

Pulmonary embolism: Acute management

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Acute pulmonary embolism: Acute management

- Diagnosis
- Risk stratification
- Treatment

Non-high risk PE: diagnosis

Suspected PE without shock or hypotension

Assess clinical probability of PE
Clinical judgment or prediction rule^a

Low/intermediate clinical probability or PE unlikely

High clinical probability or PE likely

D-dimer

CT angiography

negative

positive

no PE

PE confirmed^c

no PE

PE confirmed^c

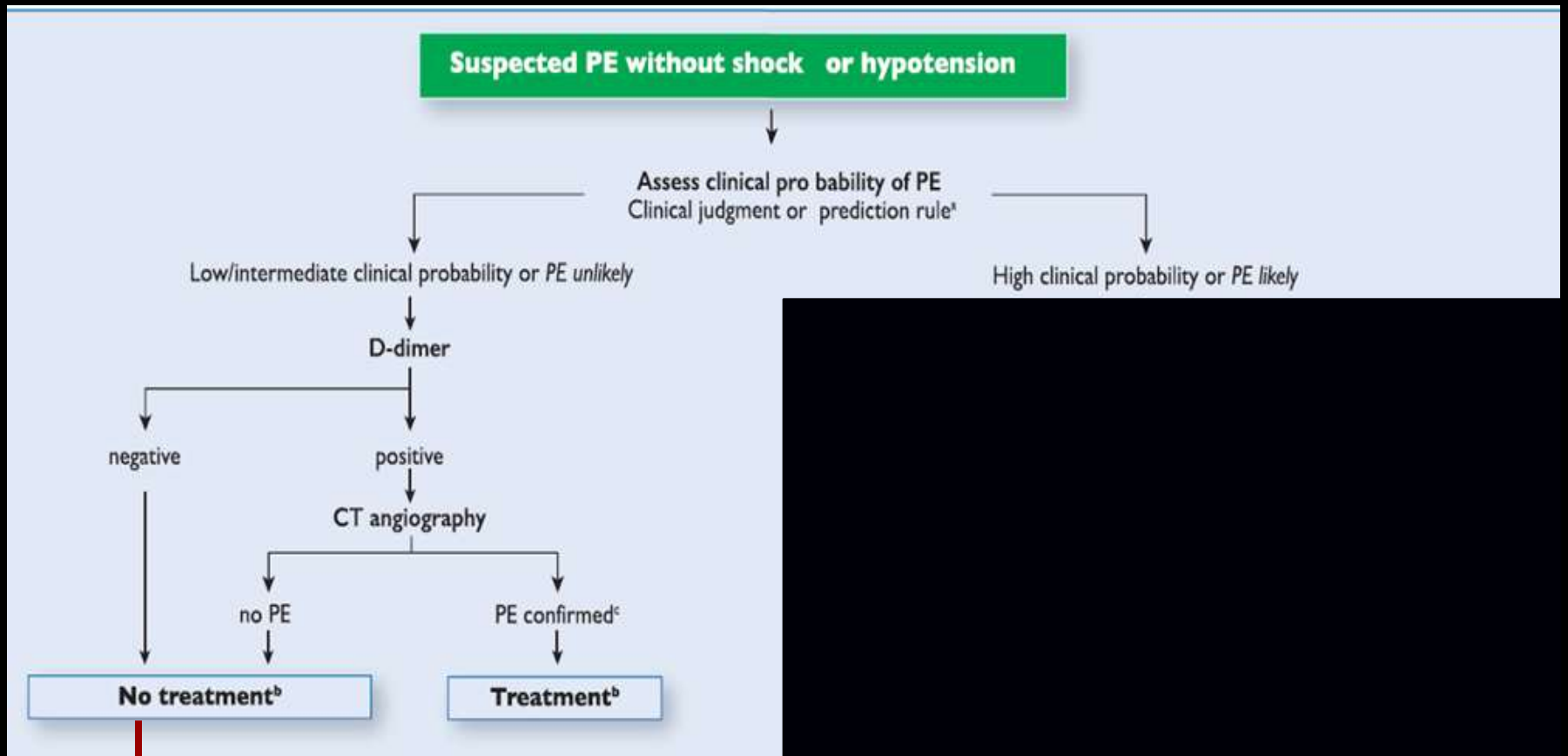
No treatment^b

Treatment^b

**No treatment^b
or investigate further^d**

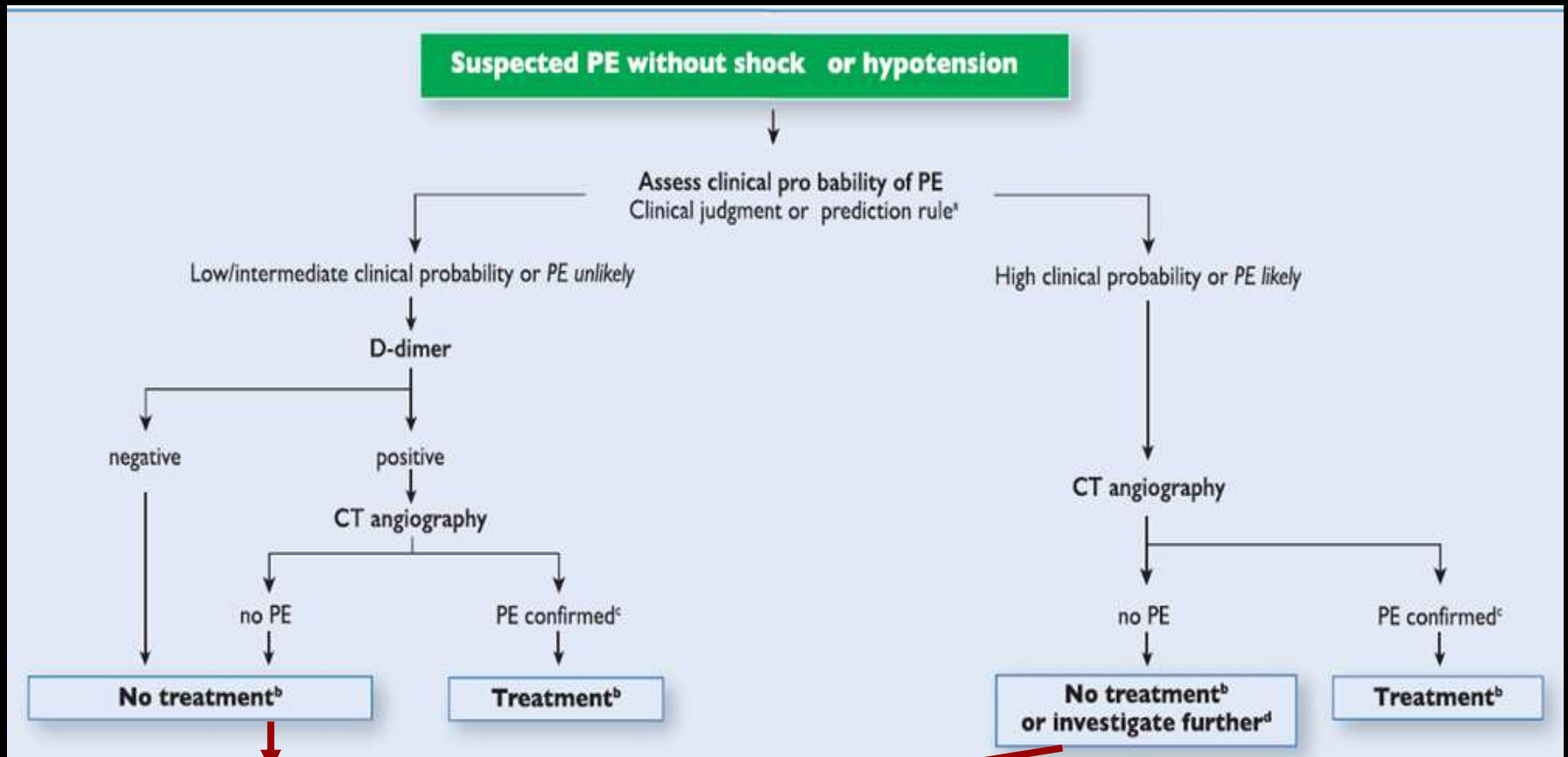
Treatment^b

Non-high risk PE: diagnosis



3-mo VTE 0.14%
95% CI 0.05-0.41

Non-high risk PE: diagnosis



3-mo VTE 1.5%
95% CI 0.8-3.0

Pre-test clinical probability

None of the clinical rules by itself is able to avoid
overuse of imaging tests

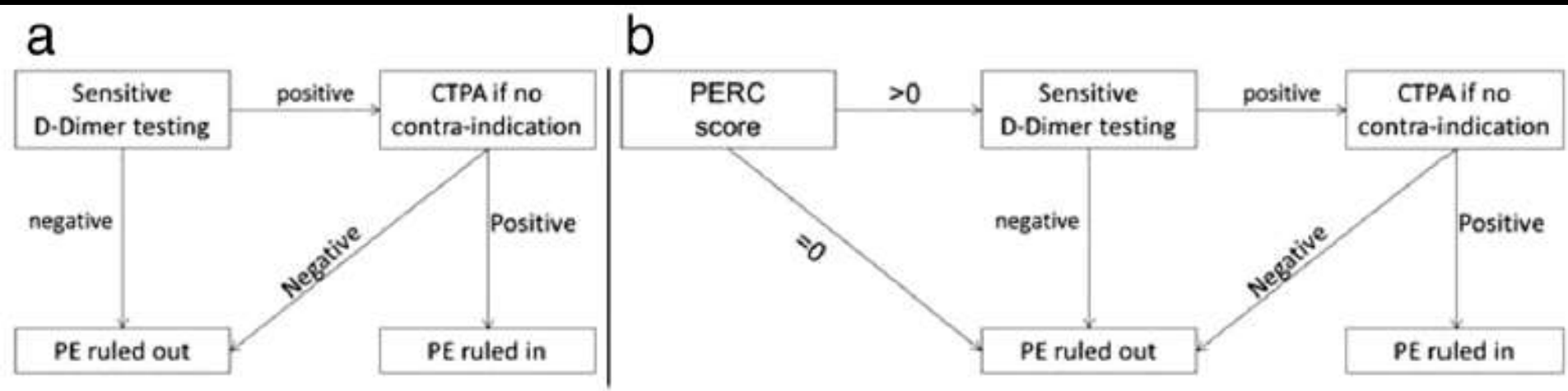
The PERC rule

1. Is the patient older than 49 years of age?
2. Is the pulse rate above 99 beats min⁻¹?
3. Is the pulse oximetry reading <95% in room air?
4. Is there a present history of hemoptysis?
5. Is the patient taking exogenous estrogen?
6. Does the patient have a prior diagnosis of VTE?
7. Has the patient had recent surgery or trauma? (Requiring endotracheal intubation or hospitalization in the previous 4 weeks.)
8. Does the patient have unilateral leg swelling? (Visual observation of asymmetry of the calves.)

PROPER study

A cluster randomized trial in France.

Primary objective to assess the non-inferiority of a PERC-based diagnostic strategy for PE low-risk emergency patients, compared to the standard strategy of D-dimer testing, on the occurrence of undiagnosed VTE events.



PROPER study: results

Characteristics	No. (%)		Mean Difference, % (95% CI)	Number Needed to Treat	P Value
	PERC	Control			
Intention-to-treat population, No. ^a	962	954			
Thromboembolic event at 3 mo (primary outcome)	32 (3)	29 (3)	0.2 (-∞ to 1.6) ^b		.12
CTPA performed	129 (13)	220 (23)	9.7 (6.1 to 13.2)	10	<.001
Length of ED stay, median (IQR), h:min	4:36 (3:16 to 6:21)	5:14 (3:50 to 7:18)	-00:36 (-1:08 to -0:04)		<.001
Hospital admission	121 (13)	152 (16)	3.3 (0.1 to 6.6)	30	.04
Anticoagulation therapy introduced	21 (2)	33 (3)	1.3 (0.3 to 2.9)	78	.09
Hospital readmission at 3 mo	43 (4)	62 (7)	2.1 (-0.1 to 4.3)	48	.051
All-cause death at 3 mo	3 (0.3)	2 (0.2)	0.1 (-0.5 to 0.7)		>.99

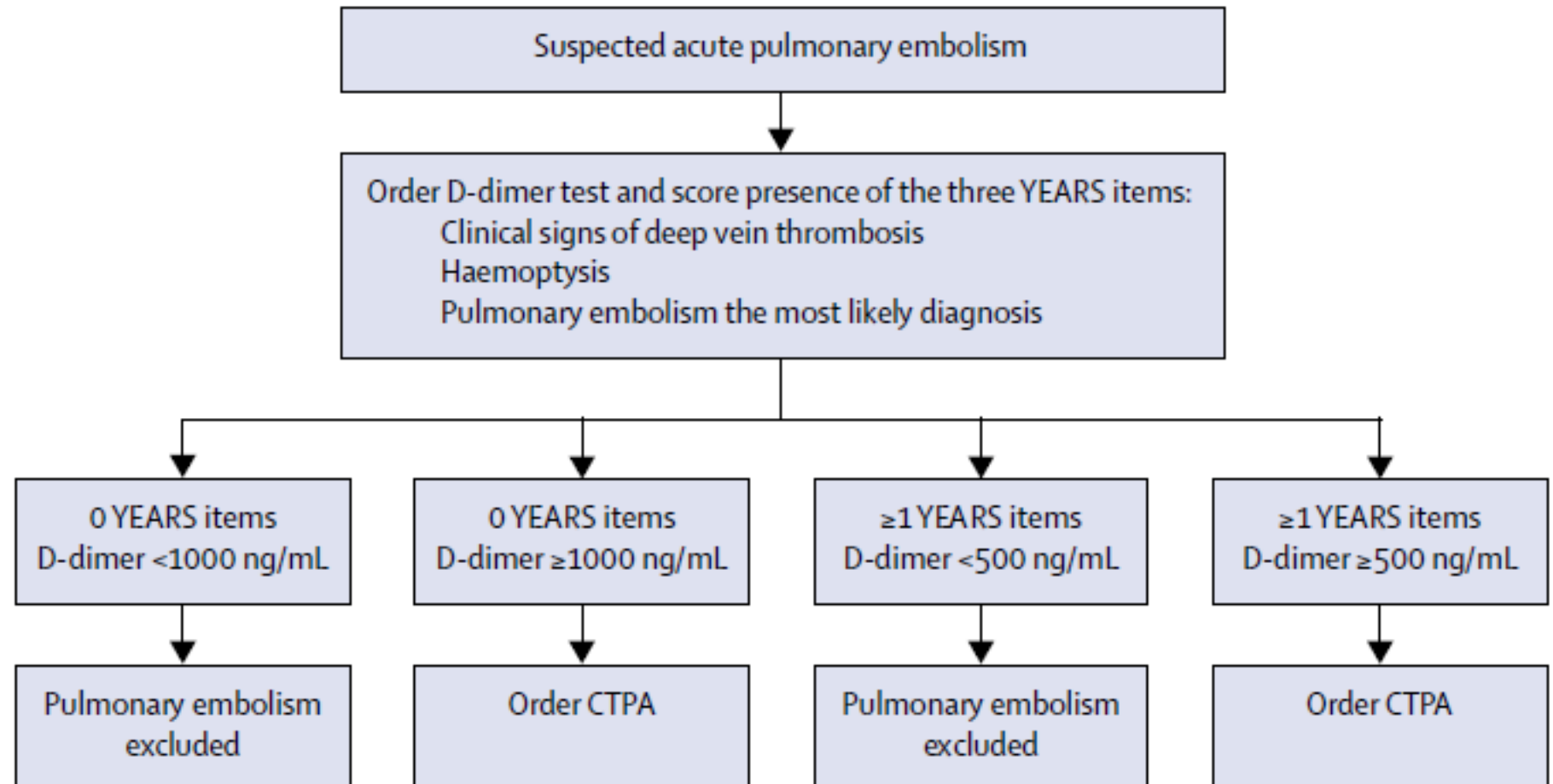
Among very low-risk patients with suspected PE, randomization to a PERC strategy vs conventional strategy did not result in an inferior rate of thromboembolic events over 3 months. These findings support the safety of PERC for very low-risk patients presenting to the emergency department

Pre-test clinical probability

Clinical prediction rules for pulmonary embolism

Wells rule	Clinical decision rule points	
	Original version	Simplified version
Previous PE or DVT	1.5	1
Heart rate ≥ 100 b.p.m.	1.5	1
Surgery or immobilization within the past 4 weeks	1.5	1
Haemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
<i>Three-level score</i>		
Low	0-1	N/A
Intermediate	2-6	N/A
High	≥ 7	N/A
<i>Two-level score</i>		
PE unlikely	0-4	0-1
PE likely	≥ 5	≥ 2

The YEARS algorithm



The YEARS algorithm

	Patients (n)	Total venous thromboembolism (n [%], 95% CI)	Fatal pulmonary embolism* (n [%], 95% CI)
Completed algorithm	2946	18 (0.61%, 0.36–0.96)	6 (0.20%, 0.07–0.44)
Patients managed without CTPA	1629	7 (0.43%, 0.17–0.88)	2 (0.12%, 0.01–0.44)
Patients managed with CTPA	1317	11 (0.84%, 0.47–1.5)	4 (0.30%, 0.12–0.78)

Patients in whom pulmonary embolism was excluded by either a low YEARS score or CT scanning were left untreated. CTPA=computed tomography pulmonary angiography. * Patients who remained untreated and were not lost to follow-up.

Table 2: Primary outcomes of venous thromboembolism events during 3-month follow-up

The YEARS algorithm

the YEARS approach should not lead to the indiscriminate use of D-dimer testing in all outpatients or inpatients with dyspnoea or chest pain

Age-adjusted D-dimer

3324 Patients with clinical probability assessment

2898 PE unlikely or non-high probability

426 PE likely or high probability

817
D-d < 500

337
D-d > 500 but
< age-adjusted

1744
D-d \geq age-adjusted

**2170
CTPA**

3-month VTE risk

0.01
(0-0.7)

0.3
(0.1-1.7)

Age-adjusted D-dimer

Using the age-adjusted (instead of the 'standard' (500 $\mu\text{g/L}$) D-dimer cut-off) increased the number of patients in whom PE could be excluded from 6.4% to 30%, without additional false-negative findings

Acute pulmonary embolism: Acute management

- Diagnosis
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- Treatment

The spectrum of clinical presentation of PE

PE-related shock

Mild clinical symptoms



The spectrum of clinical outcome of PE

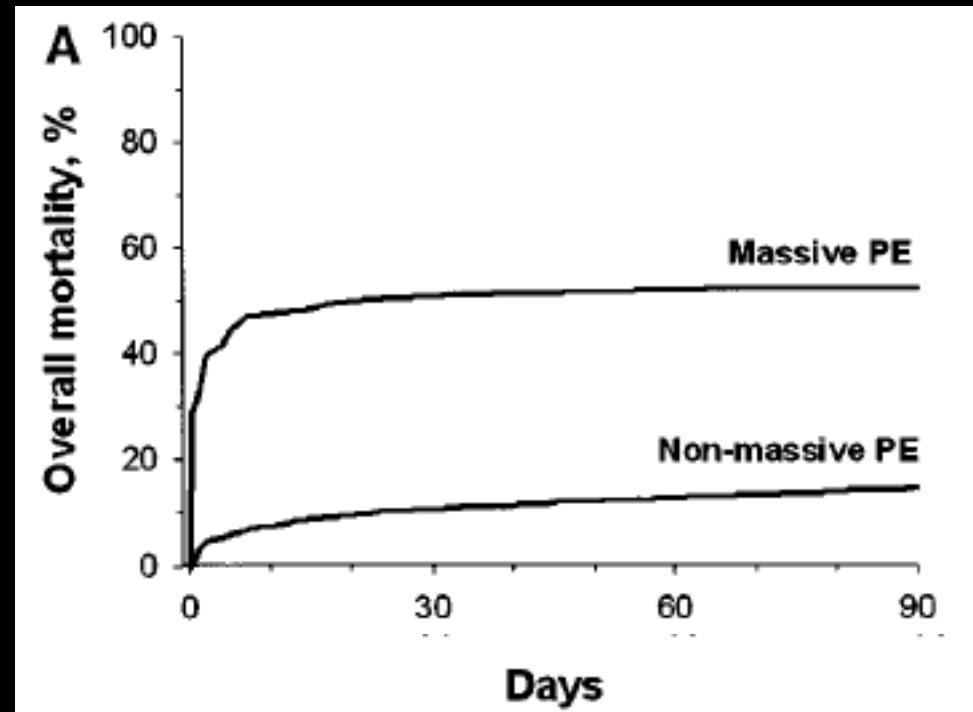
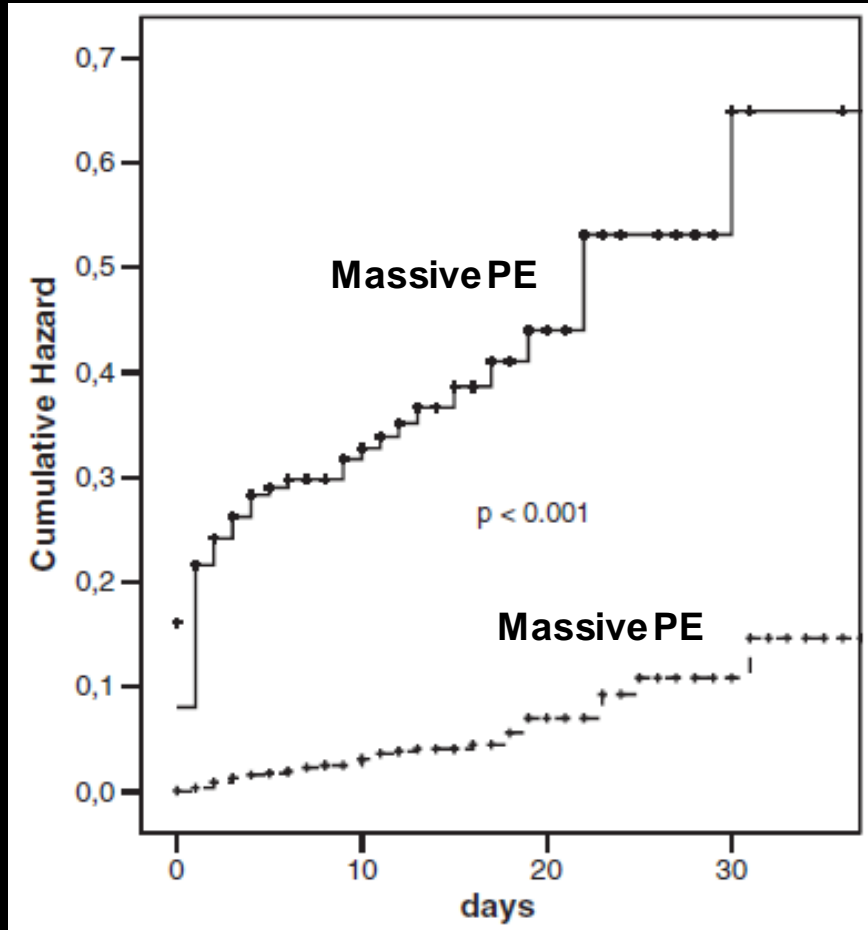
>30%

Mortality

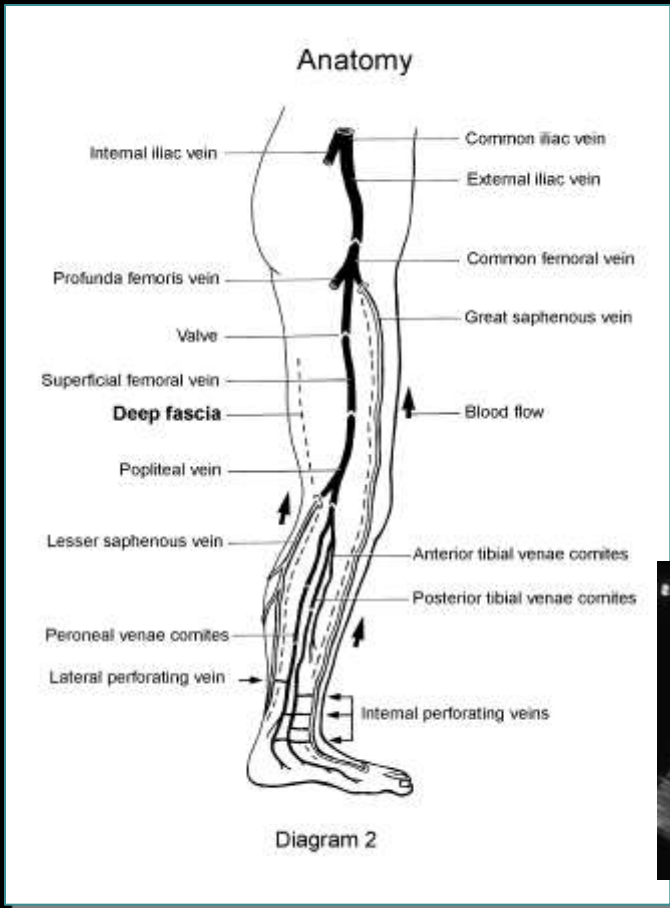
1%



PE: blood pressure

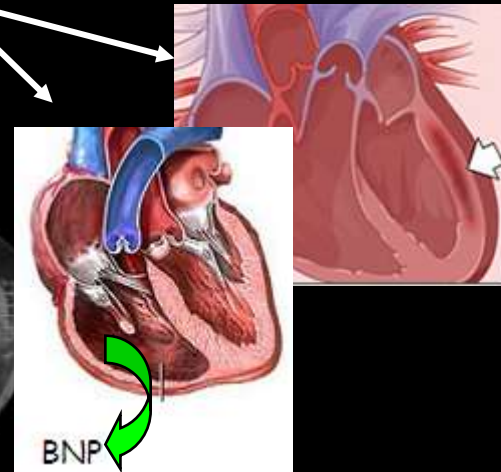
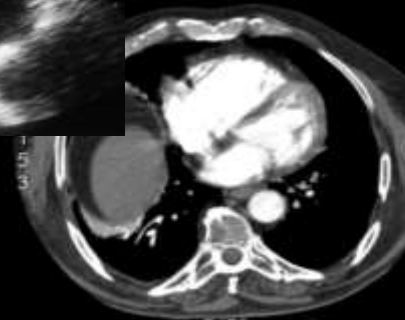
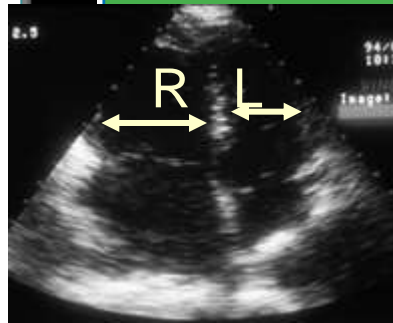


PE: across the severity spectrum



Classification of patients with acute PE based on early mortality risk

Early mortality risk		Risk parameters and scores			
		Shock or hypotension	PESI Class III-V or sPESI >1 ^a	Signs of RV dysfunction on an imaging test ^b	Cardiac laboratory biomarkers ^c
High		+	(+) ^d	+	(+) ^d
Intermediate	Intermediate-high	-	+	Both positive	
	Intermediate-low	-	+	Either one (or none) positive ^e	
Low		-	-	Assessment optional; if assessed, both negative ^e	



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

PE: ESC model for risk stratification

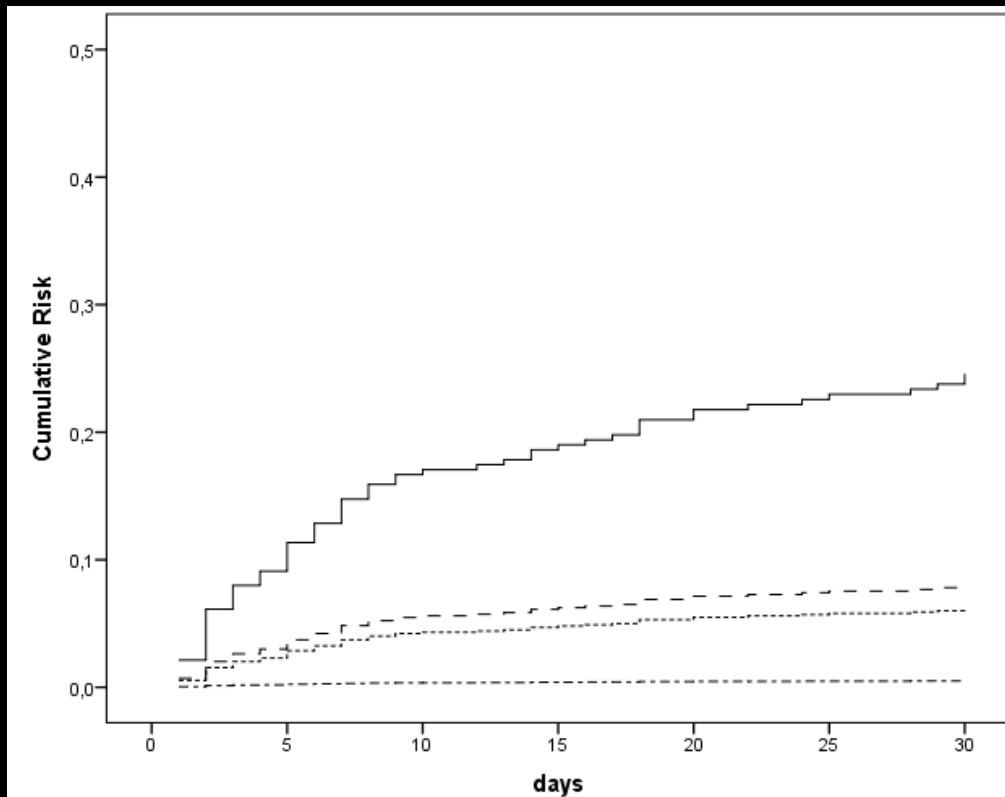


Classification of patients with acute PE based on early mortality risk

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Low		-	-	Assessment optional; if assessed, both negative ^e	

2014 ESC model... in clinical practice

906 patients with acute symptomatic objectively confirmed PE



30-day Mortality based on risk category

High —————
Intermediate high - - - - -
Intermediate low - · - - -
Low - · - - - -

CONTEMPORARY CLINICAL MANAGEMENT OF ACUTE PULMONARY EMBOLISM (COPE Observational Study)

Cecilia Becattini

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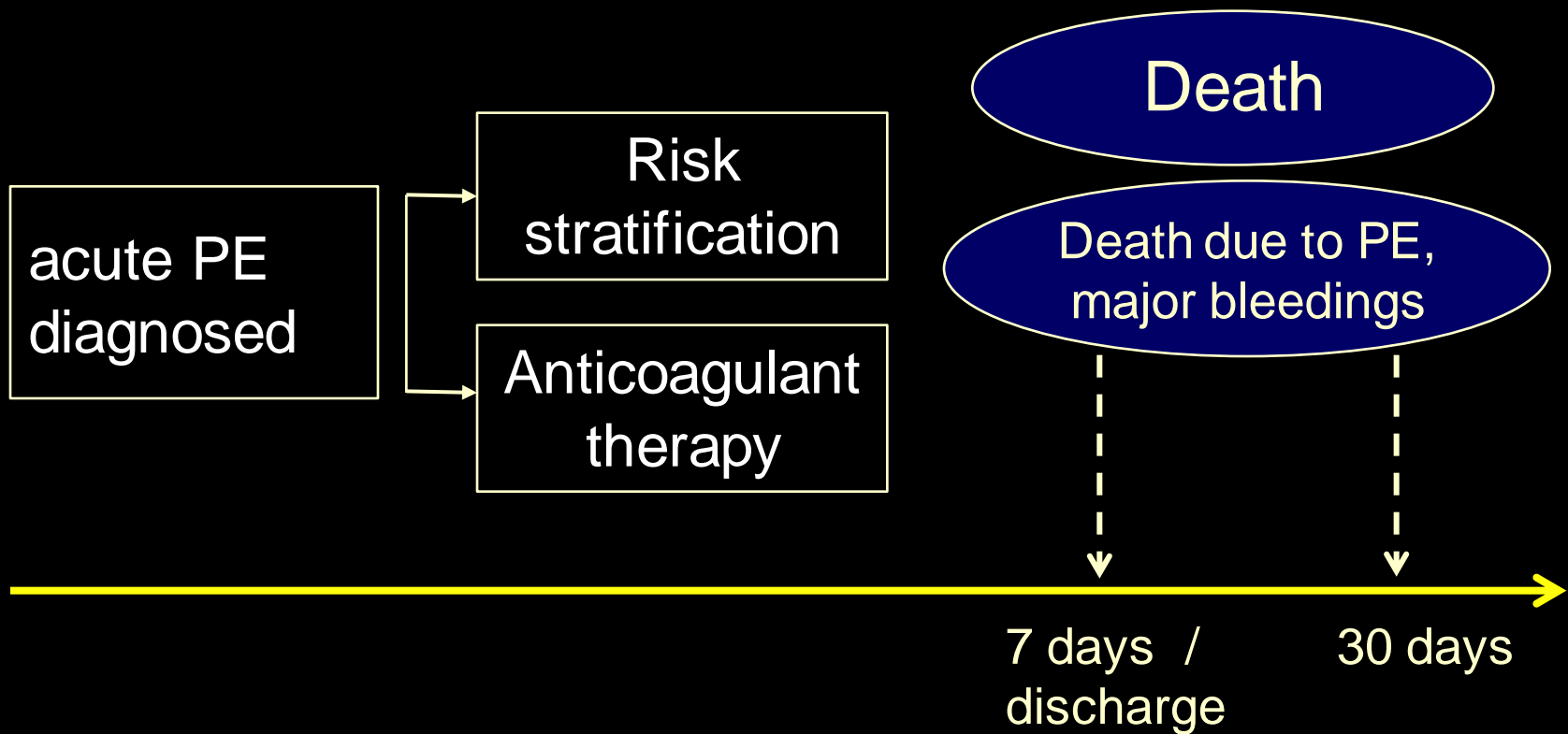
On behalf of



Study design

This is a prospective, non-interventional, multicenter study in patients with acute pulmonary embolism admitted to Cardiology, Emergency and Internal Medicine Departments in Italy

CONTEMPORARY CLINICAL MANAGEMENT OF ACUTE PULMONARY EMBOLISM



Acute pulmonary embolism: Acute management

- Diagnosis
- Risk stratification
- Treatment

Treatment for PE

Goals of acute treatment

Reduce mortality
Reduce early recurrences

Goals of long-term treatment

Complete treatment of acute PE
Reduce recurrences

Goals of extended treatment

Reduce recurrences in high risk pts



Initial treatment

Long-term treatment

Extended treatment

≥ 5 days

at least 3 months

indefinite

Treatment for PE

Acute treatment

UFH
LMWH/Fonda
Thrombolysis
Interventional
Surgery

Rivaroxaban
Apixaban

Initial treatment

≥ 5 days

Long-term treatment

VKAs
LMWH

DOACs

Long-term treatment

at least 3 months

Extended treatment

VKAs

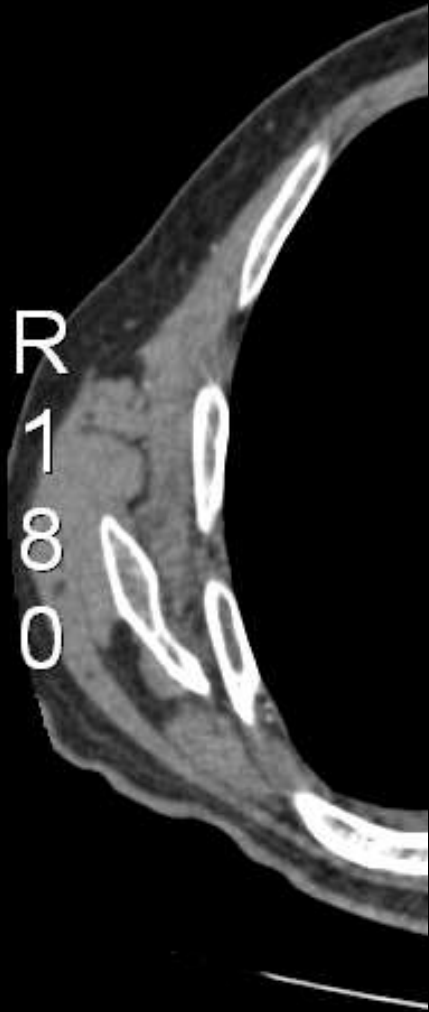
DOACs, ASA, sulodexide

Extended treatment

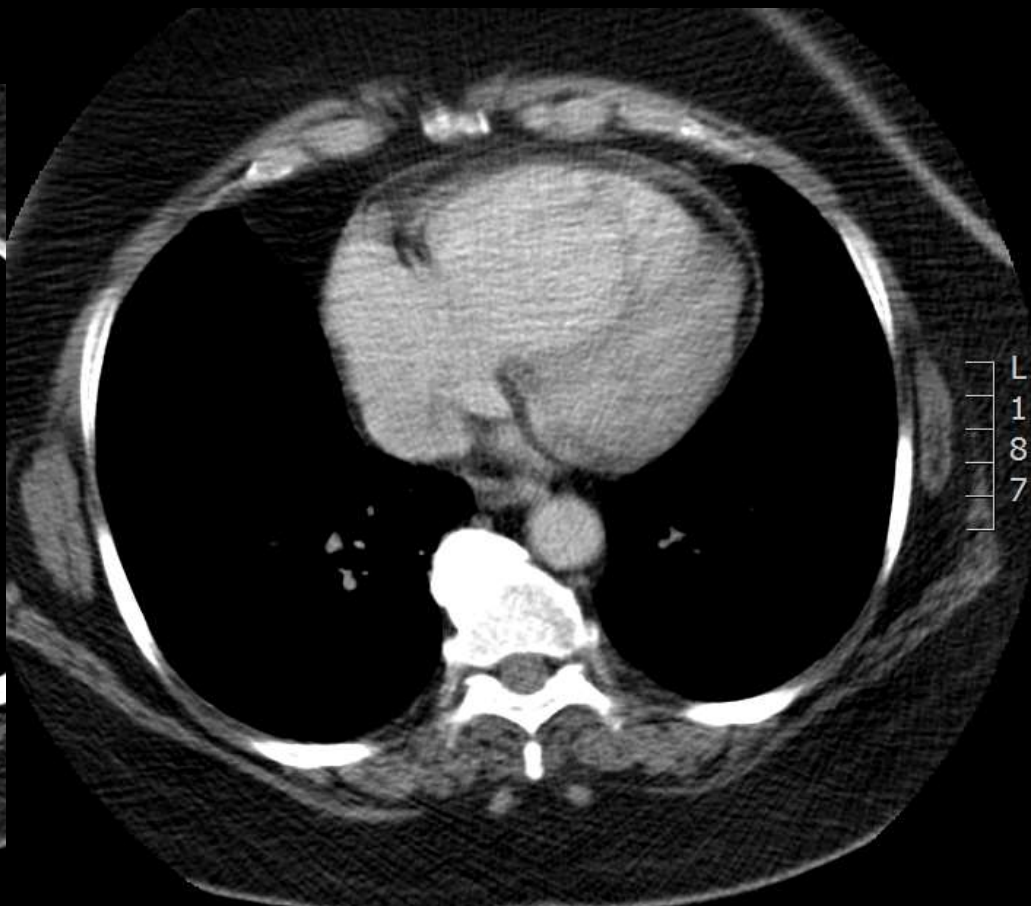
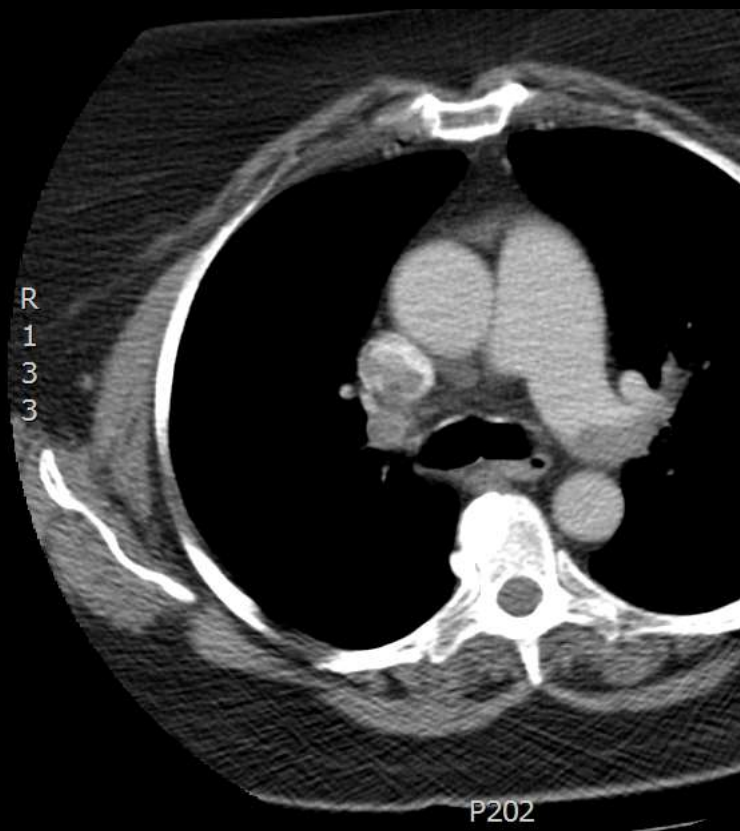
indefinite



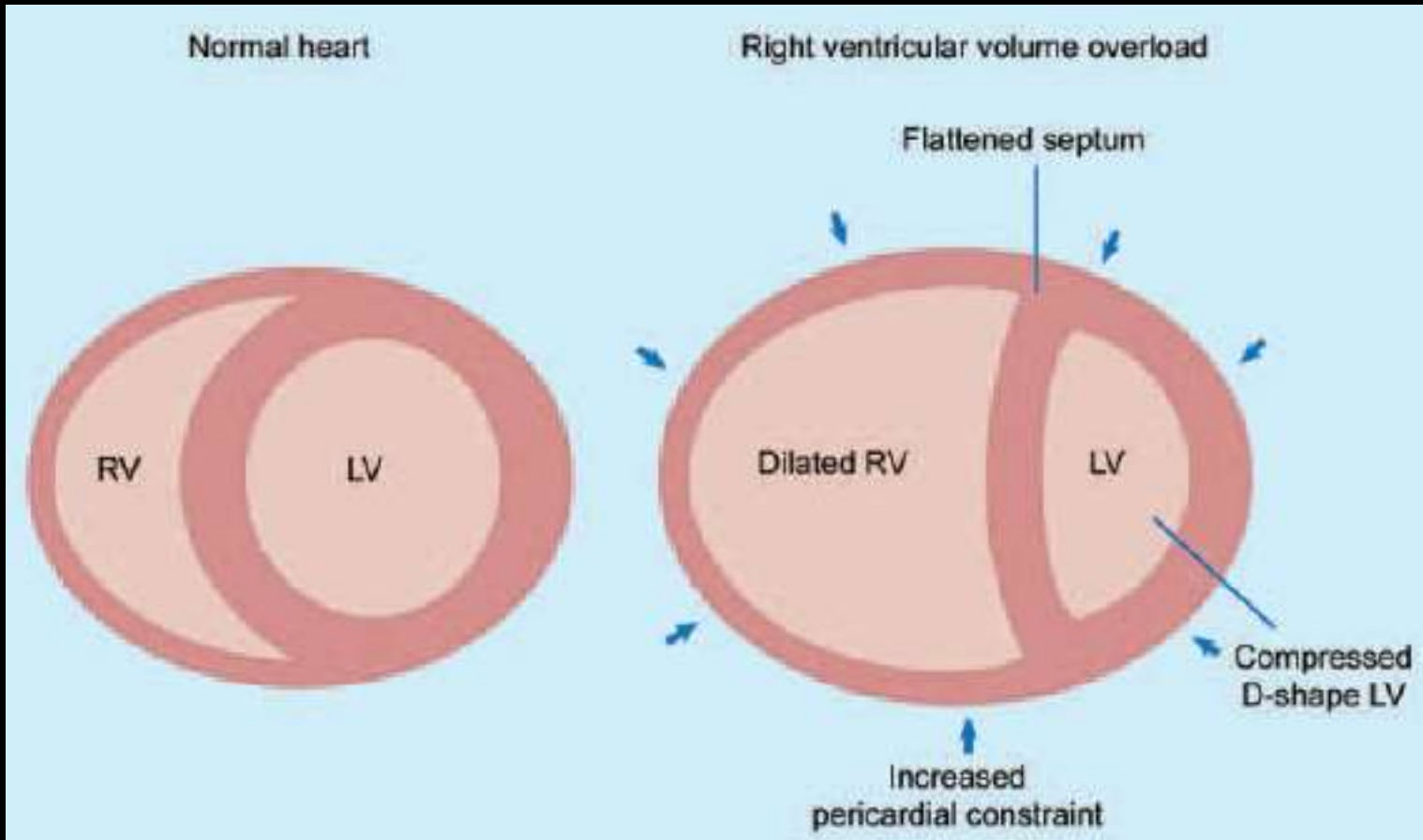
PE: abrupt closure of pulmonary arteries



PE: acute right heart overload



PE: acute right heart overload



Acute PE: intrapulmonary vs systemic rt-PA

35 patients with acute PE undergoing thrombolysis

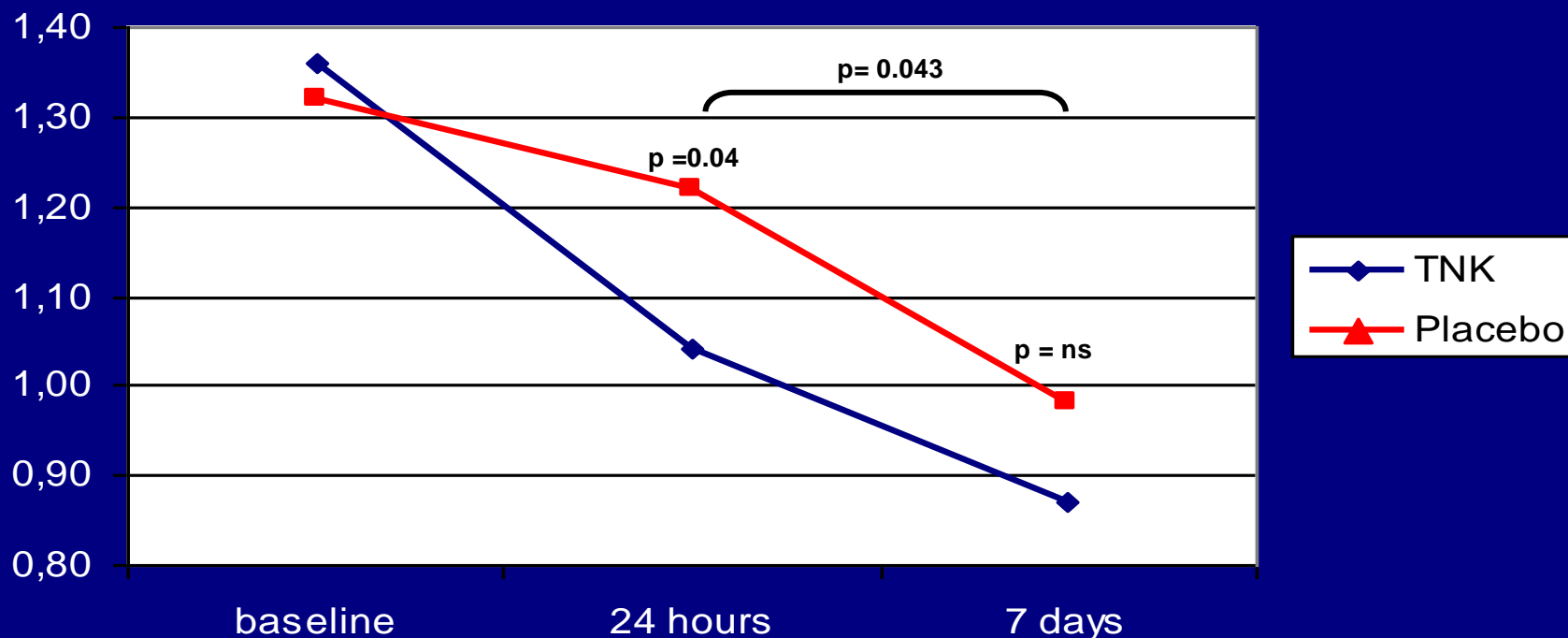
	pre- rt-PA	2-hours
<u>Intrapulmonary</u>		
Mean PA systolic pressure	31±7	18±7
Mean modified Miller index	25±4	16±6
<u>systemic</u>		
Mean PA systolic pressure	31±12	12±5
Mean modified Miller index	26±2	16±6



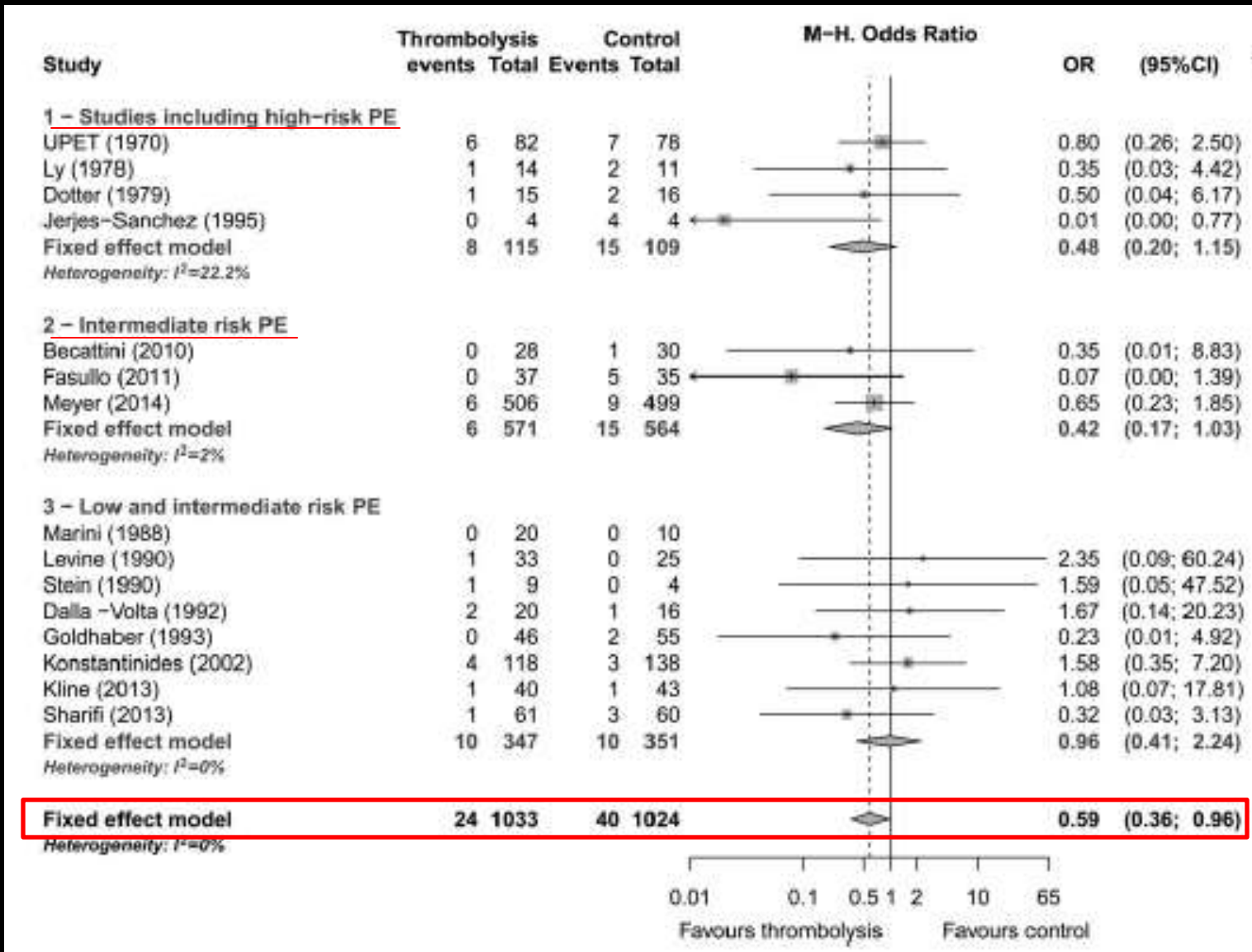
TNK vs placebo in acute PE patients

Patients with acute PE Randomized to TNK or placebo

Time course of R/L end-diastolic dimension ratio at echocardiography



Acute PE: thrombolysis and mortality



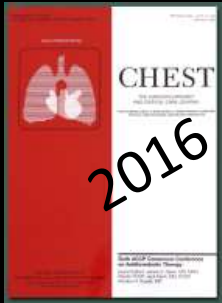
Thrombolysis for PE: the counterbalance

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

Tenecteplase for intermediate-high risk PE



	Tenecteplase (n=506)		Placebo (n=499)		<i>P</i> value
	n	(%)	n	(%)	
All-cause mortality within 7 days	6	(1.2)	9	(1.8)	0.43
Hemodynamic collapse within 7 days	8	(1.6)	25	(5.0)	0.002
Major	32	(6.3)	6	(1.5)	<0.001
Hemorrhagic stroke	10		1		



The Guidelines: clinical management

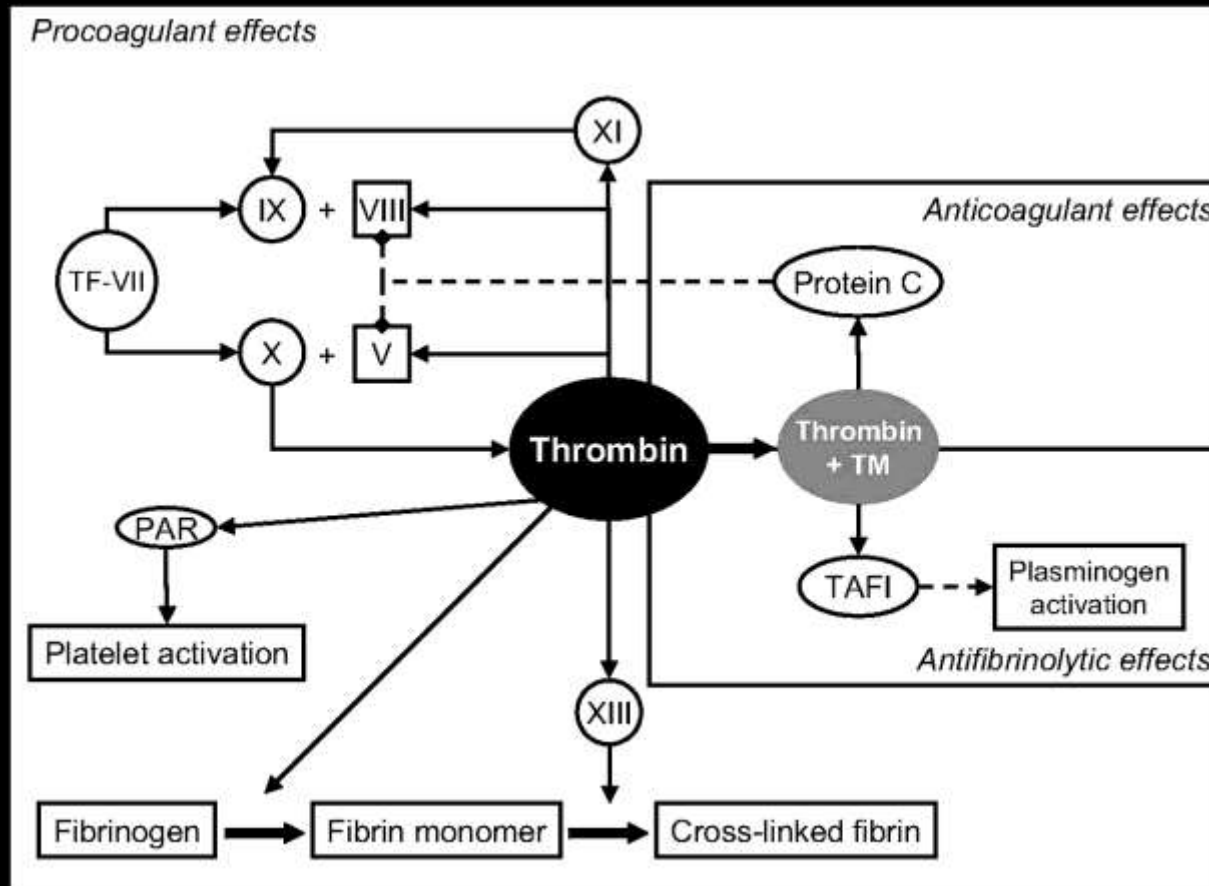


- ✓ Thrombolysis IS NOT RECOMMENDED in hemodynamically stable patients with acute PE
- ✓ Close monitor for early assessment of hemodynamic deterioration
- ✓ Use thrombolysis in case of deterioration
- ✓ Limit percutaneous procedures to high-risk patients at high risk for bleeding

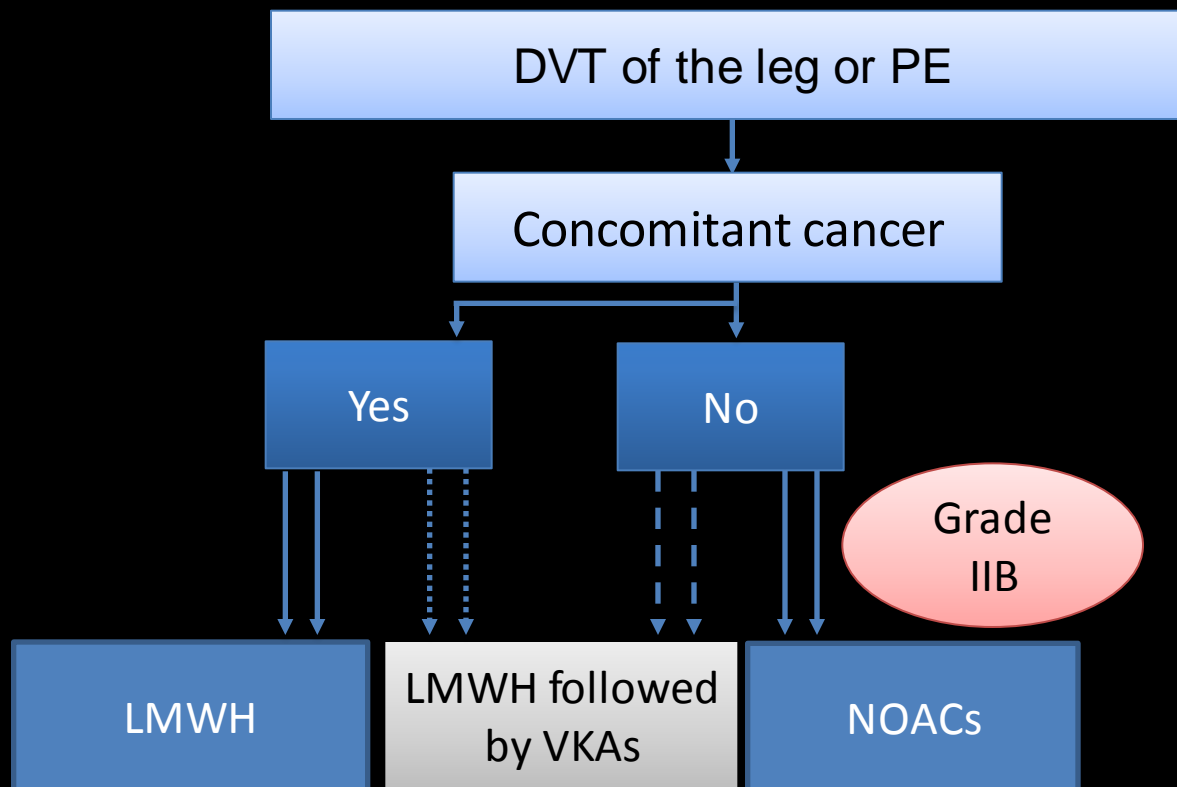
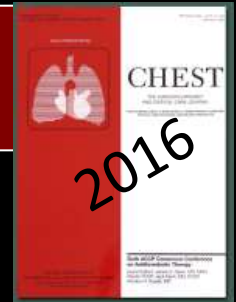
Low-dose thrombolysis

	Odds ratio (95% CI) for dying			
Odds ratio (95% CI) for bleeding	<i>Full-dose thrombolysis</i>	1.28 (0.40 to 4.12)	1.93 (0.07 to 51.33)	0.60 (0.36 to 1.01)
	2.22 (0.71 to 6.89)	<i>Low-dose thrombolysis</i>	1.50 (0.05 to 47.94)	0.47 (0.14 to 1.59)
	2.07 (0.03 to 126.08)	0.93 (0.01 to 65.65)	<i>Catheter-directed thrombolysis</i>	0.31 (0.01 to 7.96)
	2.00 (1.06 to 3.78)	0.90 (0.25 to 3.21)	0.97 (0.02 to 56.03)	<i>Placebo</i>

TAFI Inhibitor



The CHEST guidelines



***Same grade of recommendation for different NOACs**

Efficacy & safety of DOACs in VTE

Meta-analysis of RCT studies with DOACs in
initial and long-term VTE treatment

6 studies 27023 patients

	OR	95% CI
Recurrent VTE	0.89	(0.75-1.05)
Major bleeding	0.63	(0.51-0.77)
CRNMB	0.74	(0.59-0.93)

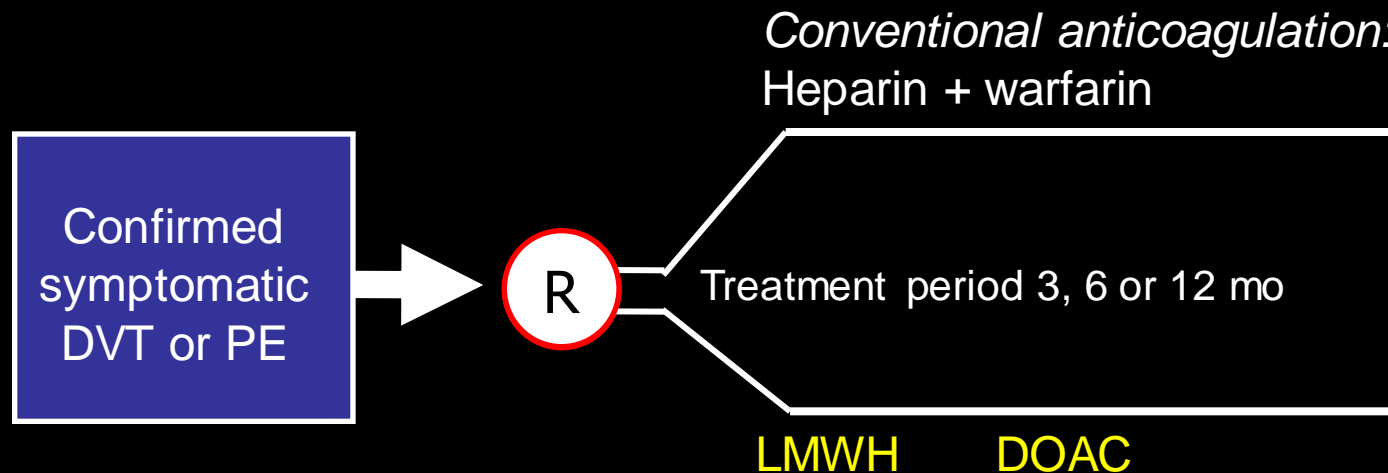
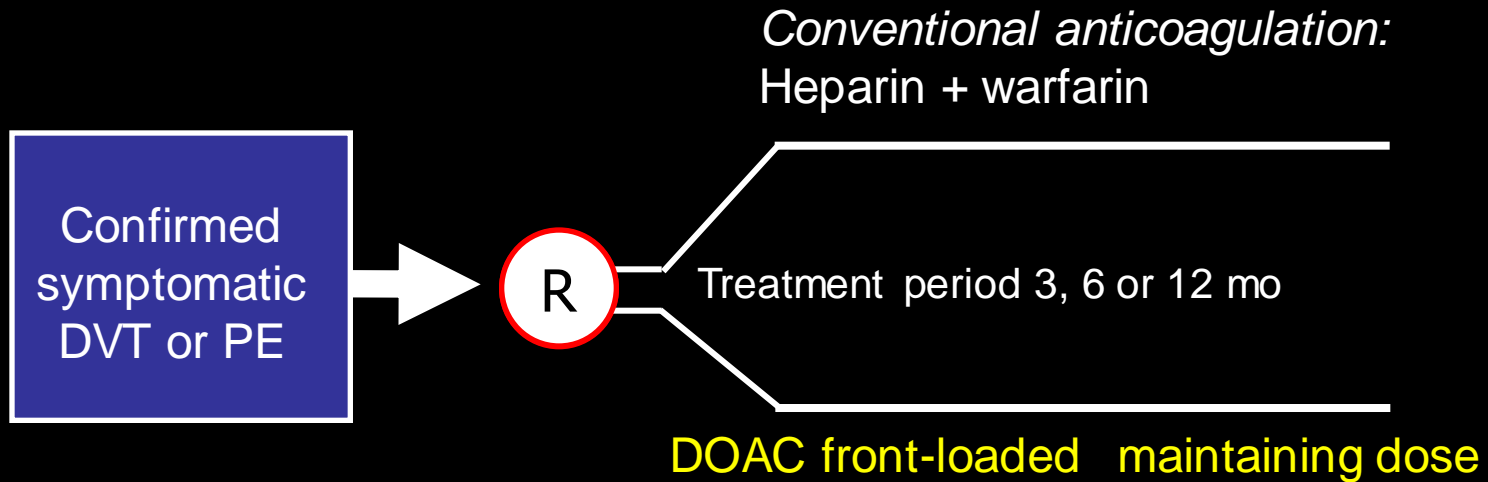
DOACs in pulmonary embolism

5 phase III studies included: 11,539 patients

	OR	95% CI
Recurrent VTE	0.89	(0.70-1.12)
anti-Xa	0.89	(0.69-1.15)
anti-IIa	0.87	(0.46-1.64)
Major Bleeding*	0.30	(0.10-0.95)
Clinically Relevant Bleeding*	0.89	(0.77-1.03)

* two studies included

DOACs for VTE: study design

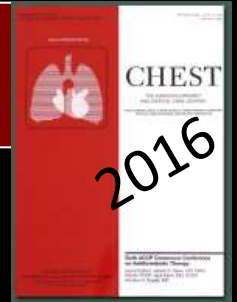


PE: anatomical extent of PE as defined in DOACs trials

- Limited extent
 - $\leq 25\%$ of the vasculature of a single lobe
- Intermediate extent
 - $>25\%$ of vasculature of a single lobe or multiple lobes with $\leq 25\%$ of entire vasculature
- Extensive extent
 - multiple lobes with $\geq 25\%$ of entire vasculature



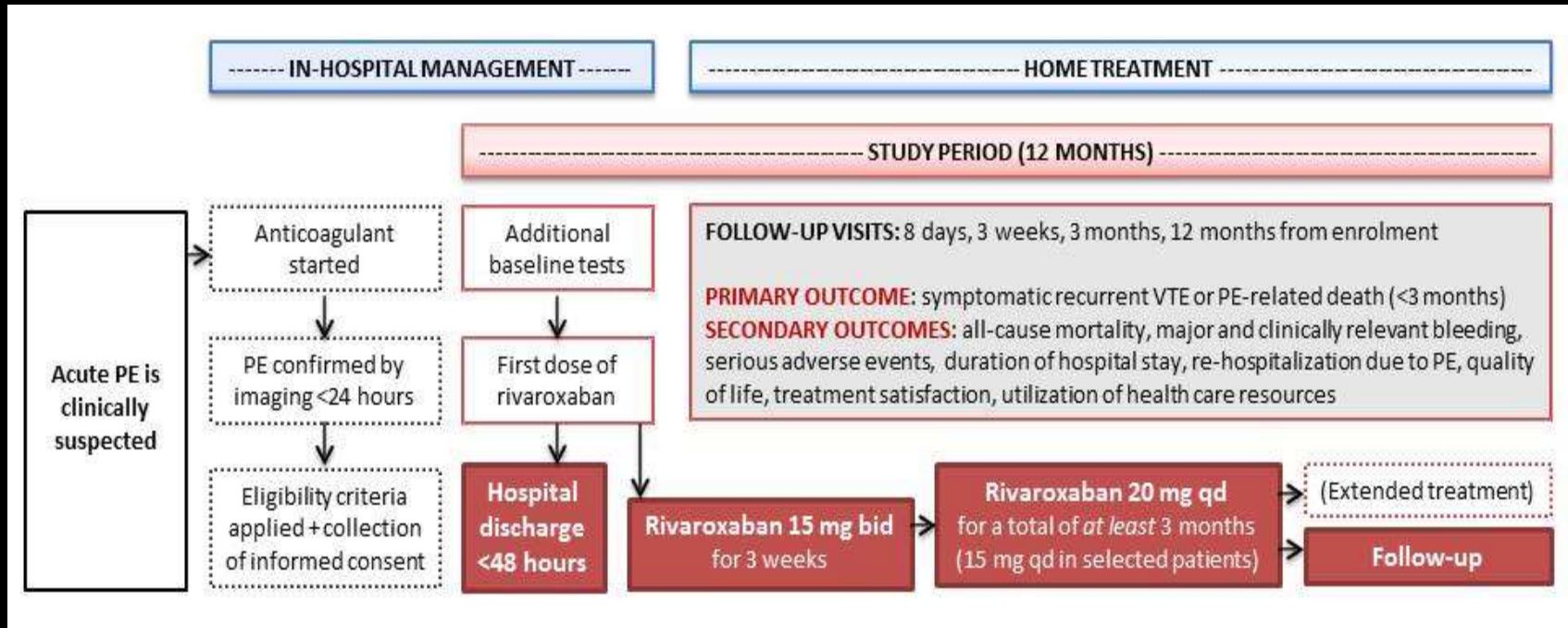
The guidelines



5.5. In patients with low-risk PE and whose home circumstances are adequate, we suggest early discharge over standard discharge (eg, after first 5 days of treatment) (Grade 2B).

Remarks: Patients who prefer the security of the hospital to the convenience and comfort of home are likely to choose hospitalization over home treatment.

Home treatment: the Hot-PE trial



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