Practical treatment approach for patients with PE

Cecilia Becattini

University of Perugia

The spectrum of clinical presentation of PE

PE-related shock — Mild clinical symptoms

The spectrum of clinical outcome of PE

>30% — Mortality — 1%

Practical treatment approach for patients with PE

- Which treatment?
- Which management?

Treatment for VTE

Goals of acute treatment

Reduce mortality
Reduce early recurrences

Goals of long-term treatment

Complete treatment of acute VTE
Reduce recurrences

Goals of extended treatment

Reduce recurrences in high risk pts

Treatment for VTE

Acute treatment

UFH
LMWH/Fonda
Thrombolysis
Interventional
Surgery

Long-term treatment

VKAs (INR 2.0-3.0)
LMWH

Extended treatment

VKAs (INR 2.0-3.0 or 1.5-2.5)

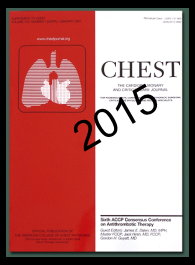
Initial treatment

Long-term treatment

Extended treatment

≥ 5 days **at least 3 months** **indefinite**

Treatment for VTE



Acute treatment

UFH
LMWH/Fonda
Thrombolysis
Interventional
Surgery

Rivaroxaban
Apixaban

Long-term treatment

VKAs (INR 2.0-3.0)
LMWH

Rivaroxaban
Apixaban
Dabigatran

Extended treatment

VKAs (INR 2.0-3.0 or 1.5-2.5)

Rivaroxaban
Apixaban
Dabigatran

Initial treatment

Long-term treatment

Extended treatment

≥ 5 days **at least 3 months** **indefinite**

Initial Treatment for HD stable PE

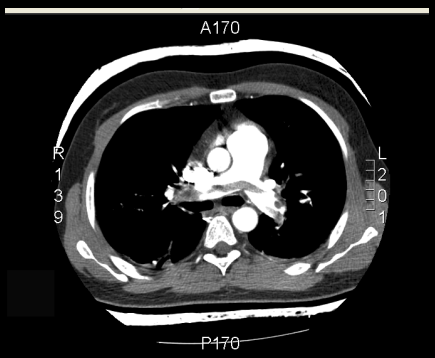
Acute treatment

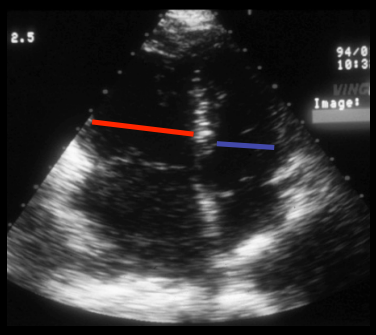
UFH
LMWH/Fonda
Thrombolysis
Interventional
Surgery

Rivaroxaban
Apixaban

Initial treatment

≥ 5 days





Initial Treatment for HD stable PE

Acute treatment

UFH
LMWH/Fonda
Thrombolysis
Interventional
Surgery

Rivaroxaban
Apixaban

Initial treatment

≥ 5 days

→ Thrombolysis
Interventional/Surgery
Active bleeding
Recent trauma/surgery
Dialysis

Initial Treatment for HD stable PE

Acute treatment

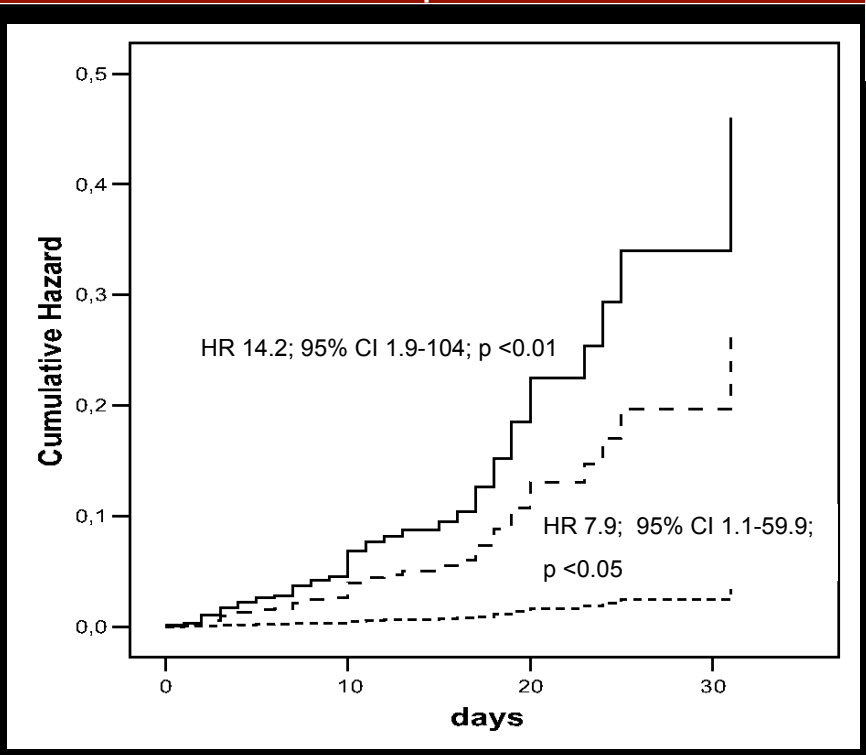
UFH
LMWH/Fonda
Thrombolysis →
Interventional
Surgery

Rivaroxaban
Apixaban

Initial treatment

≥ 5 days

Acute PE: RV dysfunction and injury & in-hospital outcome



Becattini et al, Chest 2013

PEITHO: efficacy outcome (within 7 days)

	Tenecteplase (n=506)		Placebo (n=499)		*P* 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**
Need for CPR	1		5		
Hypotension / blood pressure drop	8		18		
Catecholamines	3		14		
Resulted in death	1		6		

Meyer G, N Eng J Med2014

PEITHO: safety outcomes (within 7 days)

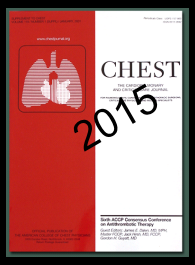
	Tenecteplase (n=506)		Placebo (n=499)		*P* value
	n	(%)	n	(%)	
Non-intracranial bleeding					
Major	32	(6.3)	6	(1.5)	<0.001
Minor	165	(32.6)	43	(8.6)	<0.001
Strokes by day 7					
Hemorrhagic	10		1		

Meyer G, N Eng J Med2014

ESC Guidelines: clinical management

PE without shock or hypotension (intermediate or low risk)[c]		
Reperfusion treatment		
Routine use of primary systemic thrombolysis is not recommended in patients without shock or hypotension.	III	B
Close monitoring is recommended in patients with intermediate-high-risk PE to permit early detection of haemodynamic decompensation and timely initiation of rescue reperfusion therapy.	I	B
Thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of haemodynamic decompensation.	IIa	B
Surgical pulmonary embolectomy may be considered in intermediate-high-risk patients, if the anticipated risk of bleeding under thrombolytic treatment is high.[f]	IIb	C
Percutaneous catheter-directed treatment may be considered in intermediate-high-risk patients, if the anticipated risk of bleeding under thrombolytic treatment is high.[f]	IIb	B

Initial Treatment for HD stable PE



Acute treatment

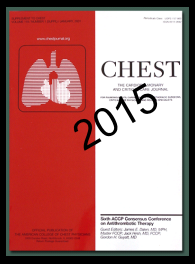
UFH
LMWH/Fonda
Thrombolysis → Deteriorating to HD unstable
Interventional
Surgery

Rivaroxaban
Apixaban

Initial treatment

≥ 5 days

Initial Treatment for HD stable PE



Acute treatment

UFH
LMWH/Fonda
Thrombolysis
Interventional
Surgery

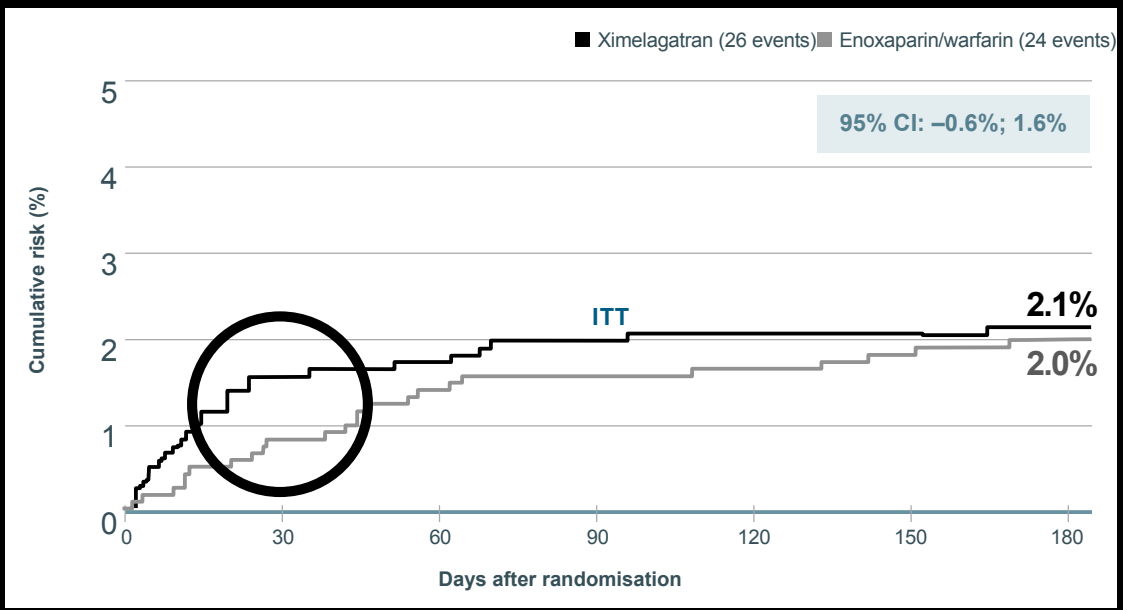
Rivaroxaban
Apixaban

Initial treatment

≥ 5 days

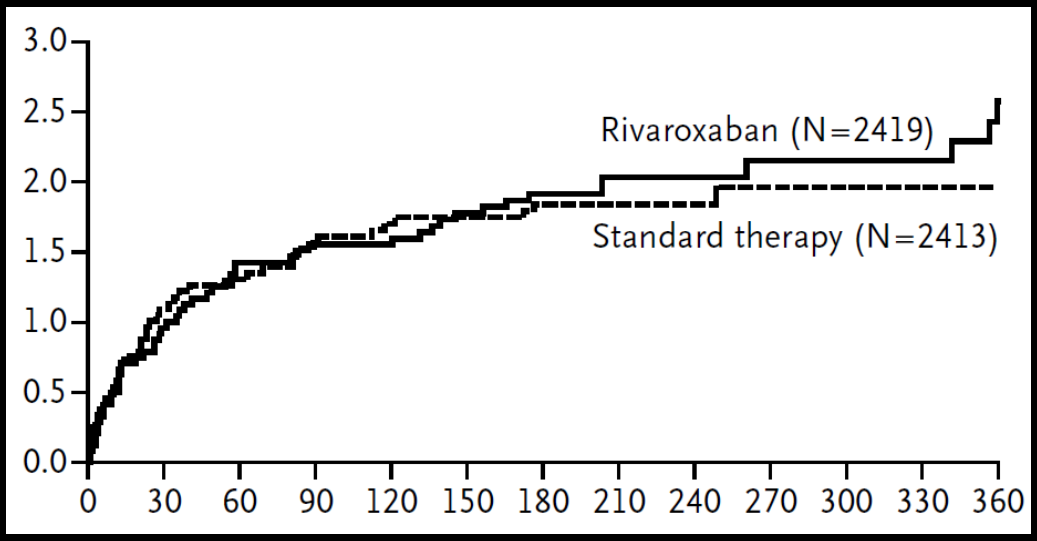
Treatment for PE & DVT

THRIVE TREATMENT



Fiessinger J-N et al. JAMA 2005;293:681–689

Rivaroxaban for PE



Einstein PE Investigators. N Eng J Med 2012

NOACs for Treatment of PE

Study	Primary endpoint	Event, % (n/N)		HR*/RR† (95%CI)
		NOAC	Warfarin	
RECOVER I & II (index PE)	VTE/VTE-related death	**2.9** (23/795)	**3.1** (25/807)	**0.93** (0.53–1.64)
EINSTEIN-PE	Recurrent VTE	**2.1%** (50/2419)	**1.8%** (44/2413)	**1.12*** (0.75–1.68)
AMPLIFY (Index PE)	Recurrent VTE / VTE-related death	**2.3%** (21/900)	**2.6%** (23/886)	**0.90†** (0.50–1.61)
HOKUSAI (Index PE)	Recurrent VTE	**2.8%** (47/1650)	**3.9%** (65/1669)	**0.73*** (0.50–1.06)
HOKUSAI (Severe PE) (ProBNP ≥500 pg/mL)	Recurrent VTE	**3.3%** (15/454)	**6.2%** (30/485)	**0.52*** (0.28–0.98)

NOAC for PE: meta-analysis

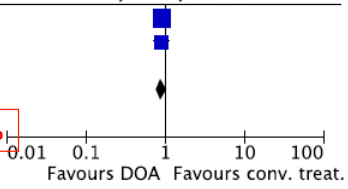
Clinically Relevant Bleeding

Study or Subgroup	DOA Events	DOA Total	conv. treat. Events	conv. treat. Total	Weight	Odds Ratio M-H, Fixed, 95% CI
EINSTEIN-PE 2012	249	2412	274	2405	59.5%	0.90 [0.75, 1.07]
HOKUSAI 2013	166	1650	187	1669	40.5%	0.89 [0.71, 1.11]
Total (95% CI)		**4062**		**4074**	**100.0%**	**0.89 [0.77, 1.03]**
Total events	415		461			

Heterogeneity: $Chi^2 = 0.00$, df = 1 (P = 0.95); $I^2 = 0\%$

Test for overall effect: Z = 1.60 (P = 0.11)

10.2% vs 11.3%



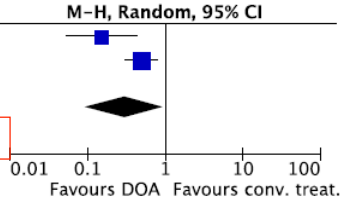
Major Bleeding

Study or Subgroup	DOA Events	DOA Total	conv. treat. Events	conv. treat. Total	Weight	Odds Ratio M-H, Random, 95% CI
AMPLIFY 2013	4	928	25	902	41.7%	0.15 [0.05, 0.44]
EINSTEIN-PE 2012	26	2412	52	2405	58.3%	0.49 [0.31, 0.79]
Total (95% CI)		**3340**		**3307**	**100.0%**	**0.30 [0.10, 0.95]**
Total events	30		77			

Heterogeneity: $Tau^2 = 0.53$; $Chi^2 = 4.03$, df = 1 (P = 0.04); $I^2 = 75\%$

Test for overall effect: Z = 2.04 (P = 0.04)

0.9% vs 2.3%



Vedovati et al. Int J Cardiol 2014

PE: ESC model for risk stratification

2014 EUROPEAN SOCIETY OF CARDIOLOGY®

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]	

Eur Heart J 2014

Edoxaban for PE: efficacy

	Edoxaban (N=4118)	Warfarin (N=4122)	Hazard ratio (95% CI)
First recurrent VTE - no. (%)			
Subgroup severe PE (RV dysfunction ProBNP) **n/N (%)**	**15/454 (3.3)**	**30/485 (6.2)**	0.52 (0.28 to 0.98)

Hokusai Investigators. N Eng J Med 2013

Initial Treatment for HD stable PE

Acute treatment

UFH
LMWH/Fonda
Thrombolysis
Interventional
Surgery

Rivaroxaban
Apixaban

→ Cancer patients
Stage IIIb renal failure

Initial treatment

≥ 5 days

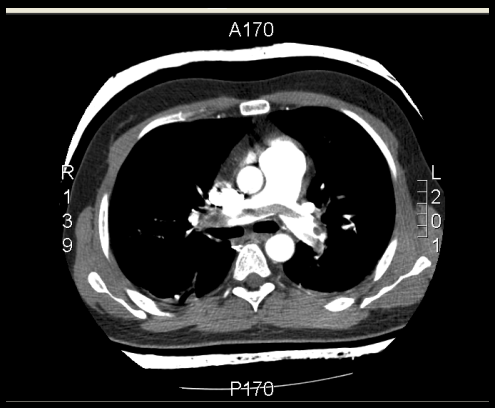
Practical treatment approach for patients with PE

- Which treatment?
- Which management?

Practical treatment approach for acute PE

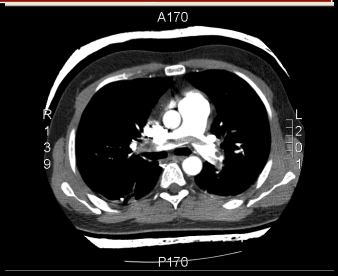
Hospital admission?

- ICU?
- Internal Medicine?
- Cardiology?



Practical treatment approach for acute PE

Hospital admission?



Treatment for pulmonary embolism

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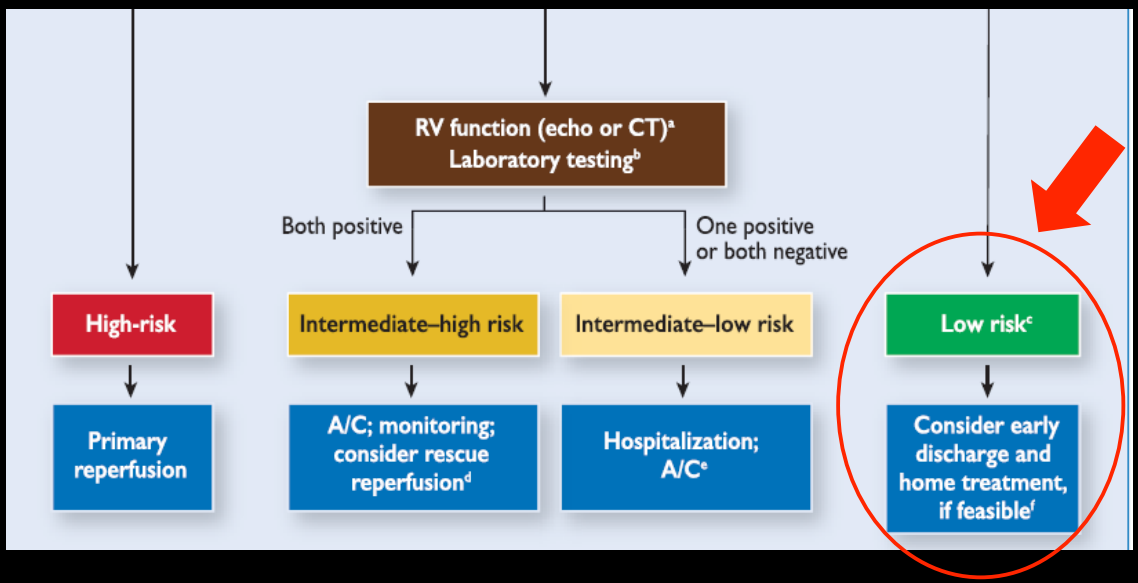
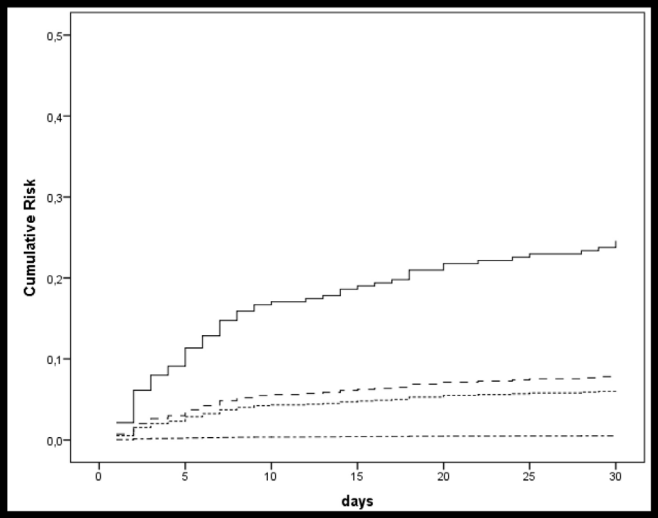


Eur Heart J 2014

2014 ESC model… in clinical practice

906 patients with acute symptomatic objectively confirmed PE



30-day Mortality based on risk

High ———

Intermediate high - - - - - - - -

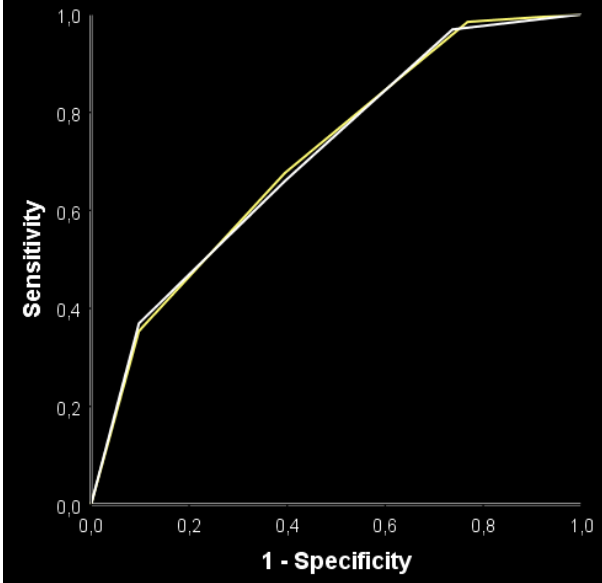
Intermediate low ----------

Low —·—·—·—

Becattini et al, *submitted*

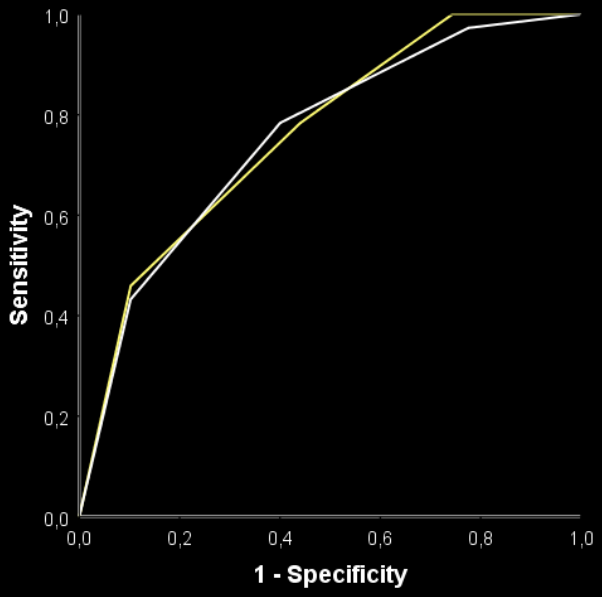
2014 vs. 2008-ESC model: accuracy

Death at 30 day



2014 ESC model ———

Death due to PE



2008 ESC model ———

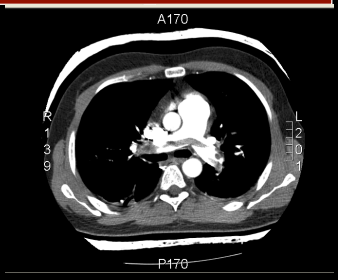
Acute pulmonary embolism: the PESI score

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

Arch Intern Med 2006

Hospital admission for acute PE

The HESTIA Criteria



- ✓ Is the patient HD unstable?
- ✓ Is thrombolysis/embolectomy necessary?
- ✓ Active bleeding or high risk for?
- ✓ Oxygen supply necessary >24h?
- ✓ PE diagnosed during anticoagulation?
- ✓ Severe pain requiring i.v. therapy?
- ✓ Medical or social reason?
- ✓ Creatinine clearance <30ml/min
- ✓ Severe liver impairment
- ✓ Pregnancy
- ✓ History of HIT

Practical treatment approach for patients with PE

- ✓ Thrombolysis to be used in deteriorating stable patients
- ✓ NOACs and conventional therapy for the large majority of PE patients
- ✓ Obtaining information on RVD is easy (diagnostic CT); this should encourage to claim for RVD assessment in every patient, particularly in candidates to home treatment/ short hospital stay.