RISK STRATIFICATION OF PATIENTS WITH ACUTE SYMPTOMATIC PULMONARY EMBOLISM

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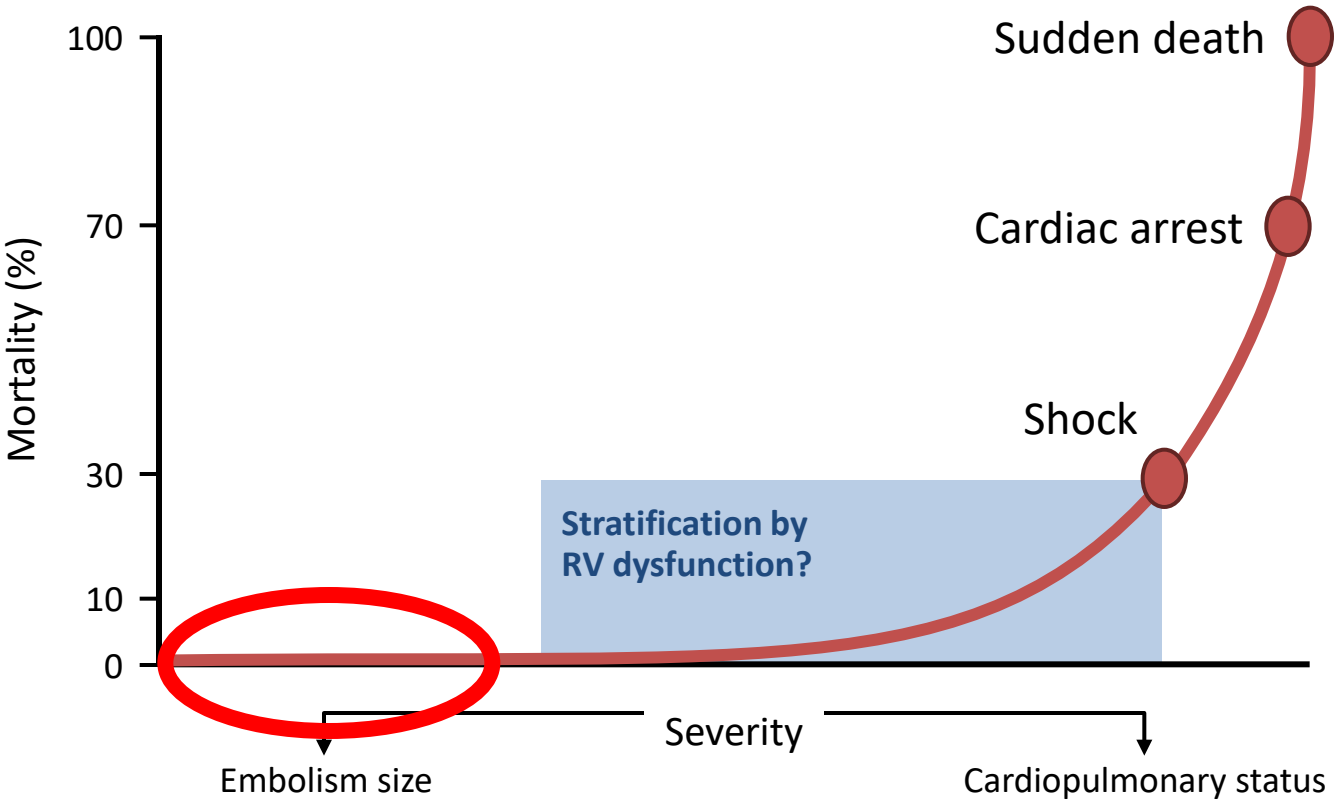
Potential Conflicts of Interest

- Financial conflicts of interest
  - None related to this topic

Risk stratification

Outcomes in pulmonary embolism

The relationship of severity and mortality in patients with PE



Wood KE, Chest 2002

Definition of low-risk PE

AHA 2011

Normotensive PE patients with normal biomarkers and no RV dysfunction on imaging

ESC 2014

The PE-related risk and the patient's clinical status and comorbidities should be taken into consideration

Jimenez's definition of low-risk PE

Normotensive PE patients at low-risk for all-cause mortality, recurrent VTE and major bleeding soon after diagnosis

No other indication for hospitalization, treatment feasible, home support, patient compliance

Reasons to use clinical scores for risk stratification

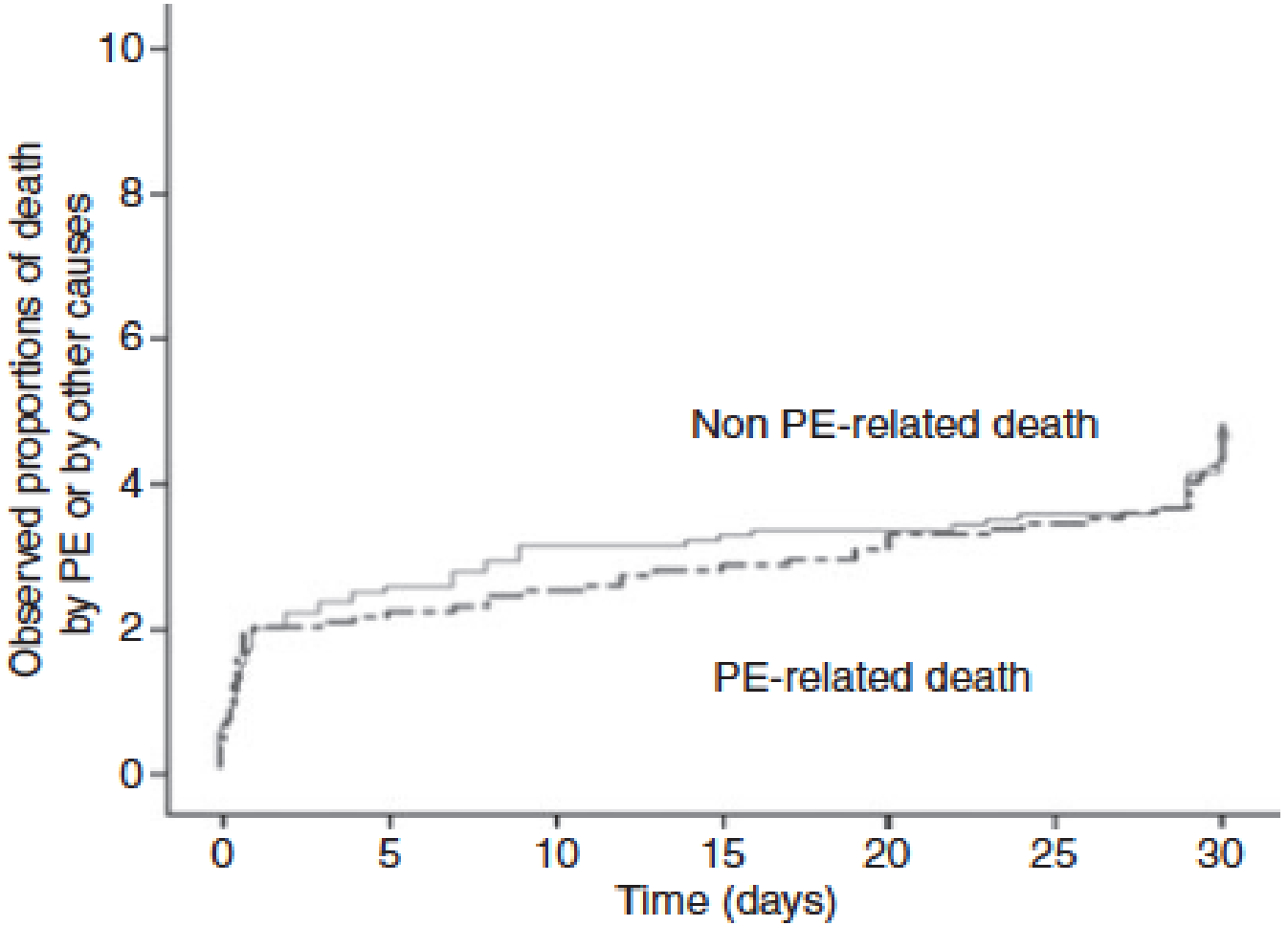
- A minority of normotensive patients will die because of PE itself
- Direct comparisons favor clinical scores
- Cheaper
  - Echo: 150 €
  - sPESI: 1 neuron
- Availability 24 h a day, 365 d a year

IPER registry

Event	PE patients (n=1716)	HD unstable (n=201)	HD stable (n=1515)
All-cause mortality	116 (6.7)	64 (31.8)	52 (3.4)
Death from PE	68 (3.9)	47 (23.3)	21 (1.4)
Death from intracranial hemorrhage	6 (0.3)	1 (0.5)	5 (0.3)
Death from malignancy	6 (0.3)	2 (1)	4 (0.3)
Death from other causes	36 (2.1)	14 (7)	22 (1.4)
Documented recurrent PE	22 (1.3)	2 (1)	20 (1.4)

Casazza F, Throm Res 2012

Etiologies and time to death of 1,291 patients with acute PE



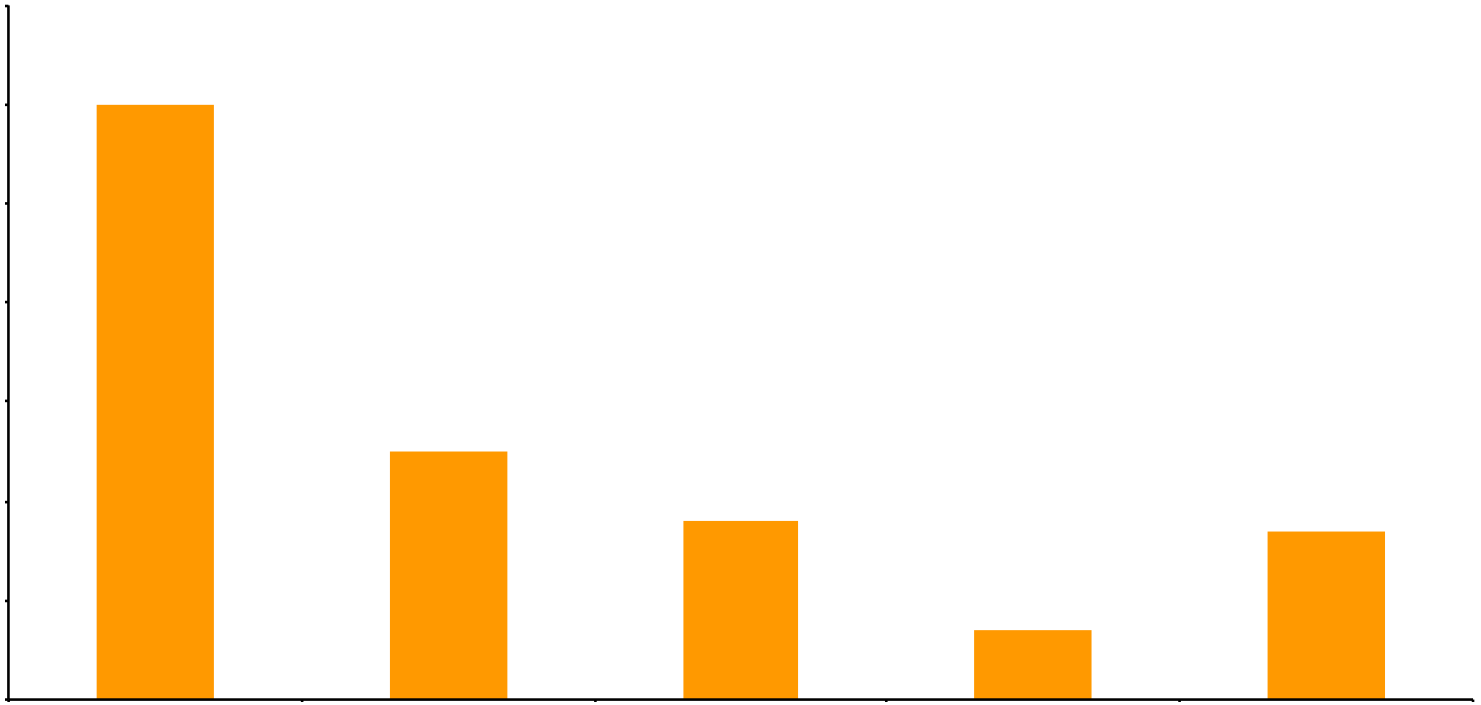
Sánchez D, J Thromb Haemost 2011

Etiologies and time to death of 1,291 patients with acute PE

sPESI

OR 5.97*

OR 8.79*



*$P < 0.05$

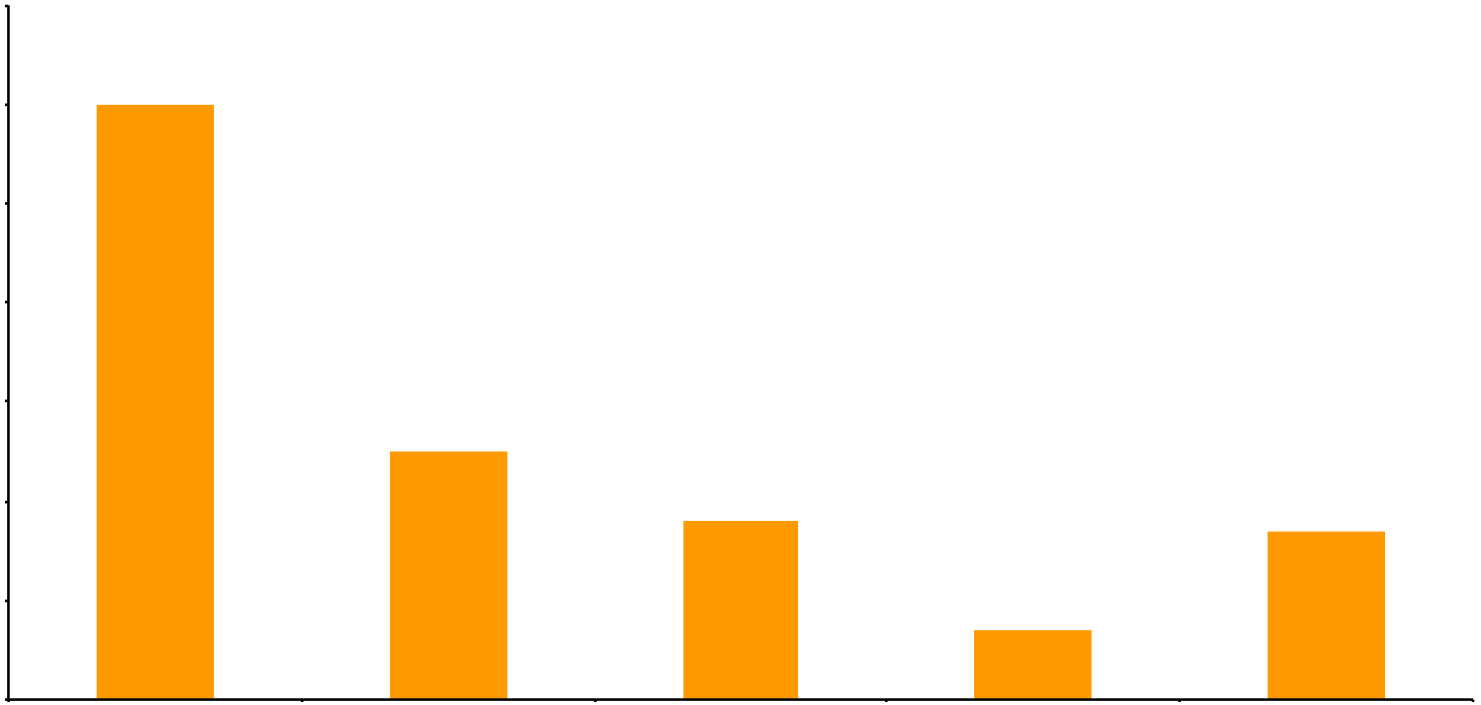
Sánchez D, J Thromb Haemost 2011

Etiologies and time to death of 1,291 patients with acute PE

cTnI

OR 1.34

OR 2.39*



*$P < 0.05$

Sánchez D, J Thromb Haemost 2011

PROTECT study

848 normotensive patients from 11 centres

	Adjusted OR	P value
Simplified PESI > 0 points	5.37 (2.08-13.82)	< 0.001
BNP > 100 pg/mL	2.13 (1.13-4.01)	0.02
cTnI > 0 ng/mL	1.95 (1.05-3.61	0.03
Presence of DVT by CCUS	2.08 (1.19-3.64)	0.01

Jimenez D, Am J Respir Crit Care Med 2014

Simplified PESI

995 patients from a single centre	
Age >80 years	1 point
Cancer	1 point
Cardiopulmonary disease	1 point
HR ≥110 bpm	1 point
SBP <100 mmHg	1 point
O_2 saturation <90%	1 point

Jiménez D, Arch Intern Med 2010

Hestia criteria

- Is the patient haemodynamically unstable?
- Is thrombolysis or embolectomy necessary?
- Active bleeding or high risk of bleeding?
- >24 hours of oxygen supply to maintain oxygen saturation >90%?
- Was PE diagnosed during anticoagulant treatment?
- Severe pain needing intravenous pain medication for >24 hours?
- Medical or social reason for treatment in the hospital for >24 hours (infection, malignancy, no support system)?
- Does the patient have a creatinine clearance of <30 ml/min?
- Does the patient have severe liver impairment?
- Is the patient pregnant?
- Does the patient have a documented history of heparin-induced thrombocytopenia?

Zondag W, Thromb Haemost 2013

Hestia criteria vs. sPESI

HESTIA	sPESI
17 items NPV 99% Reproducibility issues?	6 items NPV 100% Good reproducibility Not used in a RCT or management study

Zondag W, Thromb Haemost 2013

OTPE trial

	Outpatient (n=171)	Inpatient (n=168)	P*
	N (%)		
Recurrent VTE	1 (0.6)	0	0.011
Major bleeding			
14 days	2 (1.2)	0	0.031
90 days	3 (1.8)	0	0.086
Overall mortality	1 (0.6)	1 (0.6)	0.005

*Non-inferiority margin = 4%

Aujesky D, Lancet 2011

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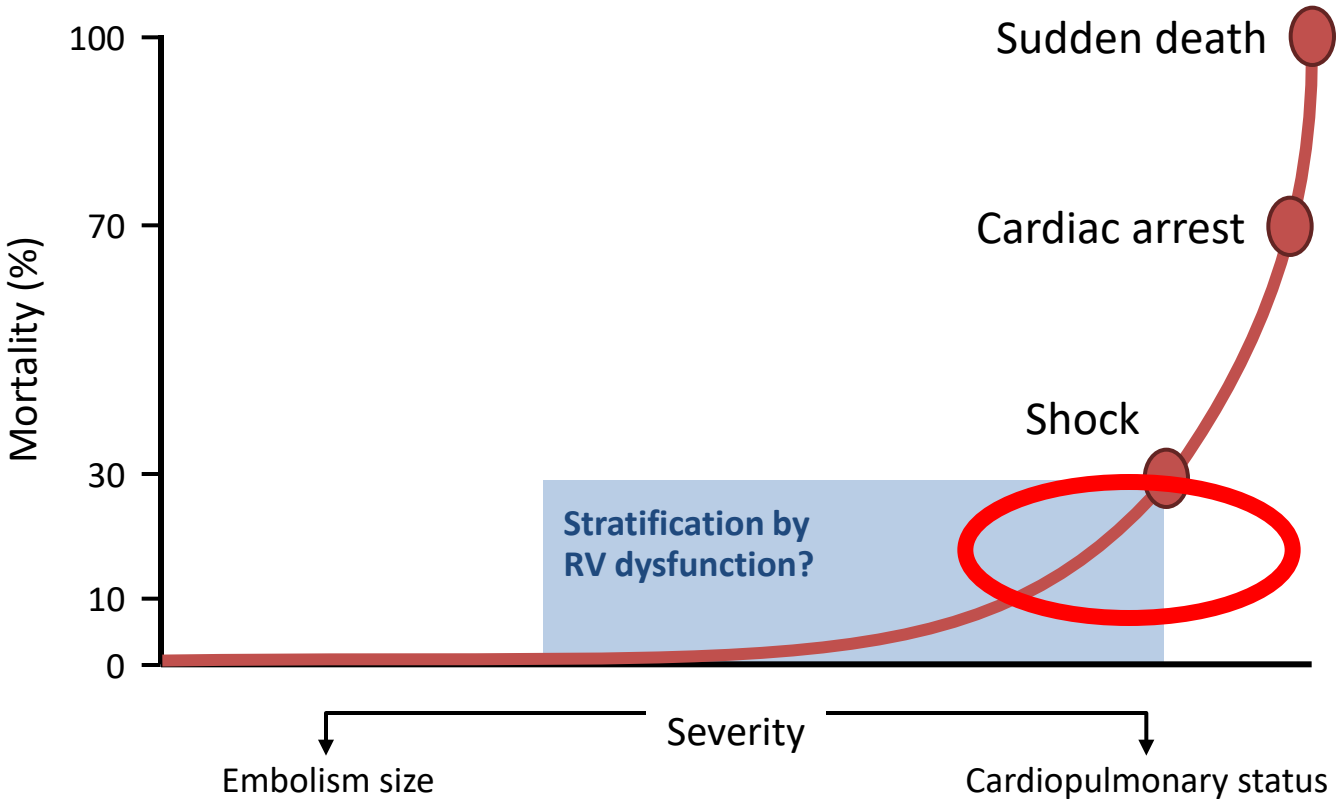


Wood KE, Chest 2002

Definition of intermediate-risk PE

American Heart Association 2011

PE in the setting of a hemodynamically stable patient with echo-proven evidence of RVD

European Society of Cardiology 2014

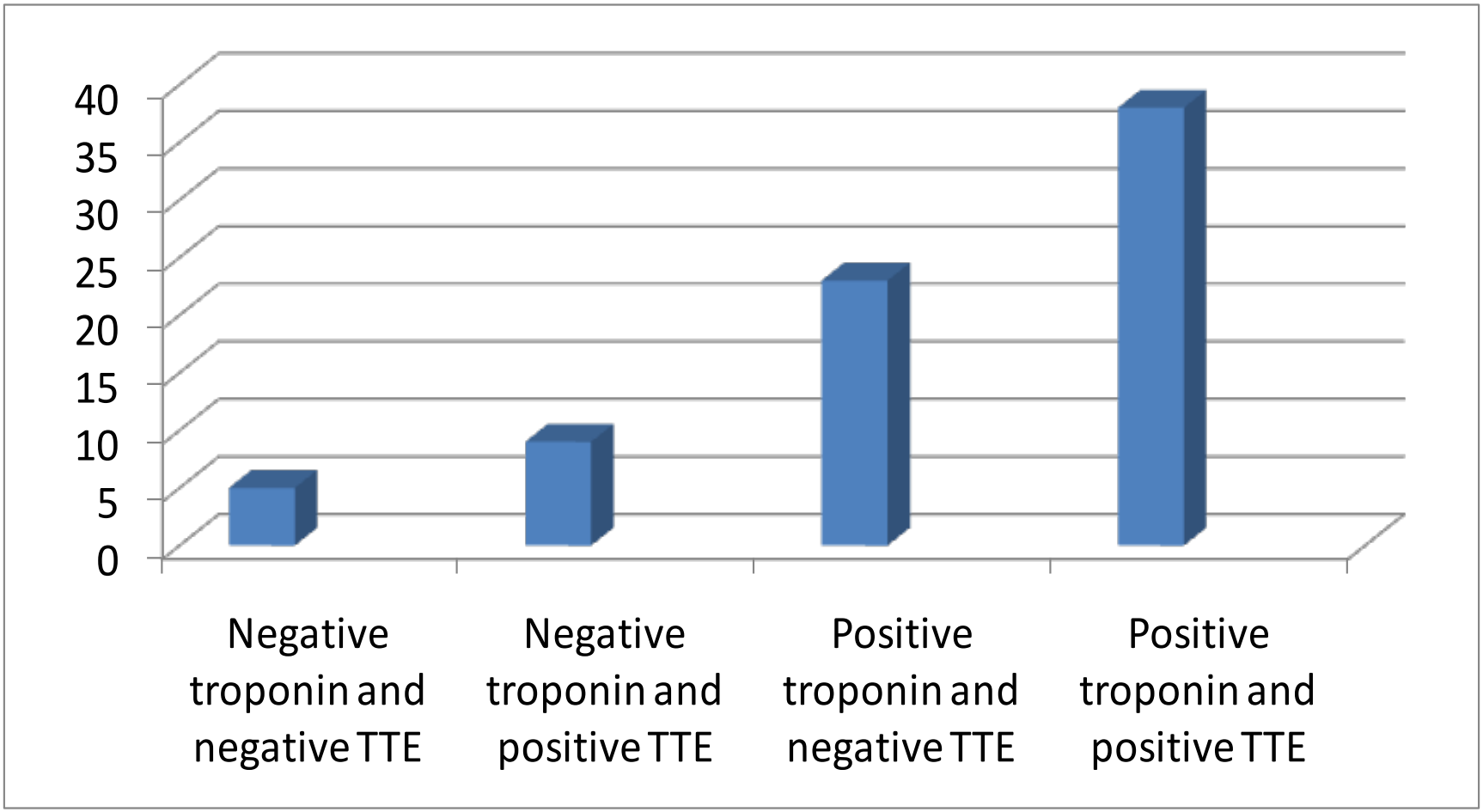
Intermediate-risk PE is defined if at least one RVD or one myocardial injury marker is positive

Jimenez's definition of intermediate-risk PE

Confirmed PE, normal blood pressure and an increased PE-related mortality…

…similar to patients with PE and cardiovascular instability

Transthoracic echocardiography plus cardiac biomarkers



Scridon T. Am J Cardiol 2005

Thrombolysis for submassive PE

	Thrombolysis (n = 506)	Heparin (n = 499)	P value
PEITHO			
7-day death	1.2%	1.8%	0.43

Meyer G, N Engl J Med 2014

	Thrombolysis (n = 118)	Heparin (n = 138)	P value
MAPPET			
In-hospital death	3.4%	2.2%	0.71

Konstantinides S, N Engl J Med 2002

Patient-level metaanalysis

2,874 normotensive patients from 6 prospective cohort studies

Predictor	Points
Systolic blood pressure 90-100 mm Hg	2
Elevated cardiac troponin	2
RVD (CT or echocardiography)	2
Heart rate ≥ 110/min	1

Stage	I	II	III
Points	0-2	3-4	> 4
Patients, %	75.5	18.6	5.8
30-day PE-related complications, %	4.2	10.8	29.2

Bova C, Eur Respir J 2014

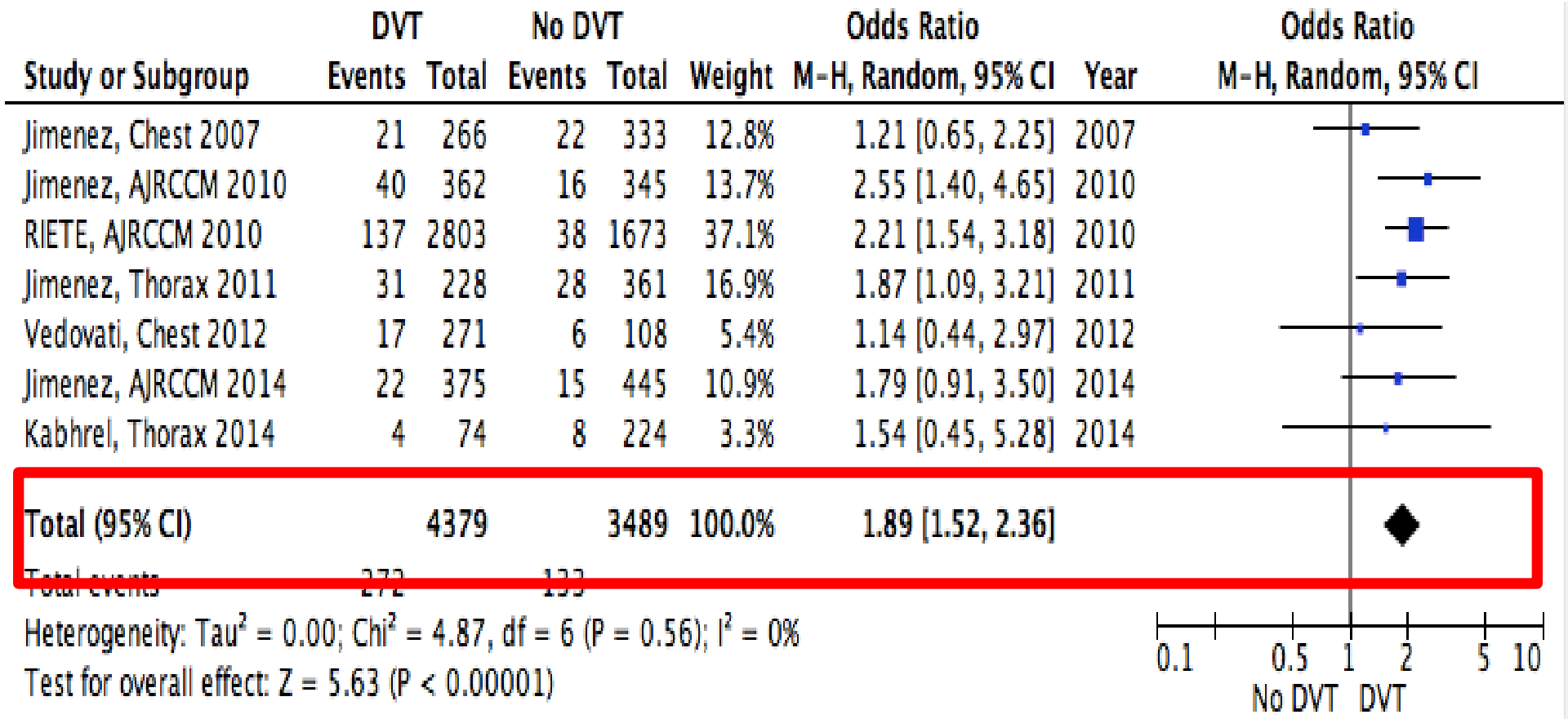
Combination of clinical variables and prognostic tests

271 normotensive patients from a single center

Predictor	Points
H-FABP $\geq$ 6 ng/mL	1.5
Syncope	1.5
Tachycardia	2
Cut-off value	$\geq$ 3

Dellas C, Thromb Haemost 2014

Residual DVT and prognosis in patients with acute PE



Study or Subgroup	DVT Events	DVT Total	No DVT Events	No DVT Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Jimenez, Chest 2007	21	266	22	333	12.8%	1.21 [0.65, 2.25]	2007
Jimenez, AJRCCM 2010	40	362	16	345	13.7%	2.55 [1.40, 4.65]	2010
RIETE, AJRCCM 2010	137	2803	38	1673	37.1%	2.21 [1.54, 3.18]	2010
Jimenez, Thorax 2011	31	228	28	361	16.9%	1.87 [1.09, 3.21]	2011
Vedovati, Chest 2012	17	271	6	108	5.4%	1.14 [0.44, 2.97]	2012
Jimenez, AJRCCM 2014	22	375	15	445	10.9%	1.79 [0.91, 3.50]	2014
Kabhrel, Thorax 2014	4	74	8	224	3.3%	1.54 [0.45, 5.28]	2014
Total (95% CI)		**4379**		**3489**	**100.0%**	**1.89 [1.52, 2.36]**	
Total events	272		133				

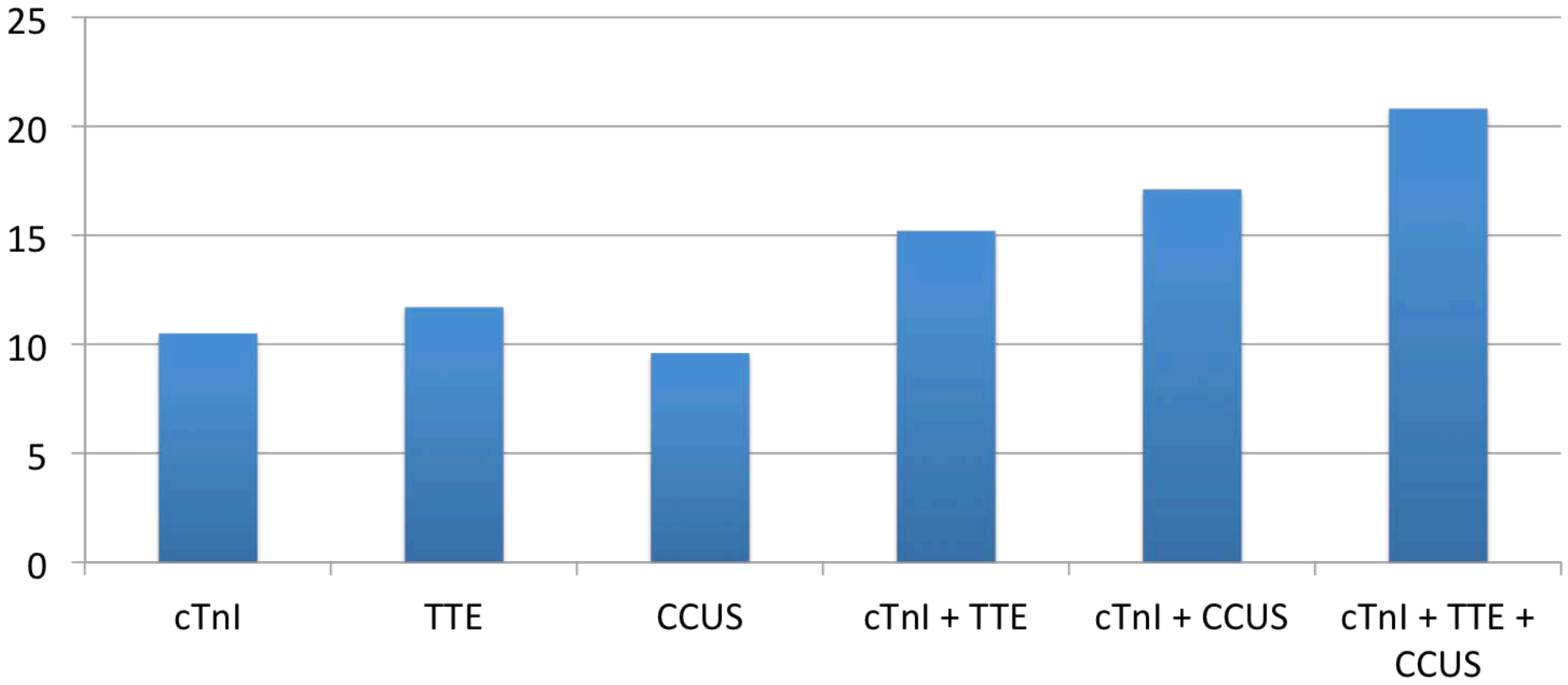
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.87$, df = 6 (P = 0.56); $I^2 = 0\%$

Test for overall effect: Z = 5.63 (P < 0.00001)

Becattini C, Chest 2017

Combination of prognostic tests

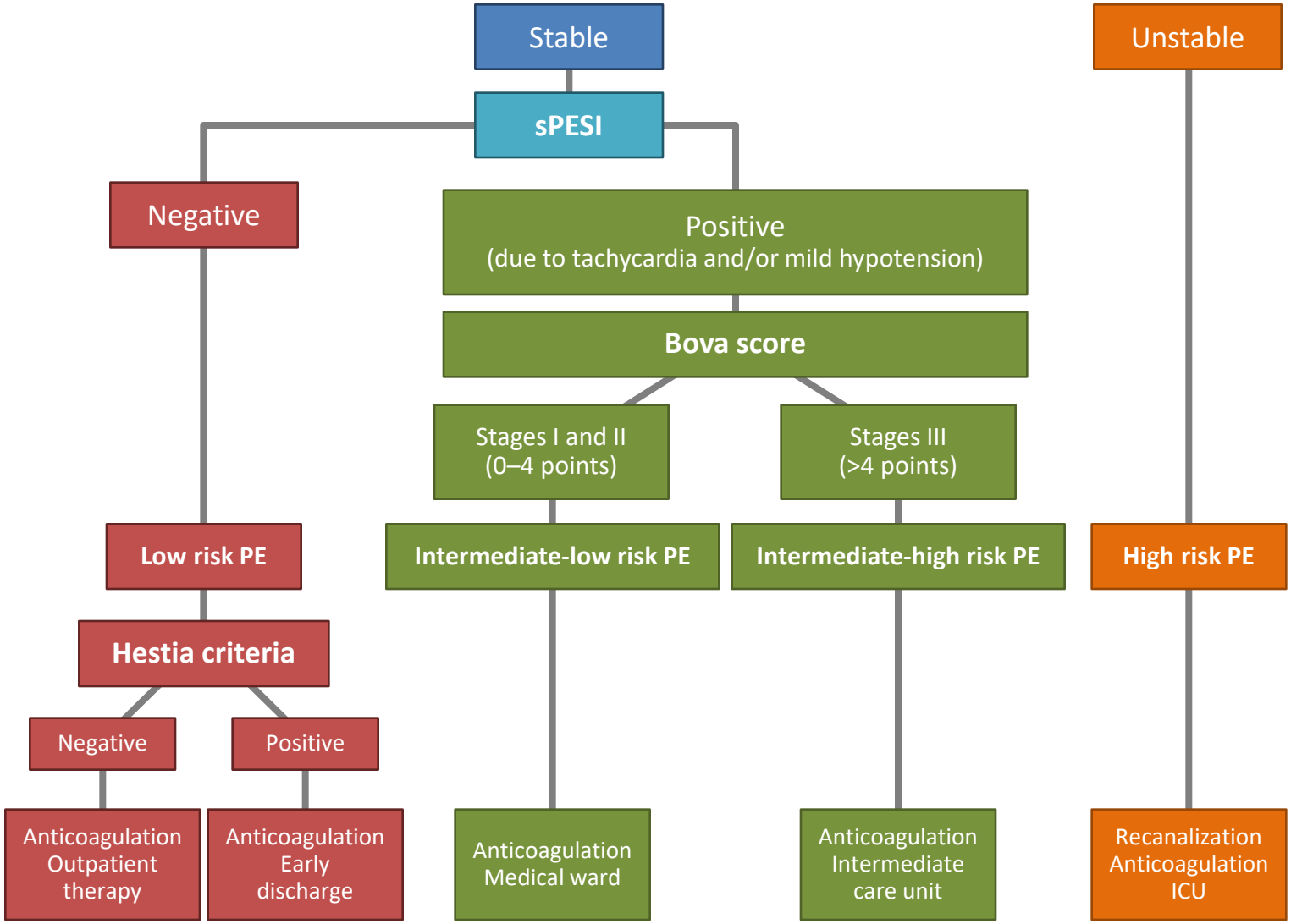
591 patients from a single center 1/2003-12/2008.



Positive predictive value for 30-day PE-related death

Jiménez D, Thorax 2011

A proposed pathway for identification of intermediate-high risk PE



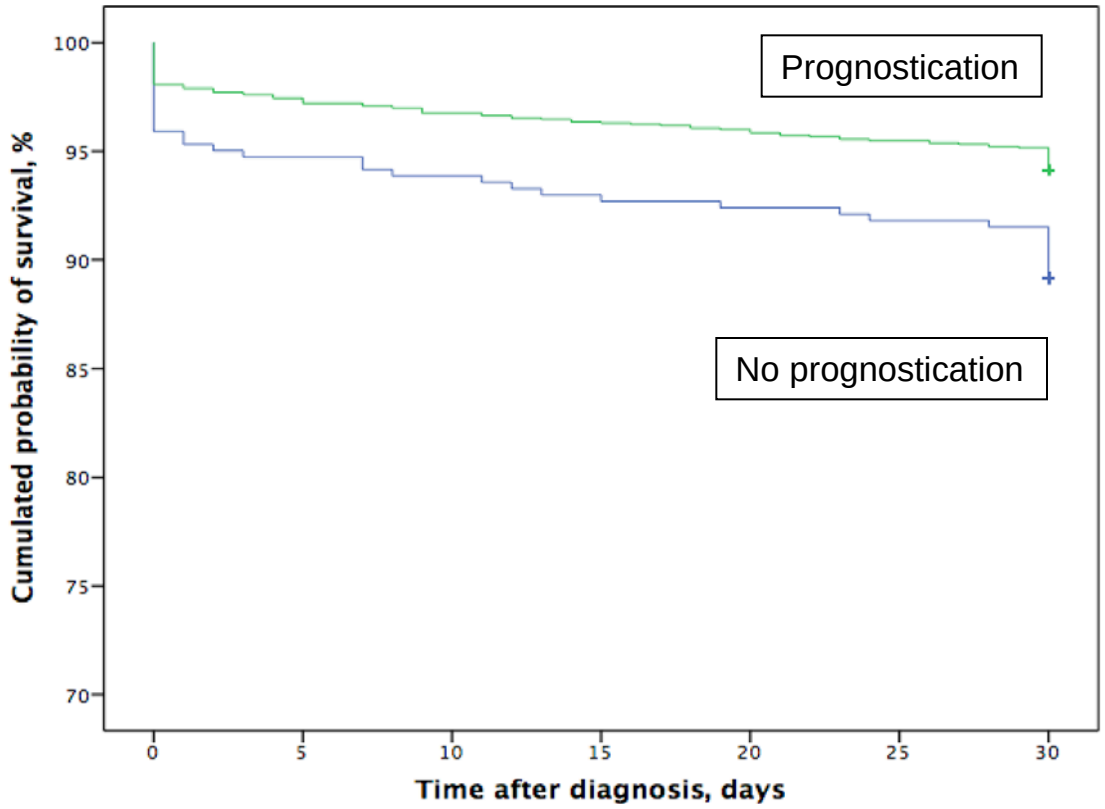
Morillo R, Semin Thromb Haemost 2017

The future in PE prognostication

- Are prognostic tools interchangeable?
- Markers to monitor response to therapy
- Does prognostication *per se* improve outcomes?

Do we need to risk stratify patients with acute PE?

2,096 patients from a single center



Log rank p < 0.01

Jimenez D, unpublished

Summary

- Patients with acute PE should undergo risk stratification
- Risk stratify starting with sPESI and/or Hestia
- Combination of clinical, echographic and biochemical variables for “real” intermediate-risk PE