinides SV, Meyer G.. Eur Heart J. 2019 Mar 14;40(11):902-910.

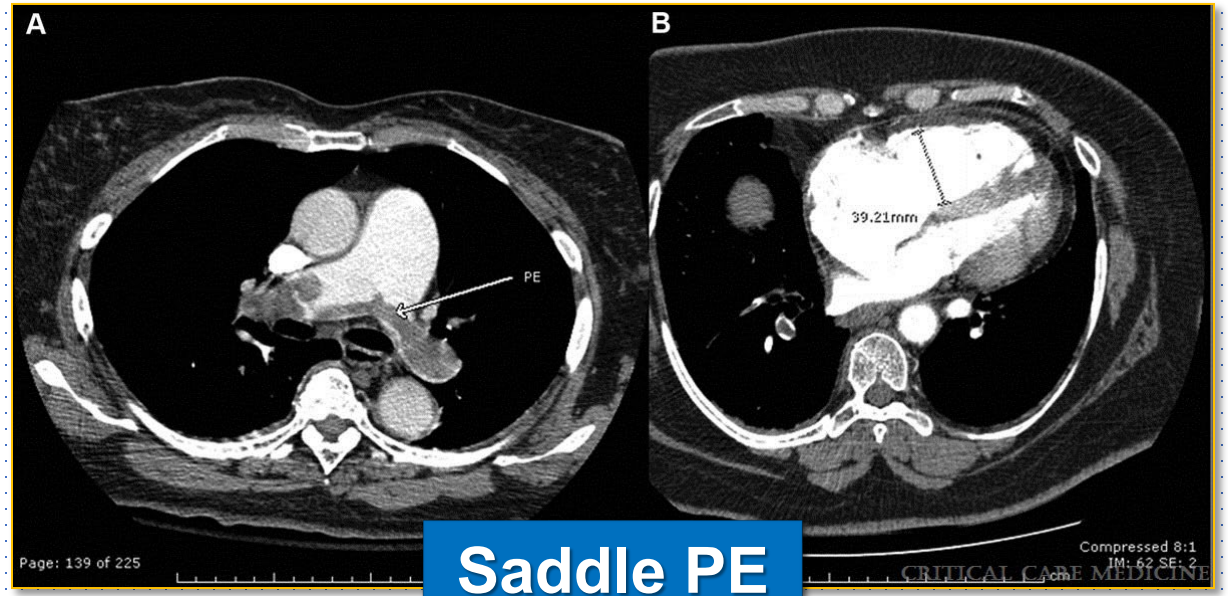
Performance of Predictors of *Negative* Outcome Tests

Diagnostic finding	Sens	Spec	PPV	NPV
RV hypokinesis on TTE	52.4	62.7	16	90.6
RV/LV diameter > 0.9 on CTA	78	38	16	92
cTnT > 0.1 ng/mL	100	57	25	98.2
BNP > 50 pg/mL	95	60	48	97
Pro-BNP > 600 ng/mL + cTnT > 0.07 ng/mL	60	89	50	93

Saddle pulmonary embolism: Is it as bad as it looks? A community hospital experience*

Alejandro Sardi, MD; Jill Gluskin, MD; Adam Guttentag, MD; Morris N. Kotler, MD; Leonard E. Braitman, PhD; Michael Lippmann, MD

Does the size matter (or NOT)?



Saddle PE
4-5%

Sardi, Alejandro; et al . Critical Care Medicine. 39(11):2413-2418, November 2011.

Clinical Investigations

Saddle pulmonary embolism: Is it as bad as it looks? A community hospital experience*

Alejandro Sardi, MD; Jill Gluskin, MD; Adam Guttentag, MD; Morris N. Kotler, MD; Leonard E. Braitman, PhD; Michael Lippmann, MD

Design	Goal	Enrollment
Retrospective evaluation	Investigate the outcomes and management of patients with saddle pulmonary embolism.	680 patients with CTA positive for PE from June 2004, to February 2009

Results

Saddle pulmonary embolism (SPE) was found in 37 of 680 patients

(5.4%)

Dyspnea **(92%)**
Leg pain/edema (43%)
Chest pain (30%)
Syncope (11%)
Mechanical ventilation (3%)
Transient hypotension (16%)
Persistent shock **(8%)**

Management and Outcome

	Number (%)
Location	
Medical ICU	9 (24)
Surgical ICU	1 (3)
Cardiac ICU	5 (14)
Intermediate care	17 (46)
General medical floor	5 (14)
Treatment	
Unfractionated heparin	32 (87)
Low molecular weight heparin	4 (11)
Inferior vena cava filter	17 (46)
Thrombolytics (Alteplase)	4 (11)
Surgical thrombectomy	1 (3)
Outcomes	
Minor bleeding	1 (3)
Major bleeding	3 (8)
In-hospital mortality	2 (5)
In-hospital length of stay (days)	9 (7)[a]

ICU, intensive care unit.
[a]Median (interquartile range).

Mortality rate is not different compared to submassive PE of around 6%

Sardi, Alejandro; et al . Critical Care Medicine. 39(11):2413-2418, November 2011.

Clinical Inv

Saddle p
hospital

Alejandro Sa
Leonard E. B

nmunity

Design

Retrospective evaluation

Enrollment

patients with CTA positive for
rom June 2004, to February
2009

Saddle pulmonary
embolism (SPE) was fo
in 37 of 680 patient

(5.4%)

anagement and Outcome

	Number (%)
Location	
Medical ICU	9 (24)
Surgical ICU	1 (3)
Cardiac ICU	5 (14)
Intermediate care	17 (46)
General medical floor	5 (14)
Treatment	
Unfractionated heparin	32 (87)
Low molecular weight heparin	4 (11)
Inferior vena cava filter	17 (46)
Thrombolytics (Alteplase)	4 (11)
Surgical thrombectomy	1 (3)
Outcomes	
Minor bleeding	1 (3)
Major bleeding	3 (8)
In-hospital mortality	2 (5)
In-hospital length of stay (days)	9 (7)[a]

ICU, intensive care unit.
[a]Median (interquartile range).

Mortality rate is not different compared to submassive PE of around 6%

Sardi, Alejandro; et al . Critical Care Medicine. 39(11):2413-2418, November 2011.

Impact of Pulmonary Arterial Clot Location on Pulmonary Embolism Treatment and Outcomes (90 Days)

C. Charles Jain, MD[a,*], Yuchiao Chang, PhD[a], Christopher Kabrhel, MD, MPH[b], Jay Giri, MD, MPH[c], Richard Channick, MD[d], Josanna Rodriguez-Lopez, MD[d], Rachel P. Rosovsky, MD[e], Annemarie Fogerty, MD[e], Kenneth Rosenfield, MD[f], Michael R. Jaff, DO[f], and Ido Weinberg, MD[f]

Does the clot location matter, peripheral vs central?

Variable	Total	Central	Peripheral	P value
Therapy				
Anticoagulation Alone	163/269 (60.6%)	96/172 (55.8%)	67/97 (69.1%)	0.03
Inferior Vena Cava Filter	62/253 (24.5%)	42/163 (25.8%)	20/90 (22.2%)	0.53
Systemic Thrombolysis	15/257 (5.8%)	11/166 (6.6%)	4/91 (4.4%)	0.47
Catheter-Directed Thrombolysis	33/254 (13.0%)	30/164 (18.3%)	3/90 (3.3%)	<0.001
Suction Thrombectomy	2/253 (0.8%)	1/163 (0.6%)	1/90 (1.1%)	0.67
Extracorporeal Membrane Oxygenation	7/254 (2.8%)	6/163 (3.7%)	1/91 (1.1%)	0.23
Surgical Embolectomy	11/253 (4.3%)	7/163 (4.3%)	4/90 (4.4%)	0.96
Outcomes*				
Mortality within 1 day	9/269 (3.3%)	4/172 (2.3%)	5/97 (5.2%)	0.22
Mortality within 3 days	13/269 (4.8%)	7/172 (4.1%)	6/97 (6.2%)	0.44
Mortality within 7 days	18/266 (6.8%)	10/170 (5.9%)	8/96 (8.3%)	0.44
Mortality within 30 days	32/254 (12.6%)	15/162 (9.3%)	17/92 (18.5%)	0.03
Mortality within 90 days	43/240 (17.9%)	21/155 (13.5%)	22/85 (25.9%)	0.02
Right Ventricular Strain on Imaging during day 31-90	16/209 (7.7%)	14/140 (10.0%)	2/69 (2.9%)	0.07
Composite Outcome†	57/240 (23.8%)	33/155 (21.3%)	24/85 (28.2%)	0.23

Reevaluation of practice is thus warranted!

Jain CC, Chang Y, Kabrhel C, Giri J, Channick R, Rodriguez-Lopez J, Rosovsky RP, Fogerty A, Rosenfield K, Jaff MR, Weinberg I. Impact of Pulmonary Arterial Clot Location on Pulmonary Embolism Treatment and Outcomes (90 Days). Am J Cardiol. 2017 Mar 1;119(5):802-807.

Risk Stratification

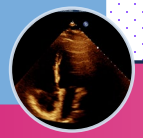
Early mortality risk		Indicators of risk			
		Hemodynamic instability	Clinical parameters of PE severity and/or comorbidity: PESI class III-V or sPESI ≥1	RV dysfunction on TTE or CTA	Elevated cardiac troponin (or BNP levels)
High		+	(+)	+	(+)
Intermediate	High	-	+	+	+
	Low	-	(+)	+	-
	Low	-	(+)	-	+
	Low	-	+	-	-
Low		-	-	-	Optional (-)

(+): can be negative

Thrombolytic Therapy for Selected Patients

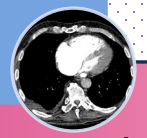
- Persistent hypotension or shock despite adequate resuscitation

Hemodynamic Instability



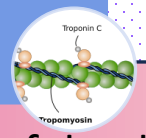
- RV/LV ratio ≥1, bulging of the RV septum into the LV, reduced RV EF
- Contrast observed in the liver
- Absence of comorbidities that affect RV function

New or worsening RV dysfunction



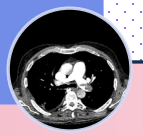
- Elevated biomarkers, including troponin and BNP

Myocardial necrosis



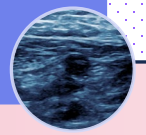
- >70% perfusion deficit on V/Q scan
- Extensive embolic burden on chest CT

A high clot burden?



- Proximal deep venous thrombosis in the lower extremities

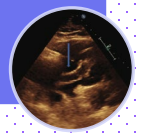
DVT



Increasing risk of death

- Clot-in-transit
- Thrombus in inferior vena cava,
- Right atrium, RV, or left atrium [+PFO]

Right-sided cardiac thrombus

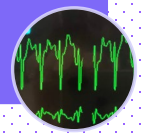


- Significant hypoxemia (eg, <90%) and/or respiratory distress

Oxygenation

- >120 beats per minute

Tachycardia



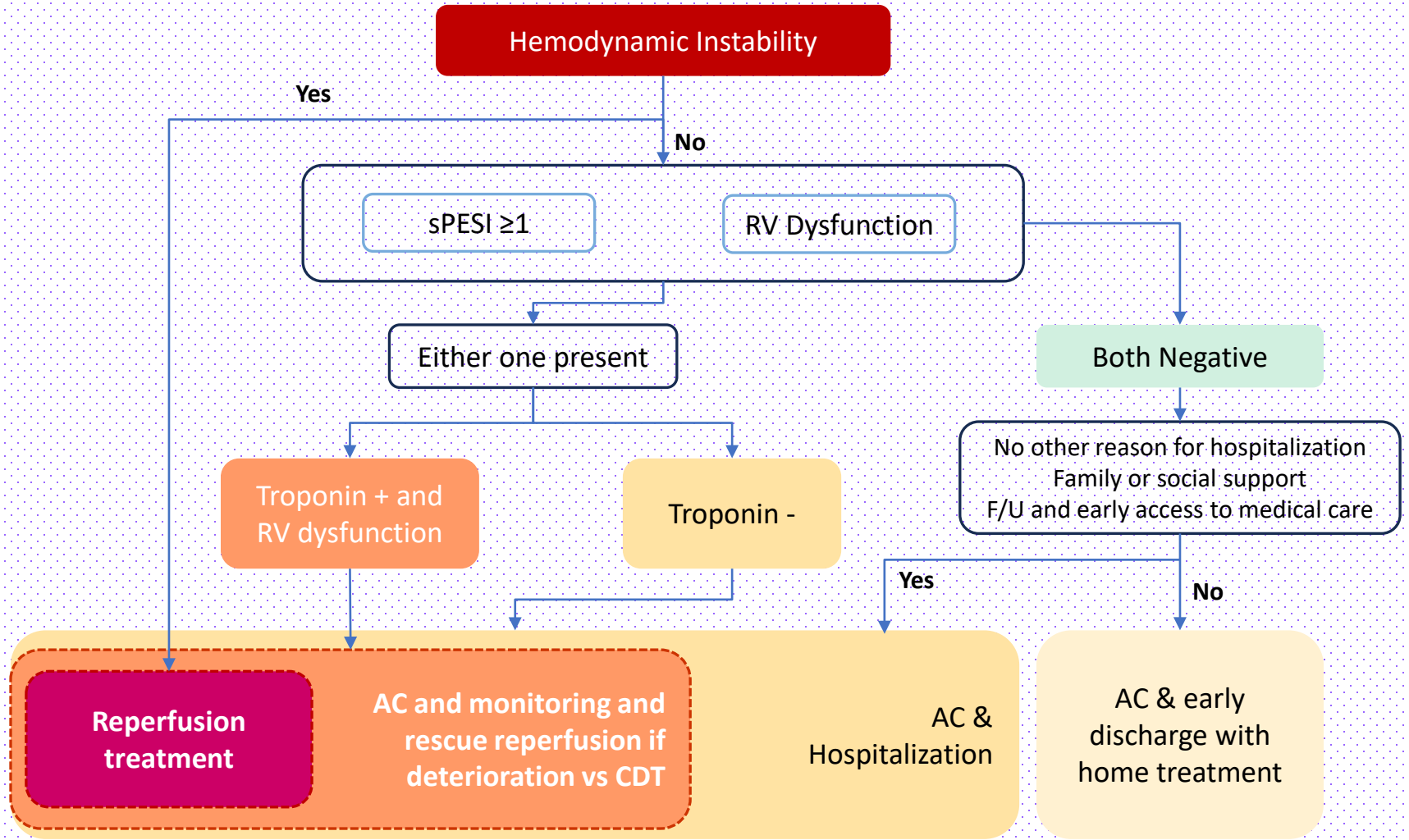
- Poor cardiopulmonary reserve

Comorbidity

- sPESI ≥1

Scoring Systems

Risk-adjusted Management Strategy for Acute Pulmonary Embolism.

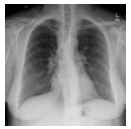
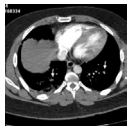


Eur Heart J, Volume 41, Issue 4, 21 January 2020, Pages 543–603

Should Subsegmental PE be Anticoagulated?

47-year-old woman with PMH of anemia and HTN who presented to ER with mild exertional dyspnea for 2 days. One week prior to presentation, she had sustained minor knee contusions and ecchymoses from a ground-level fall. No other PE risk factors.

Hemodynamics	**Clinical Parameters**	**RV Dysfunction**	**Biomarkers**
BP 117/86	RR 18/min, HR 87/min, and SpO2 100% on room air sPESI =0	RV/LV <1 on CTA	D-dimers: ↑ 632 ng/mL

CXR	**CTA**	**LE US**	**Echocardiogram**
		No DVT	Not done

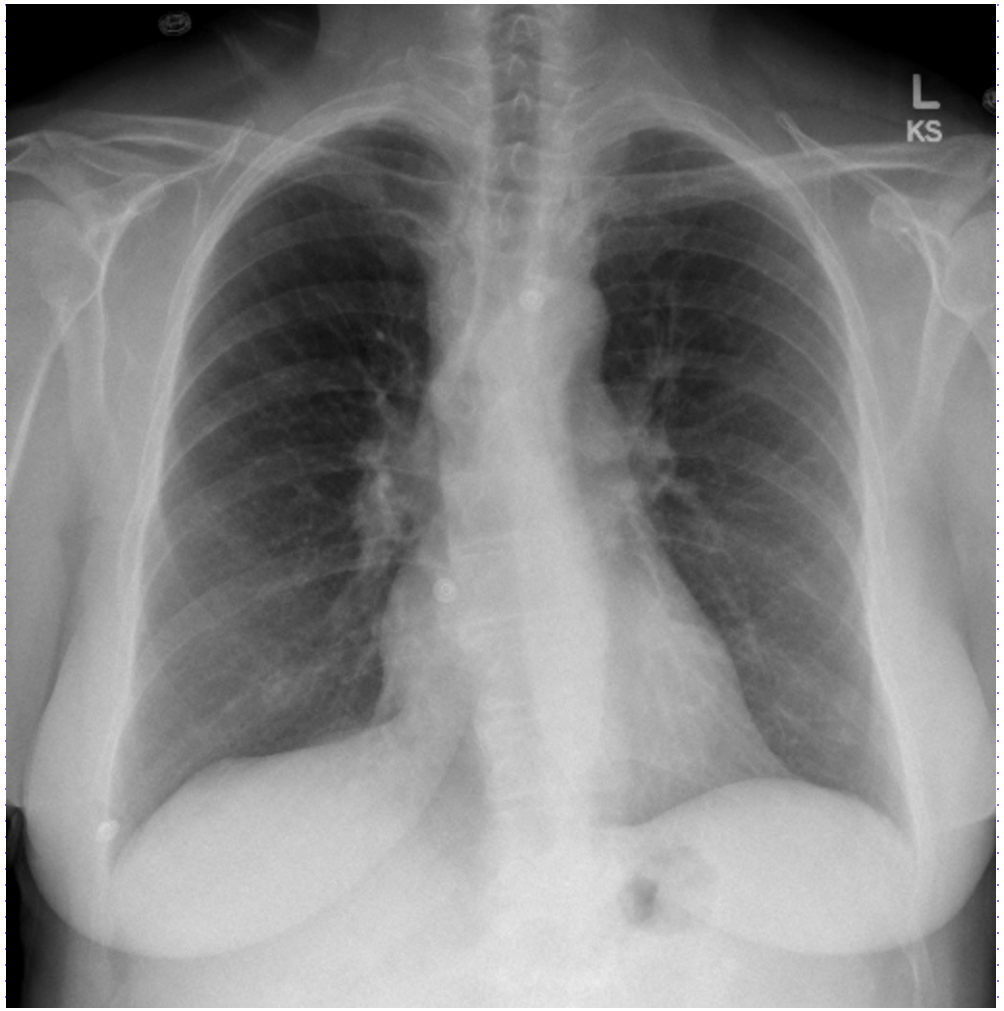
Risk of Death				**Risk of Bleeding**		
Low	Intermediate Low	Intermediate High	High	Low	Intermediate	High

Management						
Surveillance without anticoagulation	Anticoagulation	Systemic Thrombolysis Primary – Rescue – Reduced	Catheter-directed Thrombolysis	Catheter-directed Embolectomy	Surgical Embolectomy	IVC Filter

Disposition		
Home & F/U	Monitored Bed	ICU

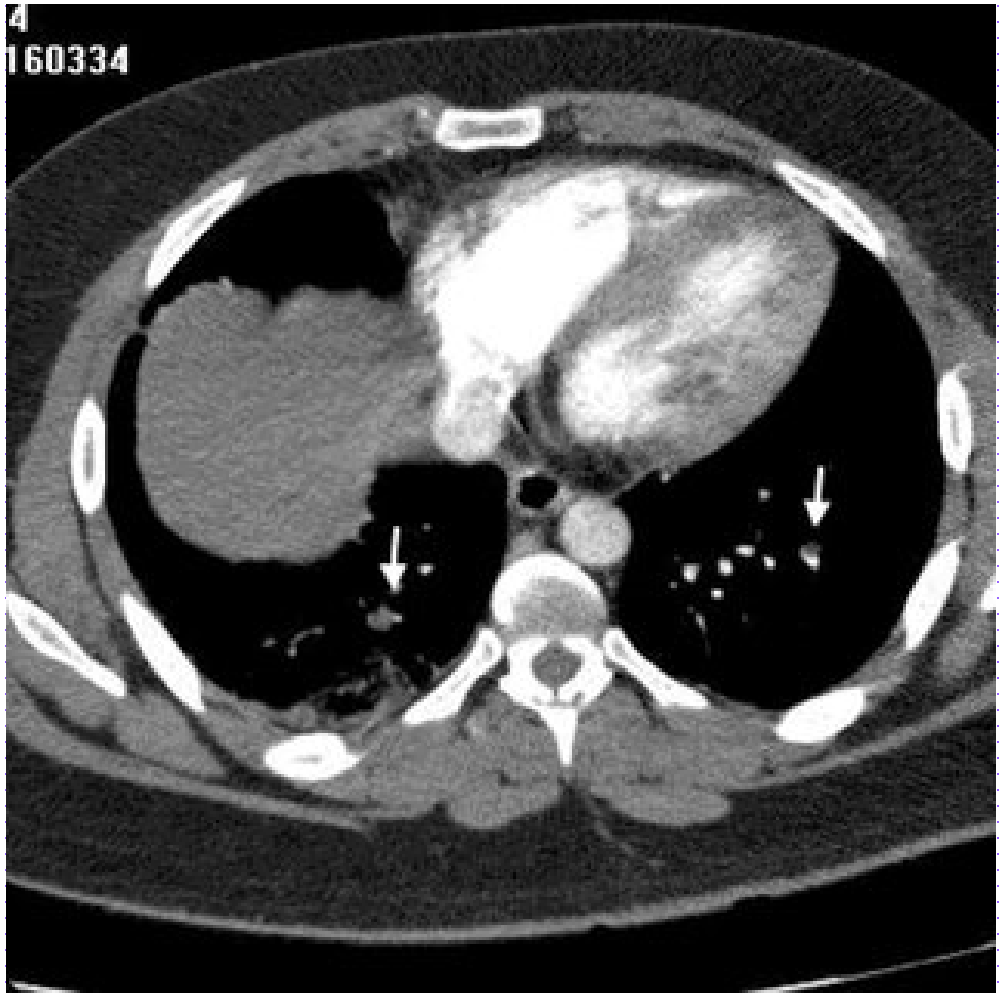
Vinson DR, Isaacs DJ, Taye E, Balasubramanian MJ. Challenges in Managing Isolated Subsegmental Pulmonary Embolism. Perm J. 2021 Dec 3;25:21.077.

Should Subsegmental PE be Anticoagulated?



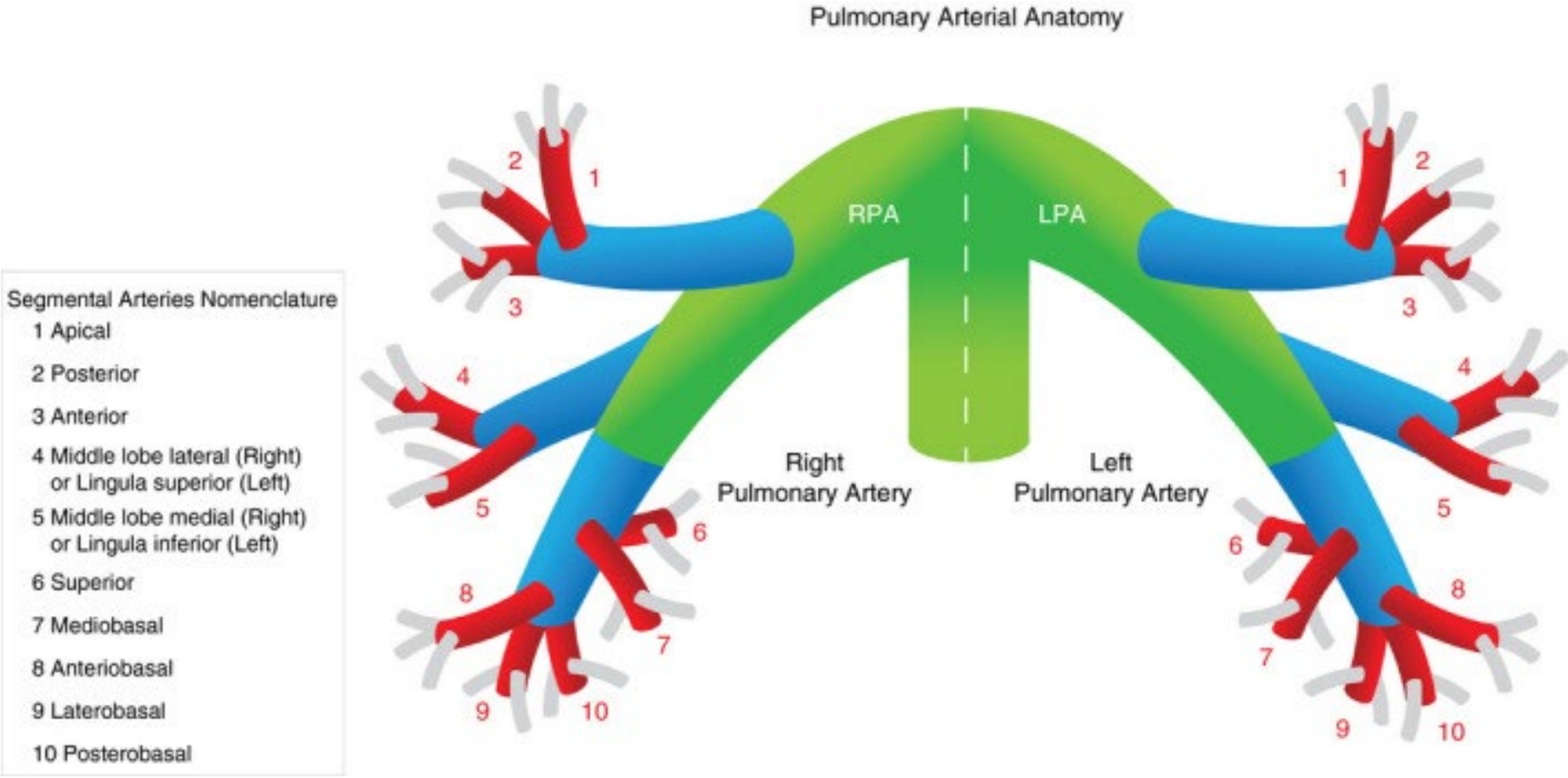
Vinson DR, Isaacs DJ, Taye E, Balasubramanian MJ. Challenges in Managing Isolated Subsegmental Pulmonary Embolism. Perm J. 2021 Dec 3;25:21.077.

Should Subsegmental PE be Anticoagulated?



Vinson DR, Isaacs DJ, Taye E, Balasubramanian MJ. Challenges in Managing Isolated Subsegmental Pulmonary Embolism. Perm J. 2021 Dec 3;25:21.077.

Subsegmental Arteries



den Exter PL, Kroft LJM, Gonsalves C, Le Gal G, Schaefer-Prokop CM, Carrier M, Huisman MV, Klok FA. Establishing diagnostic criteria and treatment of subsegmental pulmonary embolism: A Delphi analysis of experts. Res Pract Thromb Haemost. 2020 Oct 1;4(8):1251-1261.

Challenging Questions in Subsegmental PE!

Are the radiologic findings truly positive?

Is it a physiologic lung clearing process?

Is it a clinically more benign form of PE?

Is anticoagulation necessary?

Is outpatient management appropriate?

Is the patient agreeable with the treatment and follow-up plans (structured surveillance)*?

***Structured surveillance entails repeat bilateral compression ultrasonography in 5-7 days to evaluate for proximal lower-extremity deep vein thrombosis with close outpatient follow-up to monitor for emerging signs and symptoms of venous thromboembolism**

"low-certainty evidence"

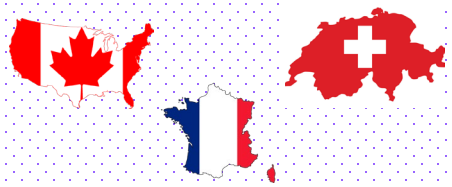
Characteristics that favor structured surveillance without anticoagulation in clinically stable outpatient adults with acute pulmonary embolism isolated to the subsegmental pulmonary arteries

Characteristics	CHEST guideline and expert panel reports (2016/2021)	European Society of Cardiology guidelines (2019)	Multispecialty panel of experts in Delphi consensus study (2020
No active cancer	√	√	√
No major risk for VTE recurrence	√		√
No current DVT (proximal)	√	√	√
No pregnancy			√
No marked PE related symptoms	√		
Normal cardiopulmonary reserve	√		
Only single subsegmental PE		√	

Anticipated Trials

SSPE

A Study to Evaluate the Safety of Withholding Anticoagulation in Patients With Subsegmental PE Who Have a Negative Serial Bilateral Lower Extremity Ultrasound



SAFE-SSPE

Clinical Surveillance vs. Anticoagulation for Low-risk Patients With Isolated Subsegmental Pulmonary Embolism

STOPAPE

STOPping Anticoagulation for Isolated or Incidental Subsegmental Pulmonary Embolism

Pm-CARD for Anticoagulation in Subsegmental PE

Cancer: **Active**

Multiple

Recurrence risk **DVT**

Vinson DR, Isaacs DJ, Taye E, Balasubramanian MJ. Challenges in Managing Isolated Subsegmental Pulmonary Embolism. Perm J. 2021 Dec 3;25:21.077.

modified

Is outpatient Treatment of Low-risk Pulmonary Embolism Safe?

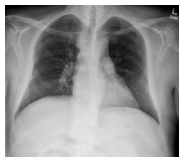
58-year-old male with PMH of hypertension and hyperlipidemia who presented with a 5-day history of pain and swelling in the right lower extremity and developed sudden onset of shortness of breath for 2 days. Recent history of a 9-hour travel between two states. No other risk factors for VTE.

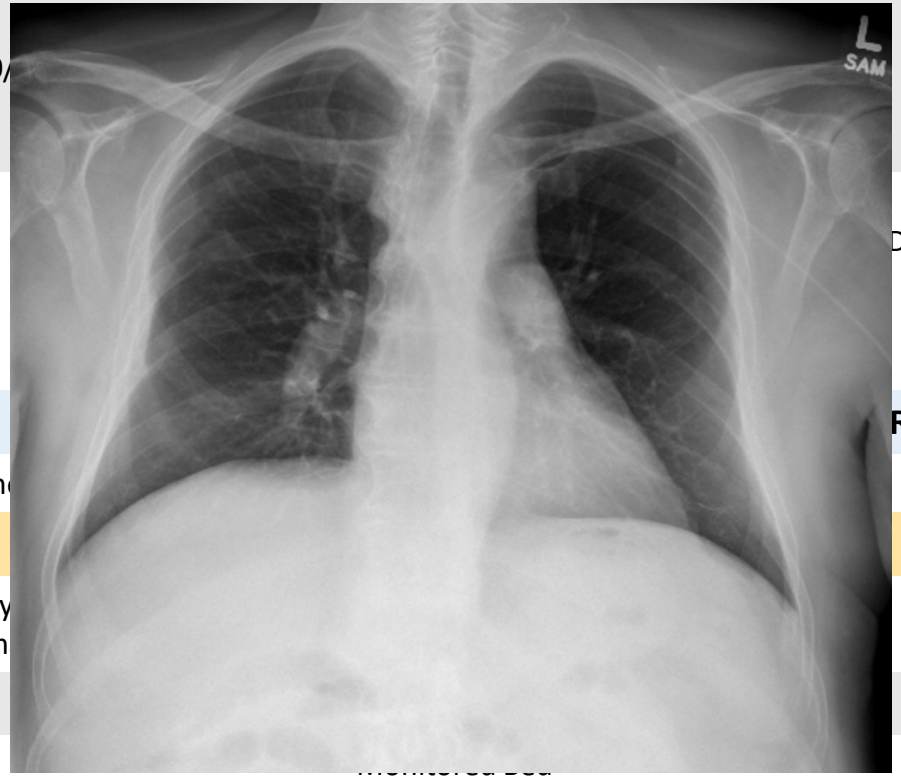
Hemodynamics
BP 132/78

RR 20/

Biomarkers
D-dimers: normal
Normal Troponin and BNP

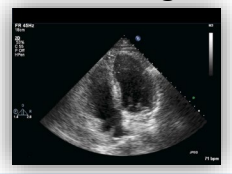
CXR





DVT in

Echocardiogram

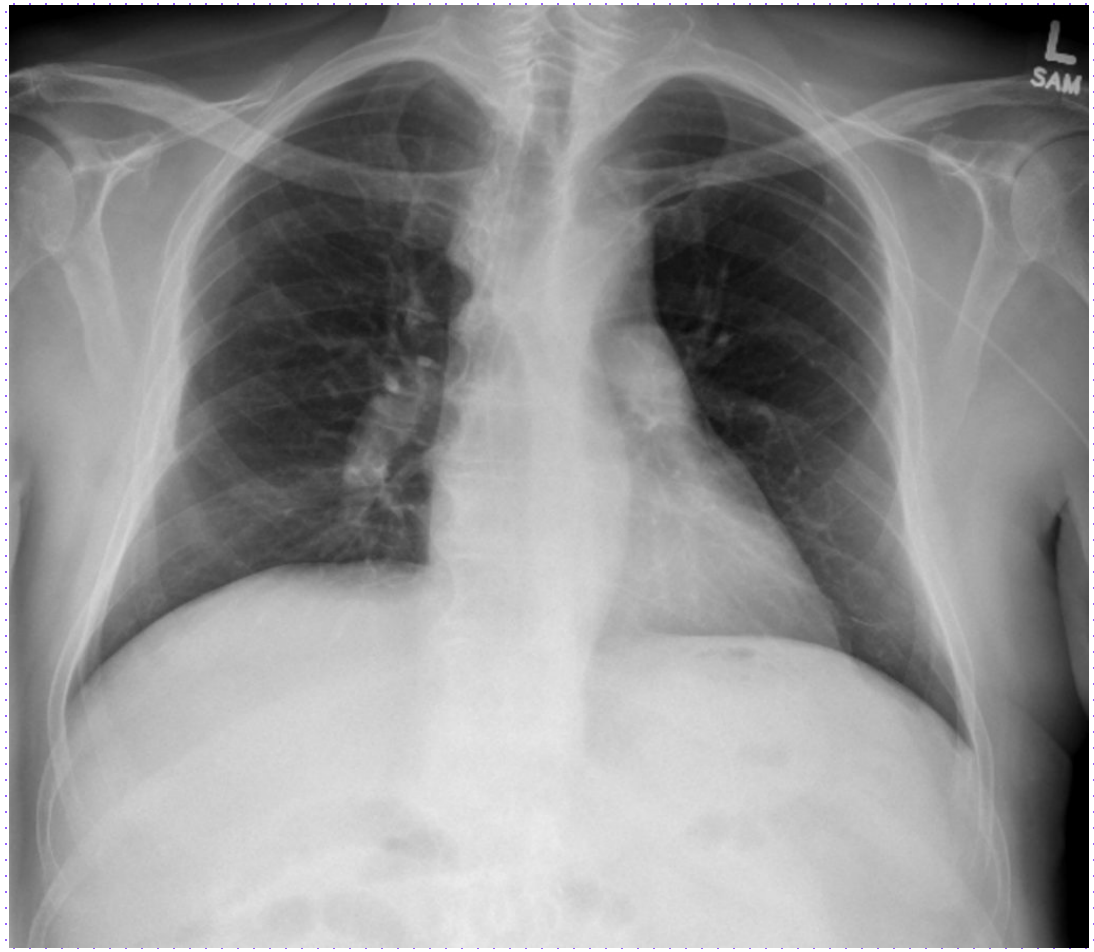


Risk of Death

Risk of Bleeding

Low	Intermediate Low	Interm		Intermediate	High
Surveillance without anticoagulation	Anticoagulation	Sy Prim		Surgical Embolectomy	IVC Filter
	Home & F/U			ICU	

Is outpatient Treatment of Low-risk Pulmonary Embolism Safe?

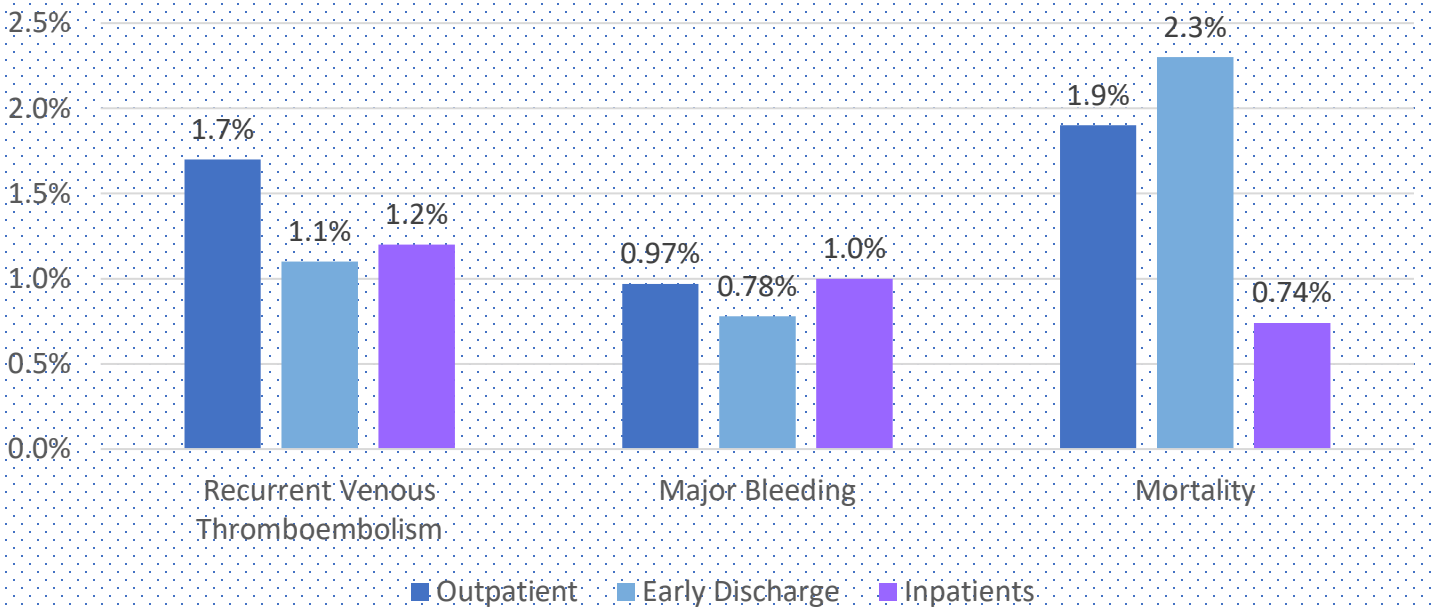


Courtesy of Dr. Talal Dahhan

Outpatient *versus* inpatient treatment in patients with pulmonary embolism: a meta-analysis

Wendy Zondag[1], Judith Kooiman[1], Frederikus A. Klok[1], Olaf M. Dekkers[2] and Menno V. Huisman[1]

Affiliations:
[1]Dept of Thrombosis and Haemostasis, LUMC, Leiden, and
[2]Dept of Epidemiology, LUMC, Leiden, The Netherlands.



15 studies of patients with low-risk PE revealed that home treatment or early discharge of selected low-risk patients with pulmonary embolism is as safe as inpatient treatment.

Zondag W, Kooiman J, Klok FA, Dekkers OM, Huisman MV. Outpatient versus inpatient treatment in patients with pulmonary embolism: a meta-analysis. Eur Respir J. 2013 Jul;42(1):134-44

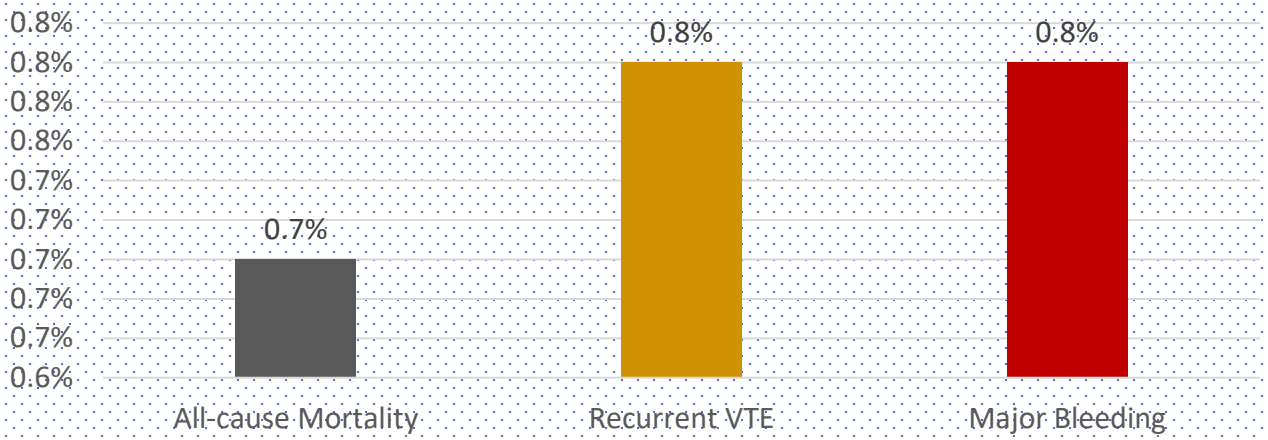
Academic Emergency Medicine
A GLOBAL JOURNAL OF EMERGENCY CARE

Systematic Reviews (With or Without Meta-analyses) | Free Access

Outpatient Treatment of Low-risk Pulmonary Embolism in the Era of Direct Oral Anticoagulants: A Systematic Review

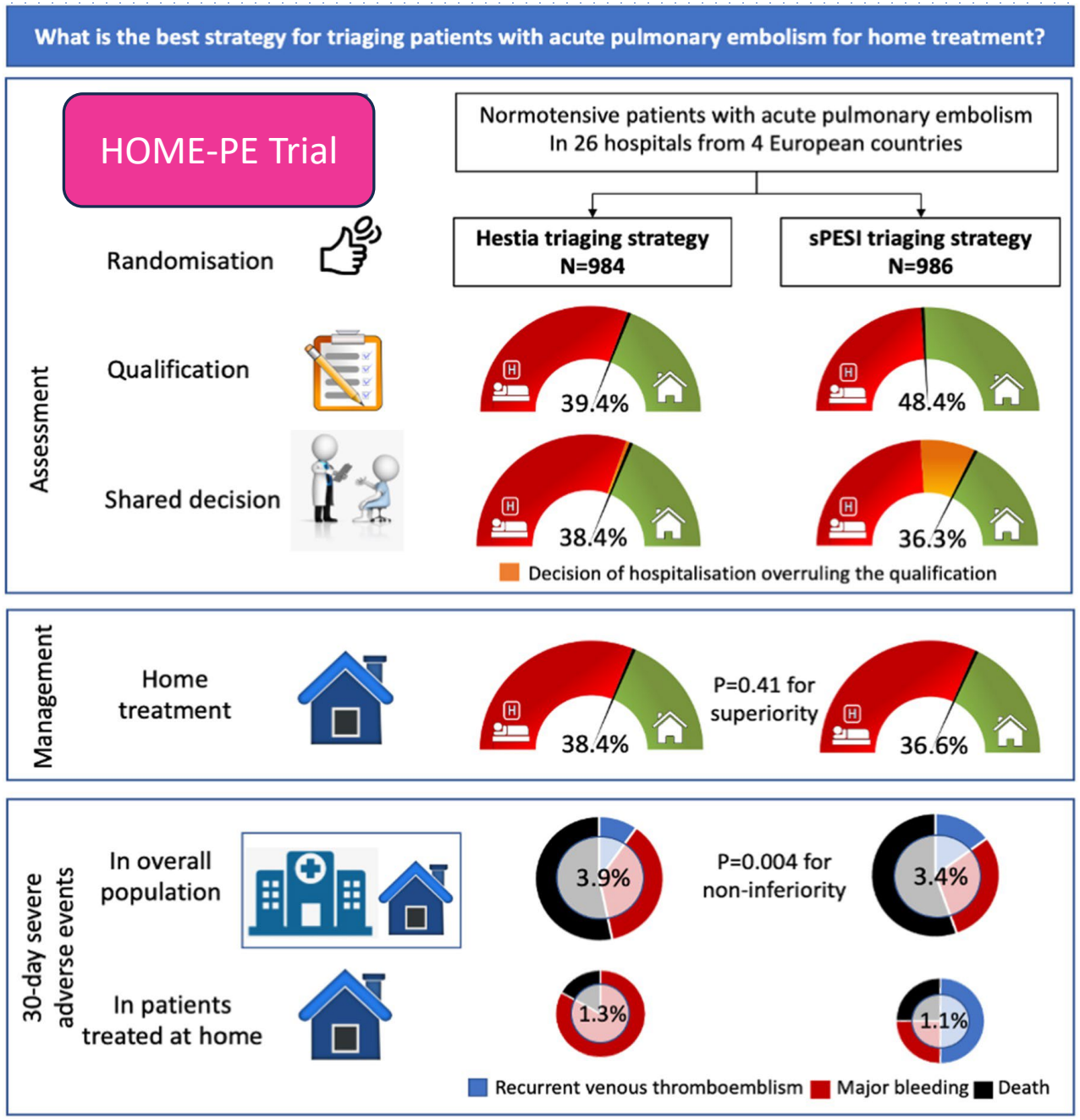
Brandon C. Maughan MD, Lisa Frueh, Marian S. McDonagh PharmD, Bryan Casciere PharmD, Jeffrey A. Kline MD

Epub 2020 Sep 20.



Among 3,191 patients in 12 studies (four RCT, eight NRT) with low-risk PE treated as outpatients, few patients experienced major adverse outcomes such as mortality, recurrent VTE, or major bleeding within 90 days

Maughan BC, Frueh L, McDonagh MS, Casciere B, Kline JA. Outpatient Treatment of Low-risk Pulmonary Embolism in the Era of Direct Oral Anticoagulants: A Systematic Review. Acad Emerg Med. 2021 Feb;28(2):226-239.



Eur Heart J, Volume 42, Issue 33, 1 September 2021, Pages 3146–3157

Criteria for Early Discharge or Home Treatment

The risk of early PE-related death or serious complications is low

- sPESI = 0 or PESI class I or II
- Heart rate <100 beats/min
- No RV dysfunction
- Negative troponin and NT-proBNP value <500 pg/mL

There is no serious comorbidity or aggravating condition(s) that would mandate hospitalization

Proper outpatient care and anticoagulant treatment can be provided, considering the patient's (anticipated) compliance, and the possibilities offered by the healthcare system and social infrastructure

modified

Intermediate Low-risk PE

72-year-old-male, COPD, CAD, and on home oxygen of 4 L/min at rest. Presented with worsening shortness of breath and chest tightness for the past two days. No pain or swelling in the lower extremities. No fever, chills, or cough.

Hemodynamics
BP 136/59-HR 78/min

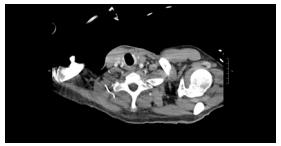
Clinical Parameters
RR 24/min and SpO2 82% on RA improved to 91% on HFNC
sPESI =2

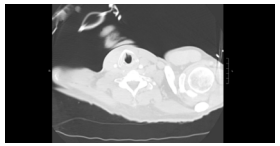
RV Dysfunction
RV/LV >1 on Echo

Biomarkers
Troponin normal,
BNP 52 ng/mL

CXR

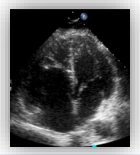
CTA





LE US
Negative

Echocardiogram



Risk of Death

Low | **Intermediate Low** | Intermediate High | High

Risk of Bleeding

Low | Intermediate | High

Management

Surveillance without anticoagulation | **Anticoagulation** | Systemic Thrombolysis Primary – Rescue – Reduced | Catheter-directed Thrombolysis | Catheter-directed Embolectomy | Surgical Embolectomy | IVC Filter

Disposition

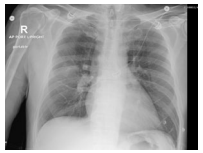
Home & F/U | **Monitored Bed** | ICU

Obstructive Shock PE

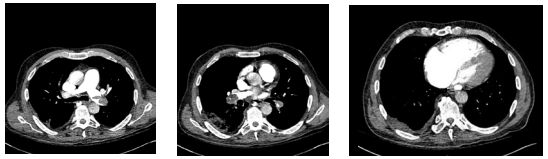
57-year-old male who is a smoker with no other significant PMH who presented to the ER with shortness of breath, hypoxemia, tachycardia, and hypotension. Predisposing factor to VTE/PE–unclear. Patient has an active lifestyle.

Hemodynamics	Clinical Parameters	RV Dysfunction	Biomarkers
BP 82/60 HR 135/min LA 4.3 mmol/L	SpO2 73% on room air sPESI =3	RV/LV 2:1 on CTA	D-dimer >20µg/mL, BNP 940 ng/mL, Troponin 0.45 ng/mL

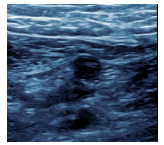
CXR



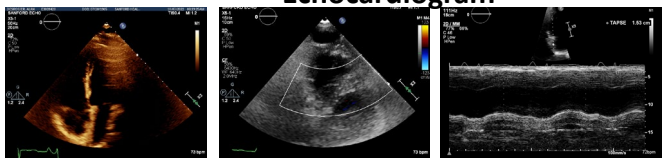
CTA



LE US (-)



Echocardiogram



Risk of Death				Risk of Bleeding		
Low	Intermediate Low	Intermediate High	**High**	**Low**	Intermediate	High

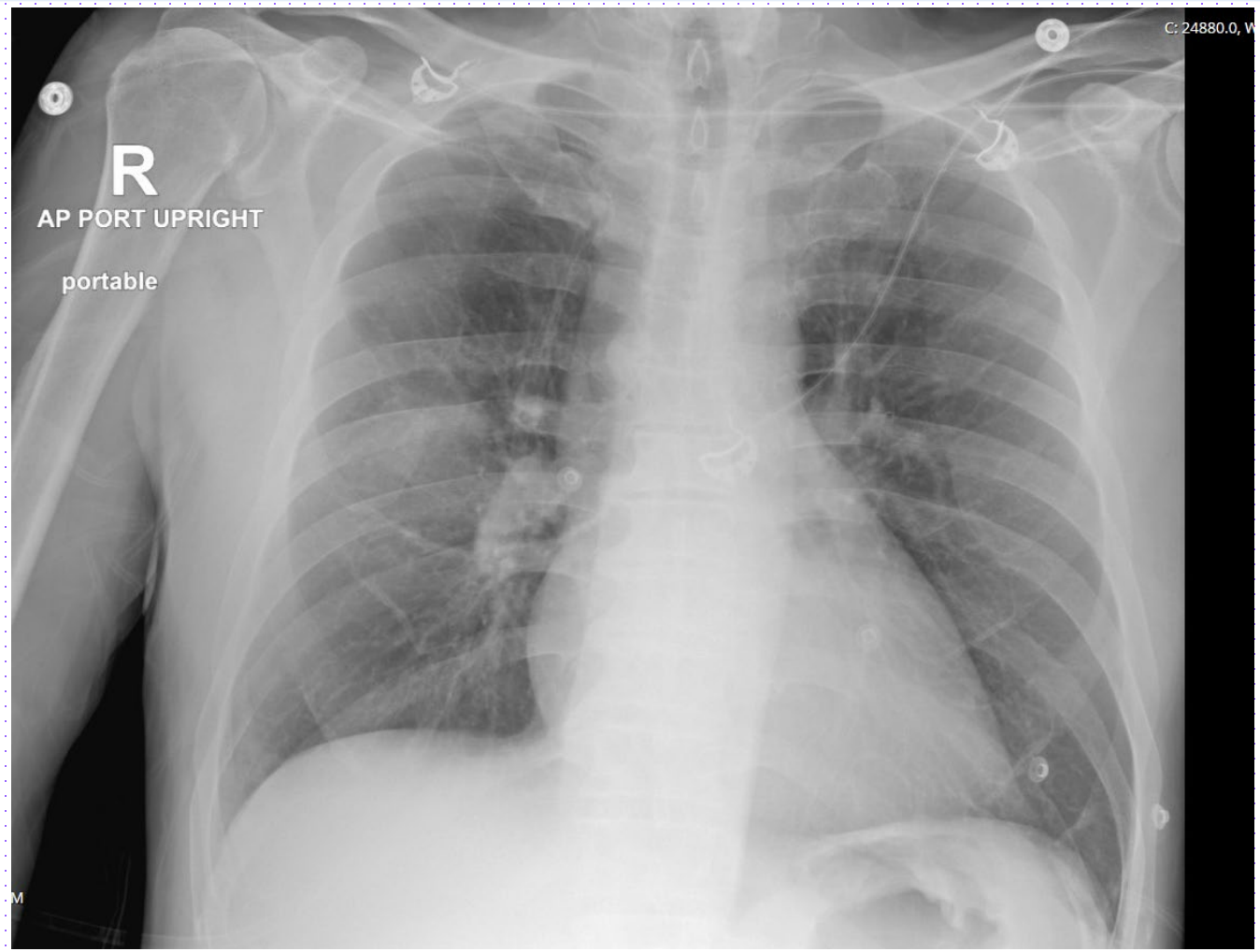
Management

Surveillance without anticoagulation	Anticoagulation	Systemic Thrombolysis Primary – ~~Rescue~~ – Reduced	Catheter-directed Thrombolysis	Catheter-directed Embolectomy	Surgical Embolectomy	IVC Filter

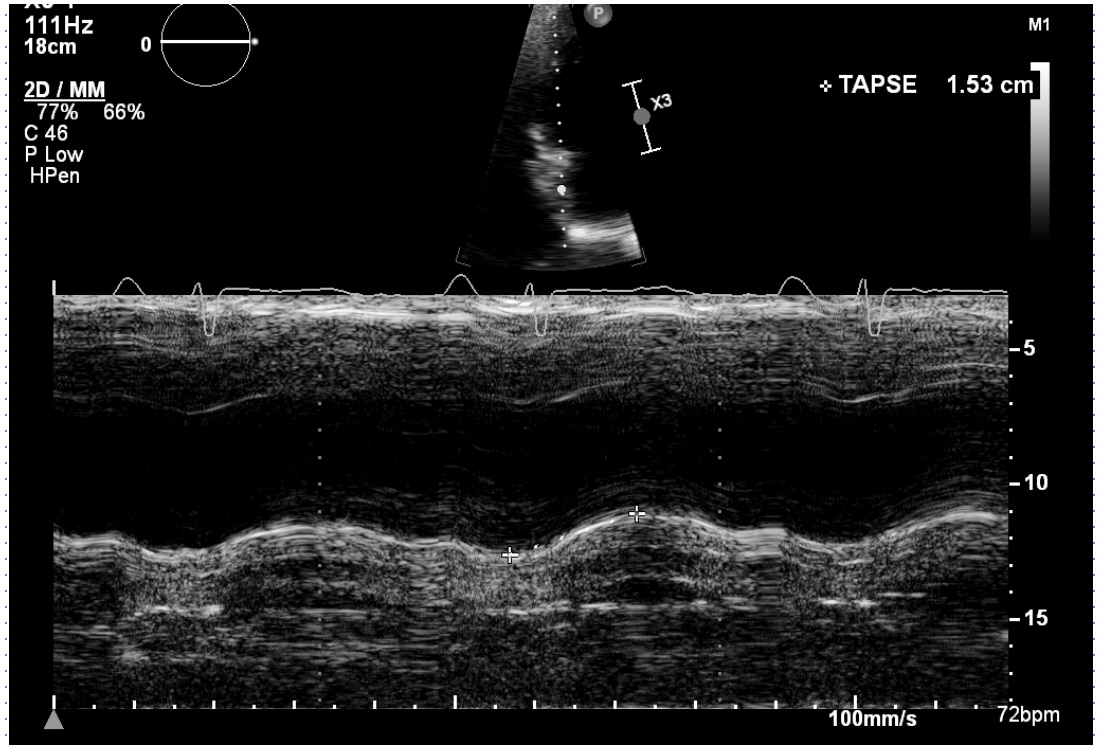
Disposition

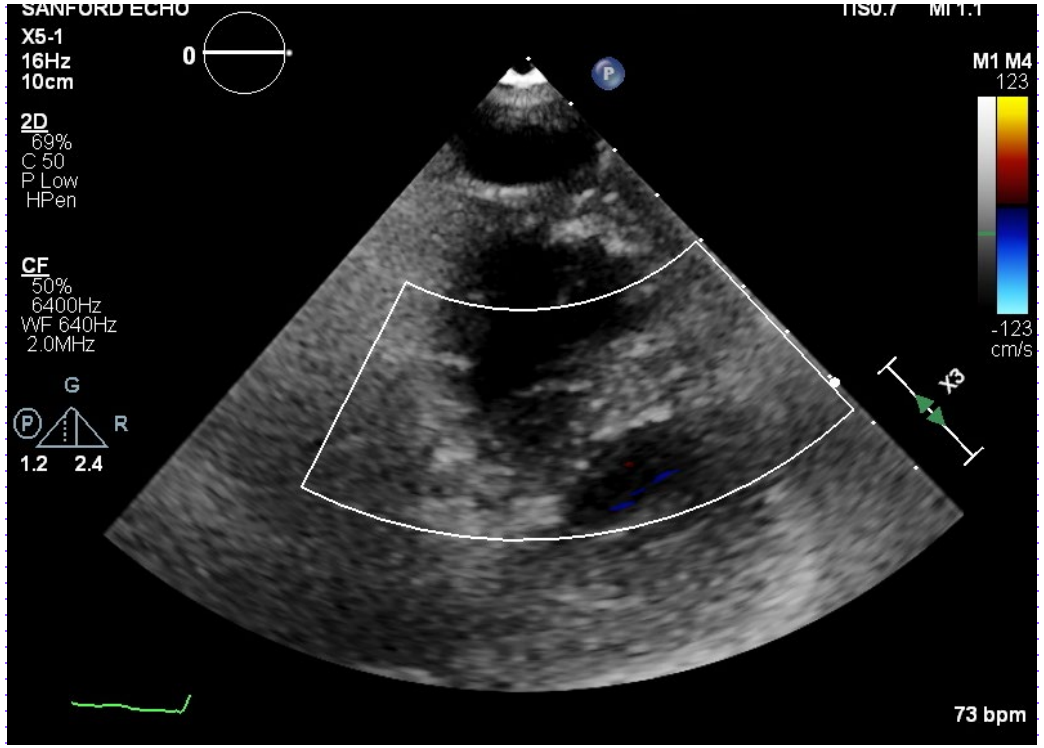
Home & F/U	Monitored Bed	**ICU**

Obstructive Shock PE

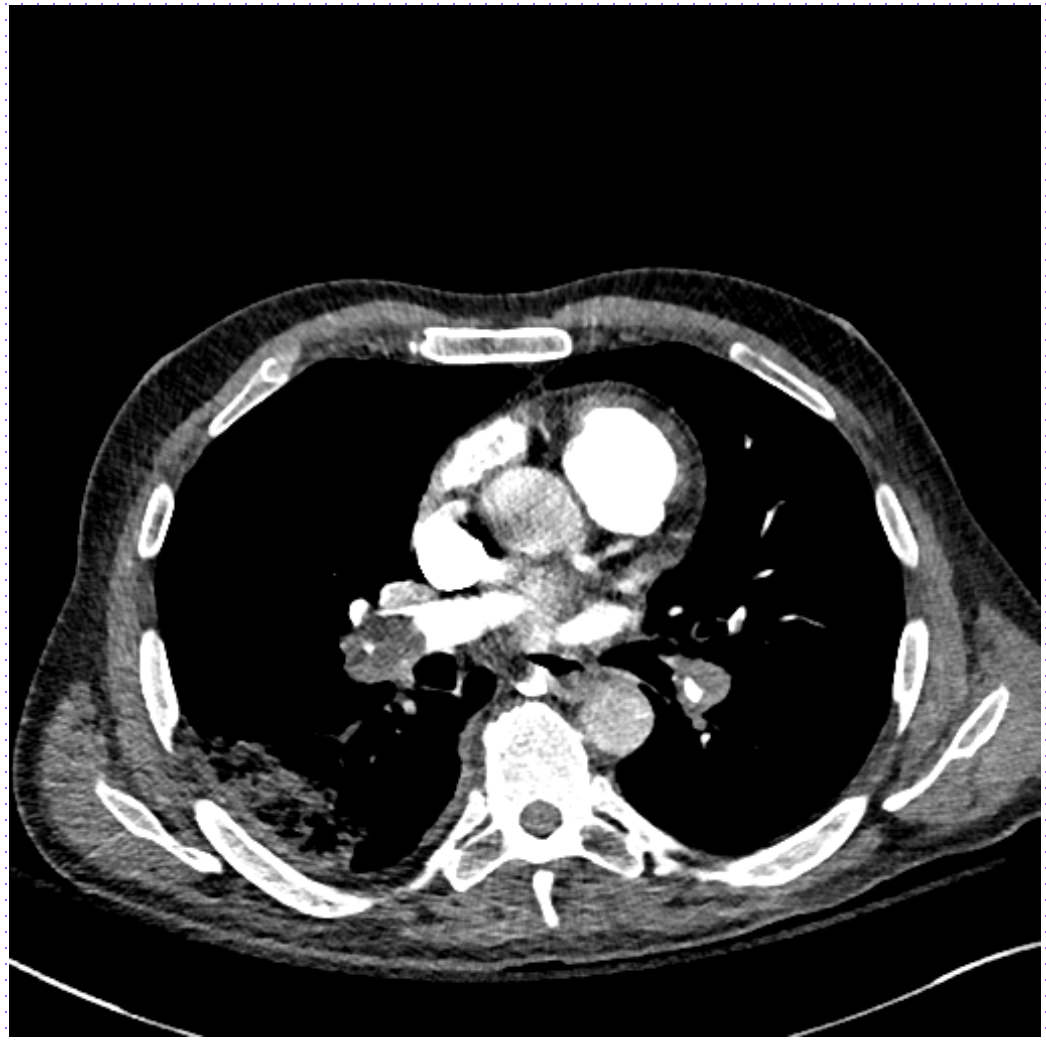


Obstructive Shock PE

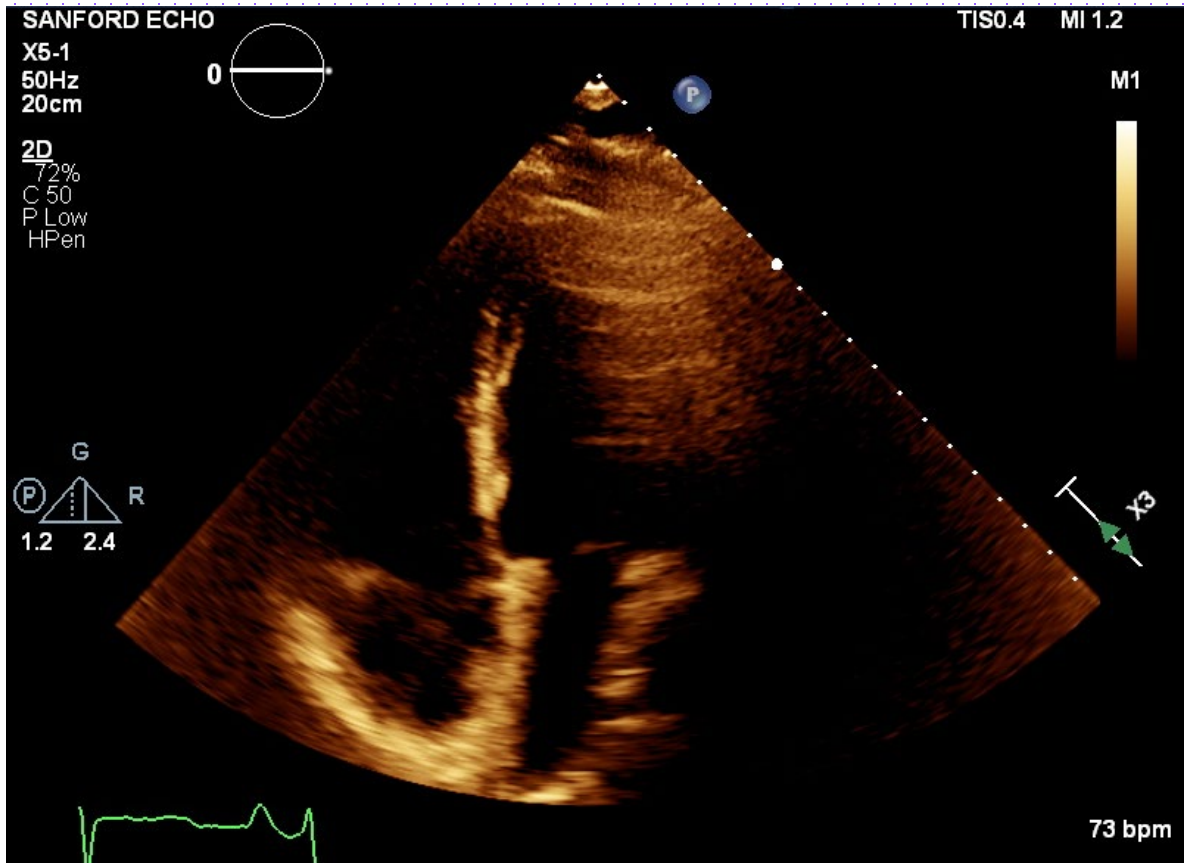


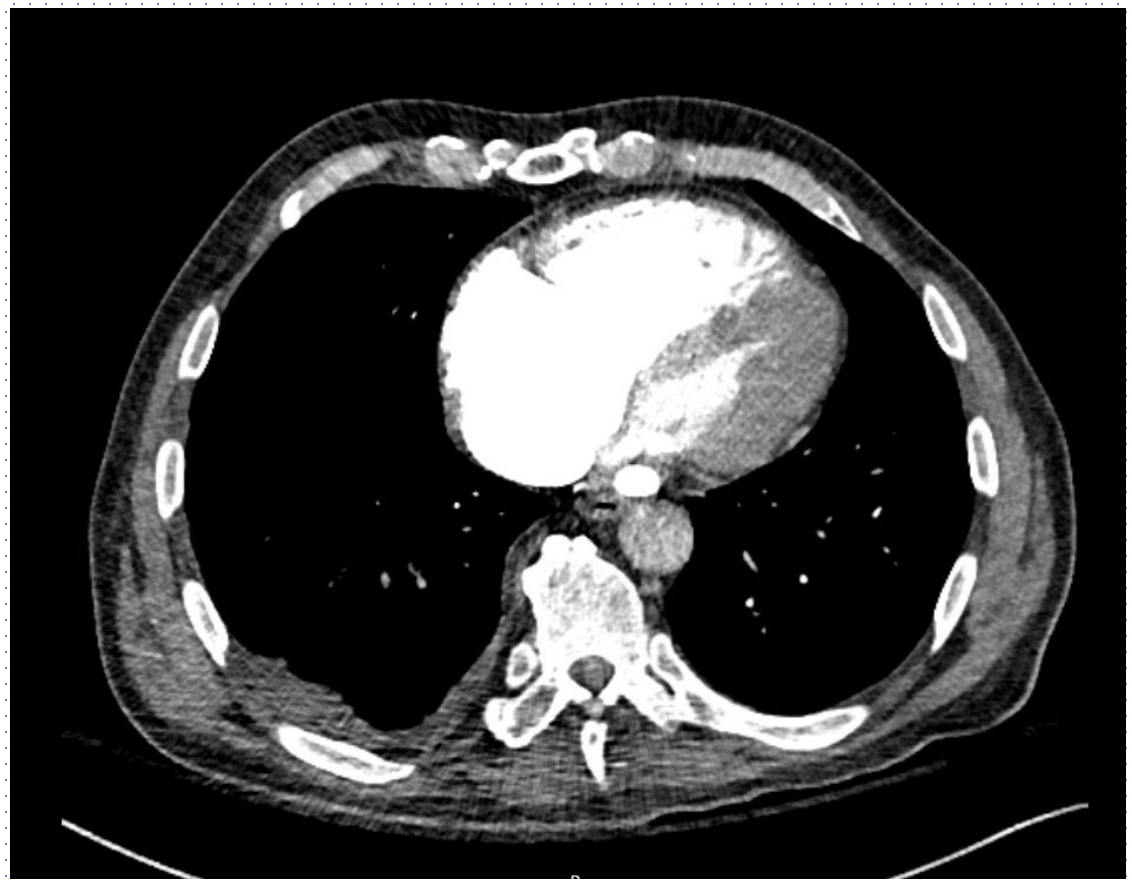


Obstructive Shock PE



Obstructive Shock PE





Streptokinase and Heparin versus Heparin Alone in Massive Pulmonary Embolism: A Randomized Controlled Trial.

Jerjes-Sanchez C[1], Ramírez-Rivera A, de Lourdes García M, Arriaga-Nava R, Valencia S, Rosado-Buzzo A, Pierzo JA, Rosas E.

Author information

1 Amores 1636 Edificio "D," Depto 503, CP 03100, Mexico City, Mexico and Emergency Care Department, Hospital de Cardiologia, National Medical Center, Mexico City, Mexico.

Design	Goal	Participants
A randomized controlled trial	To test the efficacy of thrombolytic therapy in massive pulmonary embolism	8 patients with cardiogenic shock

Results

	Streptokinase + Heparin (4)	Heparin Alone (4)	*Significance*
Death rate	All improved in the first hour after treatment, survived, and in 2 years of follow-up are without pulmonary arterial hypertension	All four patients treated with heparin alone died from 1 to 3 hours after arrival at the emergency room	P=0.02

RESEARCH ARTICLE | VOLUME 123, ISSUE 4, P684-689, FEBRUARY 15, 2019

Download Full Issue

Meta-Analysis of Prevalence and Short-Term Prognosis of Hemodynamically Unstable Patients With Symptomatic Acute Pulmonary Embolism

Carlos Andrés Quezada, MD • Behnood Bikdeli, MD • Deisy Barrios, MD • ... Manuel Monreal, PhD • Roger D. Yusen, MD • David Jiménez, PhD • Show all authors

Published: November 26, 2018 • DOI: https://doi.org/10.1016/j.amjcard.2018.11.009 • Check for updates

In unstable patients, thrombolytic therapy was associated with reduced odds of:

Short-term all-cause mortality	PE-related death
OR, 0.69; 95% CI, 0.49 to 0.95	OR, 0.66; 95% CI, 0.45 to 0.97

Contraindications to Fibrinolytic Therapy for Deep Venous Thrombosis or Acute Pulmonary Embolism

ABSOLUTE CONTRAINDICATIONS	RELATIVE CONTRAINDICATIONS
Prior intracranial hemorrhage	History of chronic, severe, poorly controlled hypertension
Known structural cerebral vascular lesion	Severe uncontrolled hypertension on presentation (SBP >180 mmHg or DBP >110 mmHg)
Known malignant intracranial neoplasm	History of ischemic stroke >3 months prior
Ischemic stroke within 3 months (excluding stroke within 3 hours*)	Traumatic or prolonged (>10 minutes) CPR or major surgery <3 weeks
Suspected aortic dissection	Recent (within 2 to 4 weeks) internal bleeding
Active bleeding or bleeding diathesis (excluding menses)	Noncompressible vascular punctures
Significant closed-head trauma or facial trauma within 3 months	Recent invasive procedure
	For streptokinase/anistreplase – Prior exposure (>5 days ago) or prior allergic reaction
	Pregnancy
	Active peptic ulcer
	Pericarditis or pericardial fluid
	Current use of anticoagulant (eg, warfarin) that has produced an elevated INR >1.7 or PT >15 s.
	Age >75 years
	Diabetic retinopathy

CDI in High-Risk PE

1988

CDT compared to tPA in 34 patients with high-risk PE

Similar impact on the degree of reduction of clot burden and the mean pulmonary arterial pressure, with similar rates of bleeding. Bleeding complications were noted in 50% of patients and were serious in 12%.

2015

A single-arm prospective trial of 150 patients, 20%"massive" PE

(SEATTLE II)

48 hours, CDT resulted in a significant reduction in pulmonary artery pressure without any episodes of major bleeding. No ICHs were reported.

2019

Retrospective review of 105 cases of both massive and submassive PE

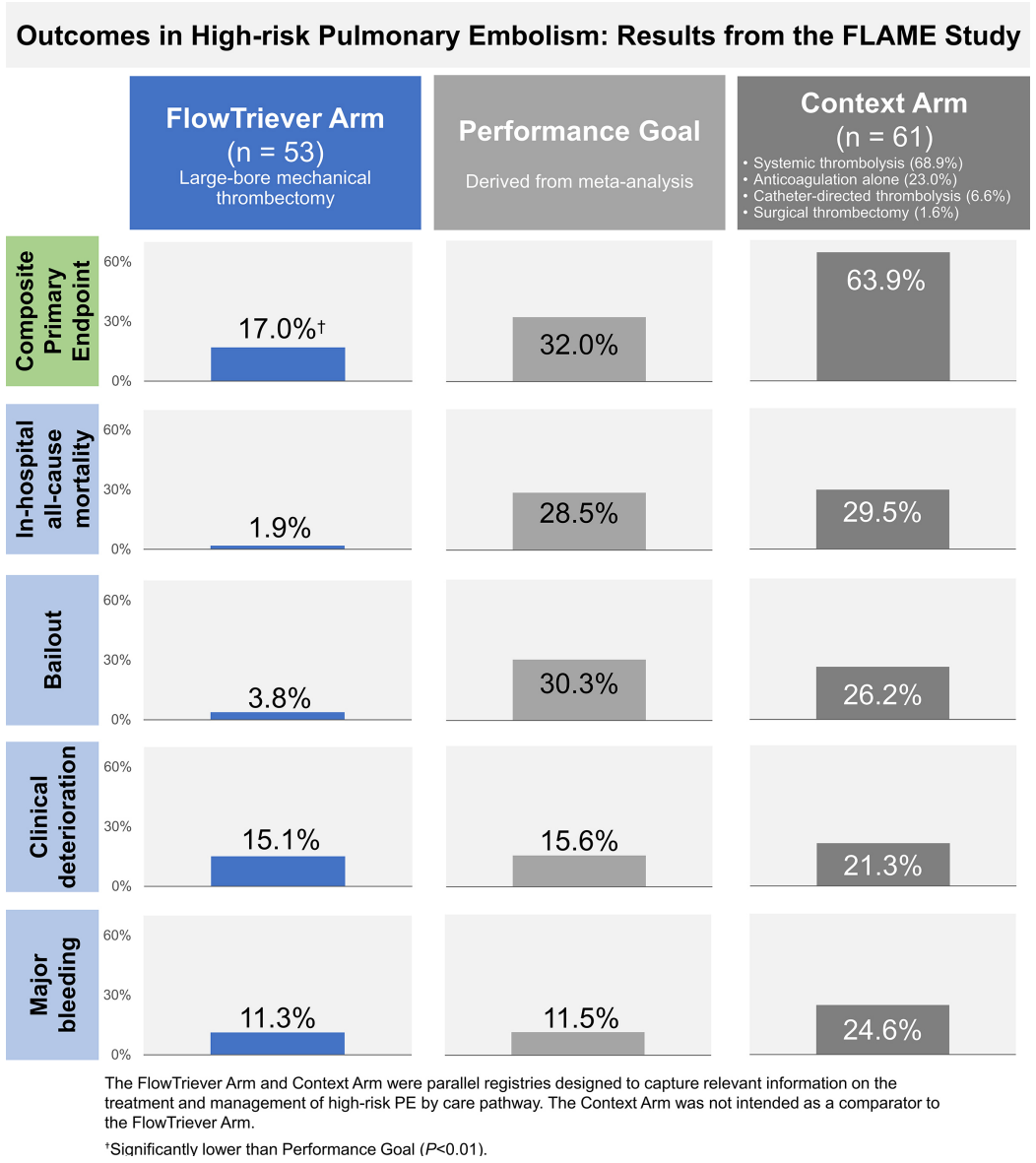
Improved RV/left ventricular ratio in patients treated with CDT compared with heparin alone without any difference in 90-day mortality or major bleeding

2019

A meta-analysis of 28 studies (2135 patients, 47% with had high-risk PE)

Significant improvement in cardiopulmonary hemodynamics with ultrasound-assisted catheter-directed thrombolysis

Small sample size
Inadequate power to estimate survival benefit
The use of surrogate outcome measures (eg, echocardiography for measuring pulmonary pressures),
The lack of data describing the effect of thrombolysis over a more extended period (weeks to months) on clinically meaningful outcomes, such as survival

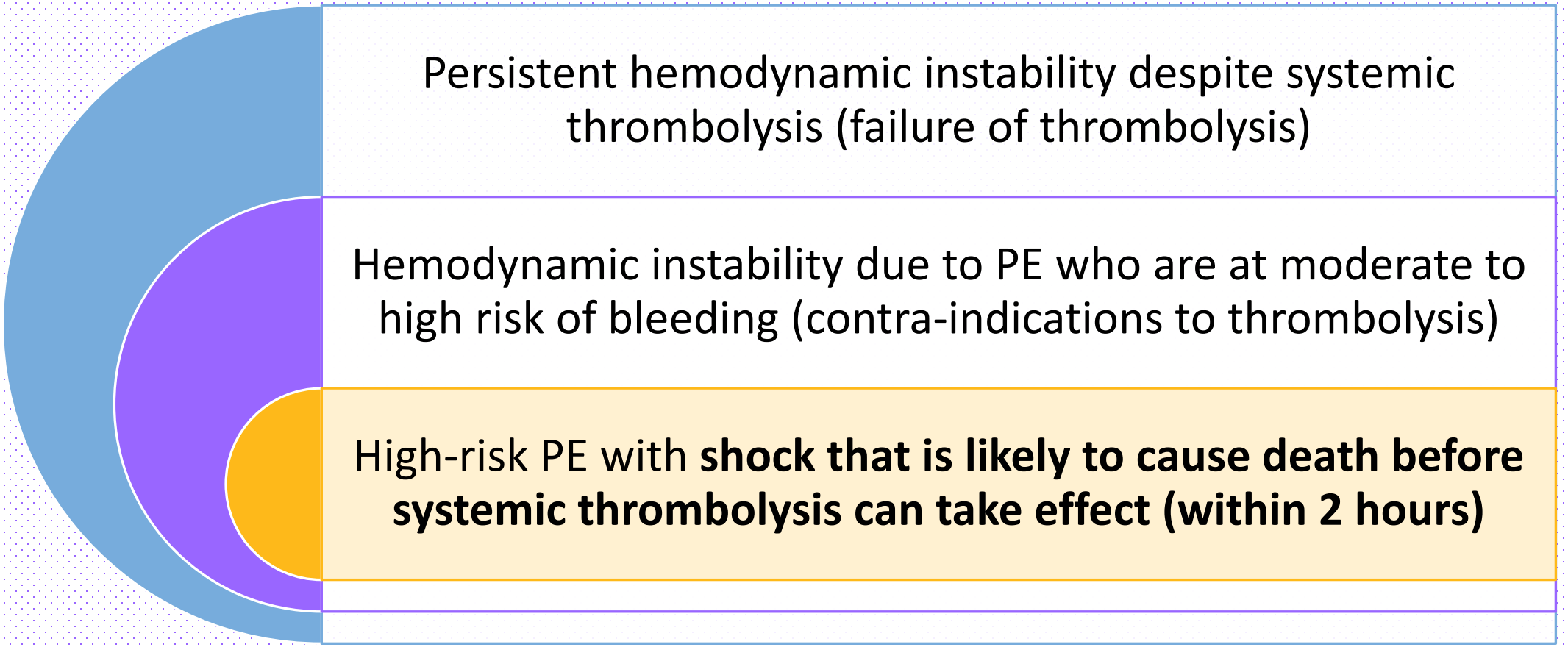


FLAME Study

Prospective, multicenter, nonrandomized, parallel group, observational study of high-risk PE

53 patients were enrolled in the FlowTriever Arm and 61 in the Context Arm (contemporary therapies)

Indications of CDI in High-risk PE

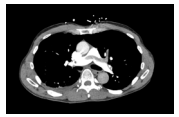


Stevens SM, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report.chest.2021.07.055. Epub 2021 Aug 2. Erratum in: Chest. 2022 Jul;162(1):269.

Intermediate High-risk PE

68-year-old male with PMH of HTN who presented to ER with syncopal episode, tachypnea, and low oxygen saturation. Patient was diagnosed few days ago with community-acquired pneumonia and was discharged on amox/clav. No other PE risk factors.

Hemodynamics	Clinical Parameters	RV Dysfunction	Biomarkers
BP 135/94-HR 100/min	RR 28 breaths/min and SpO2 100% on 10L/min sPESI =1	RV/LV >1 on CTA	D-dimers: ↑ 31,145 ng/mL, Troponin 1,030, BNP 182 ng/mL

CXR	CTA	LE US	Echocardiogram
			

Risk of Death				Risk of Bleeding		
Low	Intermediate Low	**Intermediate High**	High	**Low**	Intermediate	High

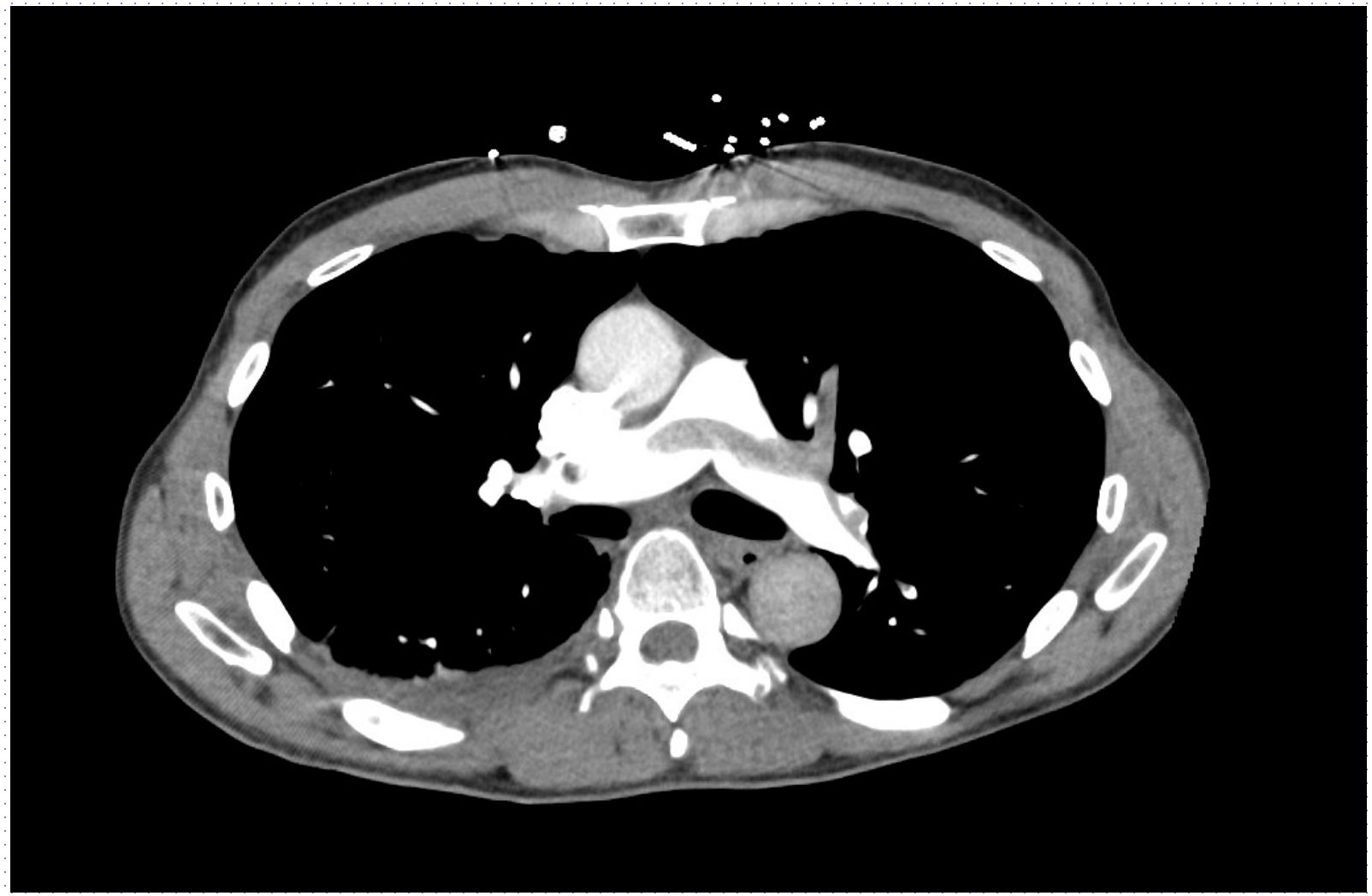
Management

Surveillance without anticoagulation	**Anticoagulation**	Systemic Thrombolysis Primary – Rescue -Reduced	**Catheter-directed Thrombolysis**	Catheter-directed Embolectomy	Surgical Embolectomy	IVC Filter

Disposition

Home & F/U	**Monitored Bed**	ICU

Intermediate High-risk PE



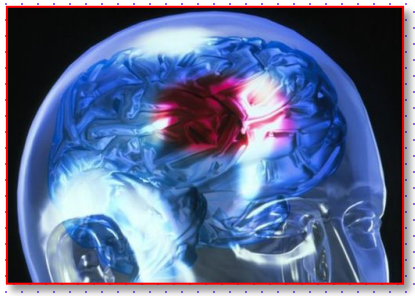
JAMA®
The Journal of the American Medical Association

Original Investigation

Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial Hemorrhage
A Meta-analysis

Saurav Chatterjee, MD; Anasua Chakraborty, MD; Ido Weinberg, MD; Mitul Kadakia, MD; Robert L. Wilensky, MD; Partha Sardar, MD; Dharam J. Kumbhani, MD, SM, MRCP; Debabrata Mukherjee, MD, MS; Michael R. Jaff, DO; Jay Giri, MD, MPH

16 trials
N= 2115 patients



JAMA. 2014;311(23):2414-2421

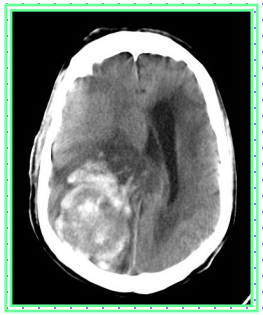
JAMA®
The Journal of the American Medical Association

Thrombolytics in *Unselected* Patients Stable and Unstable PE

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

OR 2.73

OR 0.53



Original Article

PEITHO trial

The NEW ENGLAND JOURNAL of MEDICINE

Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

Guy Meyer, M.D., Eric Vicaut, M.D., Thierry Danays, M.D., Giancarlo Agnelli, M.D., Cecilia Becattini, M.D., Jan Beyer-Westendorf, M.D., Erich Bluhmki, M.D., Ph.D., Helene Bouvaist, M.D., Benjamin Brenner, M.D., Francis Couturaud, M.D., Ph.D., Claudia Dellas, M.D., Klaus Empen, M.D., Ana Franca, M.D., Nazzareno Galiè, M.D., Annette Geibel, M.D., Samuel Z. Goldhaber, M.D., David Jimenez, M.D., Ph.D., Matija Kozak, M.D., Christian Kupatt, M.D., Nils Kucher, M.D., Irene M. Lang, M.D., Mareike Lankeit, M.D., Nicolas Meneveau, M.D., Ph.D., Gerard Pacouret, M.D., Massimiliano Palazzini, M.D., Antoniu Petris, M.D., Ph.D., Piotr Pruszczyk, M.D., Matteo Rugolotto, M.D., Aldo Salvi, M.D., Sebastian Schellong, M.D., Mustapha Sebbane, M.D., Bozena Sobkowicz, M.D., Branislav S. Stefanovic, M.D., Ph.D., Holger Thiele, M.D., Adam Torbicki, M.D., Franck Verschuren, M.D., Ph.D., and Stavros V. Konstantinides, M.D., for the PEITHO Investigators*

PE + Normotention + RV dysfunction + Myocardial injury

N Engl J Med Volume 370(15):1402-1411. April 10, 2014

ORIGINAL ARTICLE

The NEW ENGLAND JOURNAL of MEDICINE

Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

Guy Meyer, M.D., Eric Vicaut, M.D., Thierry Danays, M.D., Giancarlo Agnelli, M.D., Cecilia Becattini, M.D., Jan Beyer-Westendorf, M.D., Erich Bluhmki, M.D., Ph.D., Helene Bouvaist, M.D., Benjamin Brenner, M.D., Francis Couturaud, M.D., Ph.D., Claudia Dellas, M.D., Klaus Empen, M.D., et al., for the PEITHO Investigators*

Design	Goal	Enrollment
A randomized, double-blind trial	Assess tenecteplase plus heparin with placebo plus heparin in normotensive patients with intermediate-risk pulmonary embolism	1005 patients with RV dysfunction and myocardial injury

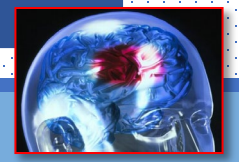
Results

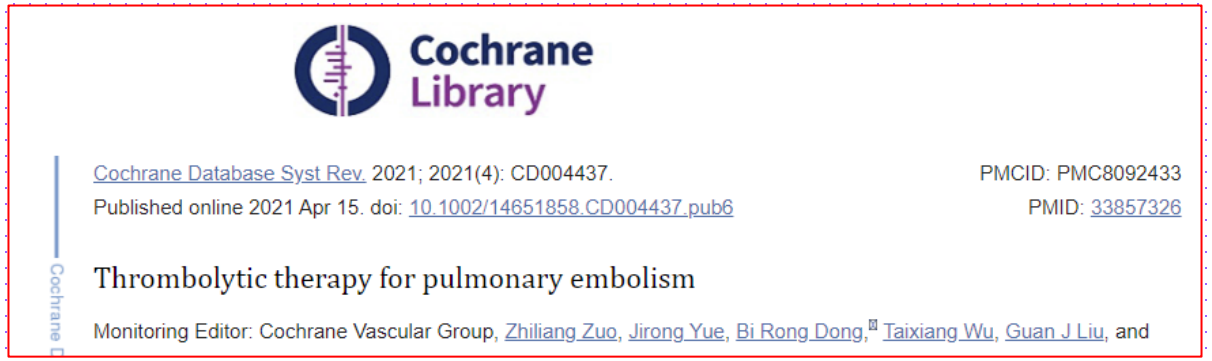
	Tenecteplase Group (506)	Placebo (499)	*Significance*

Extracranial bleeding were higher (11 versus 0.6%), suggesting that risk benefit may be more favorable in those 75 years old or younger.

Long-term follow-up of these patients (approximately 3.5 years) reported no difference in mortality (20 versus 18%)*

*Konstantinides SV, et al.. Impact of Thrombolytic Therapy on the Long-Term Outcome of Intermediate-Risk Pulmonary Embolism. J Am Coll Cardiol. 2017 Mar 28;69(12):1536-1544.





Cochrane Library

Cochrane Database Syst Rev. 2021; 2021(4): CD004437.
Published online 2021 Apr 15. doi: 10.1002/14651858.CD004437.pub6
PMCID: PMC8092433
PMID: 33857326

Thrombolytic therapy for pulmonary embolism

Monitoring Editor: Cochrane Vascular Group, Zhiliang Zuo, Jirong Yue, Bi Rong Dong, Taixiang Wu, Guan J Liu, and

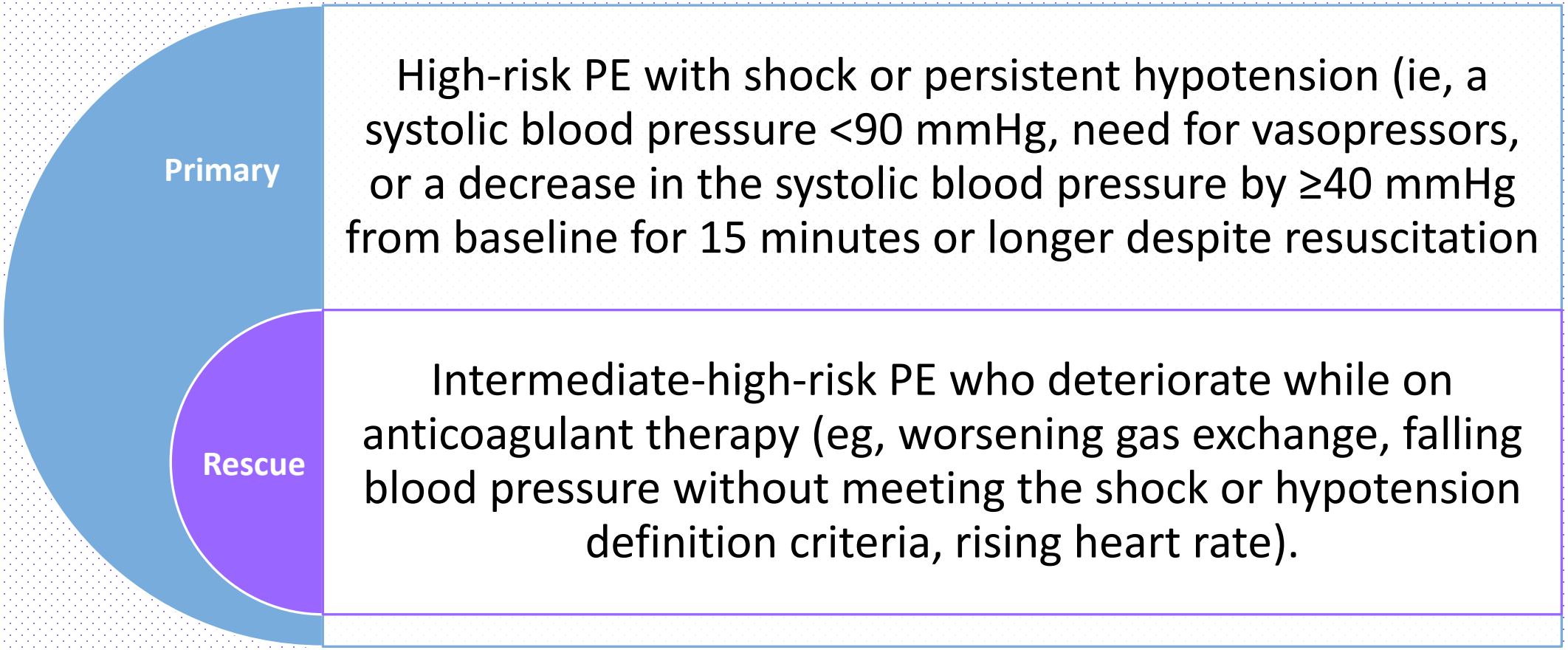
Design	Goal	Participants
A meta-analysis of 21 randomized controlled trials	To assess the effects of thrombolytic therapy for acute pulmonary embolism (massive and submassive)	2401 patients from 21 trials

Results: Odds of Death	
19 studies, 2319 participants	OR 0.58, 95% CI 0.38 to 0.88
13 studies, 2046 participants (Six trials with bias excluded)	OR 0.71, 95% CI 0.45 to 1.13
Submassive PE participants (1993)	OR 0.61, 95% CI 0.37 to 1.02

Results: Hemorrhagic stroke	
15 studies, 2101 participants	OR 2.84, 95% CI 1.92 to 4.20
2 studies, 1091 participants (low risk of bias)	OR 7.59, 95% CI 1.38 to 41.72

Zuo Z, Yue J, Dong BR, Wu T, Liu GJ, Hao Q. Thrombolytic therapy for pulmonary embolism. Cochrane Database Syst Rev. 2021 Apr 15;4(4):CD004437.

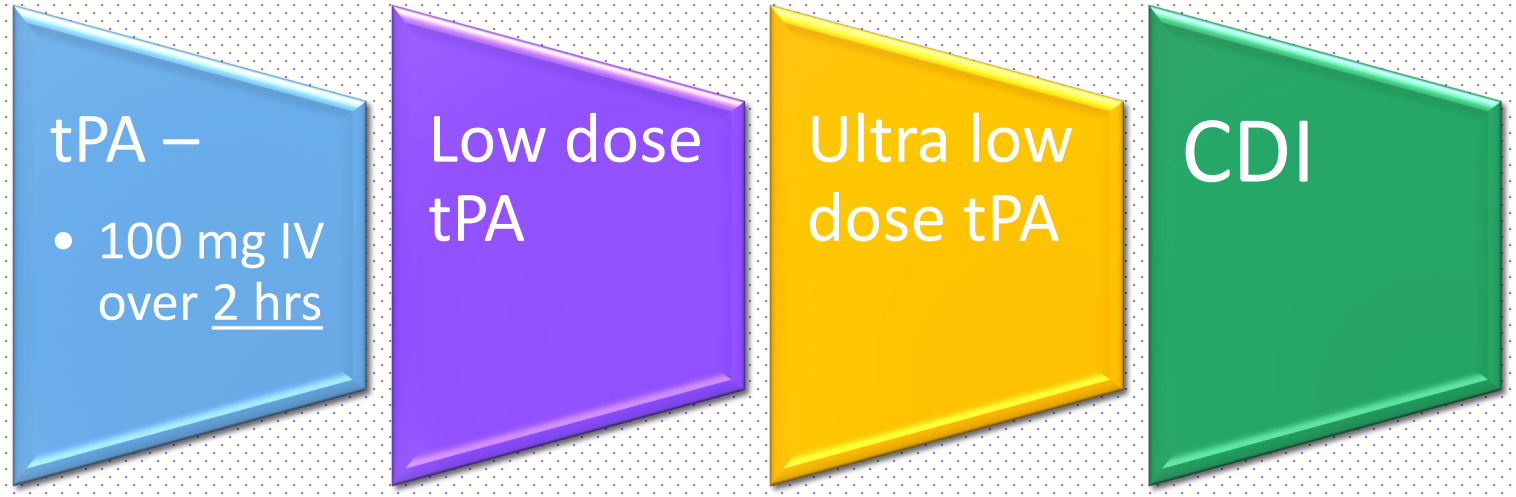
Indications of Thrombolytic Therapy



Stevens SM, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report.chest.2021.07.055. Epub 2021 Aug 2. Erratum in: Chest. 2022 Jul;162(1):269.

Thrombolytic Regimens for Intermediate High-risk PE

In patients with intermediate-risk PE systemic thrombolytic therapy MAY reduce mortality and PE recurrence compared to heparin alone but at the expense of major bleeding.



Reduced Dose tPA in PE!

Moderate Pulmonary Embolism Treated With Thrombolysis (from the "MOPETT" Trial)

Mohsen Sharifi, MD[a,b,*], Curt Bay, PhD[b], Laura Skrocki, DO[a], Farnoosh Rahimi, MD[a], and Mahshid Mehdipour, DMD[a,b], "MOPETT" Investigators

J Cardiol 2013;111:273–277

Lower rates of pulmonary hypertension
Lower combination of death plus recurrent PE

Small sample size and low prevalence of RV dysfunction (<25 percent) and RV hypokinesis (<7 percent). Additionally, "moderate PE" is not an accepted definition!

CHEST Original Research

THROMBOEMBOLISM

Efficacy and Safety of Low Dose Recombinant Tissue-Type Plasminogen Activator for the Treatment of Acute Pulmonary Thromboembolism

A Randomized, Multicenter, Controlled Trial

*Chen Wang, MD, PhD, FCCP; Zhenguo Zhai, MD, PhD; Yuanhua Yang, MD; Qi Wu, MD; Zhaozhong Cheng, MD; Lirong Liang, MD, PhD; Huaping Dai, MD; Kewu Huang, MD; Weixuan Lu, MD; Zhonghe Zhang, MD; Xiansheng Cheng, MD; Ying H. Shen, MD, PhD; for the China Venous Thromboembolism (VTE) Study Group**

Design	Goal	Participants
A prospective, randomized, multicenter trial	To compare the efficacy and safety of a 50 mg/2 h rt-PA regimen with a 100 mg/2 h rt-PA	118 patients with acute PTE and either hemodynamic instability or massive pulmonary artery obstruction

Results			
	rt-PA at 50 mg/2 h (55 patients)	rt-PA at 100 mg/2 h (48 patients)	*Significance*
Mortality rate	**1 (2%)**	**3 (6%)**	👍
Bleeding rate	**2 (3%)**	**5 (10%)**	👍

CHEST 2010; 137(2):254–262

Mayo Clin Proc. 2022 Jun;97(6):1158-1163. doi: 10.1016/j.mayocp.2022.02.011.

Ultra-Low-Dose Systemic Tissue Plasminogen Activator in High-Risk Submassive Pulmonary Embolism

Pramod K Guru [1], Abhishek R Giri [2], Devang K Sanghavi [3], Charles Ritchie [4]

A case study of four patients reported successful use of "ultra" low-dose and slow infusion of tPA (25 mg at 1 mg/hour), with all four patients demonstrating improved hemodynamics within hours of administration!

CDI in Intermediate High-Risk PE

ULTIMA Trial (2014)
59 Patients
USAT vs heparin

Statistically significantly improved RV/LV ratio, no difference in mortality, and no major bleeding events or intracranial hemorrhage.

SEATTLE II (2015)
150 patients (80% intermediate-high)
A single-arm prospective trial
USAT

CDT resulted in a significant reduction in RV/LV and pulmonary artery pressure without any episodes of major bleeding.

OPTALYSE (2018)
101 patients testing USAT tPA at different doses

Improved the RV/LV ratio. Clot burden at 48 hours improved with higher dose at longer duration. 4% bleeding rate with one ICH.

FLARE Trial (2018)
101 patients
Inari Flowtriever

Improved RV/LV ratio (Hemoptysis = 1, 1 clinical deterioration, 1 V Fib, 1 cardiogenic Shock, 1 death)

SUNSET trial (2021)
81 patients
USAT or standard CDT

No difference in thrombus score reduction

Small sample size
Inadequate power to estimate survival benefit
The use of surrogate outcome measures (eg, echocardiography for measuring pulmonary pressures),
The lack of data describing the effect of thrombolysis over a more extended period (weeks to months) on clinically meaningful outcomes, such as survival

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CANADIAN MEDICAL ASSOCIATION JOURNAL JOURNAL DE L'ASSOCIATION MÉDICALE CANADIENNE

CMAJ. 2023 Jun 19; 195(24): E833–E843. PMCID: PMC10281204
Published online 2023 Jun 19. doi: 10.1503/cmaj.220960 PMID: 37336568

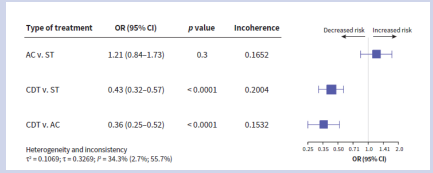
Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis

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

Design	Goal	Participants
Network meta-analysis.	Compare the efficacy and safety of CDT with anticoagulation, systemic thrombolysis	44 studies, representing 20 006 patients

Results

Death

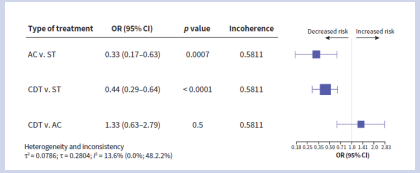


Type of treatment	OR (95% CI)	*p* value	Incoherence
AC v. ST	1.21 (0.84–1.73)	0.3	0.1652
CDT v. ST	0.43 (0.32–0.57)	< 0.0001	0.2004
CDT v. AC	0.36 (0.25–0.52)	< 0.0001	0.1532

Heterogeneity and inconsistency
$\tau^2 = 0.1069$; $\tau = 0.3269$; $I^2 = 34.3\%$ (2.7%; 55.7%)

Decreased risk Increased risk
0.25 0.35 0.50 0.71 1.0 1.41 2.0
OR (95% CI)

Intracerebral Hemorrhage

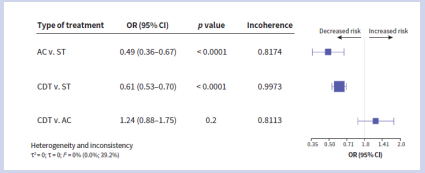


Type of treatment	OR (95% CI)	*p* value	Incoherence
AC v. ST	0.33 (0.17–0.63)	0.0007	0.5811
CDT v. ST	0.44 (0.29–0.64)	< 0.0001	0.5811
CDT v. AC	1.33 (0.63–2.79)	0.5	0.5811

Heterogeneity and inconsistency
$\tau^2 = 0.0786$; $\tau = 0.2804$; $I^2 = 13.6\%$ (0.0%; 48.2.2%)

Decreased risk Increased risk
0.18 0.25 0.35 0.50 0.71 1.0 1.41 2.0 2.83
OR (95% CI)

Major Bleeding



Type of treatment	OR (95% CI)	*p* value	Incoherence
AC v. ST	0.49 (0.36–0.67)	< 0.0001	0.8174
CDT v. ST	0.61 (0.53–0.70)	< 0.0001	0.9973
CDT v. AC	1.24 (0.88–1.75)	0.2	0.8113

Heterogeneity and inconsistency
$\tau^2 = 0$; $\tau = 0$; $I^2 = 0\%$ (0.0%; 39.2%)

Decreased risk Increased risk
0.35 0.50 0.71 1.0 1.41 2.0
OR (95% CI)

With moderate certainty of evidence, the risk of death and major bleeding complications was lower with CDT than with systemic thrombolysis.

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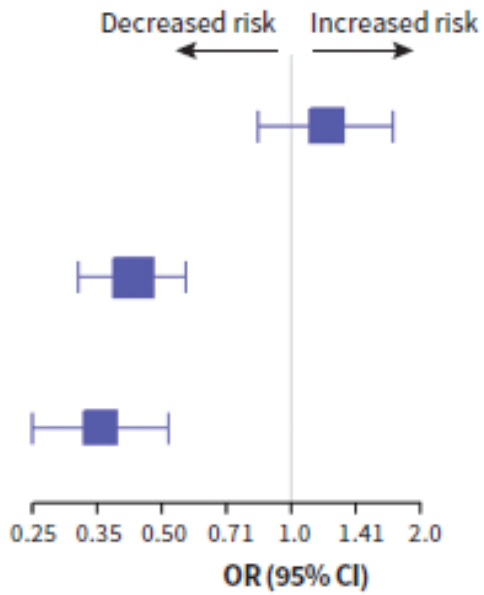
CDT v. AC	0.36 (0.25–0.52)	< 0.0001	0.1532

Heterogeneity and inconsistency
$\tau^2 = 0.1069$; $\tau = 0.3269$; $I^2 = 34.3\%$ (2.7%; 55.7%)



Death

cmaj jamc
CANADIAN MEDICAL ASSOCIATION JOURNAL JOURNAL DE L'ASSOCIATION MÉDICALE CANADIENNE

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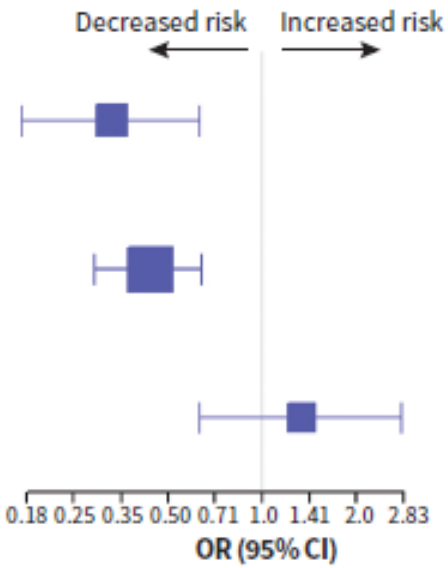
Catheter-directed thrombolysis compared with systemic thrombolysis and anticoagulation in patients with intermediate- or high-risk pulmonary embolism: systematic review and network meta-analysis

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

Type of treatment	OR (95% CI)	*p* value	Incoherence
AC v. ST	0.33 (0.17–0.63)	0.0007	0.5811
CDT v. ST	0.44 (0.29–0.64)	< 0.0001	0.5811
CDT v. AC	1.33 (0.63–2.79)	0.5	0.5811

Heterogeneity and inconsistency
$\tau^2 = 0.0786$; $\tau = 0.2804$; $I^2 = 13.6\%$ (0.0%; 48.2%)



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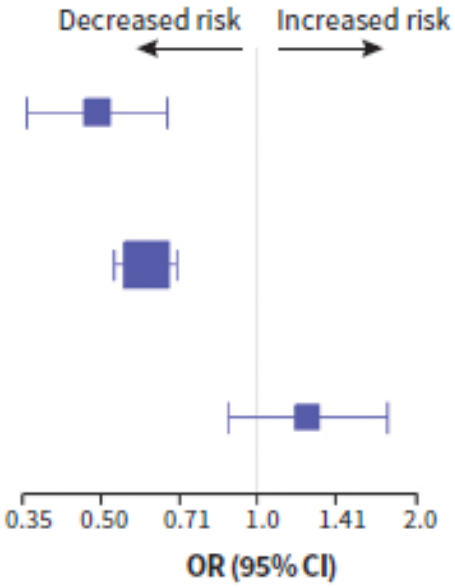
Type of treatment	OR (95% CI)	*p* value	Incoherence
AC v. ST	0.49 (0.36–0.67)	< 0.0001	0.8174
CDT v. ST	0.61 (0.53–0.70)	< 0.0001	0.9973
CDT v. AC	1.24 (0.88–1.75)	0.2	0.8113

Heterogeneity and inconsistency
$\tau^2 = 0$; $\tau = 0$; $I^2 = 0\%$ (0.0%; 39.2%)



Major Bleeding

CDI Procedures Decisions

Method

- Ultrasound
- Saline
- Rotational device
- Suction

Number of catheters

- One side or both sides

Clot removal procedure

- Large central main pulmonary artery embolus
- Right atrial clot in transit

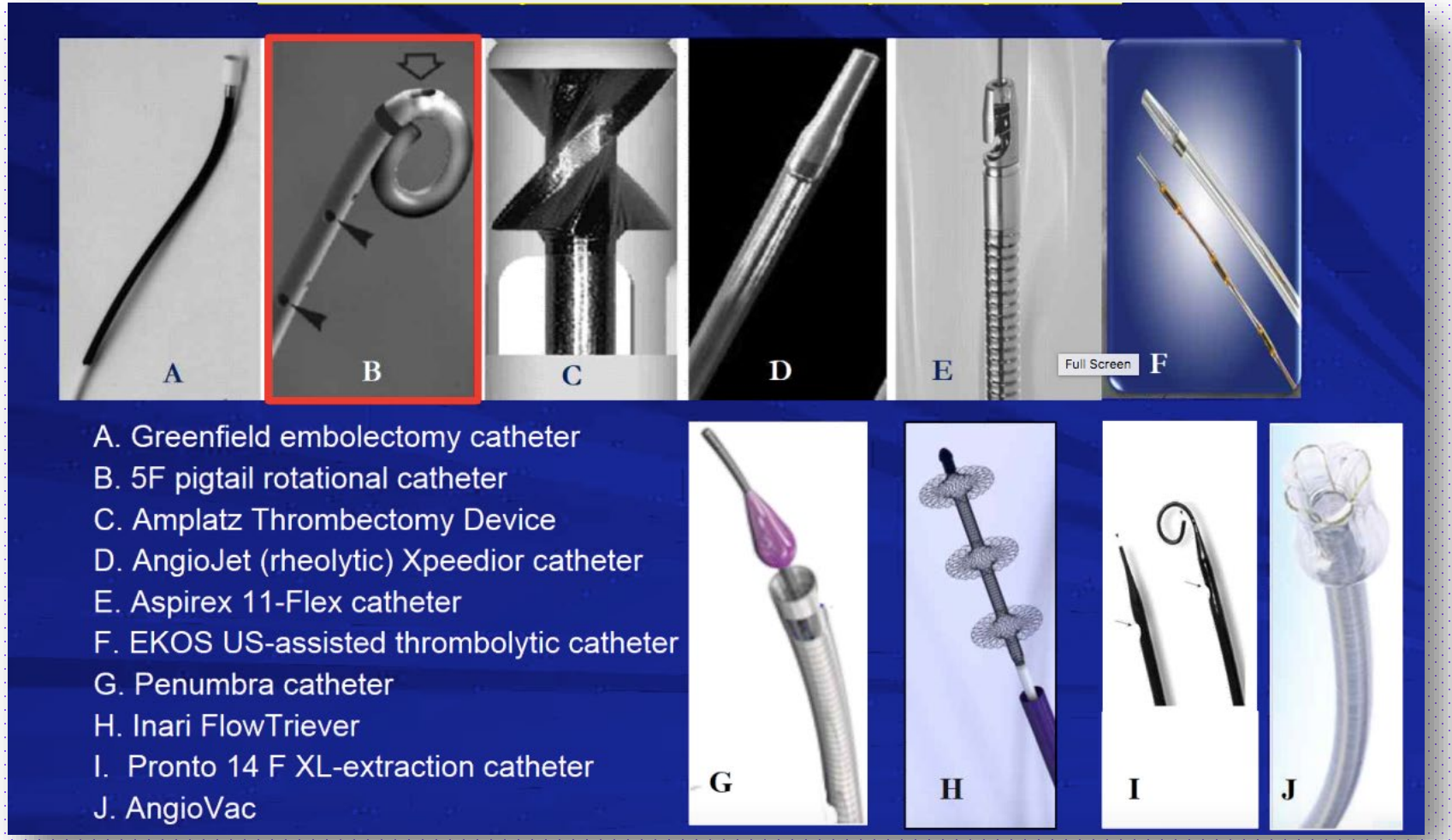
Thrombolysis

- Peripheral segmental/subsegmental embolus

Dose and duration of tPA

- Shorter duration infusions with lower doses to reduce the risk of bleeding.
- 1 mg/hour per lung over four to six hours

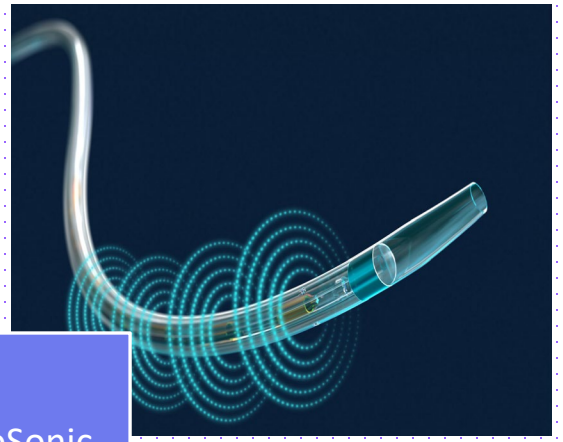
Catheter Directed Interventions



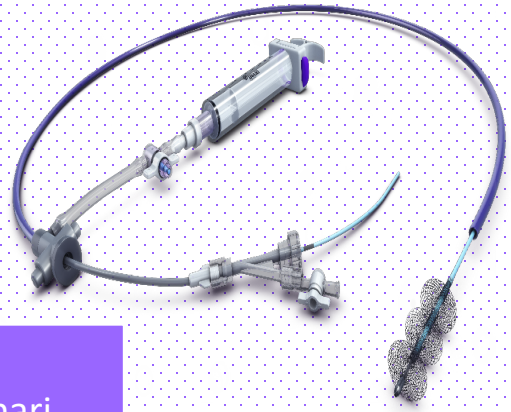
Slide Courtesy: Victor Tapson, MD

CDI Devices

AngioVac

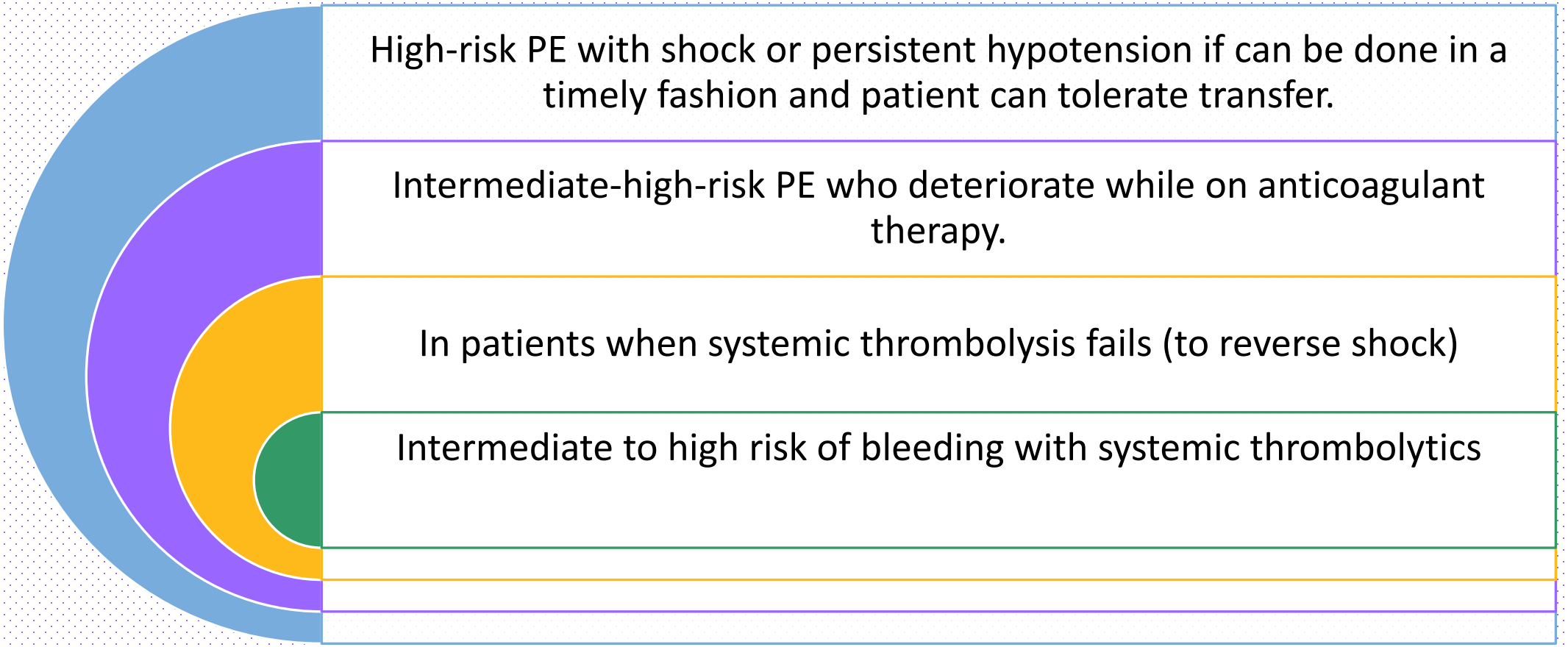


EkoSonic

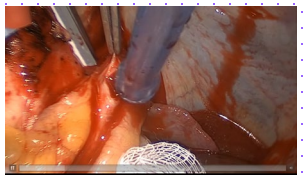


Inari Flowtriever

Indications of CDI



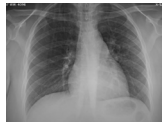
No Improvement after tPA



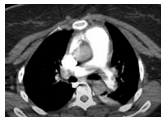
30-year-old obese female on contraceptive pills who presented to the ER with back pain and SOB associated with palpitation. She also smokes a ½ PPD. Initial BP 119/74 HR 105/min but she shortly became obtunded and hypotensive.CTA confirmed PE. Received tPA but remained hypotensive in the next 3 hours

Hemodynamics	**Clinical Parameters**	**RV Dysfunction**	**Biomarkers**
BP 82/60 HR 135/min	RR 32 breaths/min and SpO2 90% on NRM	RV/LV >1 on CTA	D-dimer 1766/ ↑Troponin

CXR



CTA



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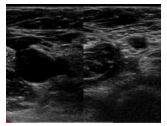
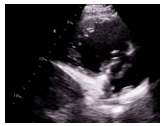


Echocardiogram



Risk of Death				**Risk of Bleeding**	
Low	Intermediate Low	Intermediate High	High	Low	Intermediate	High

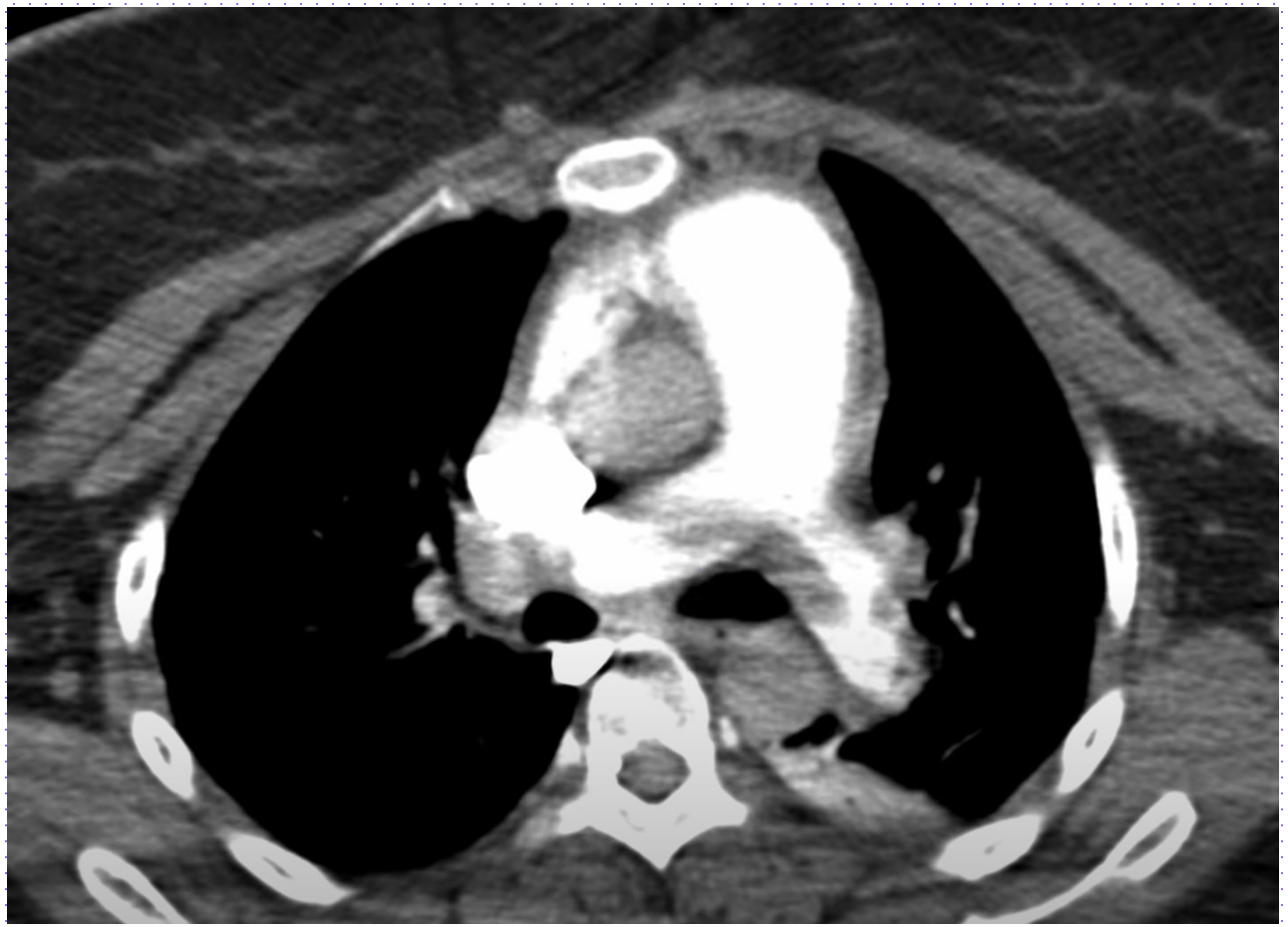
Management

Surveillance without anticoagulation	Anticoagulation	Systemic Thrombolysis Primary – Rescue -Reduced	Catheter-directed Thrombolysis	Catheter-directed Embolectomy	Surgical Embolectomy	IVC Filter

Disposition

Home & F/U	Monitored Bed	ICU

No Improvement after tPA

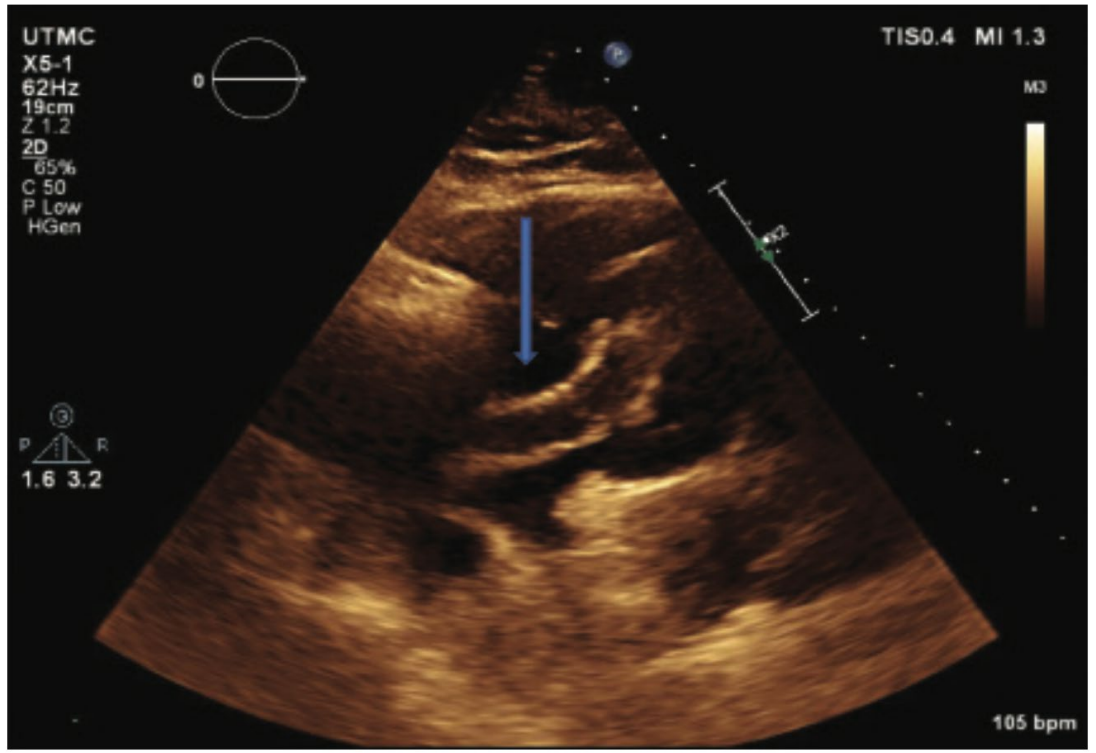


Clot in Transit

An 80-year-old male with no known past medical history presented to the emergency department at an outside facility with increasing dyspnea for the past ten days. Two weeks prior to his presentation, the patient had a fall. The patient had been immobile since then.

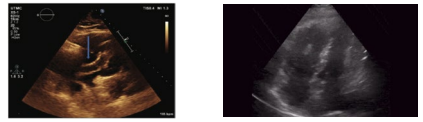
Hemodynamics
BP 132/76 HR 105/min

CXR



Biomarkers
Troponin 0.09 ng/ml

Echocardiogram



Risk of De

eeding

Low | Intermediate Low | In

diate | High

Surveillance without anticoagulation | Anticoagulation

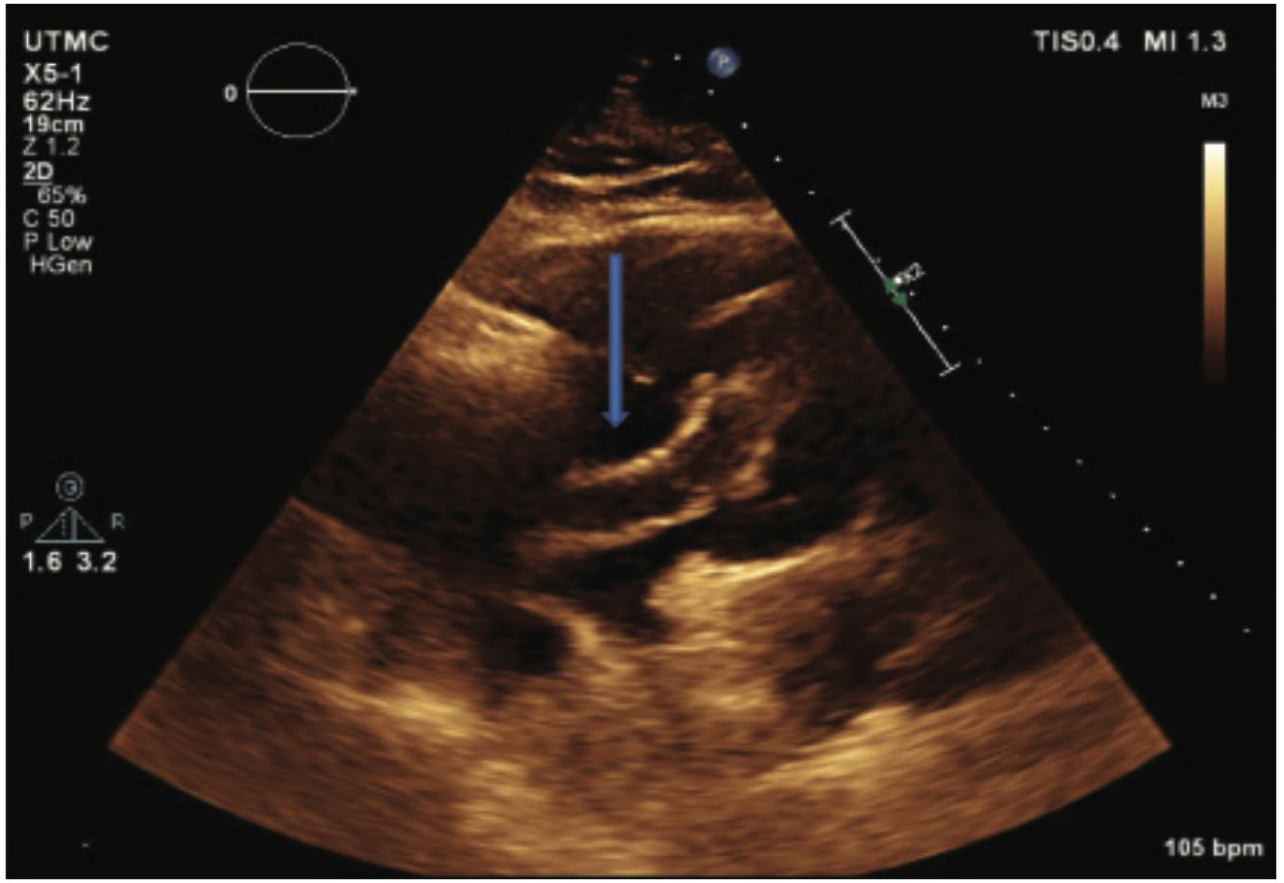
Surgical
ıbolectomy | IVC Filter

Home & F/U

ICU

[“Clot in Transit”: Percutaneous or Surgical Approach? (hmpglobalearningnetwork.com)]

Clot in Transit

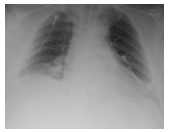


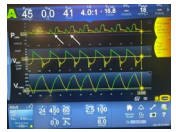
Severe Hypoxemia

A 40-year-old male with a significant PMH of schizoaffective disorder who was admitted to the ICU with RSV pneumonia and ARDS. Tracheostomy was planned due to failure to wean. Patient suddenly developed respiratory distress, increased minute ventilation and severe hypoxemia on day#18 of ICU admission. PCO2 increased from 47 to 76 mmH2O and no change in PIP or Pplateau pressure.

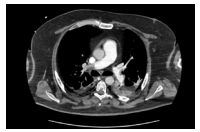
Hemodynamics	**Clinical Parameters**	**RV Dysfunction**	**Biomarkers**
BP 105/66 HR 135/min	RR 40 breaths/min and SpO2 80% on FiO2 100%	RV/LV >1	Troponin 0.9 ng/ml

CXR





CTA



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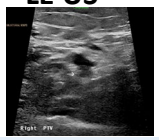
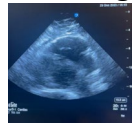


Echocardiogram



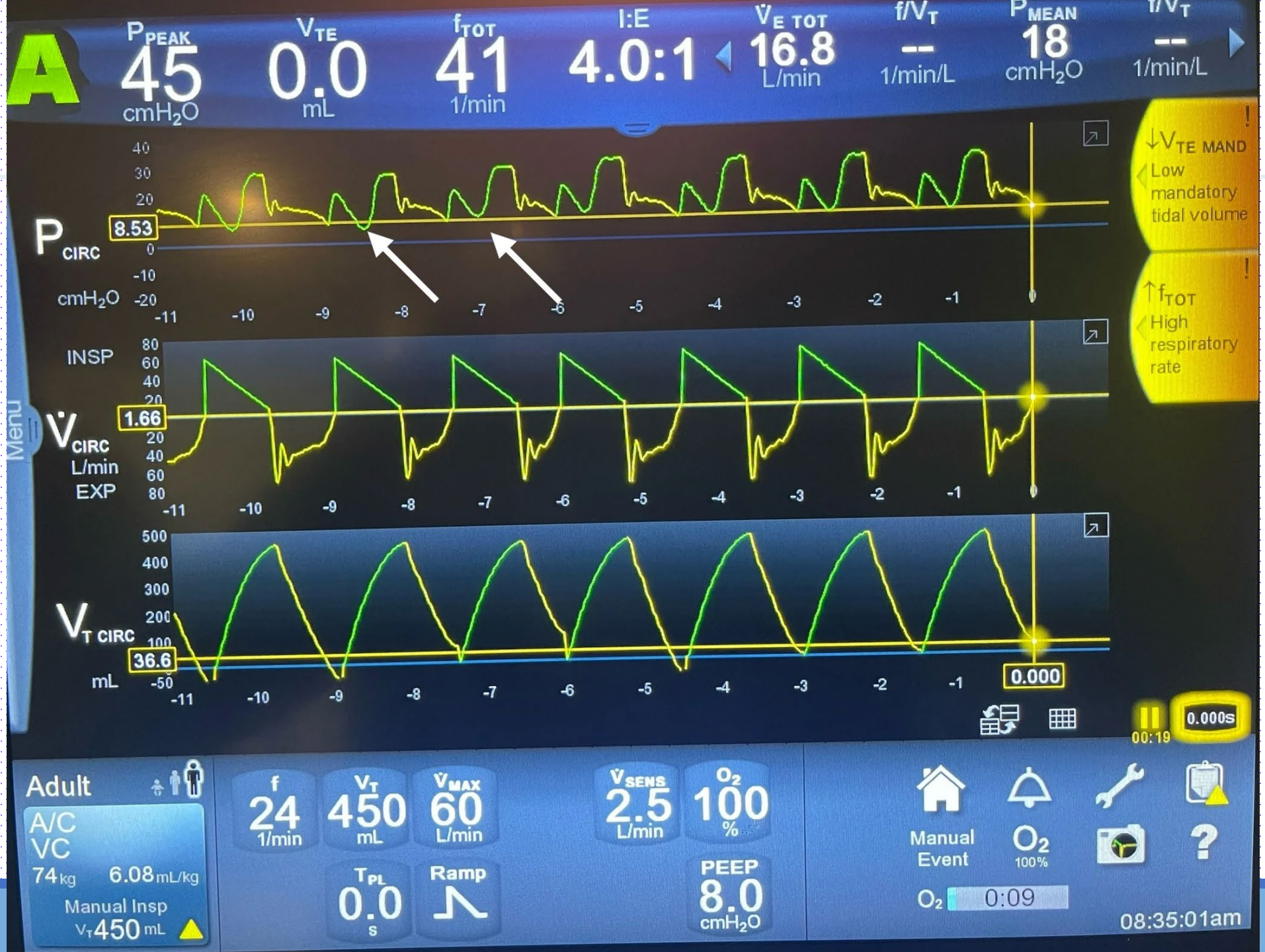
Risk of Death				**Risk of Bleeding**		
Low	Intermediate Low	Intermediate High	High	Low	Intermediate	High

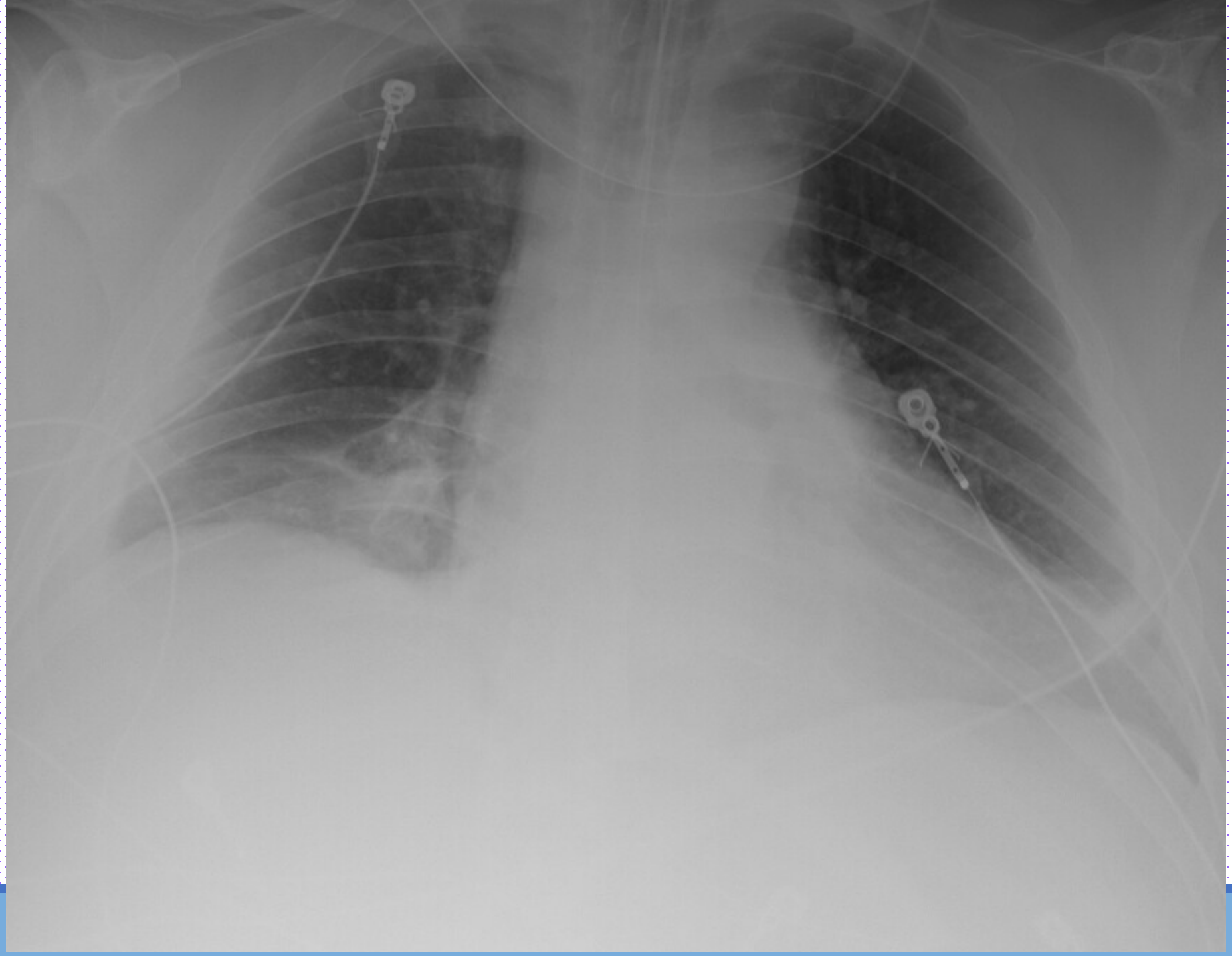
Management

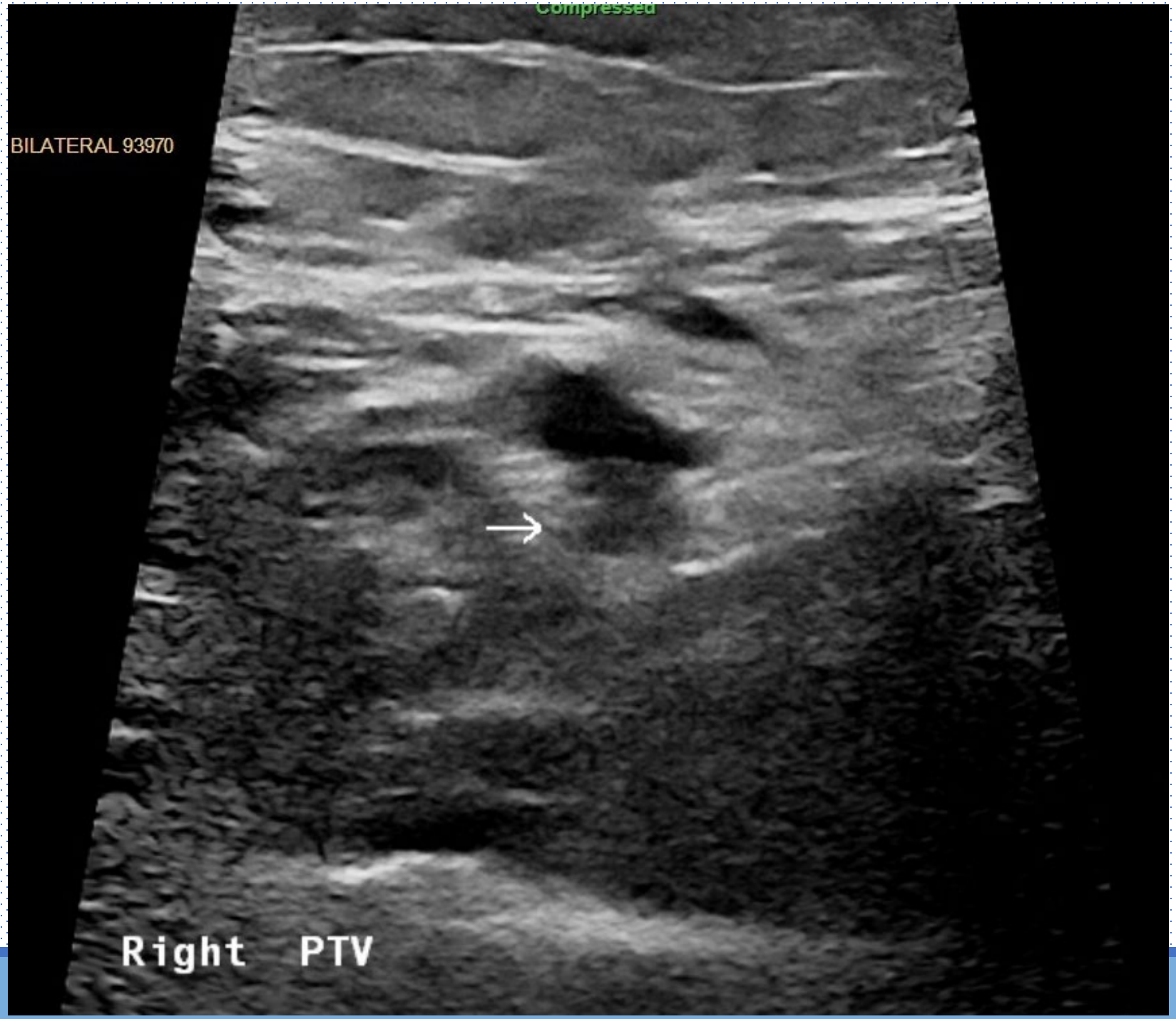
Surveillance without anticoagulation	Anticoagulation	Systemic Thrombolysis Primary – ~~Rescue – Reduced~~	Catheter-directed Thrombolysis	Catheter-directed Embolectomy	Surgical Embolectomy	IVC Filter

Disposition

Home & F/U	Monitored Bed	ICU


A
P PEAK 45 cmH2O
V TE 0.0 mL
f TOT 41 1/min
I:E 4.0:1
V̇ E TOT 16.8 L/min
f/VT -- 1/min/L
P MEAN 18 cmH2O
f/VT -- 1/min/L
↓VTE MAND
Low mandatory tidal volume
↑fTOT
High respiratory rate
P CIRC 8.53 cmH2O
INSP
V̇ CIRC 1.66 L/min EXP
V T CIRC 36.6 mL
0.000
00:19
0.000s
Menu
Adult
A/C VC
74 kg 6.08 mL/kg
Manual Insp VT 450 mL
f 24 1/min
VT 450 mL
V̇MAX 60 L/min
V̇SENS 2.5 L/min
O2 100 %
TPL 0.0 s
Ramp
PEEP 8.0 cmH2O
Manual Event
O2 100%
O2 0:09
08:35:01am

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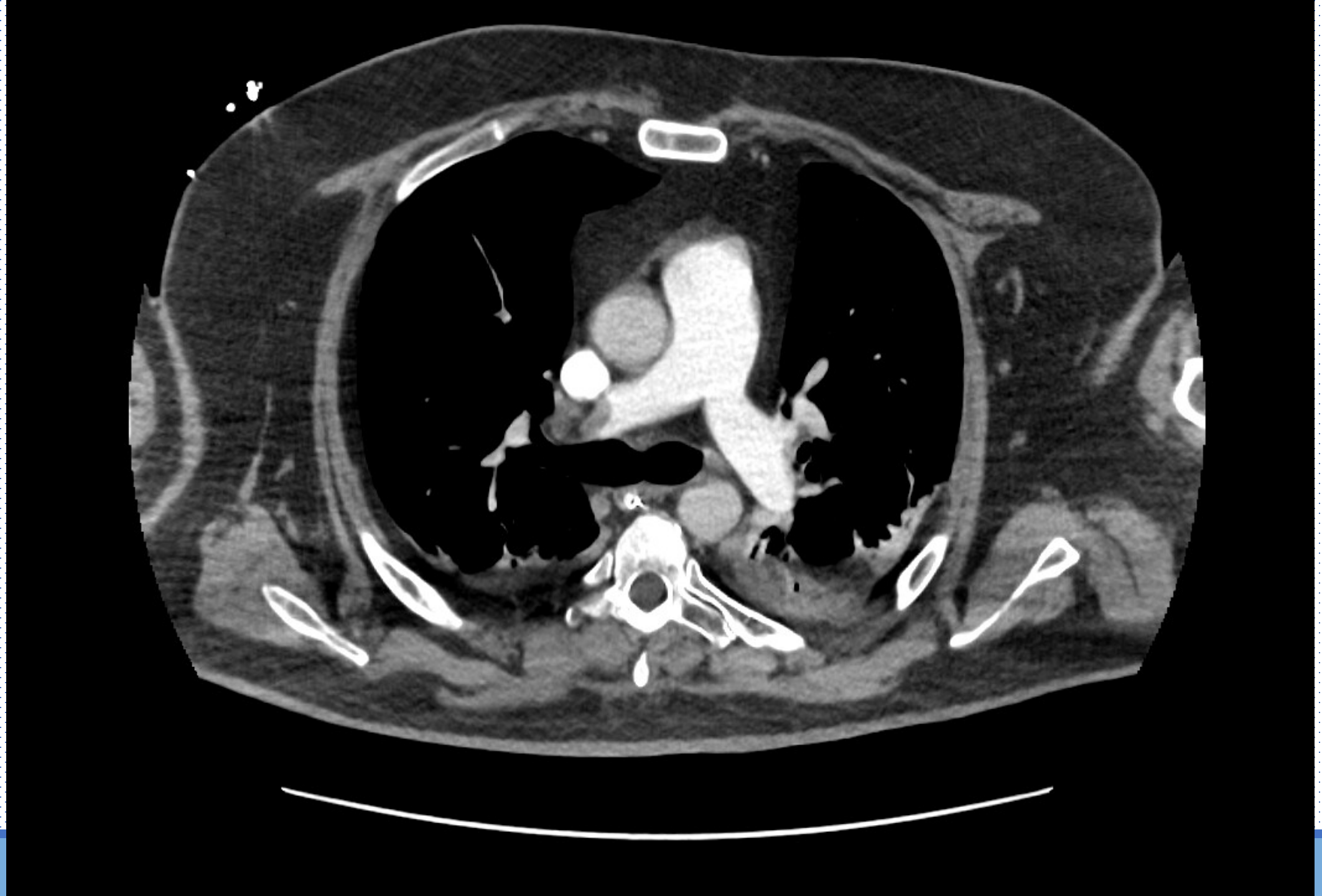
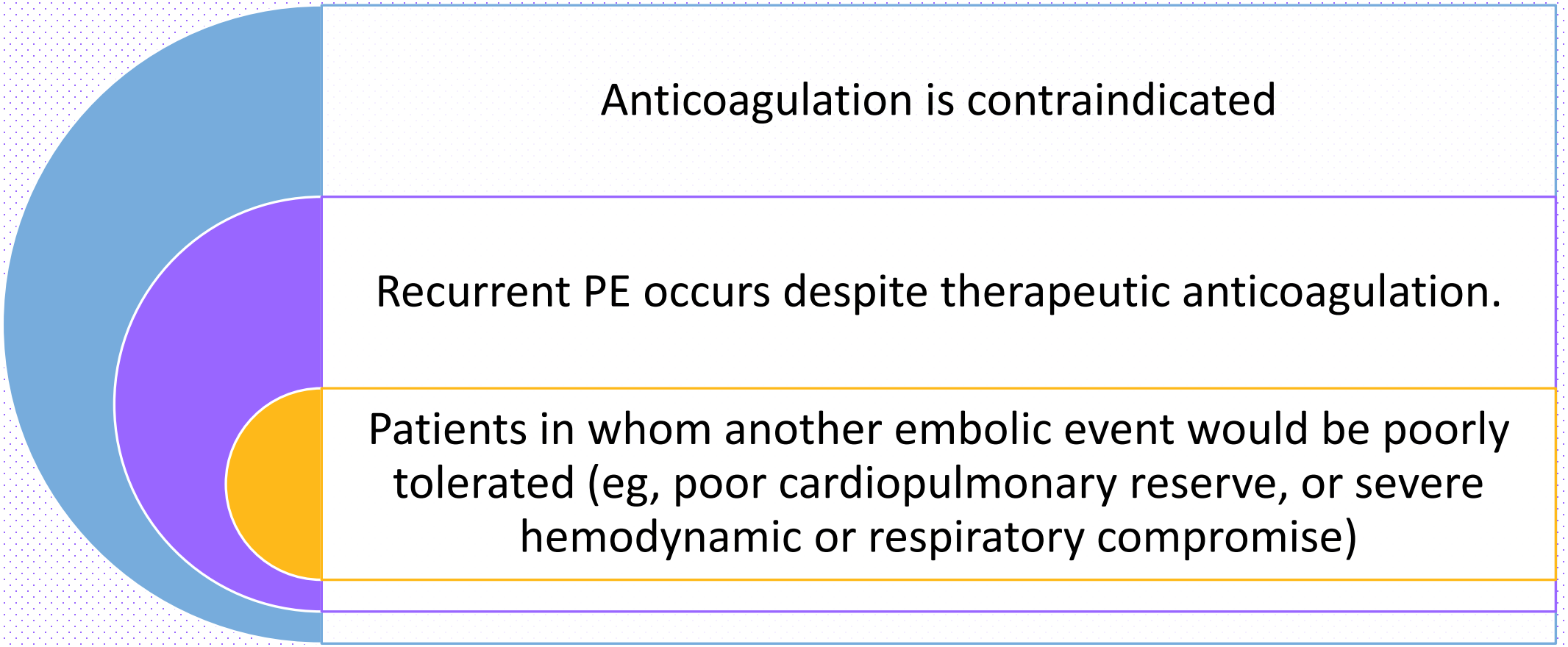
BILATERAL 93970
Right PTV



Value of PE Response Team (PERT)

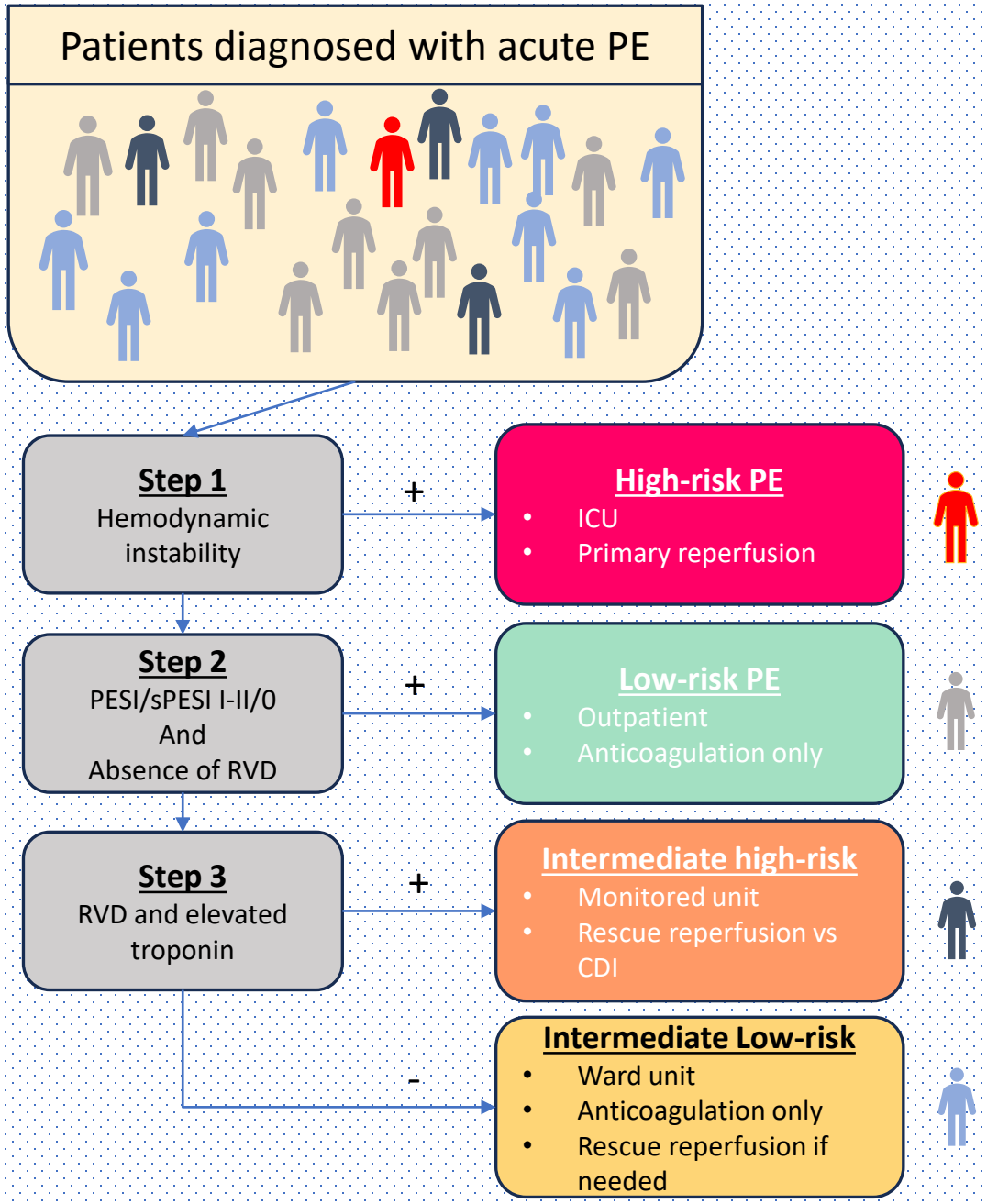
- PERT = Easy Access for multidisciplinary evaluation of a PE patient.
- Rapid evaluation.
- Diagnostic Plan.
- Mechanism to exercise full range of medical, surgical and/or interventional options.
- Expert evaluation for procedures and interventions
- Follow up after discharge

Indications of IVC Filter

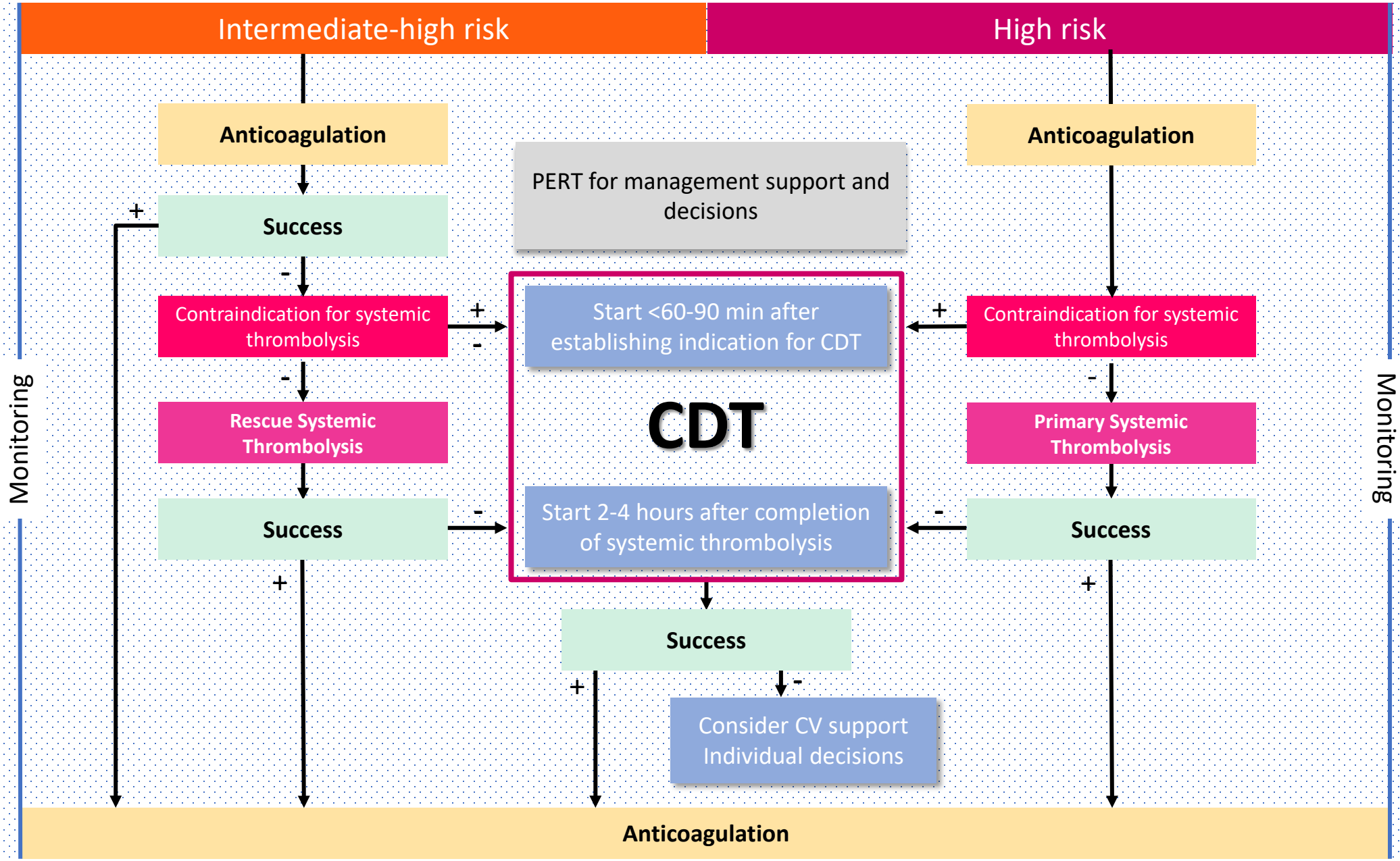


Treatment of PE

Early mortality risk		Risk of Bleeding		
		Low	Intermediate	High
Catastrophic		tPA 50 mg IV push over 2 min. May repeat in 15 min if ROSC not obtained	tPA 50 mg IV push over 2 min. May repeat in 15 min if ROSC not obtained	ECMO or tPA 50 mg IV push over 2 min. May repeat in 15 min if ROSC not obtained
High		Primary tPA 100 mg/2hr (initial 20 mg as bolus)	CDI or Primary tPA 50 mg/2hr (10 mg as bolus)	CDI or Surgical embolectomy
Intermediate	High	CDI or Rescue tPA 100 mg/2hr May consider half dose	CDI or Rescue tPA 50 mg/2hr (10 mg as bolus)	CDI
	Low	AC alone	AC alone	AC alone
Low		AC alone	AC alone	AC alone



Leidi, A.; Bex, S.; Righini, M.; Berner, A.; Grosgurin, O.; Marti, C. Risk Stratification in Patients with Acute Pulmonary Embolism: Current Evidence and Perspectives. *J. Clin. Med.* **2022**, *11*, 253


Intermediate-high risk
High risk
Anticoagulation
Anticoagulation
PERT for management support and decisions
Success
+
-
Contraindication for systemic thrombolysis
+
-
Start <60-90 min after establishing indication for CDT
+
Contraindication for systemic thrombolysis
-
Rescue Systemic Thrombolysis
CDT
Primary Systemic Thrombolysis
Success
-
Start 2-4 hours after completion of systemic thrombolysis
-
Success
+
+
Success
+
-
Consider CV support Individual decisions
Monitoring
Monitoring
Anticoagulation

BEST PRACTICES

Treatment decisions in

Pulmonary Embolism

Anitcoagulation
if
No absolute contraindication

IVC Filter
if contraindication to heparin

Monitoring

Assess Risk of Death

HIGH

Hemodyamically Unstable:
Persistent hypotension (SBP <90 mmHg, vasopressor support, or a drop in SBP ≥40 mmHg from base-line) for >15 minutes.
Obstructive shock.
Cardiac arrest

INTERMEDIATE

Hemodyamically Stable
No hypotension

RV Dysfunction
RV/LV ≥1, bulging septum into LV, enlarged RV, reduced RV ejection fraction, or RV hypokenesis

Myocardial Necrosis
Elevated biomarkers (troponin or BNP).

Significant hypoxemia
High clot burden
Tachycardia >120
sPSEI ≥1
Cardiac thrombus
LE DVT
Poor cardiopulmonary reserve
±
RV Dysfunction **AND** ↑ Biomarkers

LOW

Hemodyamically Stable:
No hypotension
No RV dilatation
No RV hypokenesis
No high troponin
No high BNP

RV Dysfunction **OR** ↑ Biomarkers

Continiue Anitcoagulation

Deterioration

Assess Risk of Bleeding

High Risk

Absolute Contraindications:
Prior intracranial hemorrhage.
Known structural cerebral vascular lesion.
Known malignant intracranial neoplasm.
Ischemic stroke within three months (excluding stroke within three hours*).
Suspected aortic dissection.
Active bleeding or bleeding diathesis (excluding menses).
Significant closed-head trauma or facial trauma within three months.

Intermediate Risk

Relative Contraindications:
History of chronic, severe, poorly controlled hypertension.
Uncontrolled hypertension on presentation (SBP >180 mmHg or DBP >110 mmHg).
History of ischemic stroke > three months prior.
Traumatic or prolonged (>10 minute) CPR or major surgery < three weeks.
Recent (within two to four weeks) internal bleeding.
Noncompressible vascular punctures.
Recent invasive procedure.
Prior exposure (> five days ago) or prior allergic reaction to streptokinase/anistreplase.
Pregnancy.
Active peptic ulcer.
Pericarditis or pericardial fluid.
Anticoagulant-induced elevated INR >1.7 or PT >15 seconds.
Age >75 years.
Diabetic retinopathy.

Low Risk

No known absolute or relative contra-indications.

Unstable

Hypotension did NOT resolve after 2-4 hours

Systemic Thrombolysis

Stable

Catheter-directed Therapies (embolectomy vs thrombolysis or both)

Sysstemic Thrombolysis
Full dose: 100 mg tissue plasminogen activator (tPA) infusion over ≤2 hours folowed by anticoagulation after 24 hours (or when PTT ≤2X normal).

Reduced dose: 50 mg tPA IV over ≤2 hours.

Ultra low dose: 25 mg tPA IV over 24 hours.

Cardiac arrest: 50 mg tPA IV bolus over 2 minutes, repeat in 15 minutes if no ROSC.

PERT:
Pulmonary Embolism Response Team

January 8, 2024

icu REACH

Take Home Messages

Not all patients with acute PE require hospitalization or anticoagulation

Risk stratification is crucial

Selected cases benefit from thrombolysis

More data on CDI

Consider PERT in your hospital!


Thank you