SALA CONCORDIA B

URGENZE CARDIOVASCOLARI

Moderatori: **Francesco Rocco Pugliese, Furio Colivicchi** (ANMCO)

Cecilia Becattini

L’embolia polmonare

XII congresso nazionale
SIMEU
RICCIONE 13-15 MAGGIO 2022

The ABC…D of Acute PE

Cecilia Becattini

University of Perugia, Italy

Speaker disclosure

C.B. received

- Speakers fees from Bayer HealthCare, Bristol Myers Squibb, Daiichi Sankyo

- Consultancies from Bayer HealthCare, Bristol Myers Squibb, Daiichi Sankyo

My agenda

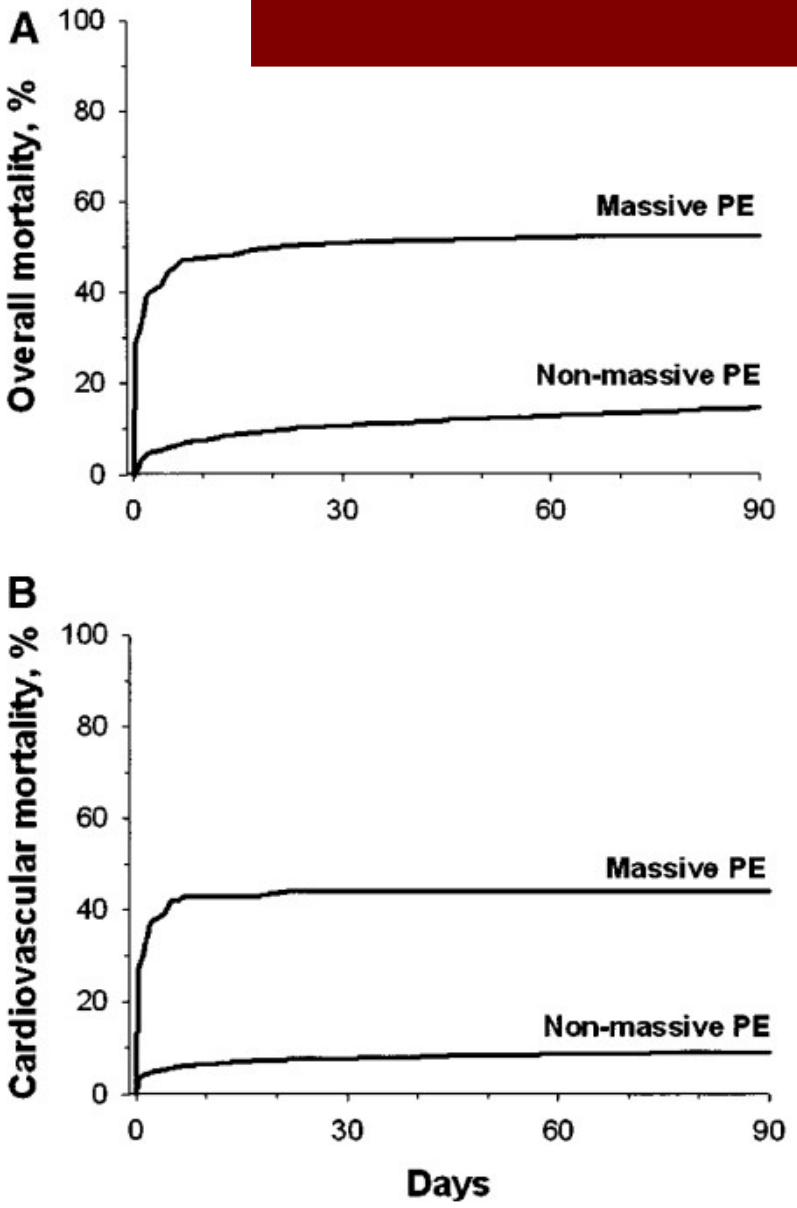
A= airway → respiratory failure

B= blood clot → anticoagulant treatment

C= circulation → assess hemodymics

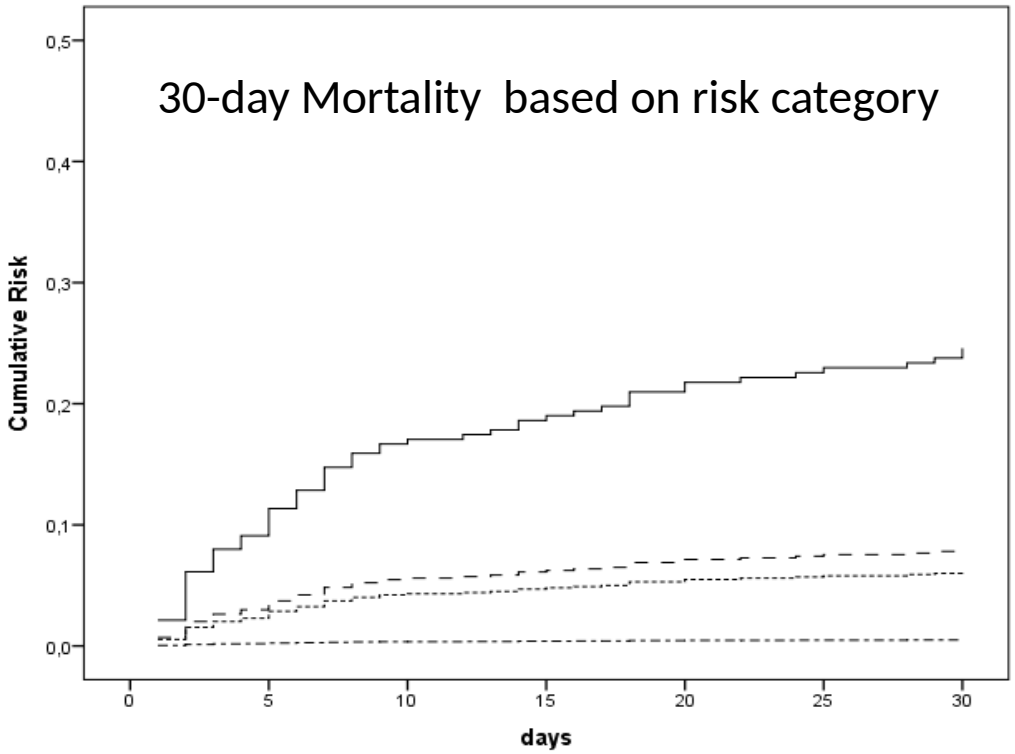
D= disposition → admission/discharge

C= hemodynamic status



Kucher N, et al. Circulation 2006;

906 patients with acute symptomatic objectively confirmed PE



High

Intermediate high

Intermediate low

Low

Becattini et al, *Eur Resp J 2016*

PE clinical course with systemic thrombolysis

	Thrombolysis		Control		OR (95% CI)
	n/N	(%)	n/N	(%)	
Early all-cause mortality (15 studies; 2057 patients)	**24/1033**	**(2.3)**	**40/1024**	**(3.9)**	**0.59 (0.36-0.96)**
Including high-risk patients	8/115	(6.9)	15/109	(13.8)	0.48 (0.20-1.15)
Intermediate risk patients	6/571	(1.1)	15/564	(2.7)	0.42 (0.17-1.03)
Low & intermediate risk patients	10/347	(2.9)	10/351	(2.8)	0.96 (0.41-2.24)
Major bleeding (12 studies; 1935 patients)	**96/974**	**(9.9)**	**35/961**	**(3.6)**	**2.91 (1.95-4.36)**
Fatal/Hemorrhagic Strokes (12 studies; 1864 patients)	**16/933**	**(1.7)**	**3/931**	**(0.3)**	**3.18 (1.25-8.11)**

Marti C et al, Eur Heart J 2015

Management of high risk/massive PE

√ High risk PE

systemic thrombolysis

<u>if contraindicated or ineffective</u>: consider percutaneous embolectomy

2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)

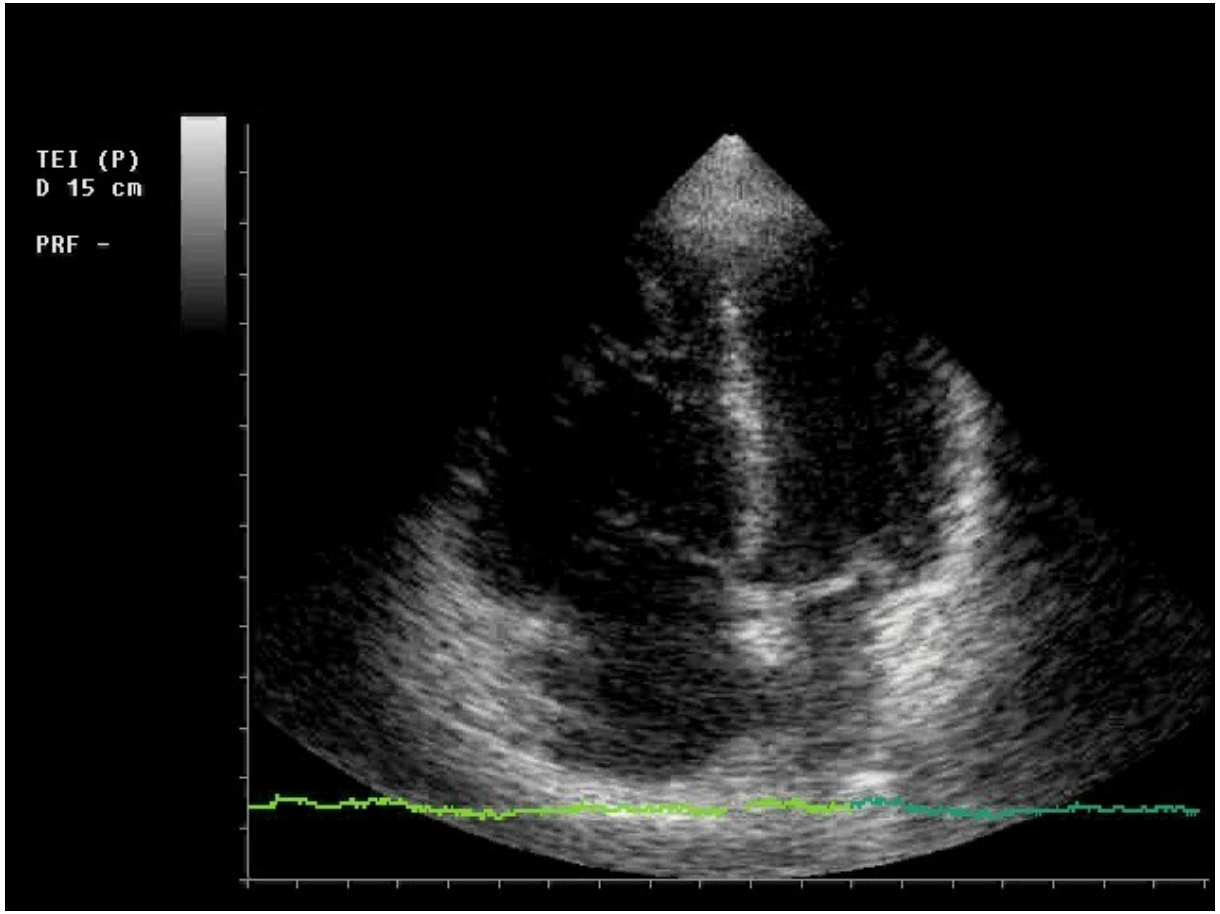
American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism

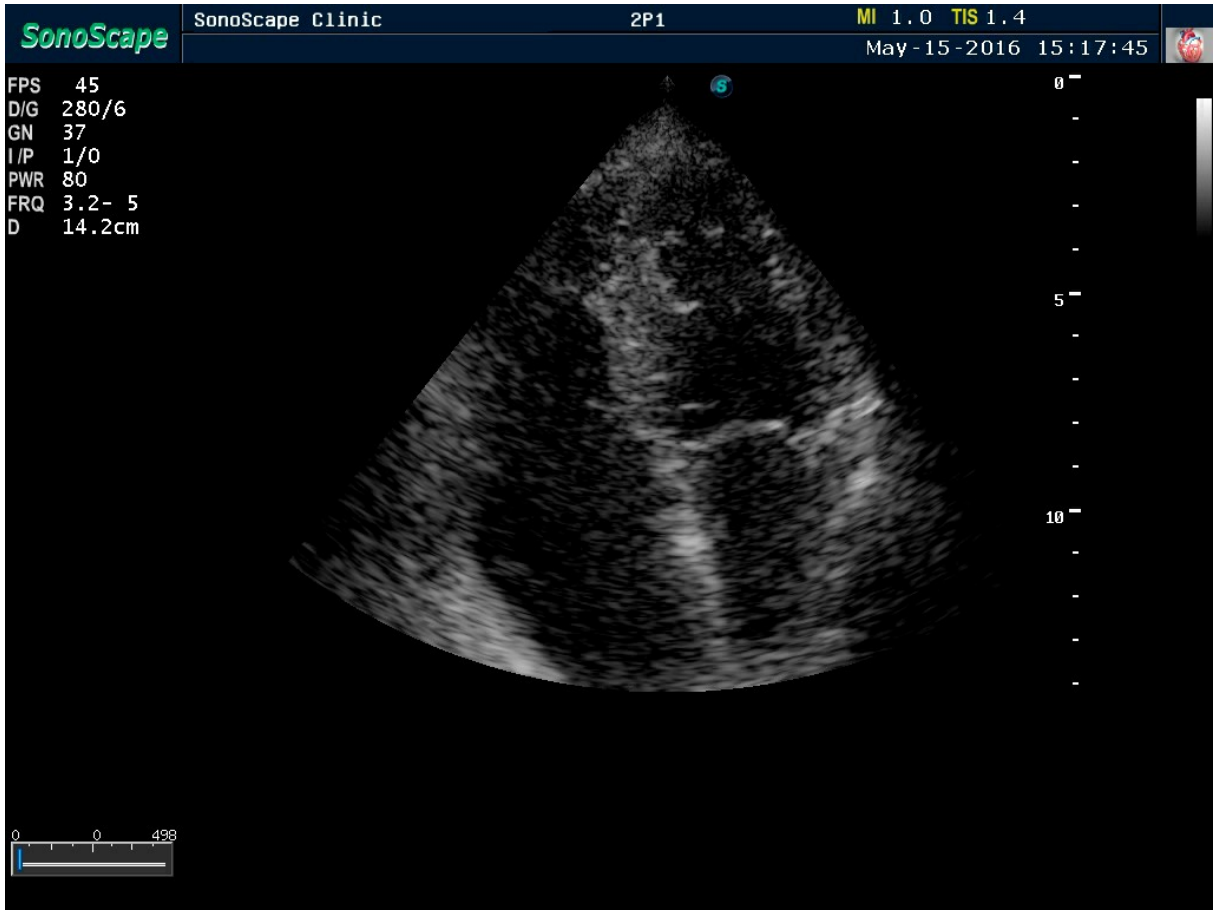
Acute phase treatment in the COPE study: reperfusion

	Overall population (N=5213)	Low risk (n=1702)	Intermediate Risk (n=3281)	High Risk (n=177)	Unknown (n=53)
Revascularization, n (%)	**253 (4.9)**	22 (1.3)	129 (3.9)	**103 (58)**	--
surgery, n	2 (0.04)	--	2	--	--
thrombolysis, n	278 (4.9)	33 (2)	142 (4)	103 (58)	--
percutaneous, n	*38 (14)*	***11 (33)***	*23 (16)*	*4 (4)*	--
systemic	*235 (84)*	*21 (64)*	*116 (82)*	***98 (95)***	--
Contraindication for thrombolysis, n (%)	435 (8)	62 (4)	335 (10)	35 (20)	3 (6)

Becattini C et al, submitted

C= hemodynamic status





Acute PE: risk stratification according to ESC

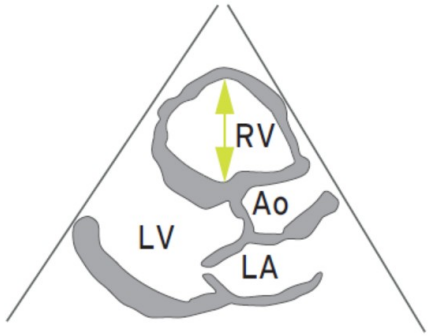
2019 EUROPEAN SOCIETY OF CARDIOLOGY®

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

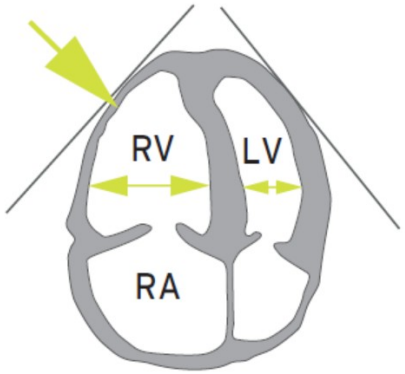
CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; TTE = transthoracic echocardiography.

Konstantinides S et al, Eur Heart J 2019

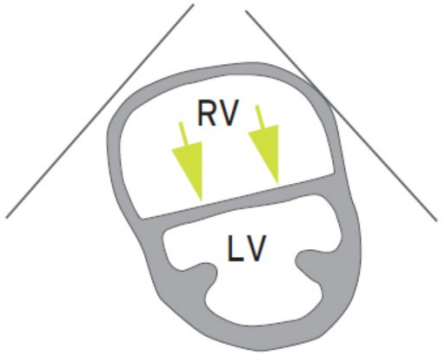
TTE parameters of RV pressure overload (1)



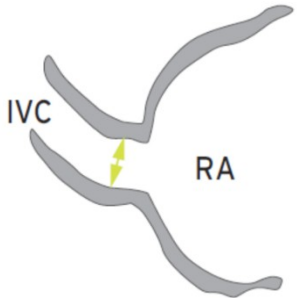
A. Enlarged right ventricle, parasternal long axis view



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



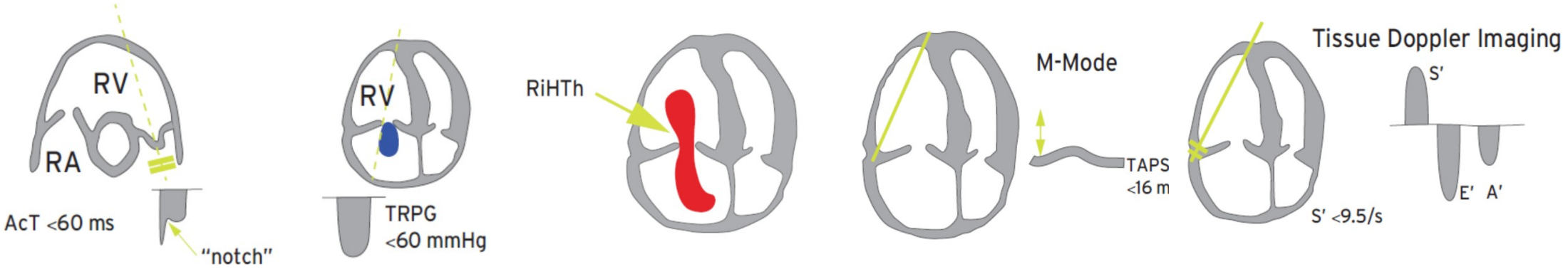
C. Flattened interventricular septum (arrows) parasternal short axis view



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

RV = right ventricular; TTE = transthoracic echocardiography/echocardiographic.

TTE parameters of RV pressure overload (2)



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

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

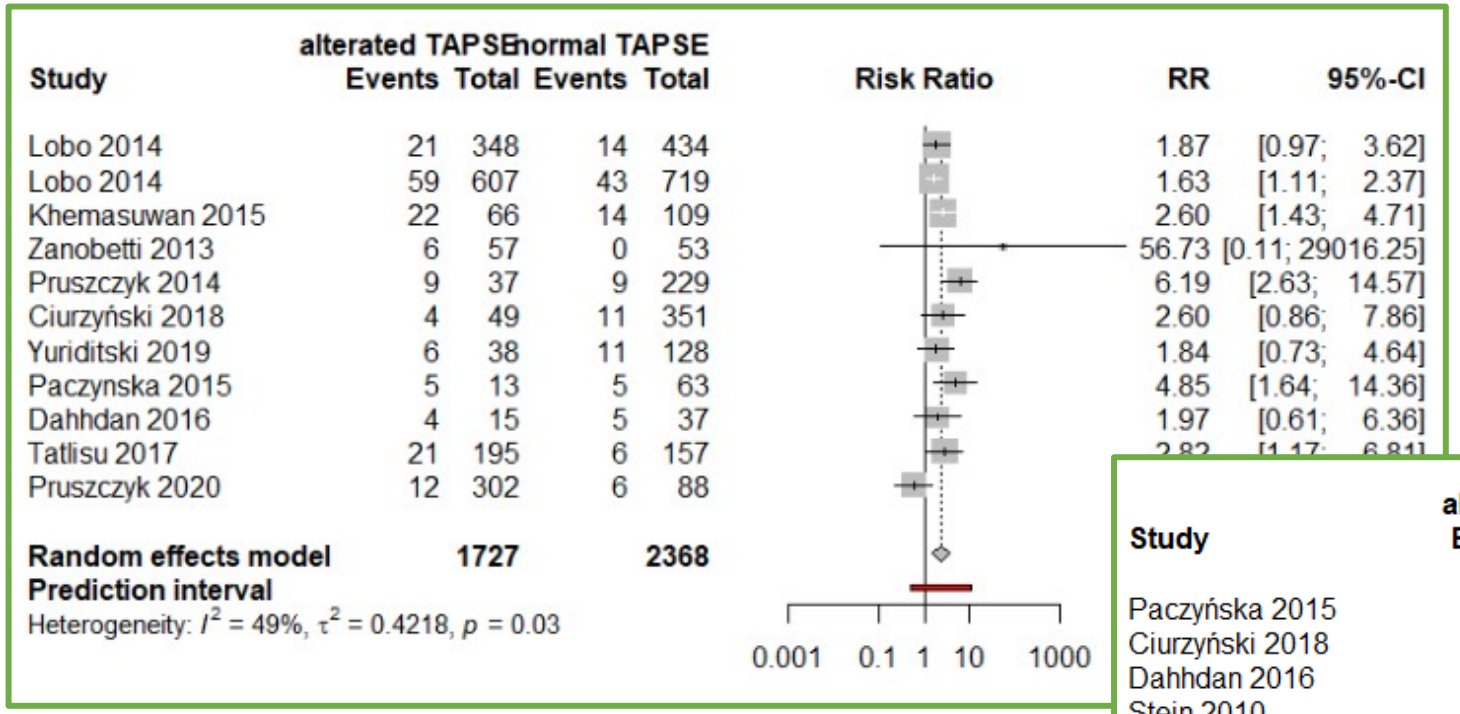
G. Decreased tricuspid annular plane systolic excursion (TAPSE) measured with M-Mode (<16 mm)

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

RV = right ventricular; TTE = transthoracic echocardiography/echocardiographic.

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

Echocardiography – which parameter for RVD?

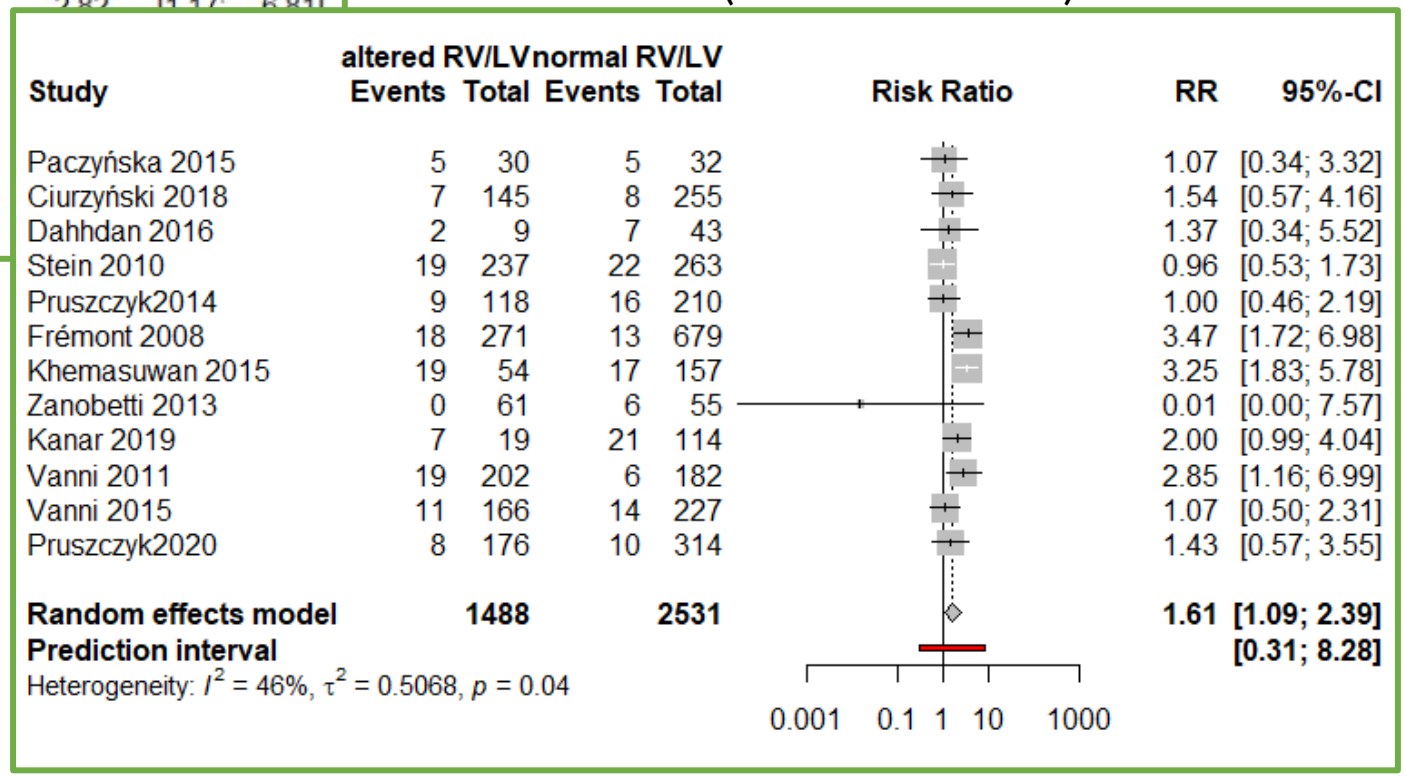


TAPSE & short term mortality

RR 2.29 (95% CI 1.45-3.59)

RV/LV Ratio & short term mortality

RR 1.61 (95% CI 1.09-2.39)



Cimini L et al, *submitted*

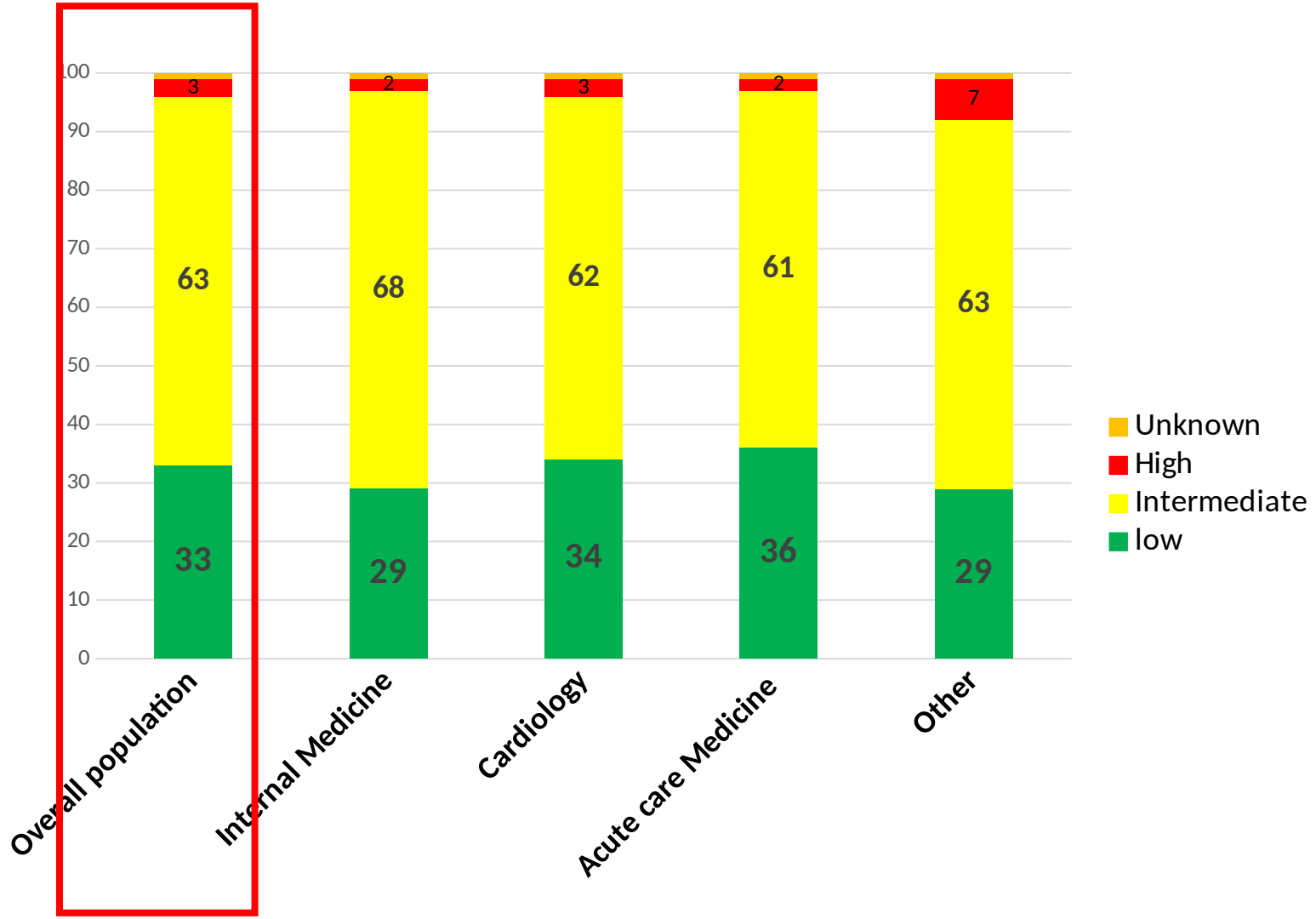
Right ventricle dysfunction or injury and death

Value of prognostic markers
in hemodynamically stable patients

	OR/HR	CI
Right ventricle dysfunction at echo	1.94	(1.23-3.06)
Right ventricle dilation at CT	1.64	(1.06-2.52)
Increased troponin	5.90	(2.68-12.95)

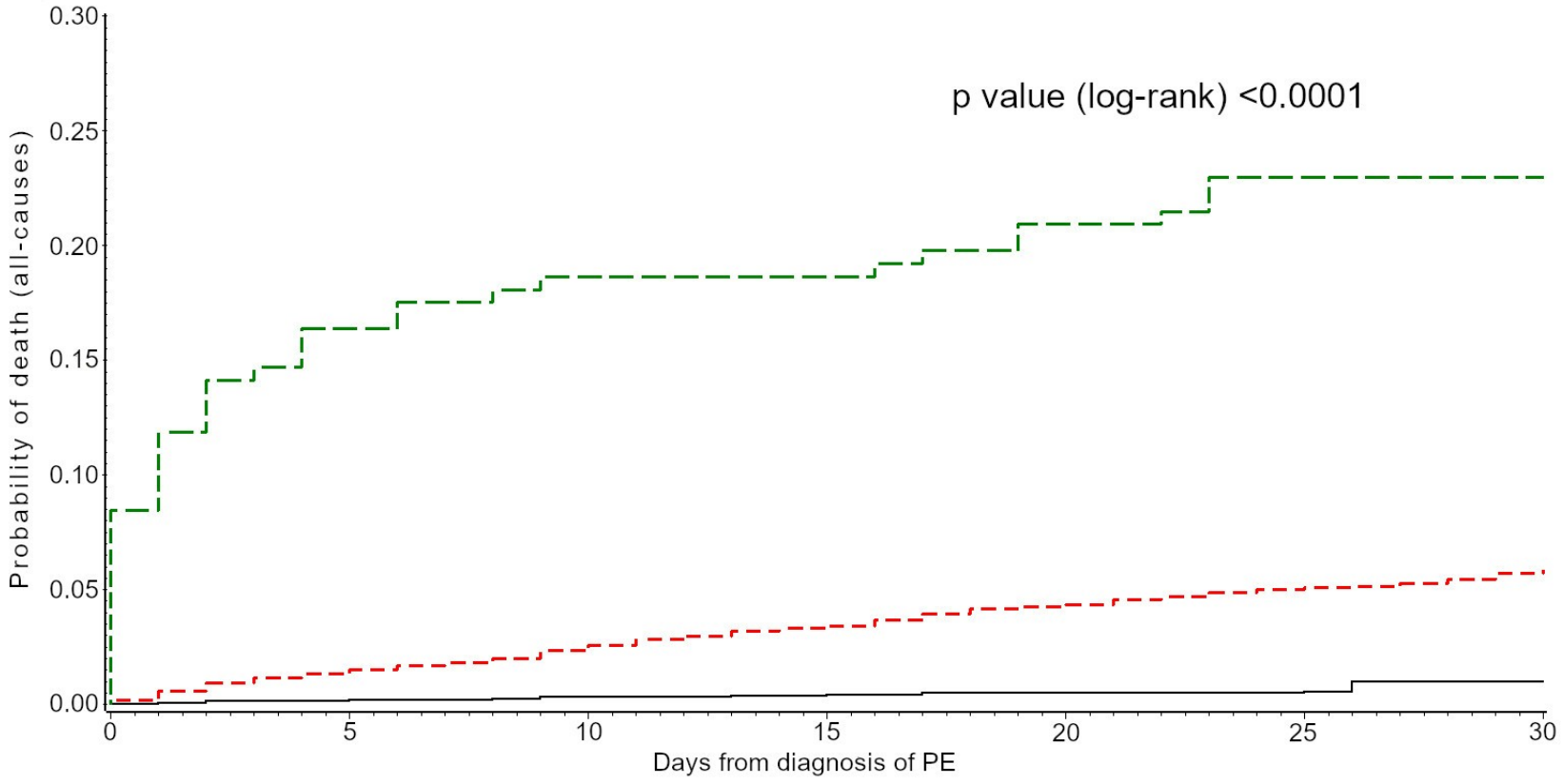
Kucher N et al. Arch Intern Med, 2005
Becattini C et al. Eur Resp J, 2014
Becattini C et al. Circulation, 2007

Severity of acute PE in the COPE study



Becattini C et al, submitted

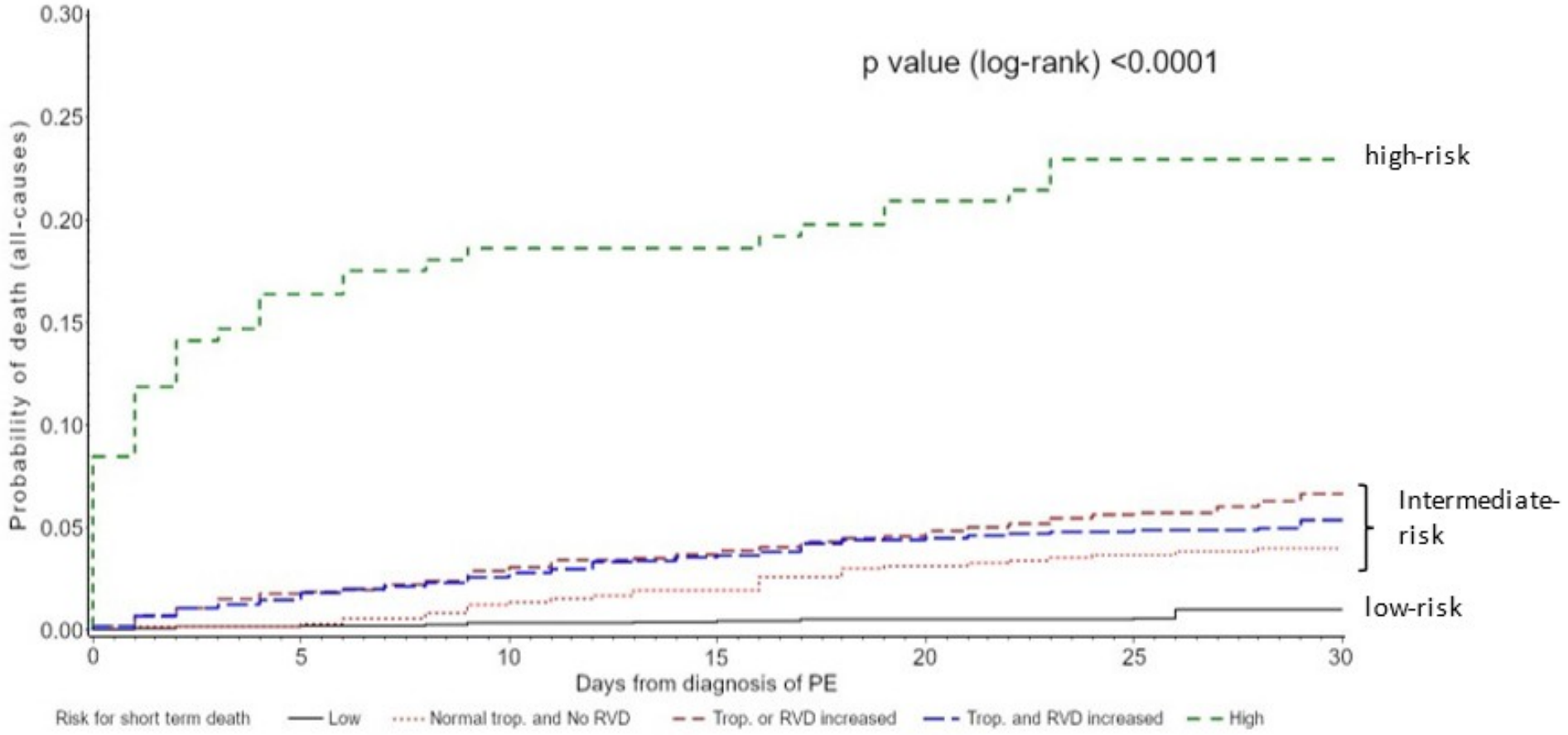
COPE: Time to all-cause death by risk category



Risk for short term death LOW INTERMEDIATE HIGH

Becattini C et al, submitted

COPE: Time to all-cause death by risk category



Becattini C et al, submitted

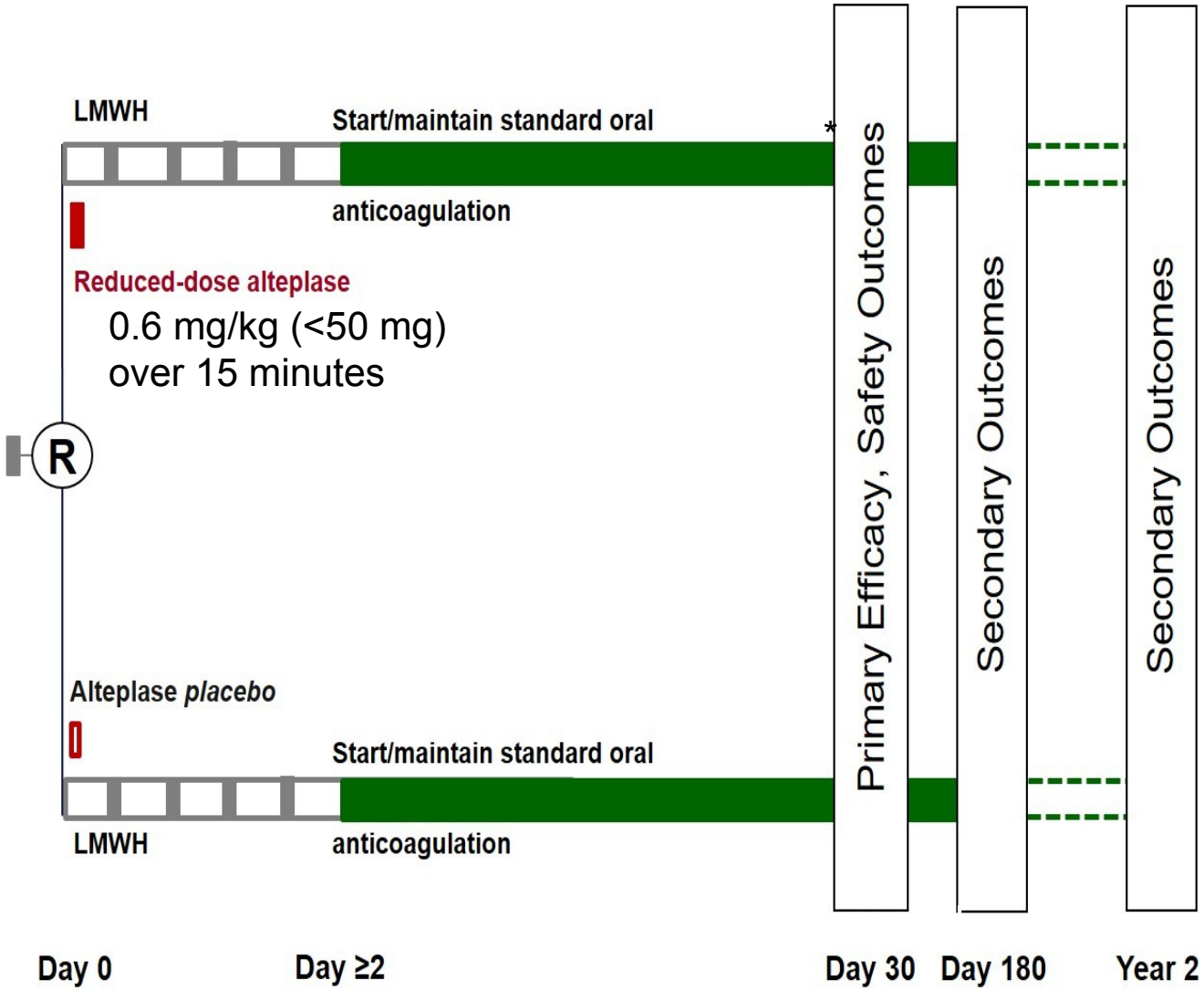
Coming soon...

PEITHO III

Confirmed acute PE, haemodynamically stable
(including stabilisation ≤2 h of admission)

≥1 criterion of severity
- Systolic blood pressure ≤110 mmHg
- Respir. rate >20 rpm / SpO2 <90%
- History of chronic heart failure

RV/LV >1.0 and positive troponin



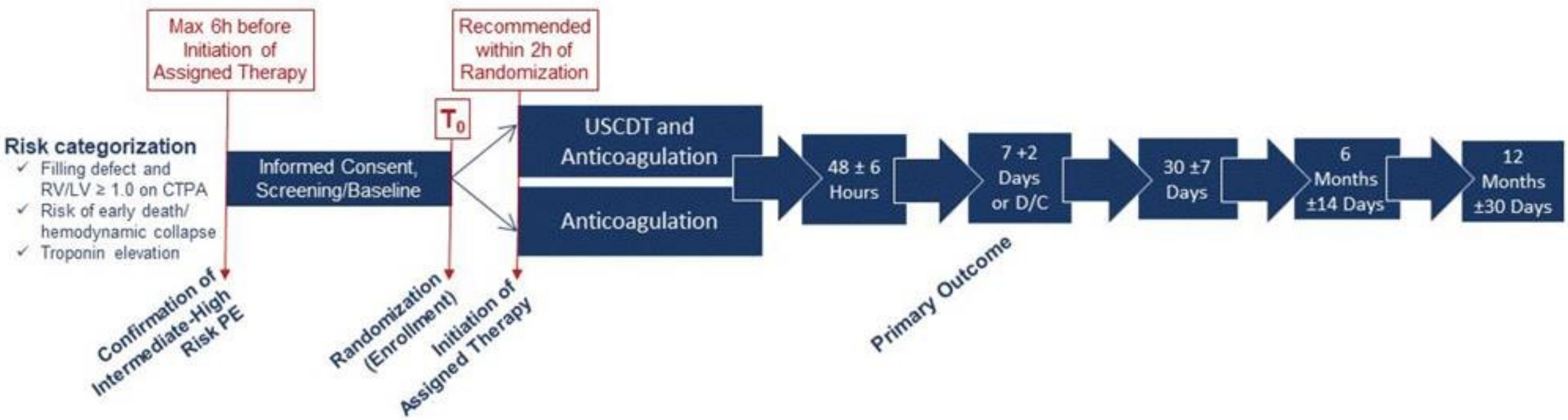
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

CTH Centrum für Thrombose und Hämostase Mainz

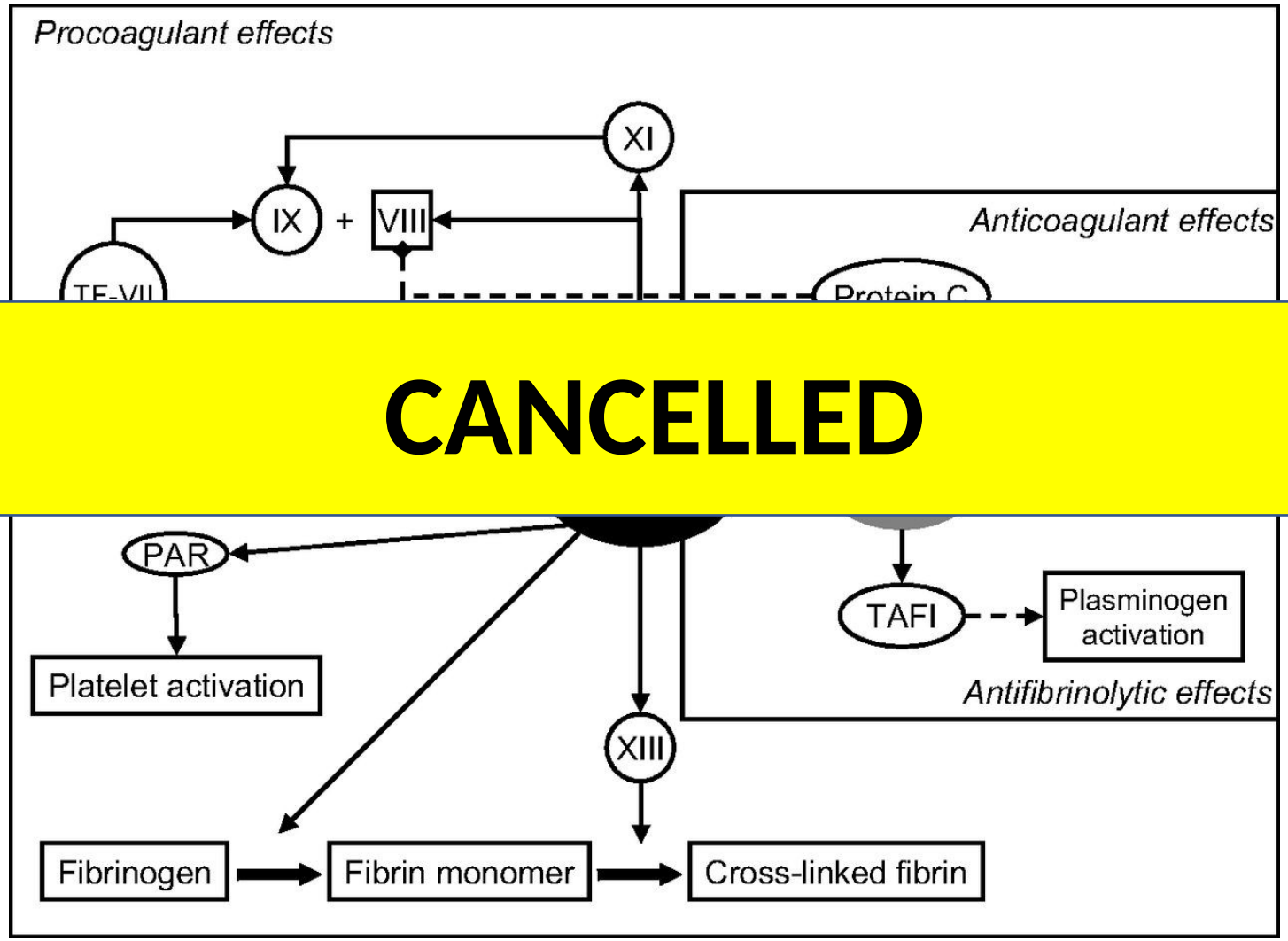
starting soon...

Hi-PEITHO

*



TAFI Inhibitor



CANCELLED

My agenda

C= circulation → assess hemodymics

B= blood clot → anticoagulant treatment

A= airway → respiratory failure

D= disposition → admission/discharge

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

Recommendations	Class	Level
It is recommended that anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with high-risk PE.[a]	I	C

Recommendations	Class	Level
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE, while diagnostic work-up is in progress.	I	C

©ESC

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

Recommendations for treatment of intermediate- or low- risk PE (1)

Recommendations	Class	Level
Oral anticoagulants		
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), **a NOAC is recommended in preference to a VKA**.	I	A
NOACs are not recommended in patients with severe renal impairment, during pregnancy and lactation, and in patients with the antiphospholipid antibody syndrome.	III	C

NOAC = non-vitamin K antagonist oral anticoagulant; LMWH = low molecular weight heparin; VKA = vitamin K antagonist; UFH = unfractionated heparin.

Treatment of VTE: ASH Guidelines

Recommendation 3

For patients with DVT and/or PE, the ASH guideline panel *suggests* using DOACs over VKAs (conditional recommendation based on moderate certainty in the evidence of effects ⊕⊕⊕◯).

Remarks: This recommendation may not apply to certain subgroups of patients, such as those with renal insufficiency (creatinine clearance <30 mL/min), moderate to severe liver disease, or antiphospholipid syndrome.

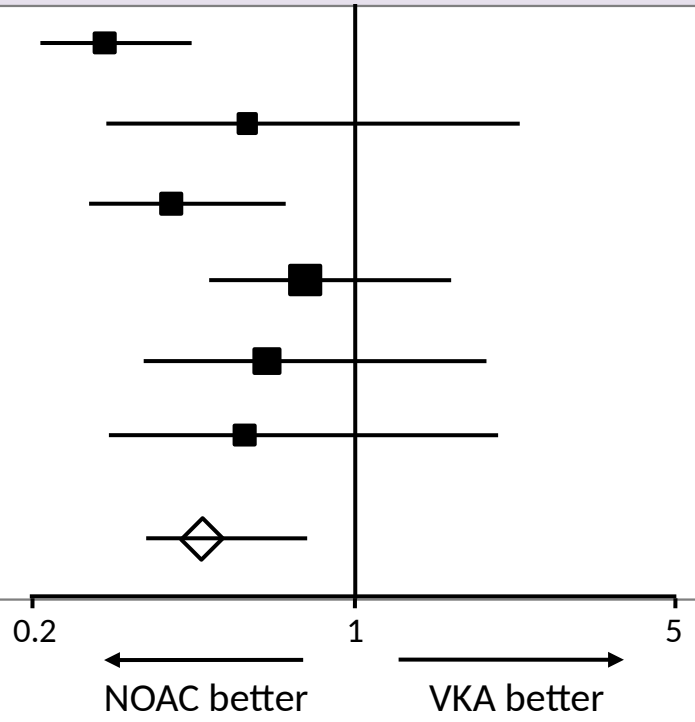
Recommendation 4

For patients with DVT and/or PE, the ASH guideline panel does not suggest 1 DOAC over another (conditional recommendation based on very low certainty in the evidence of comparative effects ⊕◯◯◯).

Ortel TL, Blood Advanc 2021

DOACs for VTE - Meta-analysis: major bleeding

	NOAC (n/N)	VKA (n/N)	RR (95% CI)	RR (95% CI)
AMPLIFY	15/2,676 (0.6%)	49/2,689 (1.8%)		0.31 (0.17–0.55)
EINSTEIN-DVT	14/1,718 (0.8%)	20/1,711 (1.2%)		0.70 (0.35–1.38)
EINSTEIN-PE	26/2,412 (1.1%)	52/2,405 (2.2%)		0.50 (0.31–0.80)
Hokusai-VTE	56/4,118 (1.4%)	66/4,122 (1.6%)		0.85 (0.60–1.21)
RE-COVER	22/1,273 (1.7%)	29/1,266 (2.3%)		0.75 (0.44–1.31)
RE-COVER II	15/1,280 (1.2%)	22/1,288 (1.7%)		0.69 (0.36–1.32)
Combined (random)	**148/13,477 (1.1%)**	**238/13,481 (1.8%)**		**0.61 (0.45–0.83)**



There are no head-to-head randomised clinical trials comparing the NOACs. Comparisons cannot be made between individual NOACs based on these data.

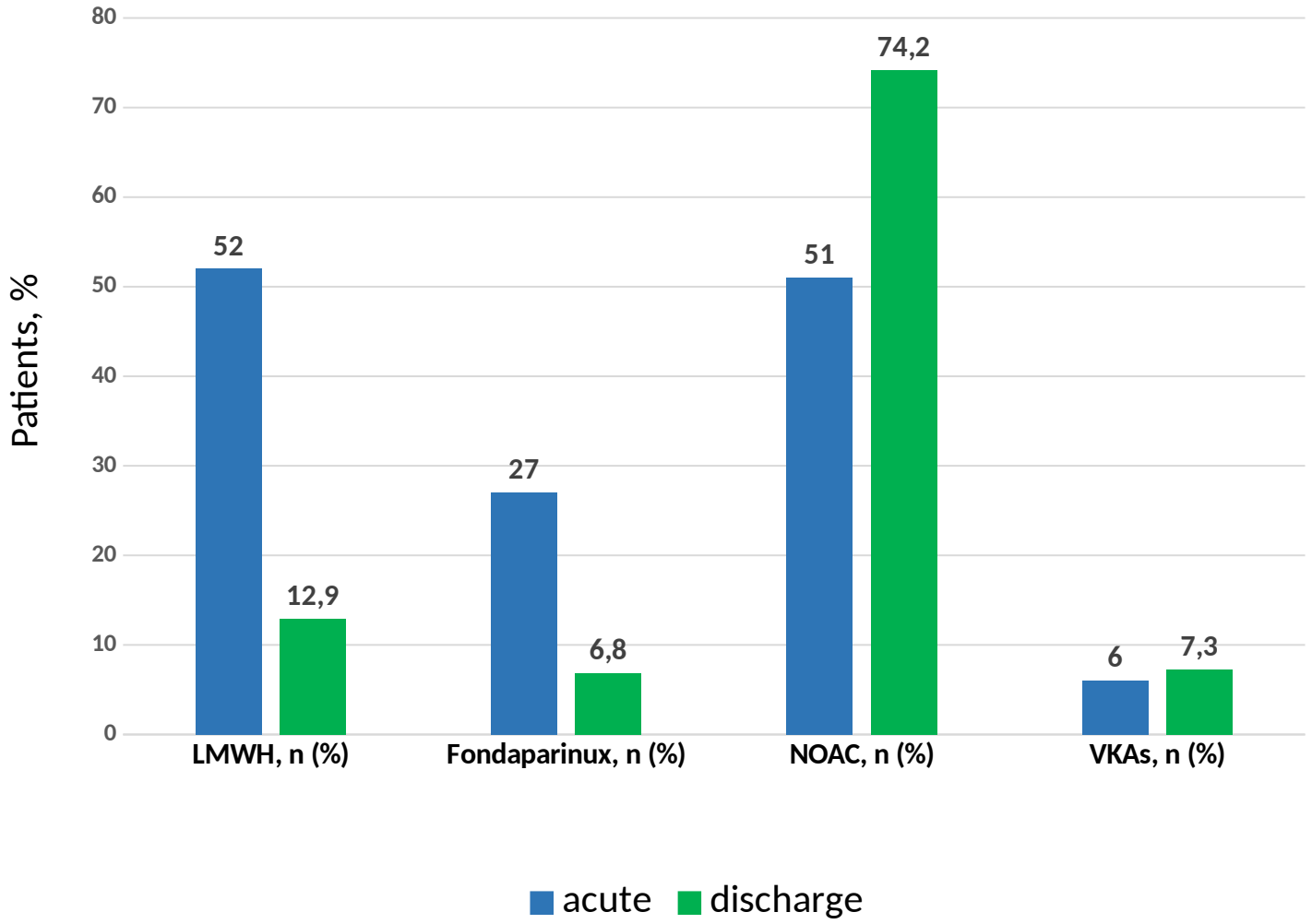
Van Es N, et al *Blood* 2014

COPE: Acute phase treatment

	Overall population (N=5213)	Risk for short-term death			
		Low risk (n=1702)	Intermediate Risk (n=3281)	High Risk (n=177)	Unknown (n=53)
UFH, n (%)	1228 (24)	300 (18)	810 (25)	110 (62)	8 (15)
LMWH, n (%)	2758 (53)	888 (52)	1771 (54)	72 (41)	27 (51)
Fondaparinux, n (%)	1424 (27)	490 (29)	892 (27)	25 (14)	17 (32)
At least 1 parenteral AC, n (%)	4801 (92)	**1538 (90)**	3049 (93)	164 (93)	59 (94)
Contraindication for AC, n (%)	105 (2)	17 (1)	79 (2)	9 (5)	--
Vena cava filter, n (%)	51 (1)	12 (0.7)	36 (1)	3 (2)	--

Becattini C et al, submitted

COPE anticoagulant Treatment: from acute phase to discharge



Becattini C et al, submitted

My agenda

C= circulation → assess hemodymics

B= blood clot → antithrombotic strategies

A= airway → respiratory failure

D= disposition → admission/discharge

Clinical scores

	Original PESI	Simplified PESI
Age >80	**Age in years**	**+1**
Male sex	**+10**	
History of cancer	**+30**	**+1**
History of heart failure	**+10**	**+1**
History of chronic lung disease	**+10**	
Heart rate ≥110 bpm	**+20**	**+1**
Systolic blood pressure < 100mmHg	**+30**	**+1**
Respiratory rate ≥30 apm	**+20**	
Temperature < 36°C	**+20**	
Altered mental status	**+60**	
Arterial oxyhemoglobin saturation <90%	**+20**	**+1**

Derivation 995 pts

30-day mortality

Low-risk 1.1% (0.0-2.1)

High risk 10.9% (8.5-13.2)

Validation 7106 pts RIETE

30-day mortality

Low-risk 1.1% (0.7-1.5)

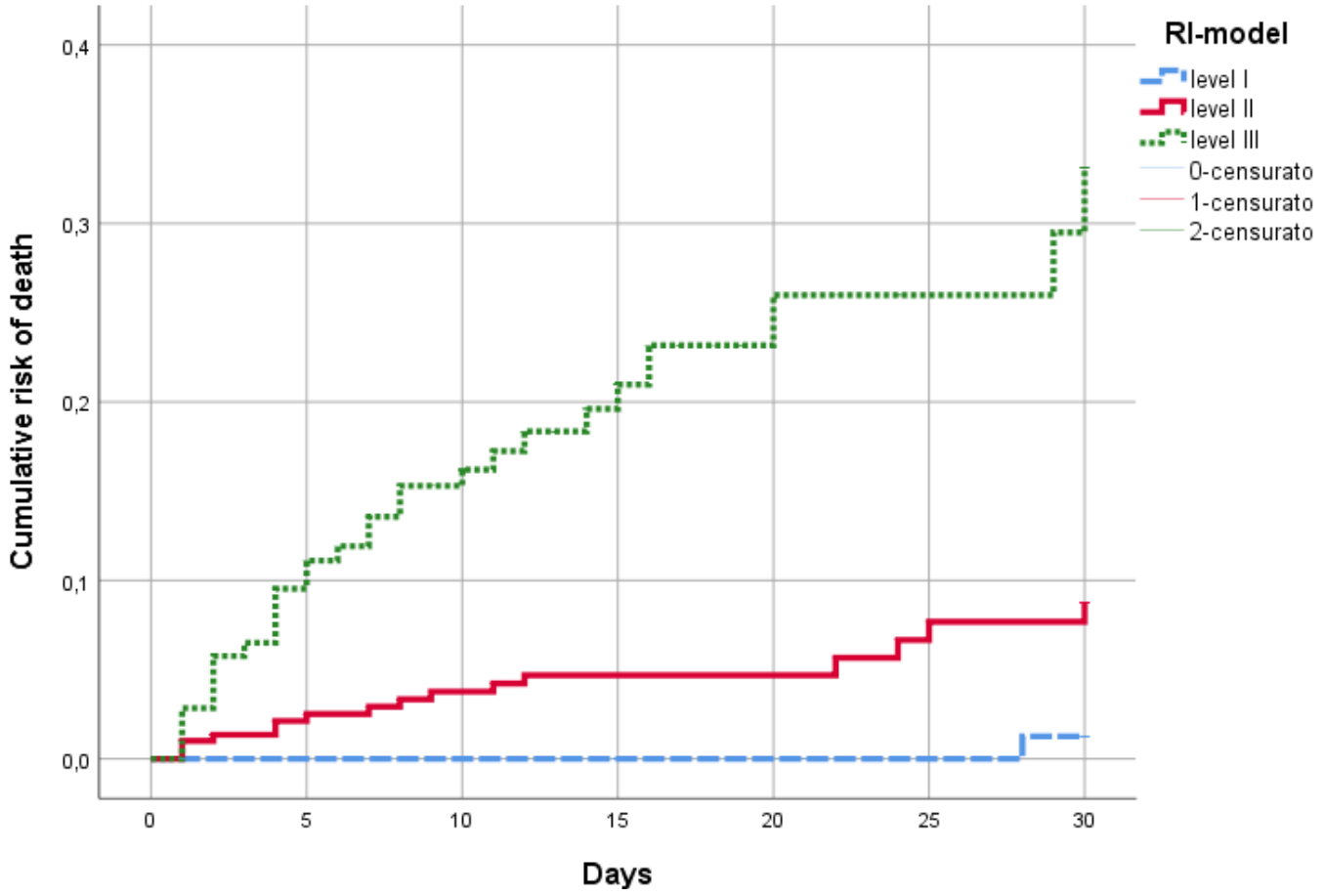
High risk 8.9% (8.1-9.8)

Low-risk 0 (30-36%); high risk ≥1

Arch Intern Med 2010

A= Airway, respiratory failure

RI-model = sPESI + Respiratoty Index (Oxy Saturation/ Respiratory Rate)



Vedovati MC,

Eur Heart J ACC 2020

My agenda

C= circulation → assess hemodymics

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Classification of PE based on early mortality risk

ESC European Society of Cardiology

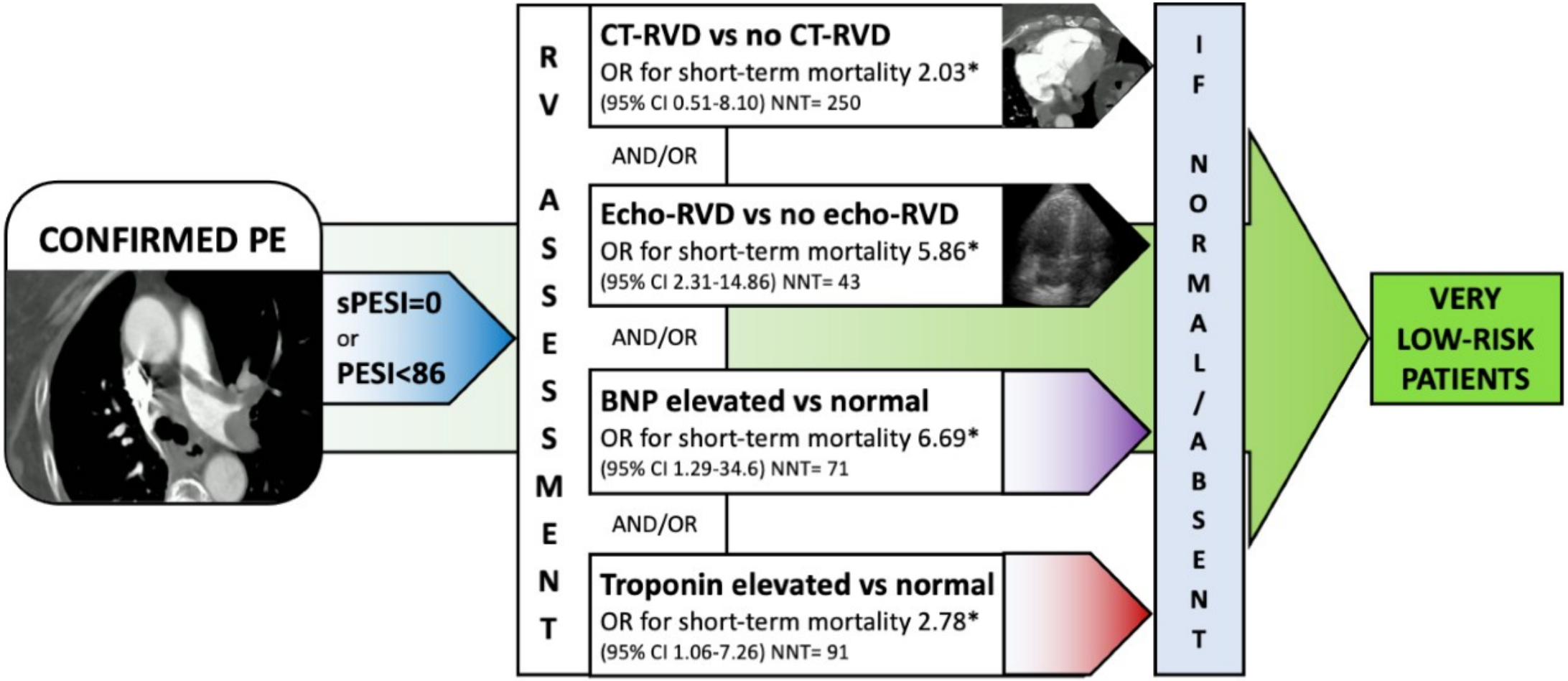
Early mortality risk		Indicators of risk			
		Haemo-dynamic instability	Clinical parameters of PE severity/ comorbidity: PESI III–V or sPESI ≥1	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High		**+**	**(+)**	**+**	**(+)**
Interme-diate	**Intermediate–high**	**-**	**+**	**+**	**+**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

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

Konstantinides S, EHJ 2019; Ortel TL, Blood Adv 2020

Identification of low-risk PE: Further stratification in sPESI zero?

DESIGN: An individual patient data meta-analysis



Becattini C et al, *Eur Heart J 2021*

Identification of low-risk PE: Further stratification in sPESI zero?

An individual patient data meta-analysis in

low-risk patients (sPESI=0 or PESI<86) with acute PE

Parameter for RVD/myocardial injury	In-hospital/30-day all-cause mortality				
	Yes vs No	OR	CI (95%)	*P* value	N. needed to test
RVD by Imaging or biomarkers (14 studies; 3266 patients)	1.5% vs 0.3%	**4.81**	**1.98-11.68**	**<0.001**	83
RVD at imaging (echo/CT) (14 studies; 2892 patients)	1.4% vs 0.3%	**4.49**	**1.80-11.18**	**0.001**	91
RVD at echocardiography (12 studies; 1843 patients)	2.8% vs 0.5%	**5.86**	**2.31-14.86**	**<0.001**	**43**
RV enlargement at CT (8 studies; 1479 patients)	0.7% vs 0.3%	2.03	0.51-8.10	0.316	250
Elevated BNP or NT-pro BNP (6 studies; 1172 patients)	1.6% vs 0.2%	**6.69**	**1.29-34.6**	**0.024**	**71**
Elevated Troponin (11 studies; 2183 patients)	1.8% vs 0.7%	**2.78**	**1.06-7.26**	**0.036**	91

Becattini C et al, *Eur Heart J 2021*

Home treatment in PE patients: the HOT PE Study

Primary Efficacy Outcome[a]	
Recurrent symptomatic VTE or fatal PE (ITT population) **One-sided 99.6% upper confidence limit**	**3/525 (0.6%)** **2.1%**
Recurrent PE (two-sided 95% CI)	**3/525 (0.6%; 0.1-1.7%)**
Recurrent deep vein thrombosis	**0**
Death related to PE	**0**
Recurrent symptomatic VTE or fatal PE *(Per-protocol population)* One-sided 99.6% upper confidence limit	2/497 (0.4%) 1.3%
Recurrent symptomatic VTE or fatal PE *(worst case scenario)* One-sided 99.6% upper confidence limit	5/525 (0.95%) 1.99%

[a] Adjudicated by an independent clinical events committee.

Barco S et al, Eur Heart J 2019

Take home messages

- ✓ **C =** assure adequate acute treatment for high and intermediate-high risk patients
- ✓ **B =** start anticoagulant treatment based on high PE suspicion

  Treat with DOACs the majority of PE patients
- ✓ **A=** consider respiratory failure and Respiratory Rate !!!
- ✓ **D=** home treatment is feasible.. in low risk patients with no RVD

Contemporary management of Pulmonary Embolism - COPE

Thanks to

- ***Patients*** *for their trust and support*
- ***Investigators***
- ***Daiichi Sankyo***

The ABC…D of Acute PE

Cecilia Becattini

University of Perugia, Italy