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Submassive and Massive PE

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Topics

- Mortality from severe disease vs non-severe disease
- Predictors of severity and mortality
- Potential interventions

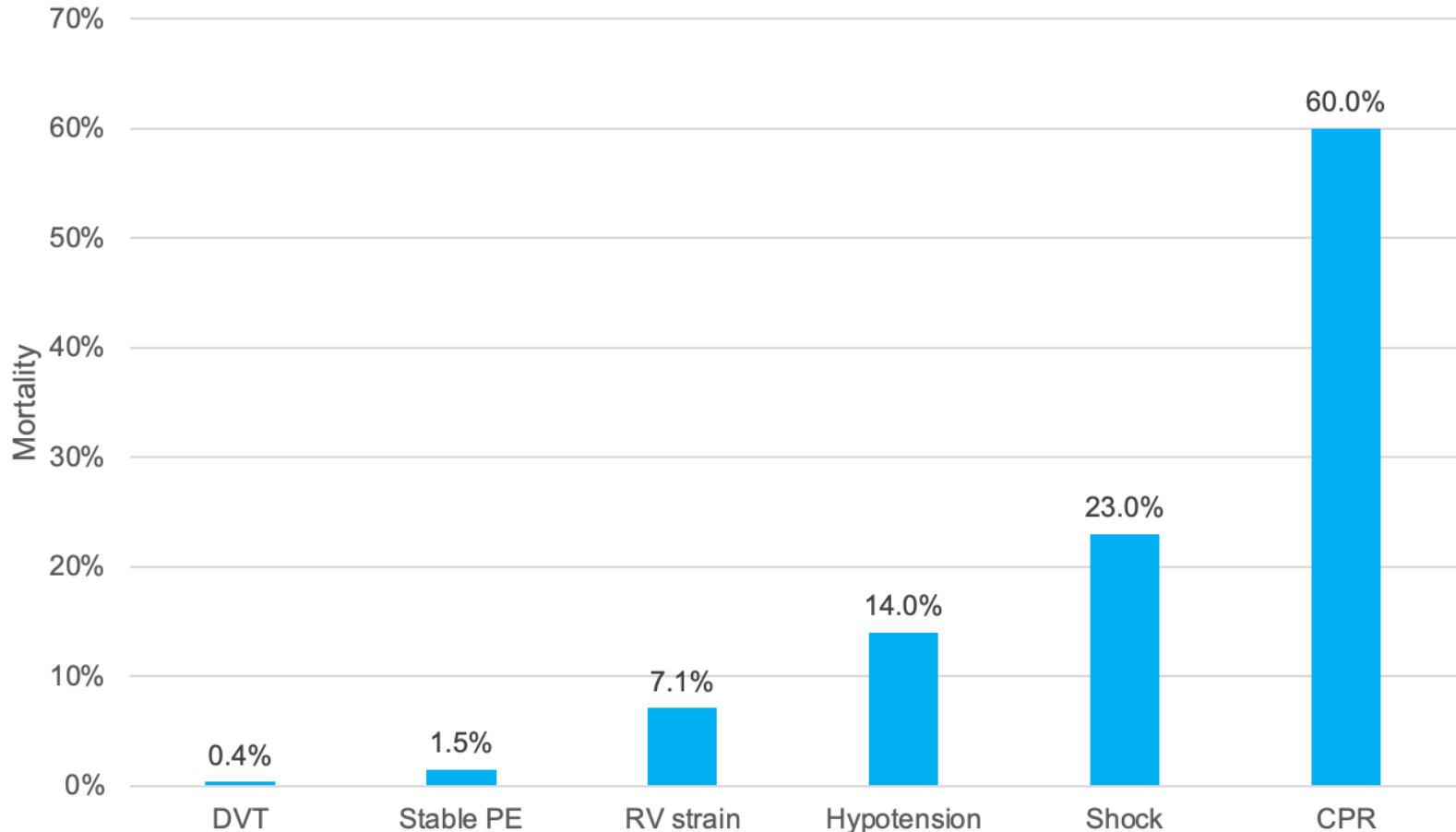


Topics

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Hemodynamics and PE Mortality



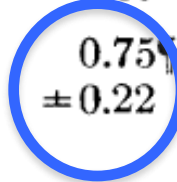
1. Douketis JD, Kearon C, Bates S, Duku EK, Ginsberg JS. Risk of fatal pulmonary embolism in patients with treated venous thromboembolism. *JAMA*. 1998;279(6):458-462.
2. Kasper W, Konstantinides S, Geibel A, et al. Management strategies and determinants of outcome in acute major pulmonary embolism: results of a multicenter registry. *J Am Coll Cardiol*. 1997;30(5):1165-1171.



RV blood flow goes down

TABLE 2. *Myocardial Blood Flow Data*

	Control			RV hypertension			Failure		
	Pericardium		Pooled data	Pericardium		Pooled data	Pericardium		Pooled data
	Open	Closed		Open	Closed		Open	Closed	
RV myocardial blood flow (ml/min/g)	0.72 ±0.27	0.61 ±0.22	0.67 ±0.25	1.01 ±0.29	1.02 ±0.31	1.01* ±0.29	0.68 ±0.36	0.74 ±0.32	0.71† ±0.33
RV endocardial blood flow (ml/min/g)	0.78 ±0.38	0.62 ±0.25	0.70 ±0.33	1.03 ±0.37	1.02 ±0.39	1.02* ±0.37	0.64 ±0.42	0.77 ±0.42	0.70† ±0.41
RV epicardial blood flow (ml/min/g)	0.82 ±0.28	0.61 ±0.21	0.71 ±0.26	1.17 ±0.28	1.08 ±0.33	1.13* ±0.30	0.89 ±0.43	0.86 ±0.32	0.88† ±0.37
RV endo:epi flow	0.94 ±0.21	1.01 ±0.23	0.97 ±0.22	0.86 ±0.15	0.96 ±0.28	0.91 ±0.22	0.69 ±0.16	0.81 ±0.28	0.75† ±0.22



1. Vlahakes GJ, Turley K, Hoffman JI. The pathophysiology of failure in acute right ventricular hypertension: hemodynamic and biochemical correlations. *Circulation* 1981;63(1):87-95.



RV has an MI, not the LV

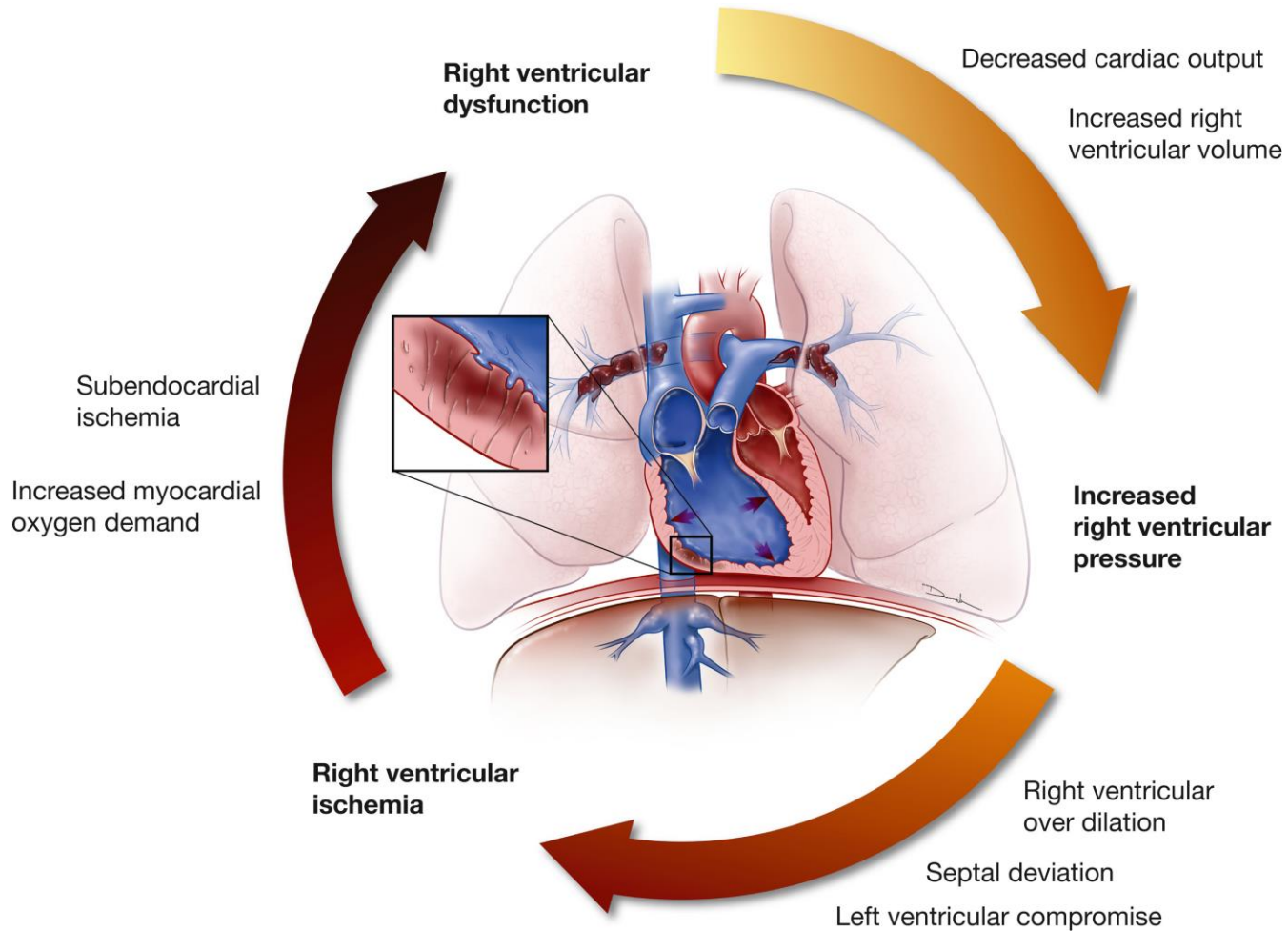
TABLE 3. *Biochemical Data*

	Control	RV hypertension	Failure
A. Right ventricular free wall			
Creatine phosphate ($\mu\text{mol/g}$)	8.37 \pm 1.56	8.17 \pm 1.41	3.75 \pm 1.98*
ATP ($\mu\text{mol/g}$)	4.01 \pm 0.48	3.95 \pm 0.47	3.03 \pm 0.85†
[lactate] : [pyruvate]	17.6 \pm 8.4	13.9 \pm 4.6	56.8 \pm 23.3*
B. Left ventricular free wall			
Creatine phosphate ($\mu\text{mol/g}$)	8.72 \pm 1.09	8.74 \pm 1.61	7.62 \pm 0.85
ATP ($\mu\text{mol/g}$)	4.48 \pm 0.35	4.57 \pm 0.57	4.23 \pm 0.56
[lactate] : [pyruvate]	19.1 \pm 9.1	17.5 \pm 7.4	16.7 \pm 4.9

1. Vlahakes GJ, Turley K, Hoffman JI. The pathophysiology of failure in acute right ventricular hypertension: hemodynamic and biochemical correlations. *Circulation* 1981;63(1):87-95.



The Perfect Storm



1. McGuire WC, Sullivan L, Odish MF, Desai B, Morris TA, Fernandes TM. Management Strategies for Acute Pulmonary Embolism in the ICU. *Chest*. 2024.



- Mortality from severe disease vs non-severe disease
- **Predictors of severity and mortality**
- Potential interventions



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Premorbid Conditions



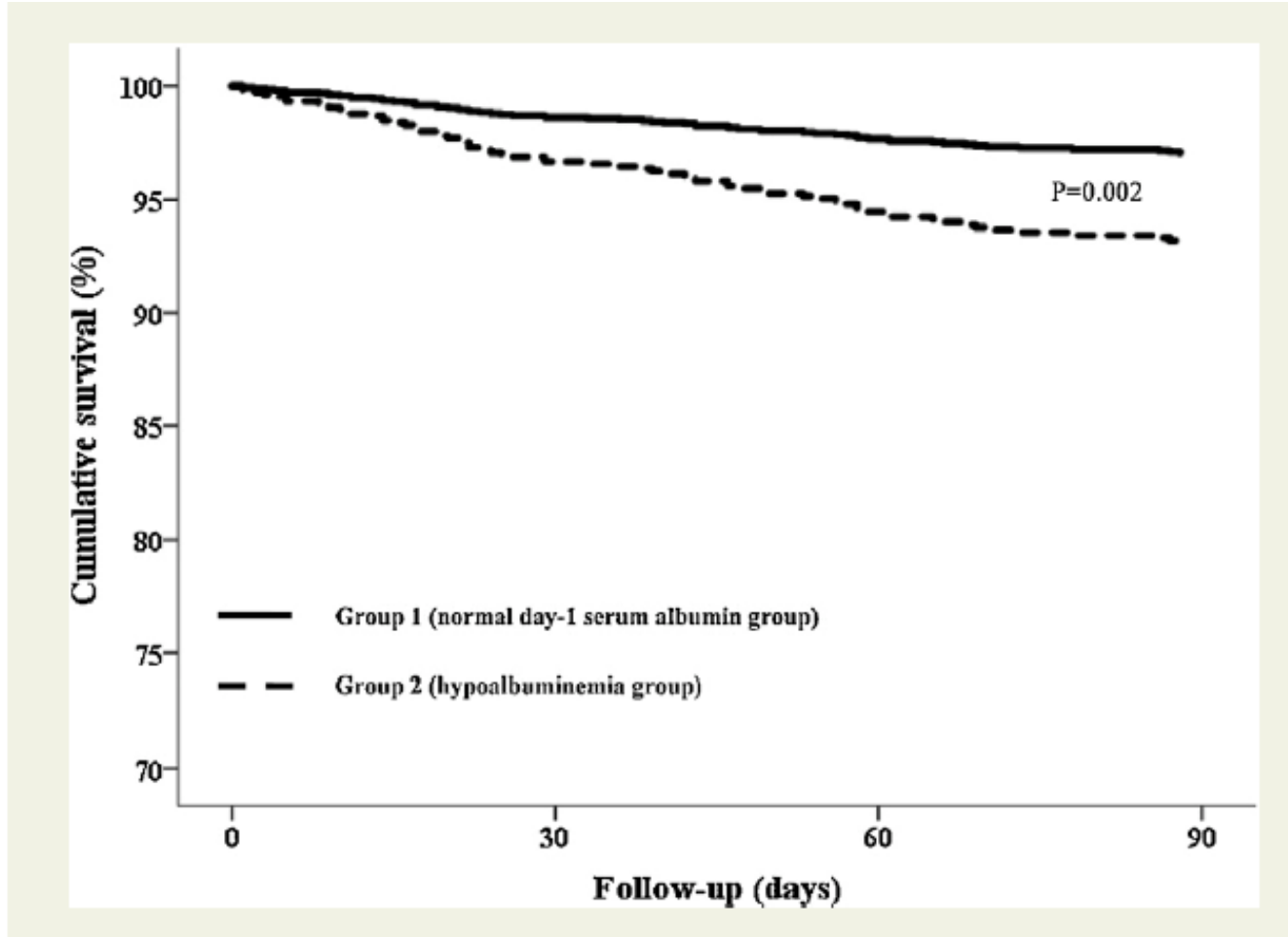
Features Associated with Worse PE Outcomes

1. Hypoalbuminemia
2. Obstructive Sleep Apnea
3. Syncope
 - Women but not men?
4. Systolic BP

1. Hoskin S, Chow V, Kritharides L, Ng ACC. Incidence and Impact of Hypoalbuminaemia on Outcomes Following Acute Pulmonary Embolism. *Heart, lung & circulation*. 2020;29(2):280-287.
2. Geissenberger F, Schwarz F, Probst M, et al. Obstructive sleep apnea is associated with pulmonary artery thrombus load, disease severity, and survival in acute pulmonary embolism. *Clinical research in cardiology : official journal of the German Cardiac Society*. 2020;109(1):13-21.
3. Dzudovic B, Subotic B, Novicic N, et al. Sex-related difference in the prognostic value of syncope for 30-day mortality among hospitalized pulmonary embolism patients. *Clin Respir J*. 2020;14(7):645-651.
4. Quezada A, Jiménez D, Bikdeli B, et al. Systolic blood pressure and mortality in acute symptomatic pulmonary embolism. *International journal of cardiology*. 2020;302:157-163.



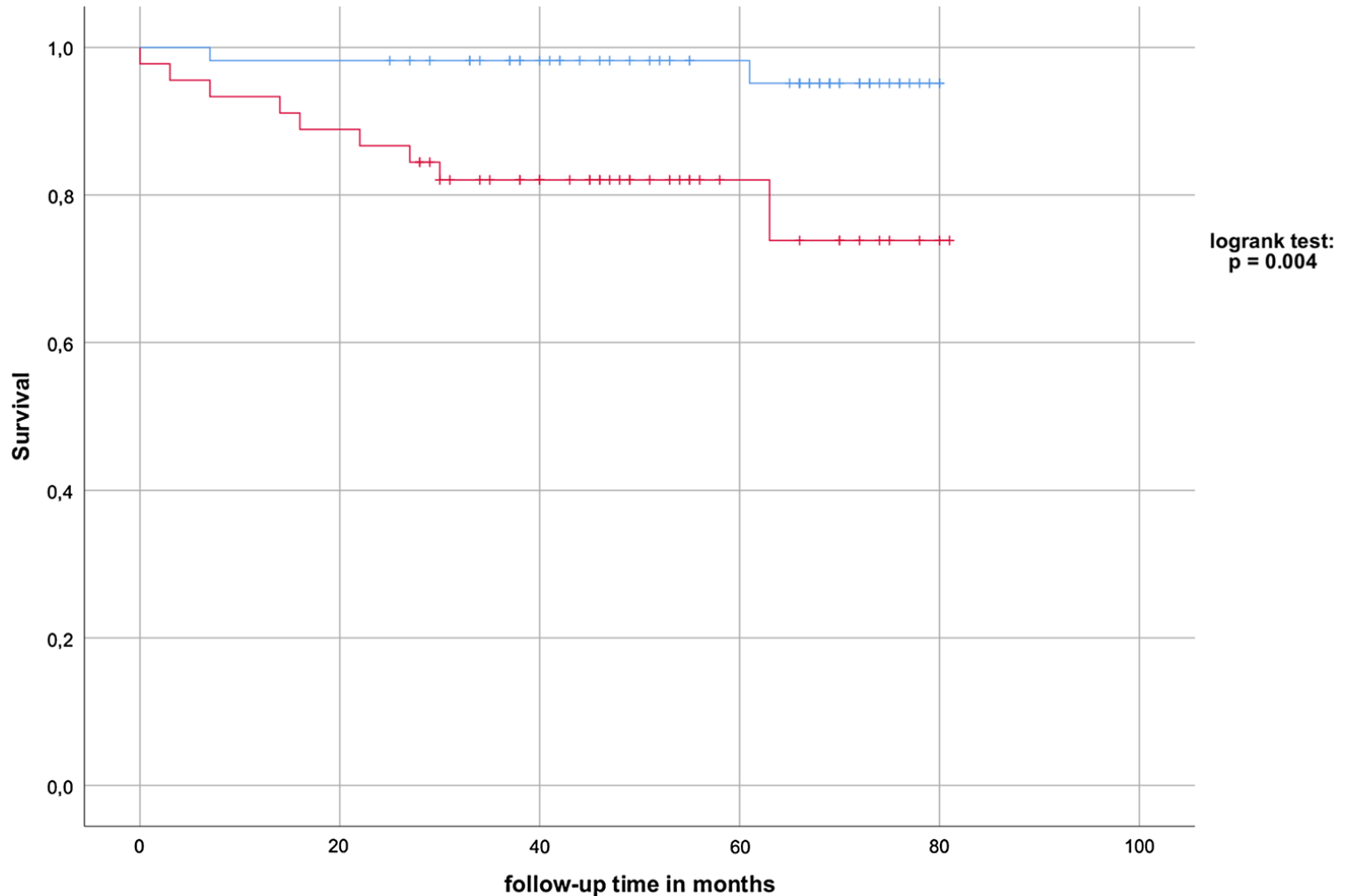
Hypoalbuminemia and Outcome after PE



1. Hoskin S, Chow V, Kritharides L, Ng ACC. Incidence and Impact of Hypoalbuminaemia on Outcomes Following Acute Pulmonary Embolism. *Heart, lung & circulation*. 2020;29(2):280-287.



Sleep apnea and outcome after PE



1. Geissenberger F, Schwarz F, Probst M, et al. Obstructive sleep apnea is associated with pulmonary artery thrombus load, disease severity, and survival in acute pulmonary embolism. *Clinical research in cardiology : official journal of the German Cardiac Society*. 2020;109(1):13-21.

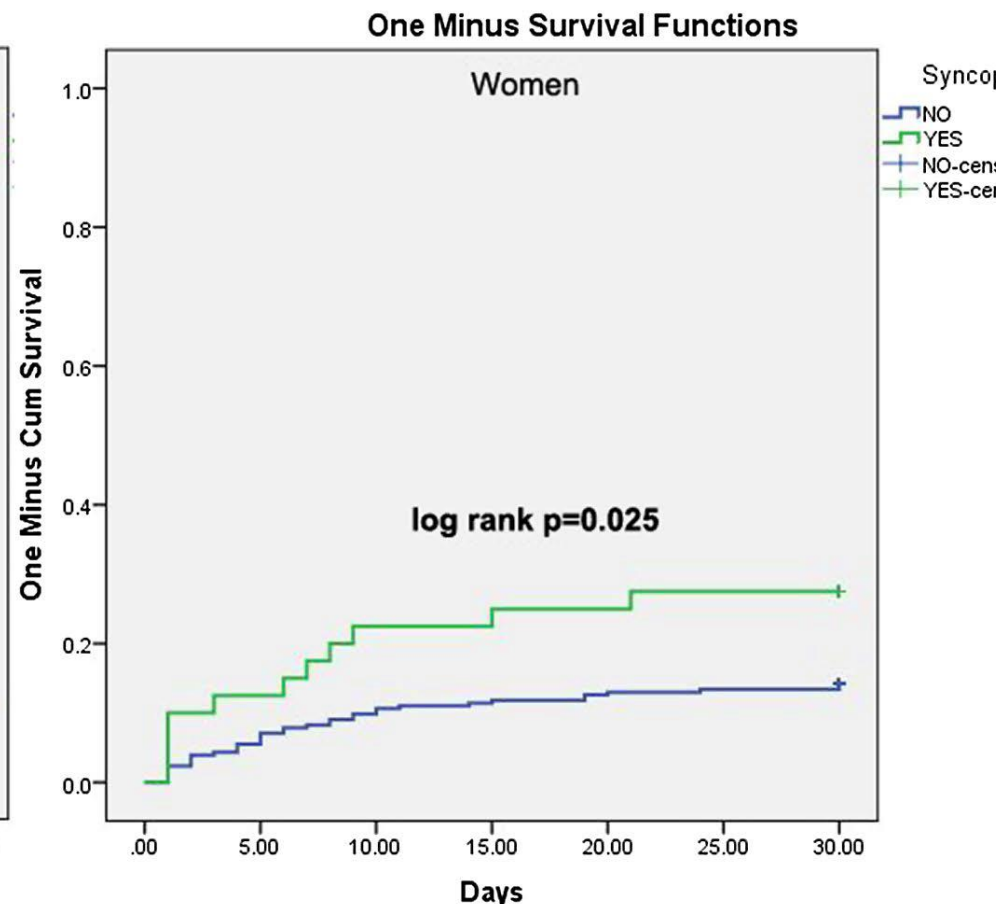
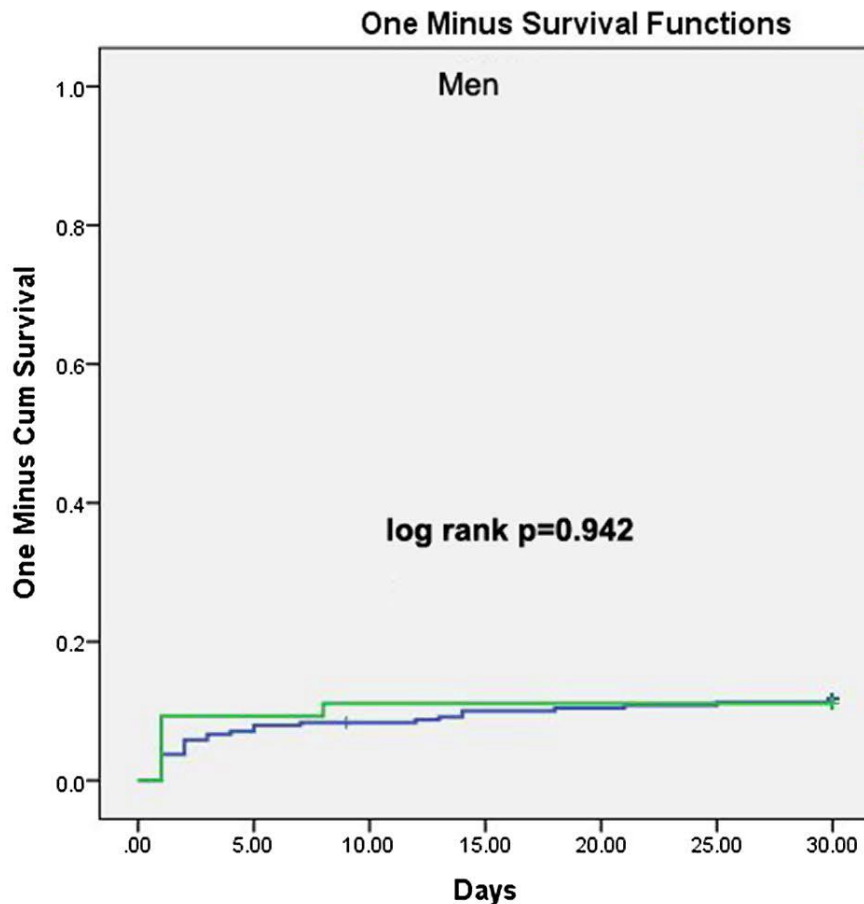


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Presentation



Syncopal and outcomes after PE



1. Dzudovic B, Subotic B, Novicic N, Matijasevic J, Trobok J, Miric M, Salinger-Martinovic S, Stanojevic D, Nikolic M, Miloradovic V, Markovic Nikolic N, Dekleva M, Lepojevic Stefanovic D, Kos L, Kovacevic Preradovic T, Obradovic S. Sex-related difference in the prognostic value of syncopal for 30-day mortality among hospitalized pulmonary embolism patients. *Clin Respir J.* 2020;14(7):645-651.



Scores to predict PE mortality

- PESI
 - Pulmonary embolism severity score
- sPESI
 - simplified Pulmonary embolism severity score
- ESC
 - European Society of Cardiology classification
- Bova
 - (the guy's name)



PESI and sPESI

Table 1. Original and Simplified Pulmonary Embolism Severity Index (PESI)

Variable	Score	
	Original PESI ^a	Simplified PESI ^b
Age >80 y	Age in years	1
Male sex	+10	
History of cancer	+30	1
History of heart failure	+10	1 ^c
History of chronic lung disease	+10	
Pulse \geq 110 beats/min	+20	1
Systolic blood pressure <100 mm Hg	+30	1
Respiratory rate \geq 30 breaths/min	+20	
Temperature <36°C	+20	
Altered mental status	+60	
Arterial oxyhemoglobin saturation level <90%	+20	1

1. Jiménez D, Aujesky D, Moores L, et al; RIETE Investigators. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. Arch Intern Med. 2010;170 (15):1383-1389.



ESC

Early mortality risk		Indicators of risk			
		Haemodynamic instability ^a	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥1	RV dysfunction on TTE or CTPA ^b	Elevated cardiac troponin levels ^c
High		+	(+) ^d	+	(+)
Intermediate	Intermediate–high	-	+ ^e	+	+
	Intermediate–low	-	+ ^e	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

© ESC 2019

1. Konstantinides SV, Meyer G, Becattini C, et al; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41(4):543-603



“Bova” Score

TABLE 5 Risk score

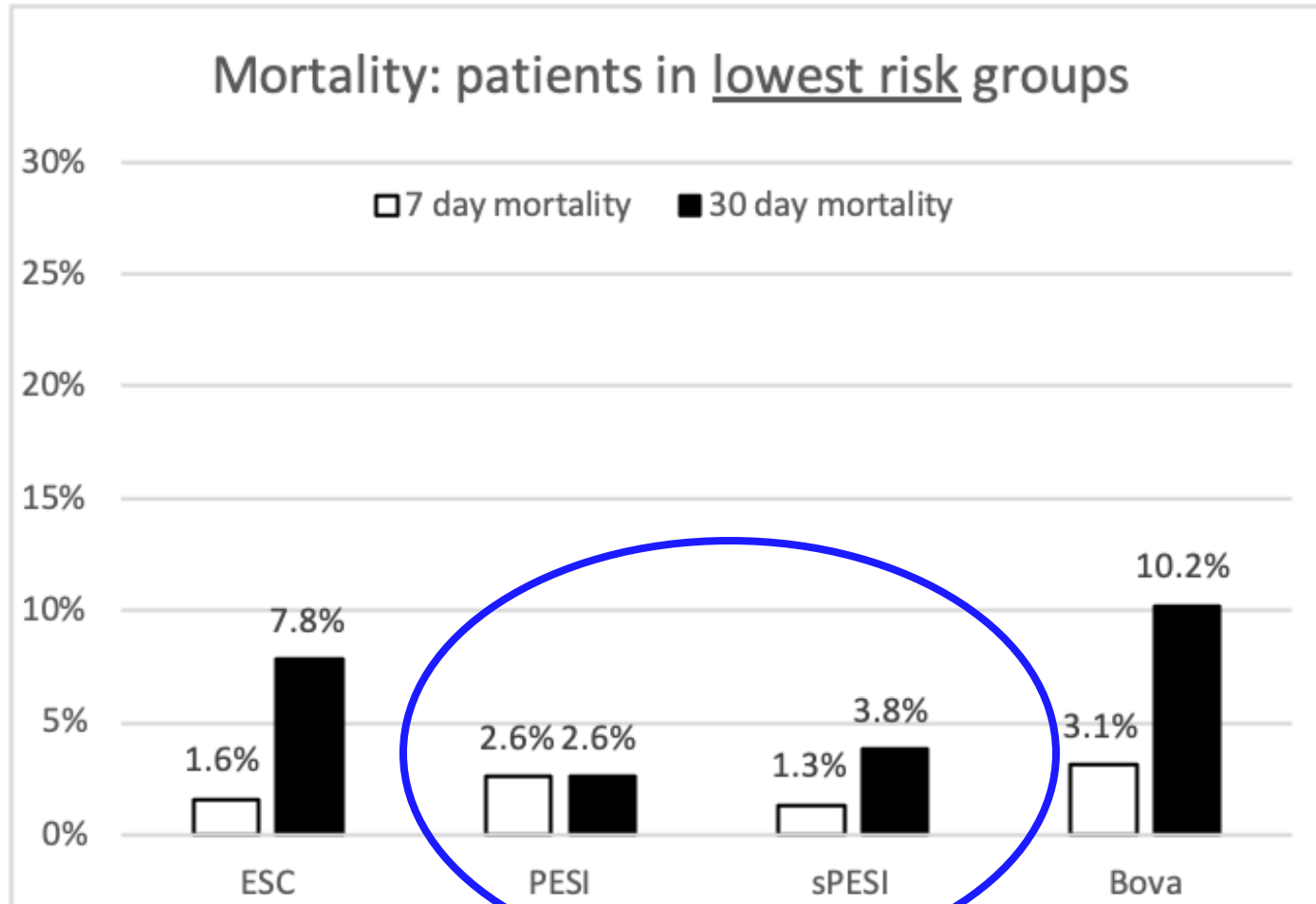
Predictor	Points
SBP 90–100 mmHg	2
Elevated cardiac troponin	2
RV dysfunction (echocardiogram or CT scan)	2
Heart rate \geq 110 beats per min	1

Points are assigned for each variable of the scoring system to obtain a total point score (range 0–7). SBP: systolic blood pressure; RV: right ventricular; CT: computed tomography.

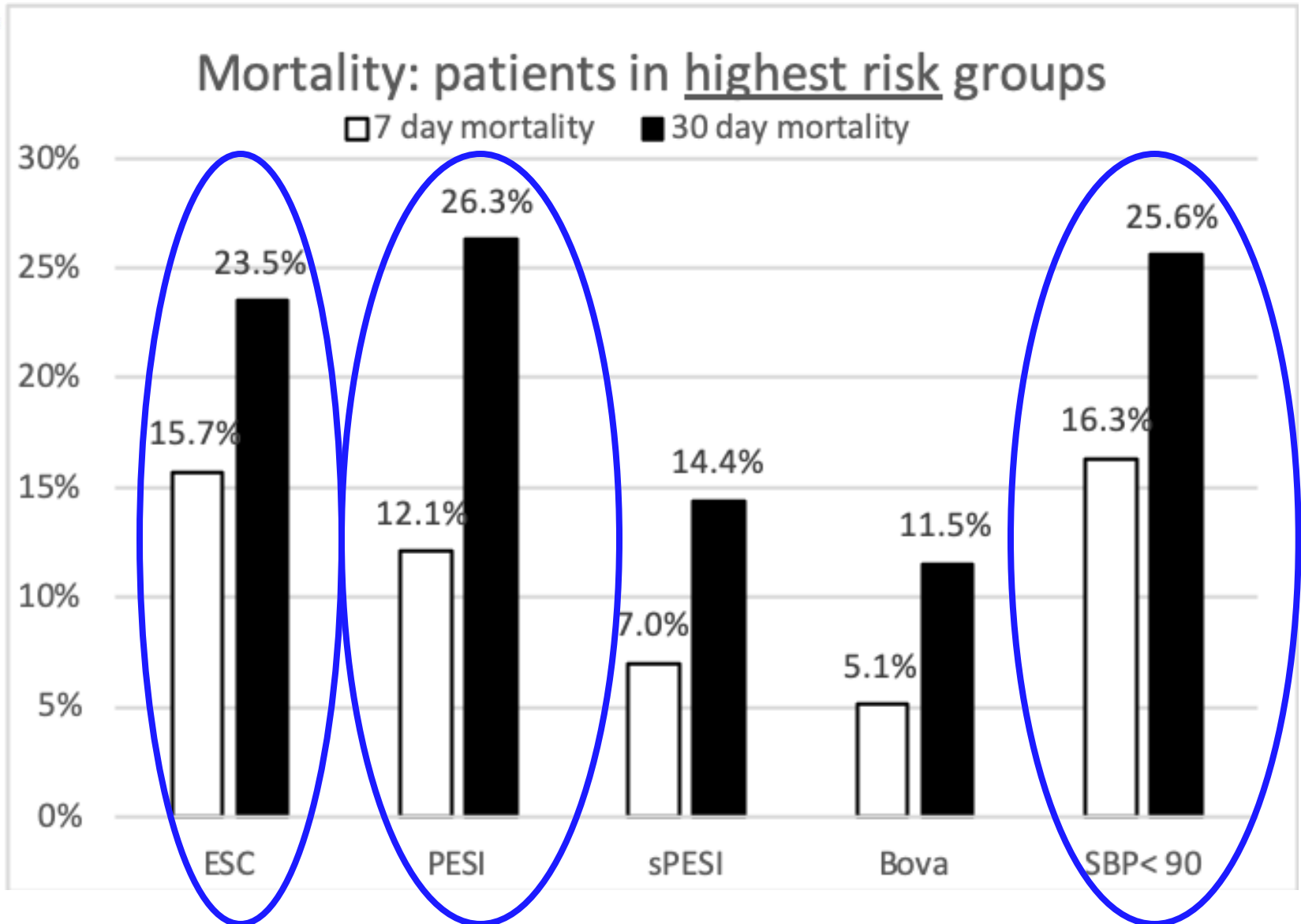
1. Bova C, Sanchez O, Prandoni P, et al. Identification of intermediate-risk patients with acute symptomatic pulmonary embolism. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology*. 2014;44(3):694-703



Severity Prediction: “Low Risk”



1. Barnes GD, Muzikansky A, Cameron S, et al. Comparison of 4 Acute Pulmonary Embolism Mortality Risk Scores in Patients Evaluated by Pulmonary Embolism Response Teams. *JAMA Netw Open.* 2020;3(8):e2010779.



1. Barnes GD, Muzikansky A, Cameron S, et al. Comparison of 4 Acute Pulmonary Embolism Mortality Risk Scores in Patients Evaluated by Pulmonary Embolism Response Teams. *JAMA Netw Open.* 2020;3(8):e2010779.



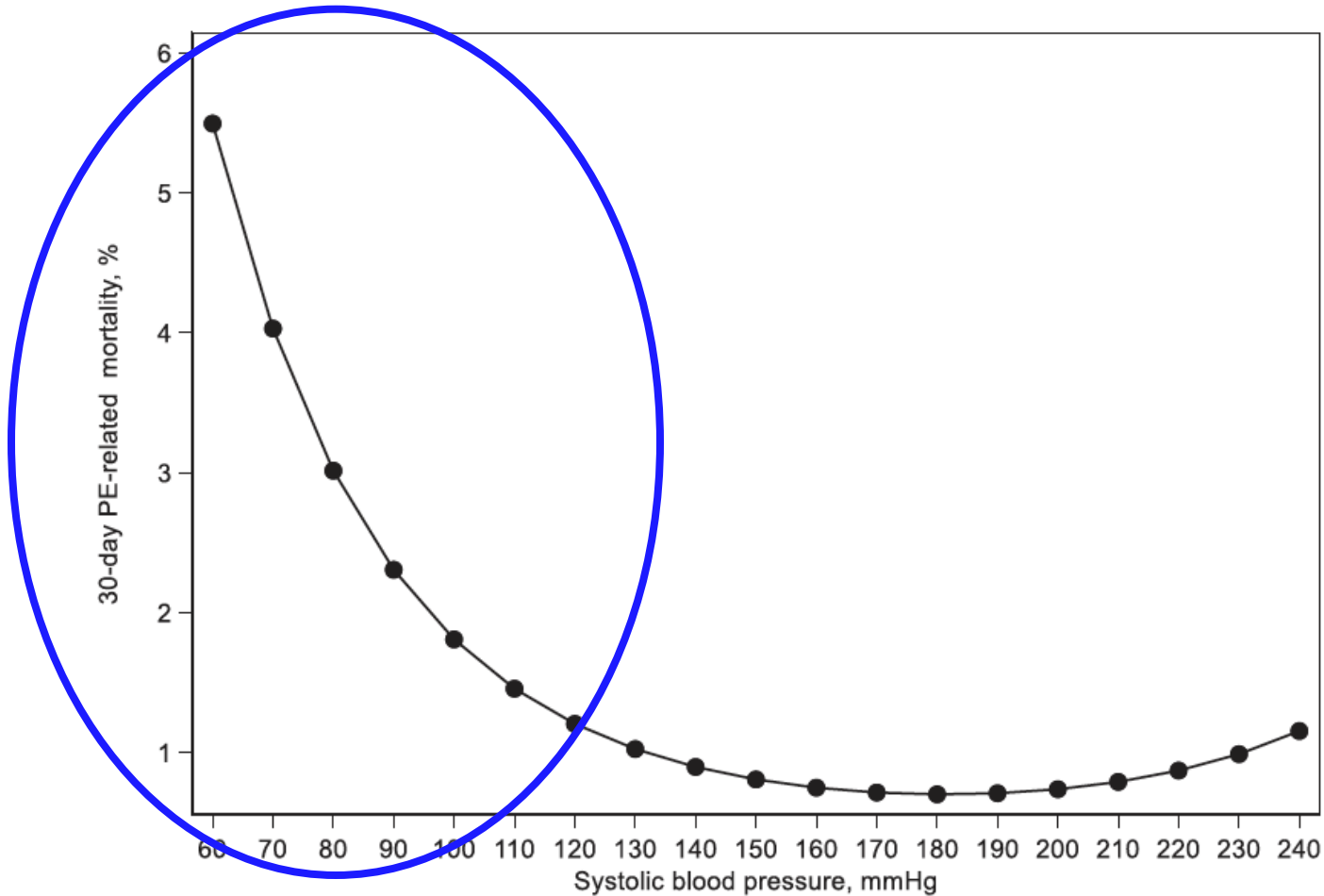
ESC “high risk” reflected low SBP

		<i>BOVA Class</i>				
		1	2	3	SBP < 90	
<i>ESC Risk Category</i>	Low	52	3	0	0	
	Intermediate-Low	64	34	6	0	
	Intermediate-High	11	61	69	0	
	High	1	1	3	43	

1. Barnes GD, Muzikansky A, Cameron S, et al. Comparison of 4 Acute Pulmonary Embolism Mortality Risk Scores in Patients Evaluated by Pulmonary Embolism Response Teams. *JAMA Netw Open.* 2020;3(8):e2010779.



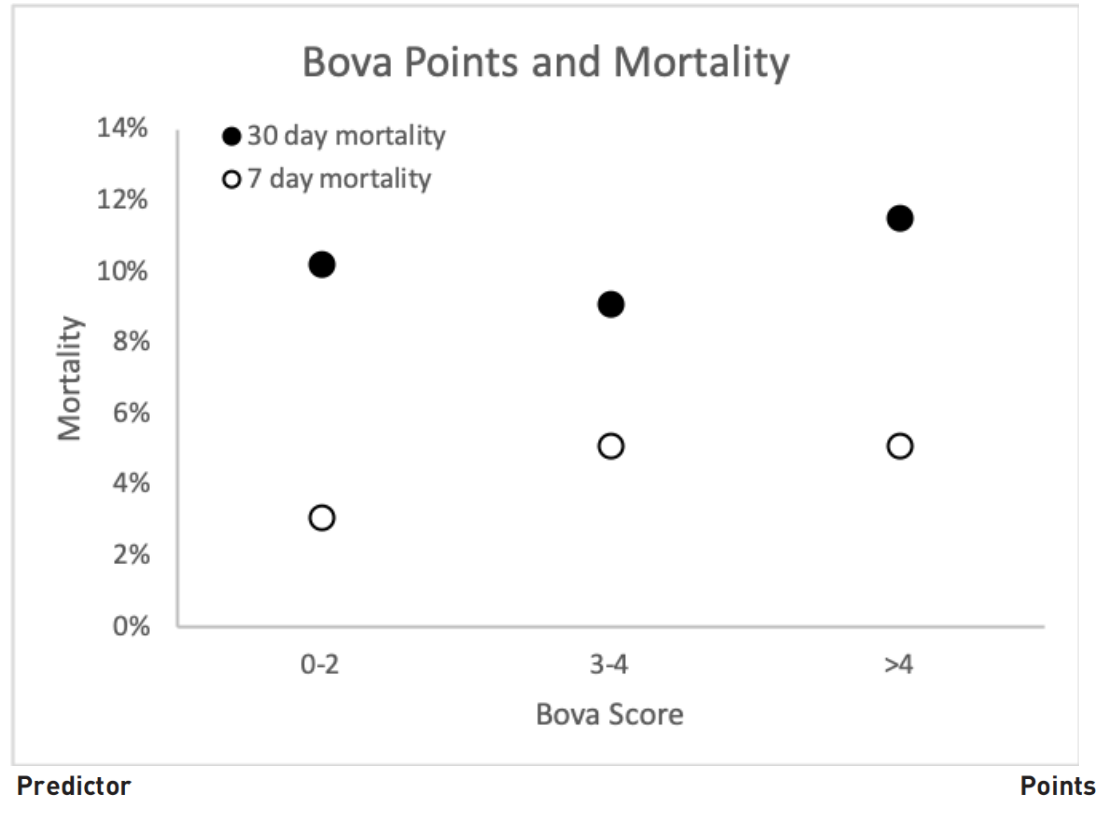
SBP and 30 day mortality after PE



1. Quezada A, Jiménez D, Bikdeli B, et al. Systolic blood pressure and mortality in acute symptomatic pulmonary embolism. *International journal of cardiology*. 2020;302:157-163.



Bova Score Didn't Predict Mortality



SBP 90-100 mmHg	2
Elevated cardiac troponin	2
RV dysfunction (echocardiogram or CT scan)	2
Heart rate ≥ 110 beats per min	1

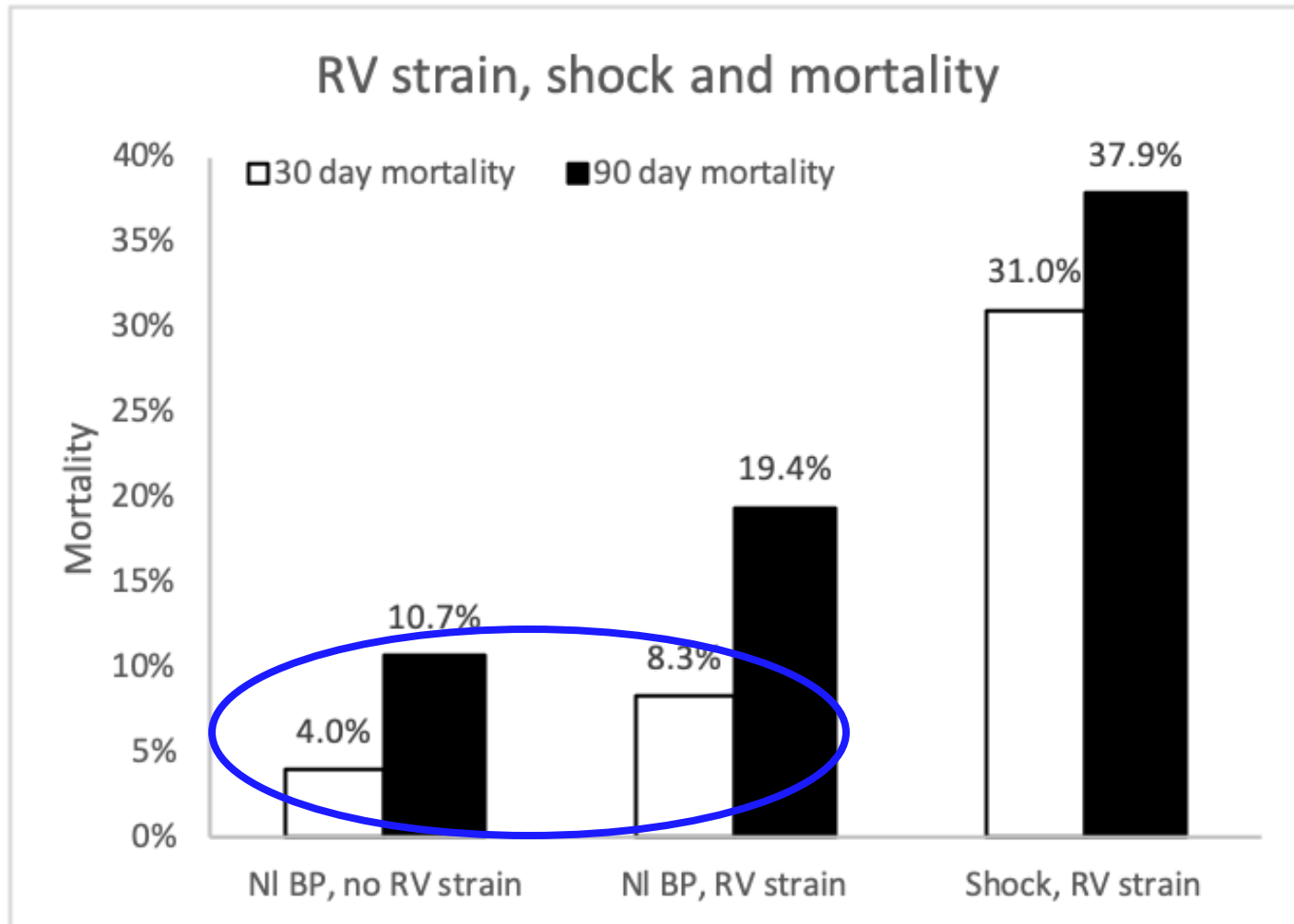
1. Barnes GD, Muzikansky A, Cameron S, et al. Comparison of 4 Acute Pulmonary Embolism Mortality Risk Scores in Patients Evaluated by Pulmonary Embolism Response Teams. *JAMA Netw Open*. 2020;3(8):e2010779.
2. Bova C, Sanchez O, Prandoni P, et al. Identification of intermediate-risk patients with acute symptomatic pulmonary embolism. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology*. 2014;44(3):694-703



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Echocardiography

RV findings as independent mortality predictor



1. Chen YL, Wright C, Pietropaoli AP, et al. Right ventricular dysfunction is superior and sufficient for risk stratification by a pulmonary embolism response team. *J Thromb Thrombolysis*. 2020;49(1):34-41.

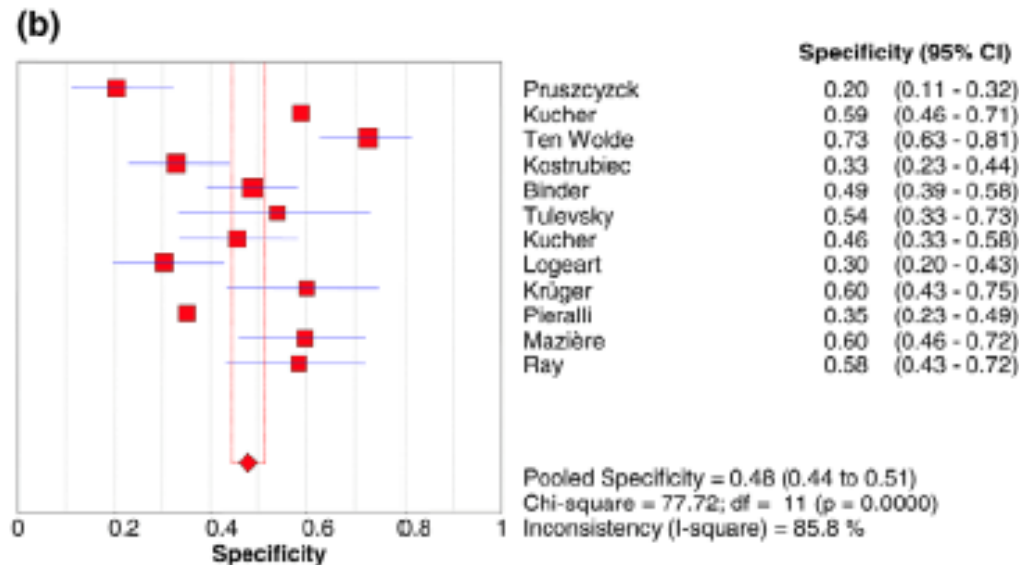
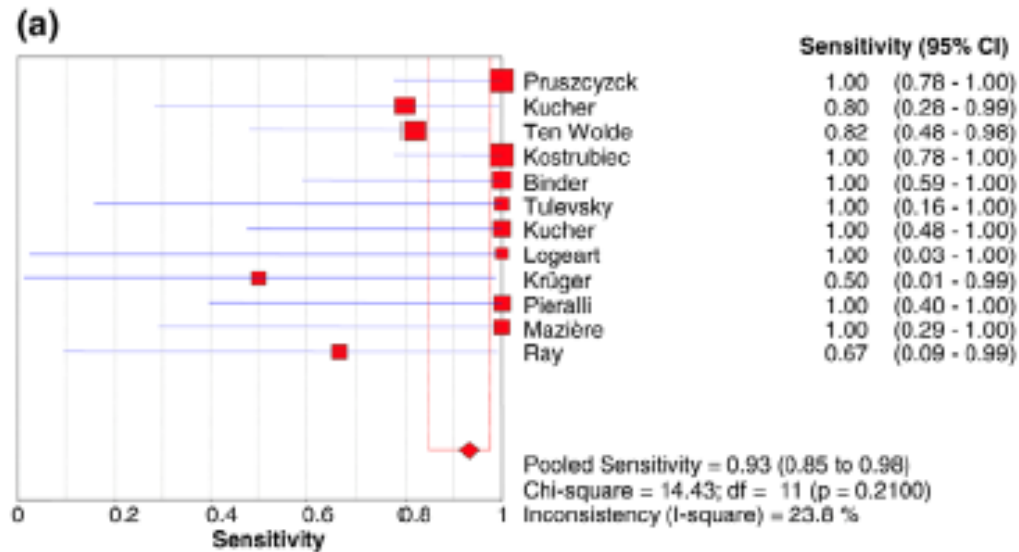


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Biomarkers

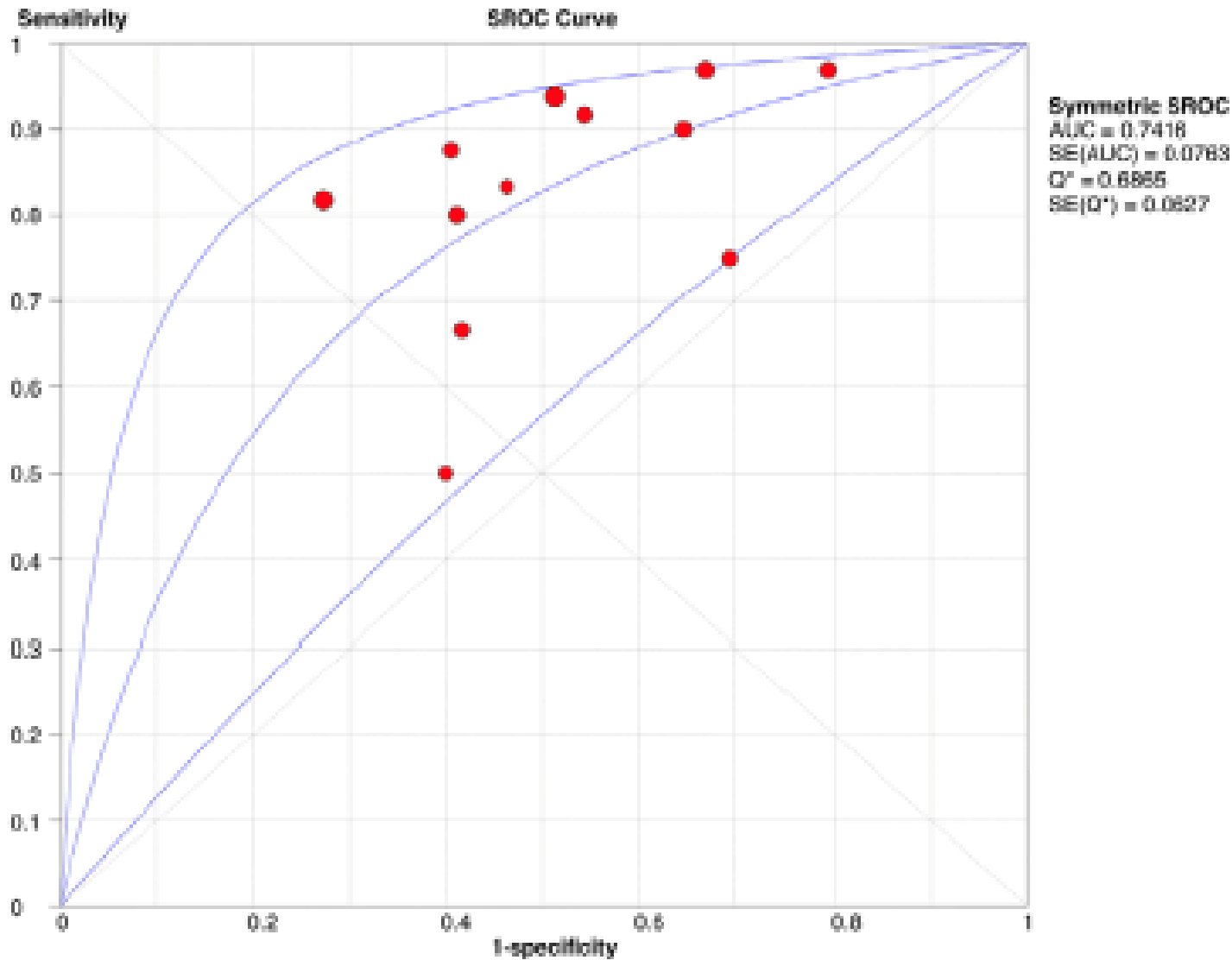


BNP: sensitive for mortality, not specific





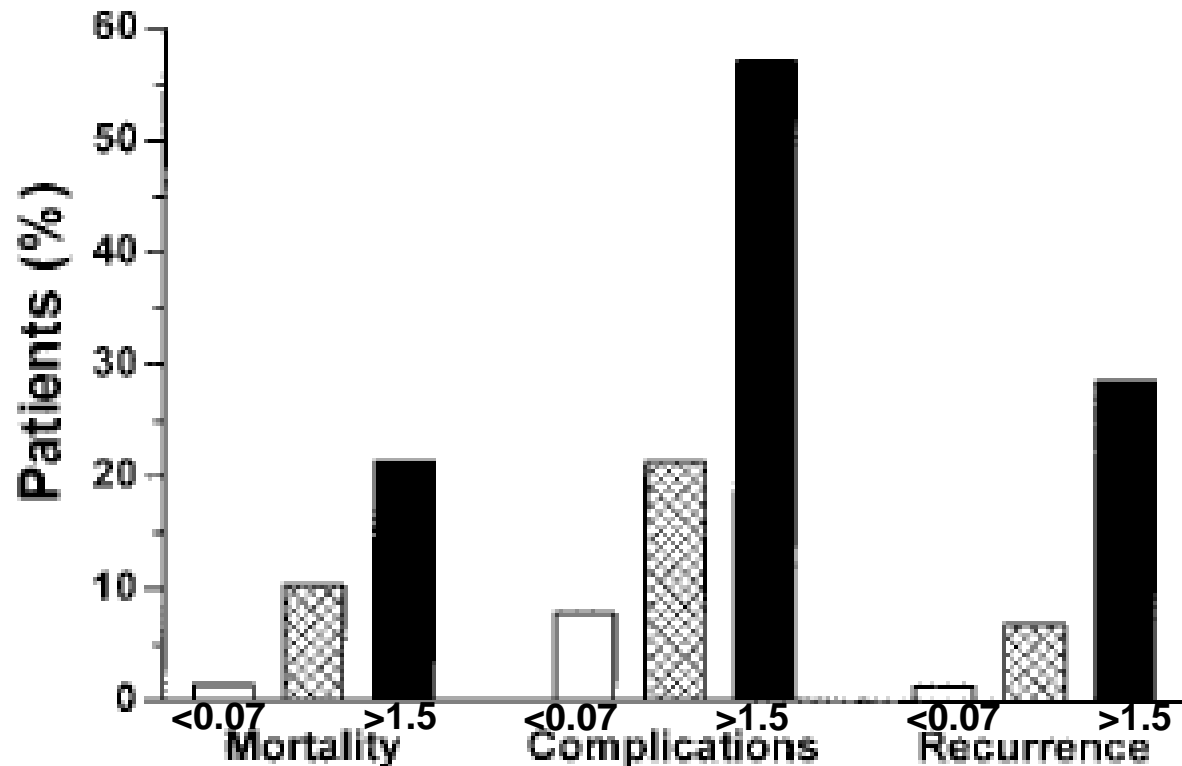
BNP: sensitive for mortality, not specific





High troponin levels predict problems

A. Troponin I



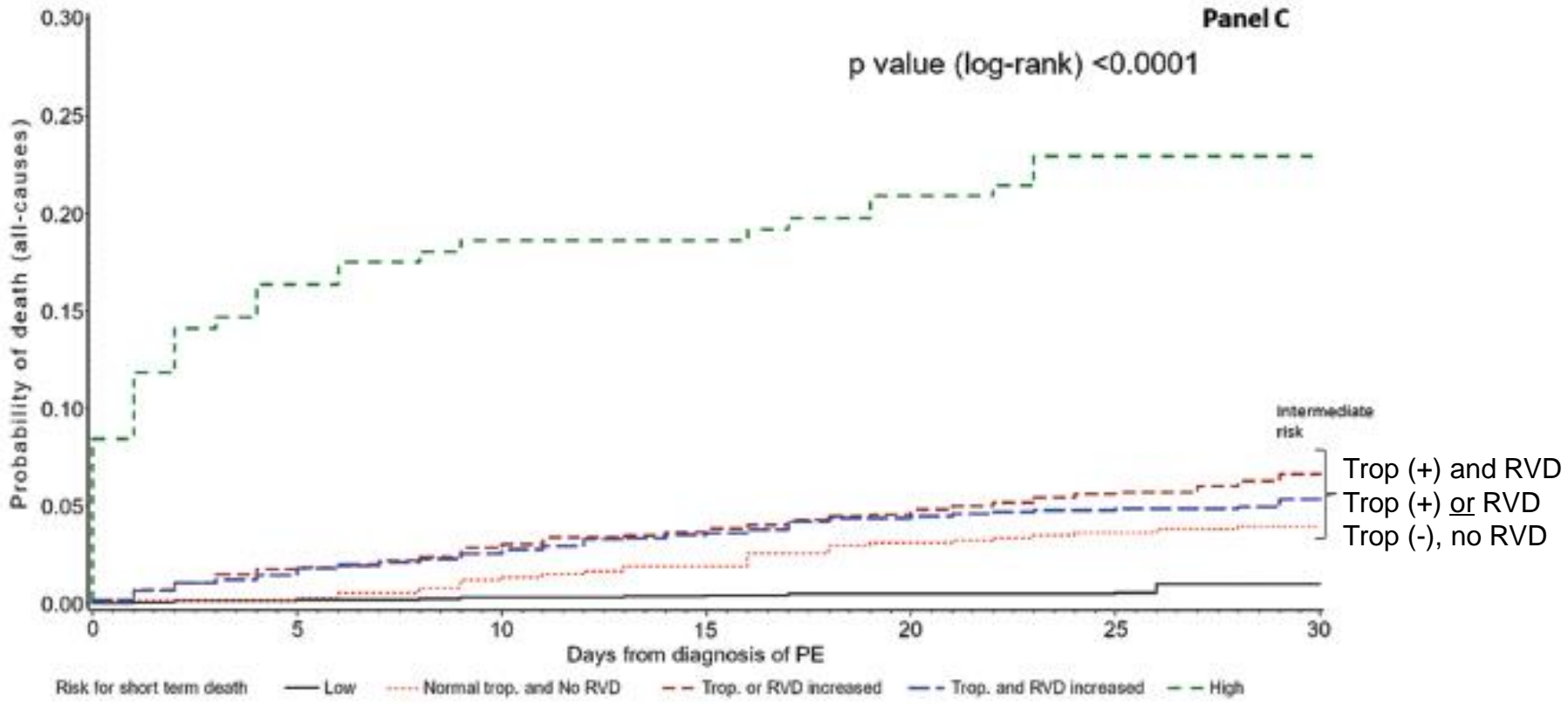


High Troponin, BNP: 2X hazard ratio

<i>Variables</i>	<i>In-hospital</i>		<i>30 days</i>	
	<i>Model I Clinical variables p HR [95% CI]</i>	<i>Model II Clinical and instrumental variables p HR [95% CI]</i>	<i>Model I Clinical variables p HR [95% CI]</i>	<i>Model II Clinical and instrumental variables p HR [95% CI]</i>
Troponin at entry ^a Increased vs. normal Not performed vs. normal	-	0.0193 1.97 [1.21-3.22] 1.95 [1.13-3.37]	-	NS
BNP/NT-pro at entry ^h Increased vs. normal Not assessed vs. normal	-	NS	-	0.0282 2.08 [1.22-3.56] 1.88 [1.10-3.20]

1. Becattini C, Agnelli G, Maggioni AP, et al. Contemporary Management and Clinical Course of Acute Pulmonary Embolism: The COPE Study. *Thromb Haemost.* 2023;123(6):613-626.

Troponin: absolute increase in risk may be modest



1. Becattini C, Agnelli G, Maggioni AP, et al. Contemporary Management and Clinical Course of Acute Pulmonary Embolism: The COPE Study. *Thromb Haemost.* 2023;123(6):613-626.



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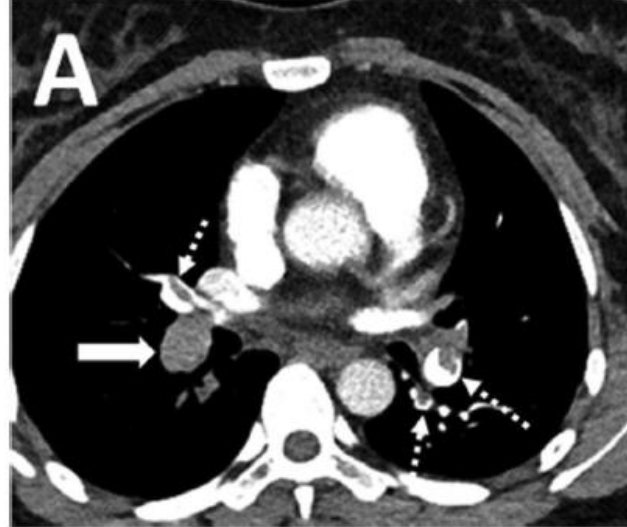
CT Imaging



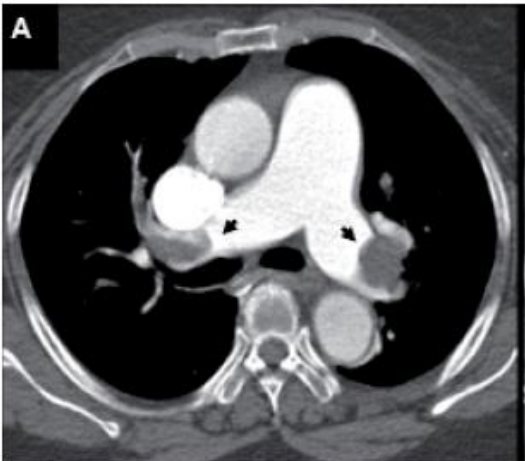
Emboli load or proximity



1. Bach, et al. 2015



6. Chaosuwanakit, et al. 2021



3. Venkatesh, et al. 2010



8. Aramberri, et al. 2022



CT clot burden doesn't predict 30d mortality

Table 2

Thrombus distribution in survivors and non-survivors.

	Survivor ^a (n = 326)	Non-survivor ^a (n = 39)	p-Value
Thrombus mass			
Global obstruction (Mastora score) [%]	30(7–67)	19(5–89)	0.810
Number of affected vessels [count]	10(3–18)	7(3–18)	0.447
Thrombus distribution by level			
Central obstruction [%]	0(0–8)	0(0–16)	0.238
Lobar obstruction [%]	13(3–33)	10(0–35)	0.846
Segmental obstruction [%]	13(4–25)	7(4–31)	0.954
Thrombus distribution by lobe			
Upper lobe obstruction [%]	10(0–28)	7(2–31)	0.962
Middle lobe obstruction [%]	7(0–27)	7(0–29)	0.668
Lower lobe obstruction [%]	17(5–32)	11(2–28)	0.676

^a Median (25–75% interquartile range).



Emboli load or proximity

Does predict mortality^{6,3}
(weakly)

Table 2
Factors associated with mortality in patients with acute pulmonary embolism.

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
CT Obstruction index	1.081 (1.050, 1.113)	1.040 (1.003, 1.079)

Table 5. Prediction of 30-day PE-related Death with Obstruction Scores*

RSLR* step	PE obstruction score	P	Odds ratio %	95% confidence Interval
1	Mastora	0.113	0.95	0.9-1.01
1	Qanadli	0.103	1.15	0.97-1.30
1	Central	0.014	1.1	1.02-1.20
2	Qanadli	0.24	1.1	0.94-1.25
2	Central	0.04	1.07	1.0-1.15
3	Central	0.003	1.01	1.03-1.16

- 6. Chaosuwannakit, et al. 2021
- 3. Venkatesh, et al. 2010

Doesn't predict mortality^{1,4,8}

Table 2
Thrombus distribution in survivors and non-survivors.

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Thrombus distribution by lobe			
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Middle lobe obstruction [%]	7(0-27)	7(0-29)	0.868
Lower lobe obstruction [%]	17(5-32)	11(2-28)	0.676

* Median (25-75% interquartile range).

Mortality

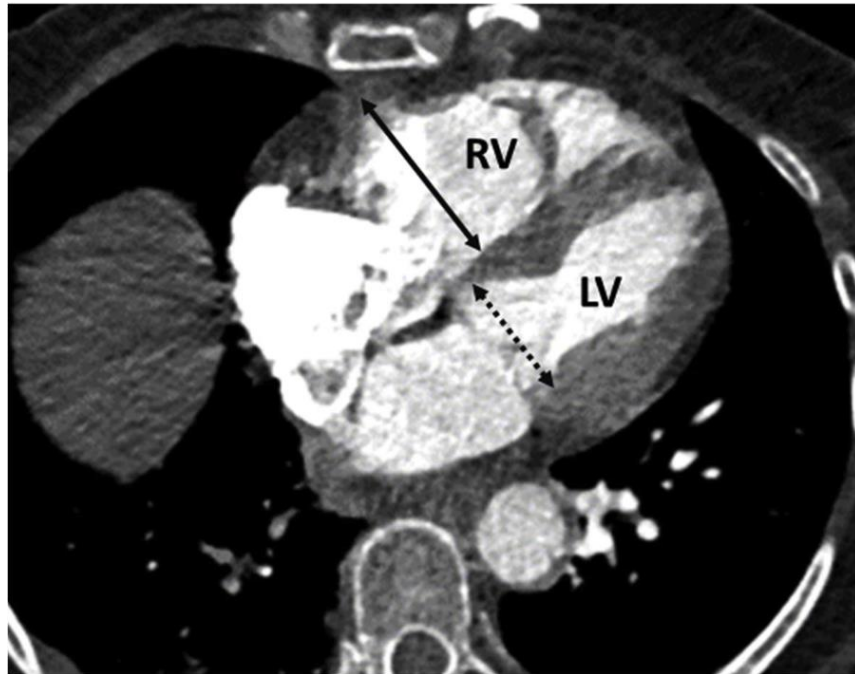
	Nonsurvivor (n = 8)		Survivor (n = 59)		P	Odds Ratio	95% CI
	Mean ± SD	Median (25%–75% Percentiles)	Mean ± SD	Median (25%–75% Percentiles)			
Qanadli, %	40.94 ± 20.65	37.50 (22.50–53.75)	44.41 ± 17.94	50 (35–52.50)	0.486	0.989	0.95–1.03

Table 2 Management of patients and 30-day outcomes according to the presence of saddle versus nonsaddle pulmonary embolism

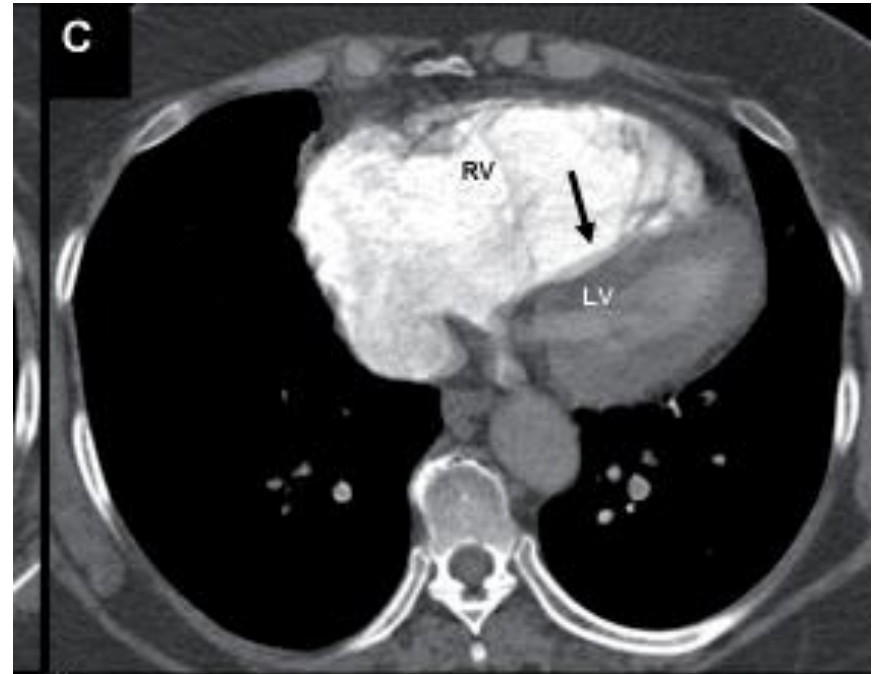
	Overall (n=289) n (%)	Saddle PE (n=36) n (%)	Nonsaddle PE (n=253) n (%)	p-Value
Outcomes within 30 days				
Overall mortality	42 (15)	5 (14)	37 (15)	>0.5
PE-related mortality	5 (2)	2 (6)	3 (1)	0.12
Cancer-related mortality	34 (12)	3 (8)	31 (12)	>0.5
VTE recurrence	6 (2)	1 (3)	5 (2)	>0.5
Major bleeding	14 (5)	1 (3)	13 (5)	>0.5
In-hospital outcomes				
In-hospital overall mortality	23 (8)	4 (11)	19 (8)	>0.5
In-hospital PE related mortality	4 (1)	2 (6)	2 (1)	0.07
In-hospital cancer related mortality	19 (7)	2 (6)	17 (7)	>0.5
In-hospital VTE recurrence	5 (2)	1 (3)	4 (2)	>0.5
In-hospital major bleeding	6 (2)	0 (0)	6 (2)	>0.5

- 1. Bach, et al. 2015
- 4. Atasoy, et al. 2015
- 8. Aramberri, et al. 2022

Right ventricular dilatation ($RV/LV \geq 1$)



6. Chaosuwannakit, et al. 2021



3. Venkatesh, et al. 2010

CT RV findings don't predict 30d mortality

Table 3

Morphometric parameters of right ventricular disorders and non-survivors sorted in order of ascending

	Survivor ^a (n = 326)	Non-survivor ^a (n = 39)	p-Value
Diameter of pulmonary trunk [mm]	28.7 (26.3–32.2)	30.6 (27.8–32.4)	0.016
Ratio short axis right ventricle/left ventricle	1.1 (0.9–1.4)	1.1 (1.0–1.7)	0.078
Short axis of the left ventricle [mm]	42 (37–48)	39 (32–48)	0.083
Interventricular septal angle [°]	44 (39–52)	48 (38–56)	0.102
Short axis of the right ventricle [mm]	48 (42–54)	50 (43–56)	0.203
Diameter of superior vena cava [mm]	23 (21–26)	22 (19–25)	0.248
Diameter of ascending aorta [mm]	33 (30–36)	33 (30–36)	0.747
Diameter of descending aorta [mm]	25 (23–27)	24 (22–26)	0.750
Diameter of IVC [mm]	25 (25–31)	25 (25–31)	0.907
Diameter of right pulmonary artery [mm]	24 (21–27)	24 (22–27)	0.922

Abbreviation: IVC inferior vena cava.

^a Median (25–75% interquartile range).



Right ventricular dilatation

Does predict mortality^{2,6,5}

Doesn't predict mortality^{1,3,4}

Table 4 Multivariable analysis.

Variable	Adjusted odds ratio	95% Confidence interval	p Value
RV dilation	2.98	1.54–5.75	0.001

Table 2
Factors associated with mortality in patients with acute pulmonary embolism.

Factors	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
RV diameter	1.344 (1.200, 1.506)	1.094 (1.007, 1.188)

Table 1
Clinical characteristics and computed tomography pulmonary ang

	Inter-reader agreement	No 30-day PE death N = 1624	PE death in 30 days N = 74	p-value
RV > LV diameter	95.2%	21.7%	35.1%	0.006

- Singanayagam, et al. 2010
- Chaosuwannakit, et al. 2021
- Kumamaru, et al. 2016

Table 3
Morphometric parameters of right ventricular dysfunction in survivors and non-survivors. Measurements are sorted in order of ascending p-value.

	Survivor ^a (n = 326)	Non-survivor ^a (n = 39)	p-Value
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Diameter of right pulmonary artery [mm]	24(21–27)	24(22–27)	0.922

Table 4. Univariate Logistic Regression Analysis for 30-day PE-related Death*

Characteristic	Odds ratio	95% confidence interval	P
RVD	0.95	0.88-1.02	0.19

Mortality

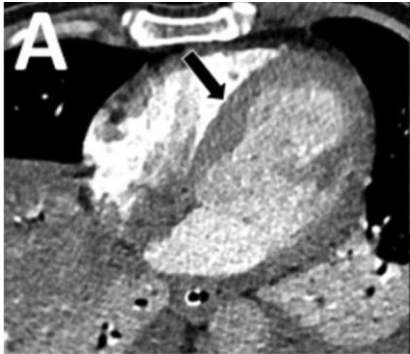
	Nonsurvivor (n = 8)		Survivor (n = 59)		P	Odds Ratio	95% CI
	Mean ± SD	Median (25%–75% Percentiles)	Mean ± SD	Median (25%–75% Percentiles)			
	RV/LV axial	1.06 ± 0.31	1.14 (0.79–1.31)	1.09 ± 0.30			

- Bach, et al. 2015
- Venkatesh, et al. 2010
- Atasoy, et al. 2015

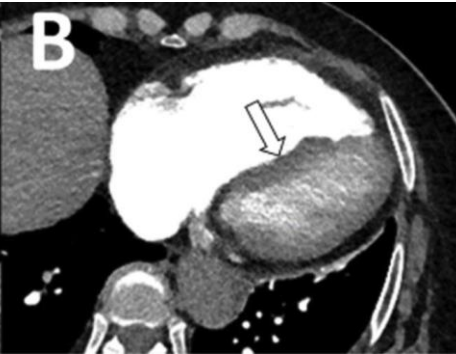


Septal deviation

Normal



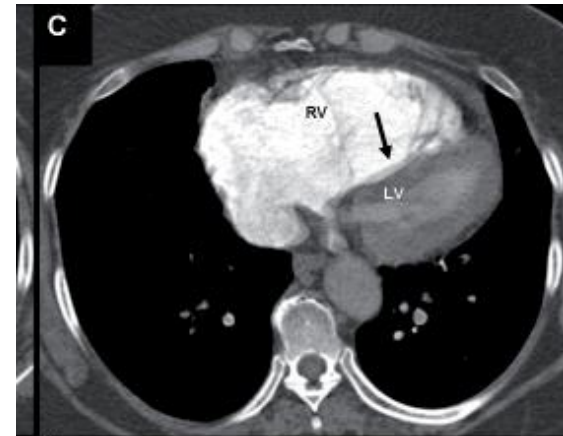
Flat



Concave



6. Chaosuwannakit, et al. 2021



3. Venkatesh, et al. 2010



Septal deviation

Does predict mortality⁴

Table 1
Baseline characteristics, physical signs, and computed tomography pulmonary angiography (CTPA) parameters of patients with acute pulmonary embolism categorized by survival outcome.

Factors	Survived N = 212	Death N = 26	p-value	Mortality
Interventricular septum, n (%)				
Normal	109 (51.42)	0	< 0.001	0%
Grade 2	72 (33.96)	8 (30.77)	0.829	10%
Grade 3	31 (14.62)	16 (61.54)	< 0.001	33%

Doesn't predict mortality^{1,3,4,6}

Table 3
Morphometric parameters of right ventricular dysfunction in survivors and non-survivors. Measurements are sorted in order of ascending p-value.

	Survivor [†] (n=326)	Non-survivor [†] (n=39)	p-Value
Ratio short axis right ventricle/left ventricle	1.1 (0.9-1.4)	1.1 (1.0-1.7)	0.078
Interventricular septal angle [°]	44(39-52)	48(38-56)	0.102

Table 4. Univariate Logistic Regression Analysis for 30-day PE-related Death*

Characteristic	Odds ratio	95% confidence interval	P
Septal deviation	0.16	0.02-1.31	0.09

Thirty patients (50.8%) showed VSB. We interpreted a smooth interventricular septum as VSB; the presence of VSB was not related to mortality in clinically nonsevere PE patients.

Table 1
Clinical characteristics and computed tomography pulmonary angiography findings.

	Inter-reader agreement	No 30-day death N = 1488	All cause death in 30 days N = 210	p-value	No 30-day PE death N = 1624	PE death in 30 days N = 74	p-value
Bowing of the septum	92.3%	8.4%	5.7%	0.40	7.8%	13.5%	0.18

6. Chaosuwanakit, et al. 2021

1. Bach, et al. 2015
3. Venkatesh, et al. 2010
4. Atasoy, et al. 2015
5. Kumamaru, et al. 2016



Septal deviation

Does predict mortality⁴

Table 1
Baseline characteristics, physical signs, and computed tomography pulmonary angiography (CTPA) parameters of patients with acute pulmonary embolism categorized by survival outcome.

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Grade 2	72 (33.96)	8 (30.77)	0.829
Grade 3	31 (14.62)	16 (61.54)	< 0.001

N. Chaosuwanakit et al.

European Journal of Radiology Open 8 (2021) 100340

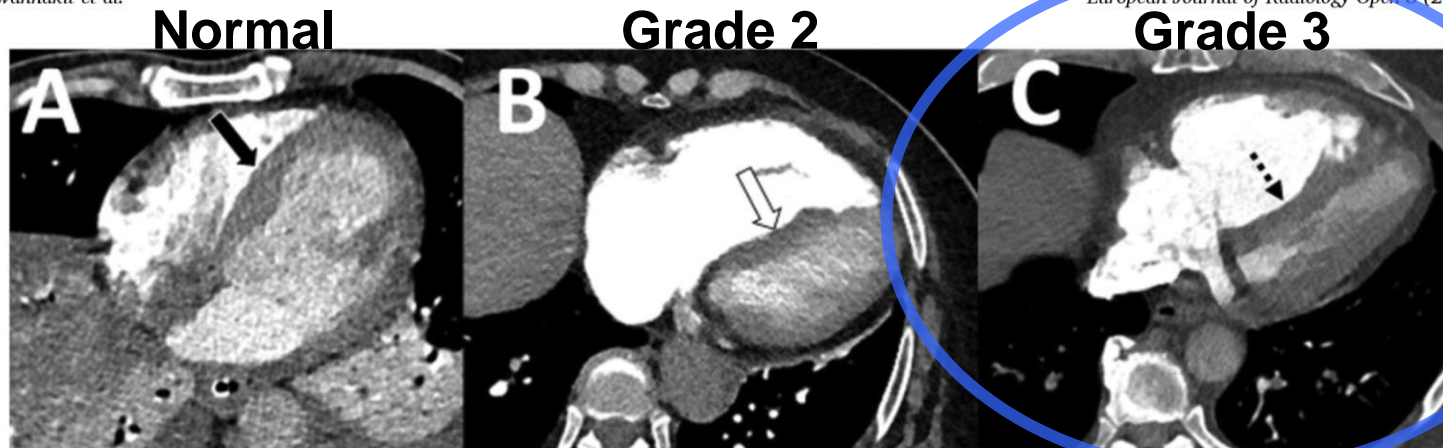
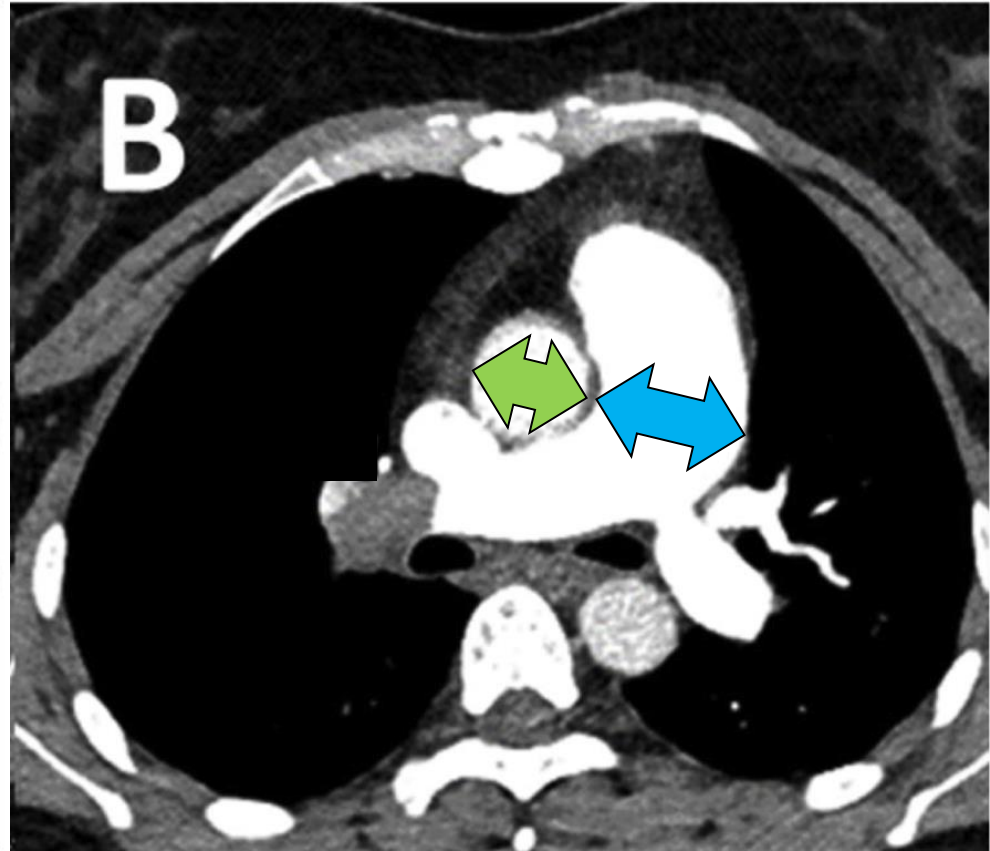


Fig. 4. Deviation of interventricular septum was evaluated on a three-point scale: 1 = normal septum (A : black arrow); 2 = flattened interventricular septum (B : white arrow); and 3 = septum deviation convex toward the left ventricle (C : dashed arrow).

Pulmonary artery enlargement (PA diameter or PA:Ao ratio)



1. Bach, et al. 2015



6. Chaosuwanakit, et al. 2021

PA diameter might predict 30d mortality

Table 3

Morphometric parameters of right ventricular disorders and non-survivors sorted in order of ascending

	Survivor ^a (n = 326)	Non-survivor ^a (n = 39)	p-Value
Diameter of pulmonary trunk [mm]	28.7 (26.3–32.2)	30.6 (27.8–32.4)	0.016
Ratio short axis right ventricle/left ventricle	1.1 (0.9–1.4)	1.1 (1.0–1.7)	0.078
Short axis of the left ventricle [mm]	42 (37–48)	39 (32–48)	0.083
Interventricular septal angle [°]	44 (39–52)	48 (38–56)	0.102
Short axis of the right ventricle [mm]	48 (42–54)	50 (43–56)	0.203
Diameter of superior vena cava [mm]	23 (21–26)	22 (19–25)	0.248
Diameter of ascending aorta [mm]	33 (30–36)	33 (30–36)	0.747
Diameter of descending aorta [mm]	25 (23–27)	24 (22–26)	0.750
Diameter of IVC [mm]	25 (25–31)	25 (25–31)	0.907
Diameter of right pulmonary artery [mm]	24 (21–27)	24 (22–27)	0.922

Abbreviation: IVC inferior vena cava.

^a Median (25–75% interquartile range).



Pulmonary artery enlargement

Does predict mortality^{1,5,6}

Table 3
Morphometric parameters of right ventricular dysfunction in survivors and non-survivors.

	Survivor* (n = 326)	Non-survivor* (n = 39)	p-Value
Diameter of pulmonary trunk [mm]	28.7 (26.3–32.2)	30.6 (27.8–32.4)	0.016

Table 1
Clinical characteristics and computed tomography pulmonary angiography findings.

	Inter-reader agreement	No 30-day PE death N = 1624	PE death in 30 days N = 74	p-value
PA > Ao diameter	95.6%	28.9%	43.2%	0.030

Table 1
Baseline characteristics, physical signs, and computed tomography pulmonary angiography (CTPA) parameters of patients with acute pulmonary embolism categorized by survival outcome.

Factors	Survived N = 212	Death N = 26	p-value
PA/Ao ratio	0.94 (0.67-2.37)	1.05 (0.85-2.10)	0.004

Doesn't predict mortality

No studies

1. Bach, et al. 2015
5. Kumamaru, et al. 2016
6. Chaosuwannakit, et al. 2021



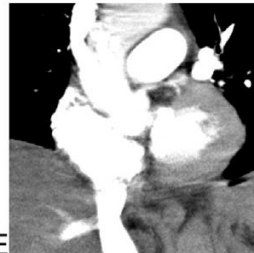
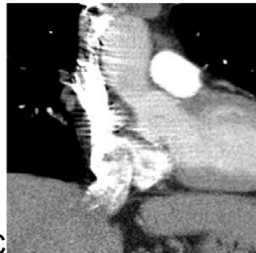
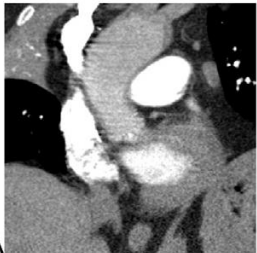
IVC Reflux

(contrast in IVC +/- hepatic vein)

IVC Reflux I
(no reflux)

IVC Reflux II
(subcardial)

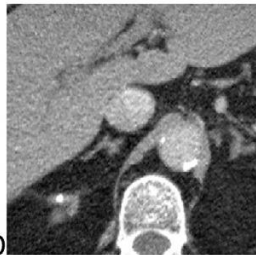
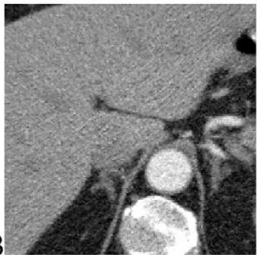
IVC Reflux III
(intrahepatic)



A

C

E

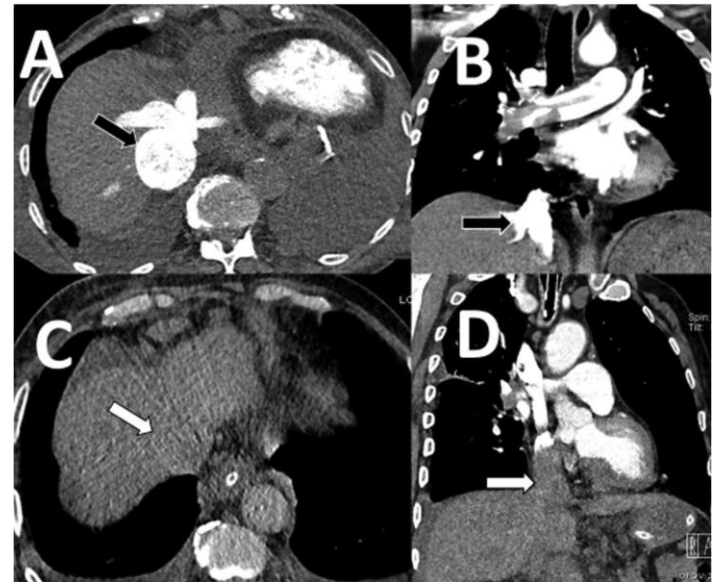


B

D

F

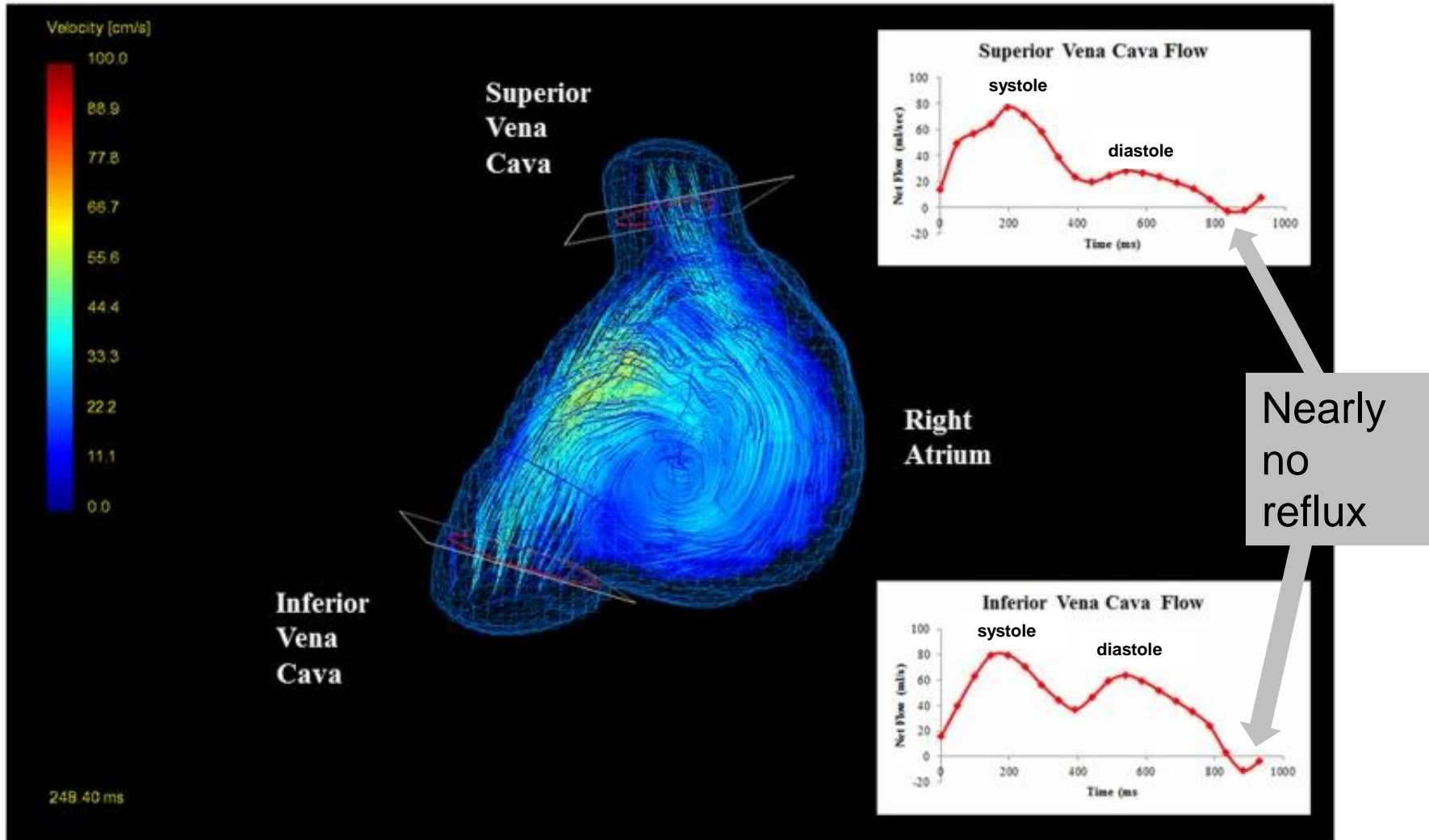
1. Bach, et al. 2015



6. Chaosuwannakit, et al. 2021



Normal flow from SVC and IVC into RA



1. Parikh JD, Kakarla J, Keavney B, O'Sullivan JJ, Ford GA, Blamire AM, Hollingsworth KG, Coats L. 4D flow MRI assessment of right atrial flow patterns in the normal heart - influence of caval vein arrangement and implications for the patent foramen ovale. PLoS One. 2017;12(3):e0173046.



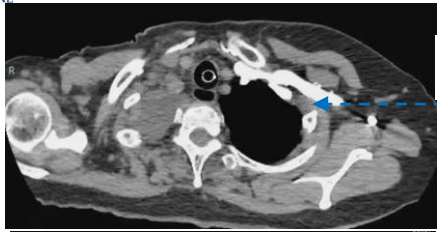
You can measure IVC reflux



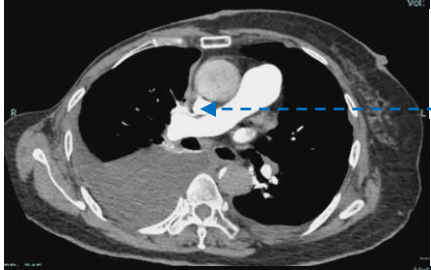
1. Bach AG, Nansalmaa B, Kranz J, Taute BM, Wienke A, Schramm D, Surov A. CT pulmonary angiography findings that predict 30-day mortality in patients with acute pulmonary embolism. *Eur J Radiol.* 2015;84(2):332-337.



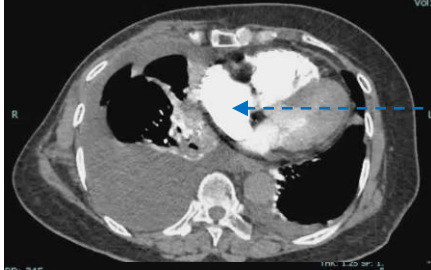
IVC reflux



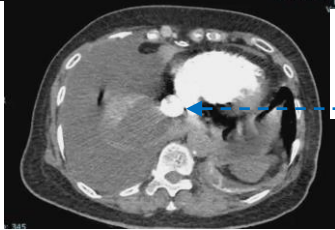
Subclavian vein



Superior Vena Cava



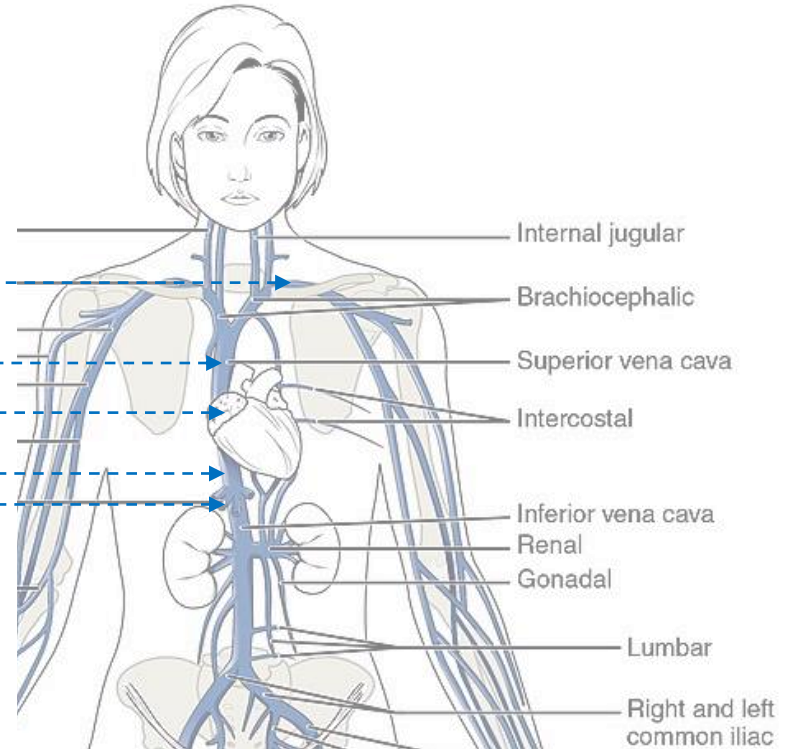
Right Atrium



Inferior Vena Cava



Hepatic Vein





IVC Reflux

Does predict mortality^{1,5,6}

Table 4

Quantification of contrast reflux in inferior vena cava in survivors and non-survivors. Measurements are sorted in order of ascending *p*-value.

	Survivor* (n=310)	Non-survivor* (n=38)	<i>p</i> -Value
Craniocaudal length of reflux in IVC [mm]	7(0-23)	33(12-57)	<0.001
Contrast of IVC intrahepatic [HU]	44(40-99)	95(55-192)	<0.001
IVC reflux III (intrahepatic) [yes]	30%(93)	58%(22)	<0.001
Contrast of IVC subcardial [HU]	106(45-187)	170(108-240)	<0.001
Ratio contrast IVC/aorta descendes	0.3 (0.2-0.6)	0.6 (0.2-1.8)	<0.001
IVC reflux II-III (subcardial or intrahepatic) [yes]	59%(183)	82%(31)	0.005
IVCI reflux I (no reflux) [yes]	41%(127)	18%(7)	0.010

Abbreviation: IVC inferior vena cava; HU Hounsfield units

Table 1

Clinical characteristics and computed tomography pulmonary angiography findings.

	Inter-reader agreement	No 30-day PE death N = 1624	PE death in 30 days N = 74	<i>p</i> -value
Contrast reflux to the hepatic portion of IVC	97.4%	21.7%	35.1%	0.006

Table 1

Baseline characteristics, physical signs, and computed tomography pulmonary angiography (CTPA) parameters of patients with acute pulmonary embolism categorized by survival outcome.

Factors	Survived N = 212	Death N = 26	<i>p</i> -value
IVC contrast reflux	39 (18.4)	18(69.2)	<0.001

Doesn't predict mortality

Twenty-one patients (35.6%) had IVC reflux. However, this reflux was not predictive of mortality.

1. Bach, et al. 2015
5. Kumamaru, et al. 2016
6. Chaosuwannakit, et al. 2021

4. Atasoy, et al. 2015



Topics

- Mortality from severe disease vs non-severe disease
- Predictors of severity and mortality
- **Potential interventions**



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Potential Interventions



Therapies beyond anticoagulation

- Systemic fibrinolysis
- Catheter-based fibrinolysis
- Catheter embolectomy



Therapies beyond anticoagulation

- Systemic fibrinolysis
- Catheter-based fibrinolysis
- Catheter embolectomy



Systemic fibrinolytics for submassive PE?

- No difference from anticoagulation in
 - 7-day mortality
 - Prolonged hospitalization
 - Rehospitalization
 - 30-day mortality
- Less hemodynamic decompensation (1.6% vs 5.0%)
 - Death from hemodynamic decompensation similar (0.2% vs 0.6%)
- Major bleeding was 5 times as high (11.5% vs 2.4%)
- Stroke was 12 times as high (2.4% vs 0.2%).



Therapies beyond anticoagulation

- Systemic fibrinolysis
- Catheter-based fibrinolysis
- Catheter embolectomy



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Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Randomized, Controlled Trial of Ultrasound-Assisted Catheter-Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism

Nils Kucher, Peter Boekstegers, Oliver J. Müller, Christian Kupatt, Jan Beyer-Westendorf, Thomas Heitzer, Ulrich Tebbe, Jan Horstkotte, Ralf Müller, Erwin Blessing, Martin Greif, Philipp Lange, Ralf-Thorsten Hoffmann, Sebastian Werth, Achim Barmeyer, Dirk Härtel, Henriette Grünwald, Klaus Empen and Iris Baumgartner

Circulation. 2014;129:479-486; originally published online November 13, 2013;
doi: 10.1161/CIRCULATIONAHA.113.005544

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Catheter fibrinolytics for submassive PE?

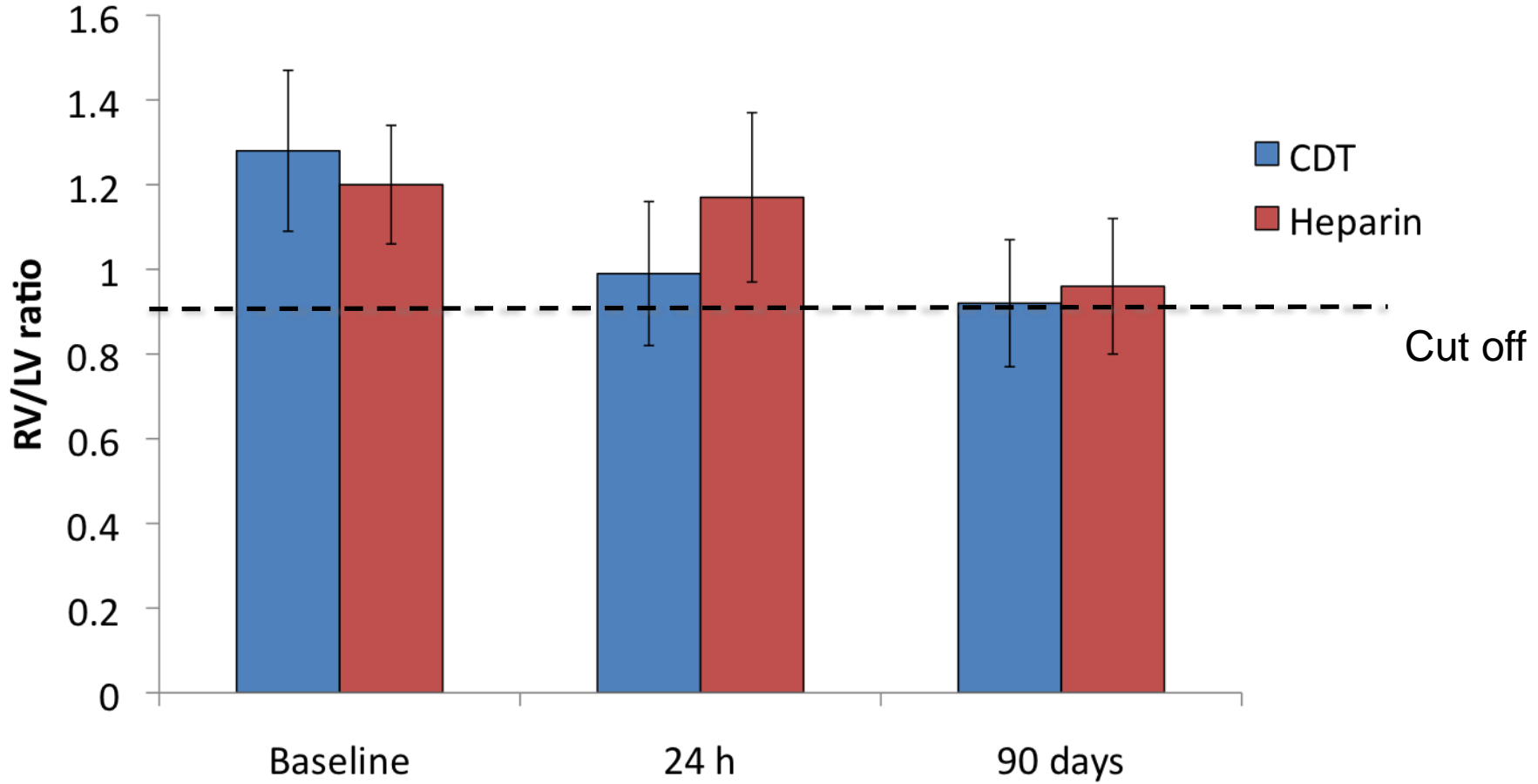
No difference in mortality

At 90 days, there were no episodes of hemodynamic decompensation or recurrent VTE among the 59 patients. There were no deaths in the USAT group and 1 death from pancreatic cancer in the heparin group 20 days after randomization ($P=1.00$).

1. Kucher N, Boekstegers P, Muller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. *Circulation*. 2014;129(4):479-486



RV/LV ratio



1. Kucher N, Boekstegers P, Muller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. *Circulation* 2014;129:479-86.



Therapies beyond anticoagulation

- Systemic fibrinolysis
- Catheter-based fibrinolysis
- Catheter embolectomy

Catheter directed thrombectomy

FlowTreiver

- FlowTreiver catheters
 - 6-10mm, 11-14 mm, 15-18 mm
- Quick aspiration into syringe
- Repeat as needed



Indigo: Extract-PE study²

- Indigo catheter
 - 8-F (2.67 mm)
- Sustained aspiration with pump
- Repeat as needed



1. Tu T, Toma C, Tapson VF, et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. *JACC. Cardiovascular interventions*. 2019;12(9):859-869.
2. Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. *JACC. Cardiovascular interventions*. 2021;14(3):319-329.



Catheter directed thrombectomy

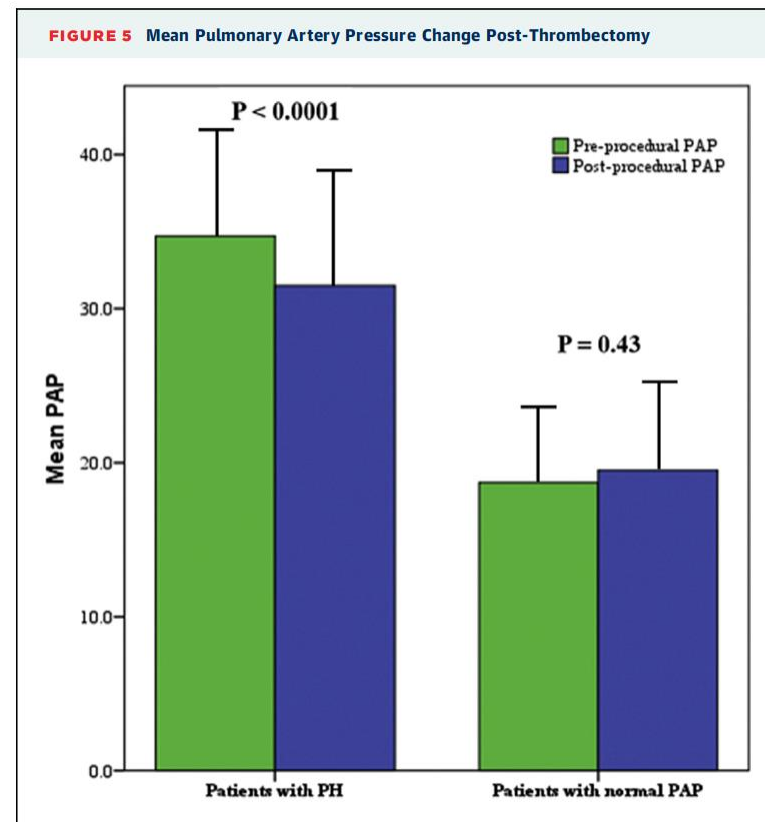
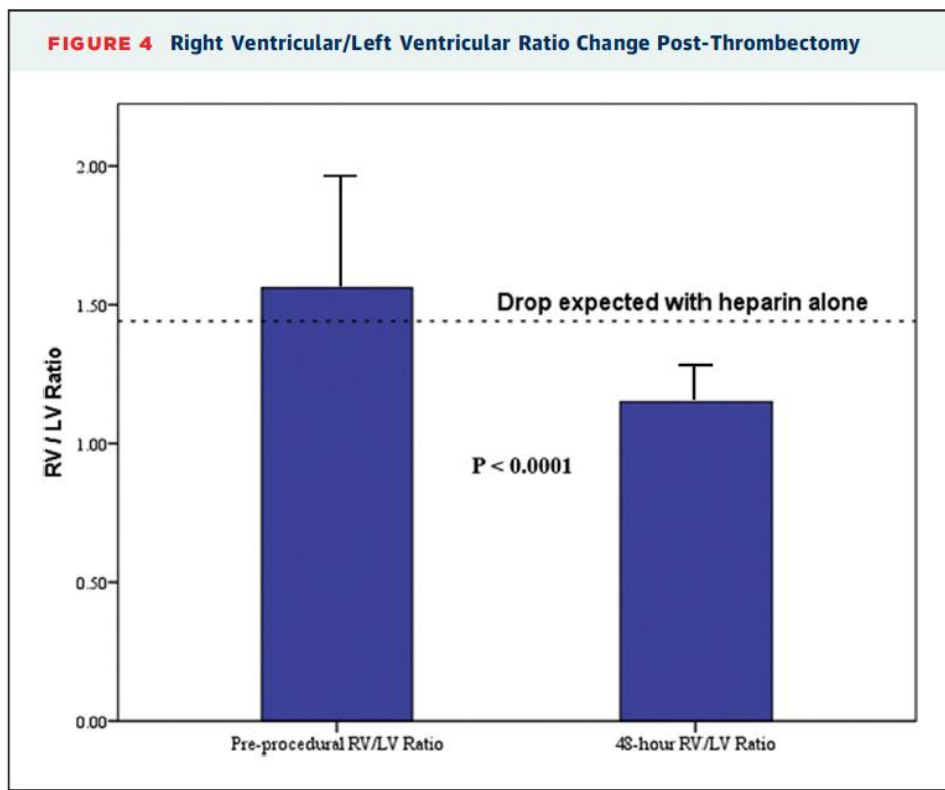
FlowTreiver: FLARE study¹

- Heparin infusion
- 0.035-inch wire into PA
- 20-F aspiration guide catheter
- FlowTreiver catheters
 - 6-10mm, 11-14 mm, 15-18 mm
- Quick aspiration into syringe
- Repeat as needed



1. Tu T, Toma C, Tapson VF, et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. *JACC. Cardiovascular interventions*. 2019;12(9):859-869.
2. Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. *JACC. Cardiovascular interventions*. 2021;14(3):319-329.

RV:LV ratio and PAP improve, but do not normalize



1. Tu T, Toma C, Tapson VF, et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. *JACC. Cardiovascular interventions*. 2019;12(9):859-869.
2. Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. *JACC. Cardiovascular interventions*. 2021;14(3):319-329.



Risks

SAFETY OUTCOMES. Four patients (3.8%) experienced 6 MAEs within 48 h of the index procedure. This rate (as well as the upper 95% confidence limit, 8.6%) was significantly lower than the performance goal of <25% ($p < 0.0001$). All MAEs were adjudicated by the clinical events committee to be procedure related but not device related: all 4 patients exhibited clinical deterioration: 1 major bleeding event and 1 pulmonary vascular injury (the major bleeding event experienced by 1 patient was also classified as pulmonary vascular injury and clinical deterioration). This patient experienced **intraprocedural pulmonary hemorrhage** likely due to pulmonary infarct and reperfusion injury, requiring a lower lobectomy. Surgical pathologic results reported residual thrombus in the PAs but did not observe PA injury. Two patients with minimal

1. Tu T., et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. *JACC Cardiovasc Interv.* 12(9) 2019

Catheter directed thrombectomy



Indigo: Extract-PE study²

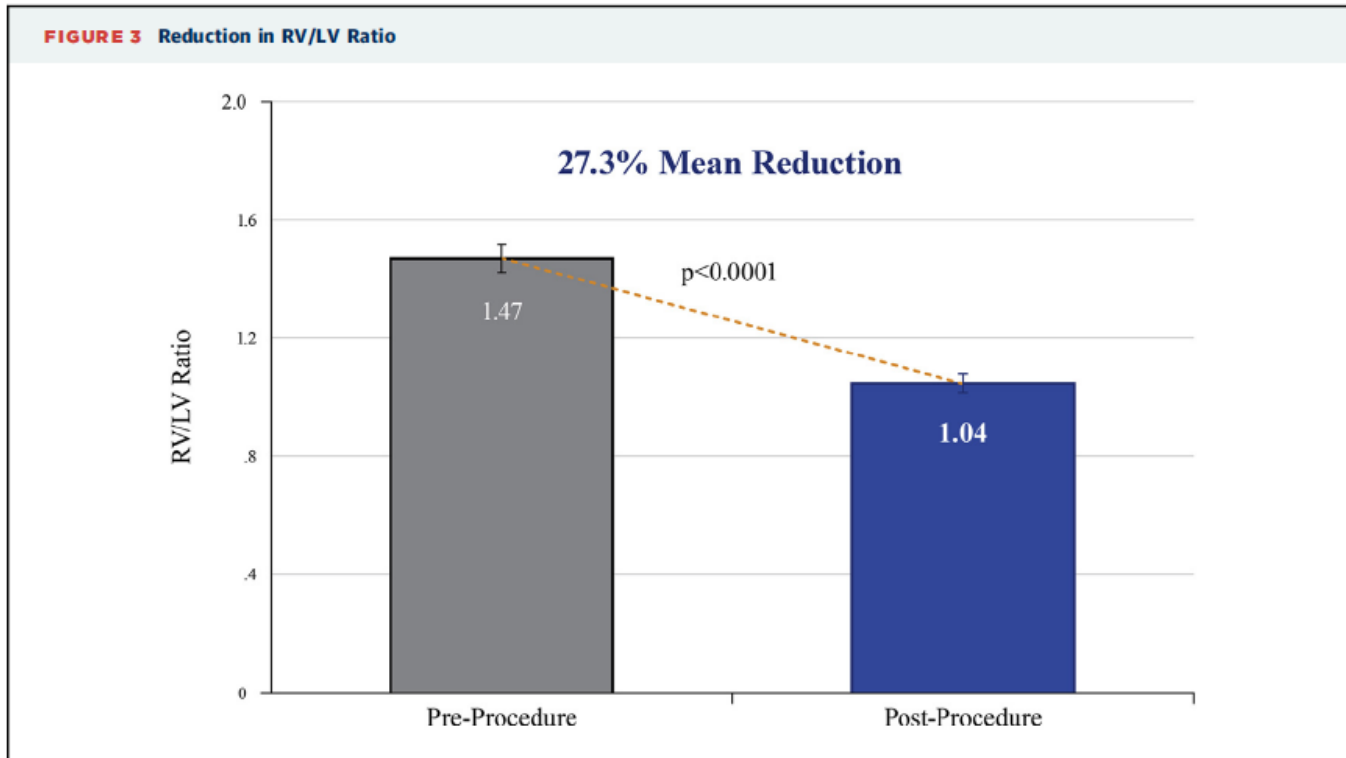
- Heparin infusion
- 0.035-inch wire into PA
- 8 F sheath (?)
- Indigo catheter
 - 8-F (2.67 mm)
- Sustained aspiration with pump
- Repeat as needed

1. Tu T, Toma C, Tapson VF, et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. *JACC. Cardiovascular interventions*. 2019;12(9):859-869.
2. Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. *JACC. Cardiovascular interventions*. 2021;14(3):319-329.



Catheter embolectomy for submassive PE?

RV improves but does not become normal



1. Tu T, Toma C, Tapson VF, et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. *JACC. Cardiovascular interventions*. 2019;12(9):859-869.
2. Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. *JACC. Cardiovascular interventions*. 2021;14(3):319-329.



Risks

The majority of patients (73.1%) had an estimated overall blood loss <400 ml. Of the patients that had blood loss >400 ml (26.9%), none required a blood transfusion due to aspiration. Three (2.5%) patients required blood transfusions for adverse events major bleeding and the third patient had pre-existing anemia. Of the 73 patients that spent time in the intensive care unit during the hospitalization, the median intensive care unit length of stay was 1.0 days and 39% of all patients did not require any intensive care unit stay.

(Table 4). One of the patients experienced 2 events that met the primary endpoint definition. One patient developed hemoptysis (device-related SAE) during the procedure from a distal vessel perforation. The hemoptysis was treated successfully during the procedure; this patient subsequently experienced a post-

1. Tu T., et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. JACC Cardiovasc Interv. 12(9) 2019



Hemoptysis after Embolectomy

Ann Thorac Surg
1999;68:2383-91

Journal of Cardiothoracic and Vascular Anesthesia 31 (2017) 633-636

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journal homepage: www.jcvaonline.com

CORRESPONDENCE 23

Management of Massive Hemoptysis After Pulmonary Thromboembolectomy Using a Double Bronchial Blocker System

Brandon Caddell, DO^{*,1}, Bryan Yelverton, MD^{*},
Jason C. Tippet, MD^{*}, Yazhini Ravi, MD[†],
Chittoor B. Sai-Sudhakar, MD[†], William C. Culp Jr., MD^{*}

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Center College of Medicine, Temple, TX

Exsanguinating Hemoptysis After Pulmonary Embolectomy

To the Editor:

We read with interest the article by Smythe and associates [1] regarding management of exsanguinating hemoptysis during cardiopulmonary bypass (CPB). We congratulate the authors on successful immediate management of such a life-threatening event by rapid airway control with rigid bronchoscopy. They report the cases of 3 patients with different sources of exsanguinating hemoptysis during CPB. We previously reported a case of massive endobronchial hemorrhage after pulmonary embolectomy [2], which is very similar to that of patient 2 reported by the authors. In our case of recurrent massive pulmonary embolism, extensive clots were removed using forceps, balloon embolectomy catheter, and bolus saline flush with suction under total CPB. Plugged and lodged thrombi in the peripheral pulmonary arteries were then repeatedly squeezed

2. Kirklin JW, Barratt Boyes BG. Cardiac tumors. In: Cardiac surgery, New York: Churchill Livingstone, 1993:1635-53.
3. Li JY, Lin FY, Hsu RB, Chu SH. Video-assisted cardioscopic resection of recurrent left ventricular myxoma. J Thorac Cardiovasc Surg 1996;112:1673-4.



How to decide?

- No technique works perfectly
- Most techniques improve PE
- Time to improvement differs



Ask yourself

- Can my patient make it
 - five days before improvement?
 - one day before improvement?
 - a few hours before improvement?
 - no time at all before improvement?



How fast they work

Method

- Heparin
- Catheter fibrinolysis
- Systemic fibrinolysis
- Catheter embolectomy

Time to resolution

- 5 days
 - 1/2 complete in 24 hours
- 24 hours
- 2 hours
- ½ - 1 hour



Thank you!