Pulmonary Emboli: Diagnosis Based on Suspicion and Management in 2017

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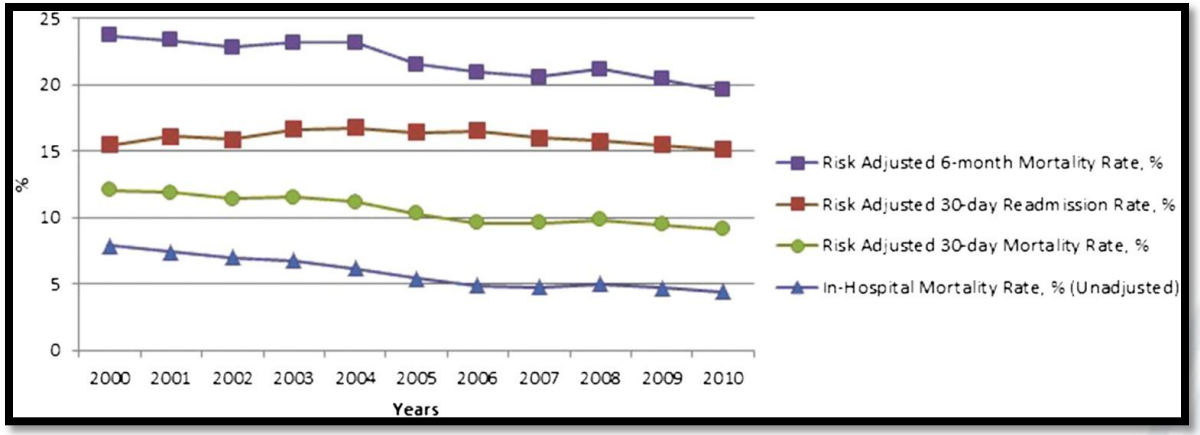
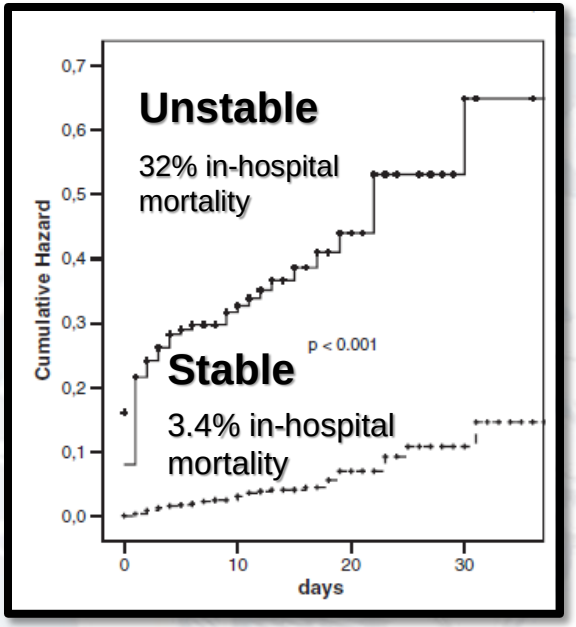
Objectives

- Review the critical pathways for pulmonary embolism (PE) diagnosis and risk stratification
- Highlight evidence-based strategies for effective management of acute PE
- Explore emerging concepts in the advanced care of PE patients

PE Epidemiology: High Mortality and Risk of Readmission





Minges KE, et al. Am J Cardiol 2015; 116:1436

Casazza F, et al. Thromb Res 2012;130:847

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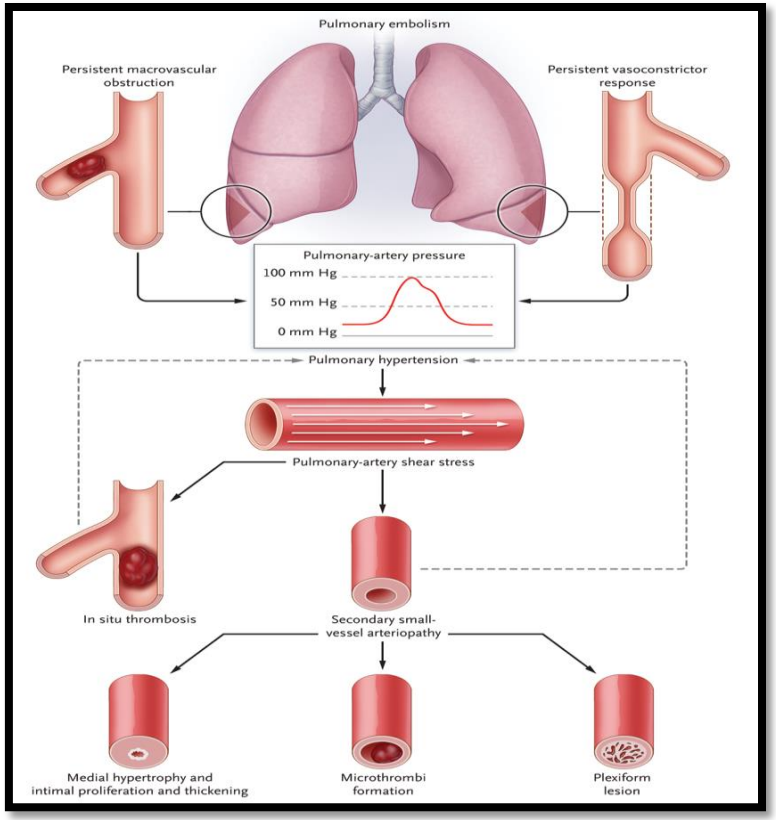
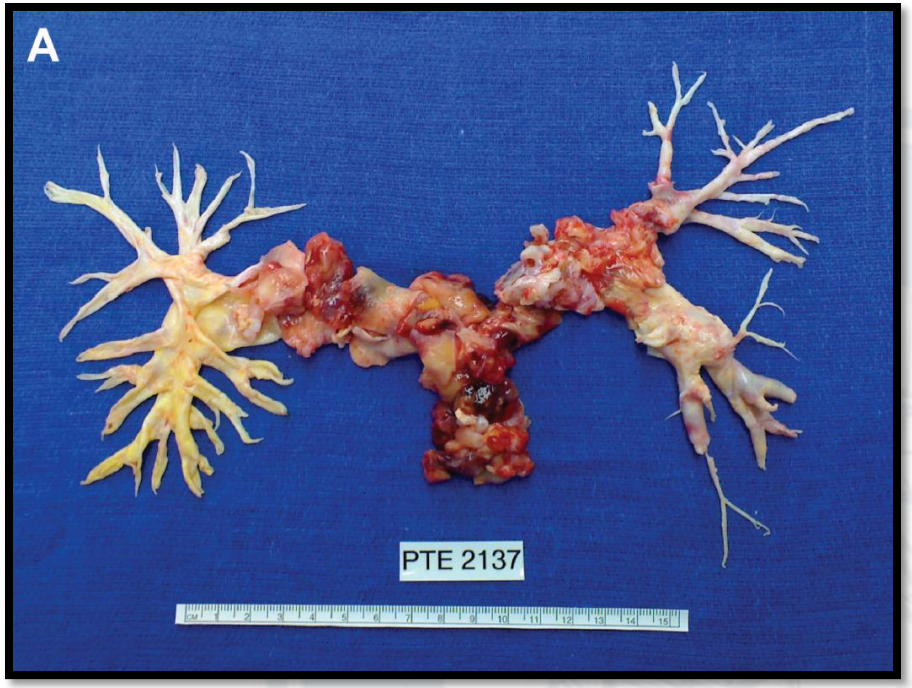
Major Risk Factors for PE

Inherited	• Thrombophilias • Family history
Lifestyle	• Smoking • Stress • Diet/obesity
Acquired	• Age • Malignancy • Recent surgery, trauma, hospitalization, immobility • Chronic medical illness
Inflammatory	• Acute and chronic infection • Chronic inflammatory diseases

Chronic Thromboembolic Pulmonary Hypertension



Piazza G, Goldhaber SZ. N Engl J Med 2011;364:351



Jaff MR, et al. Circulation 2011;123:1788

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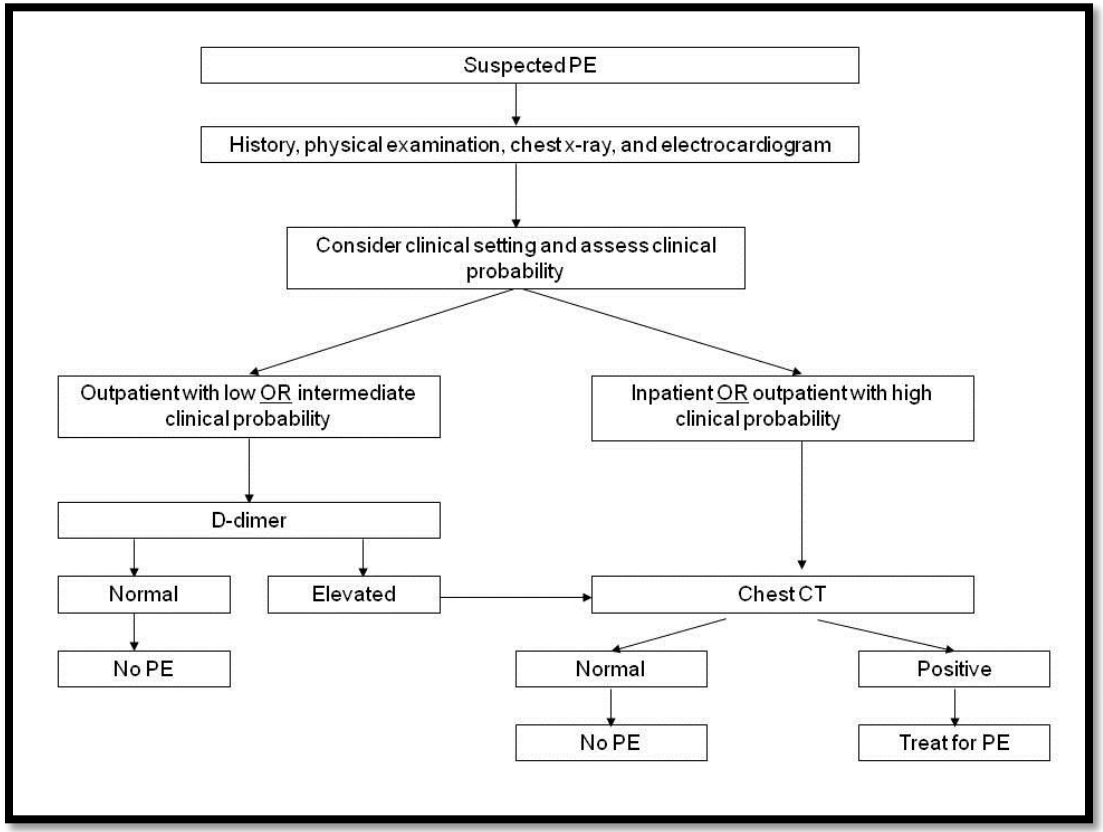
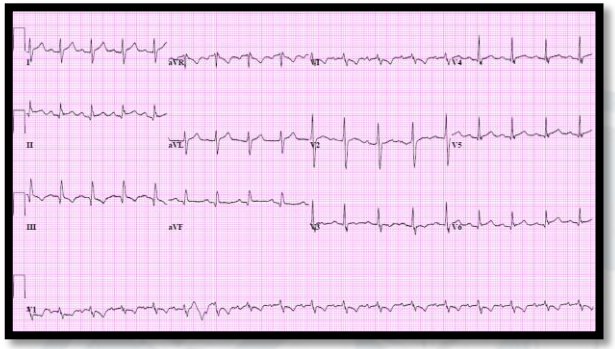
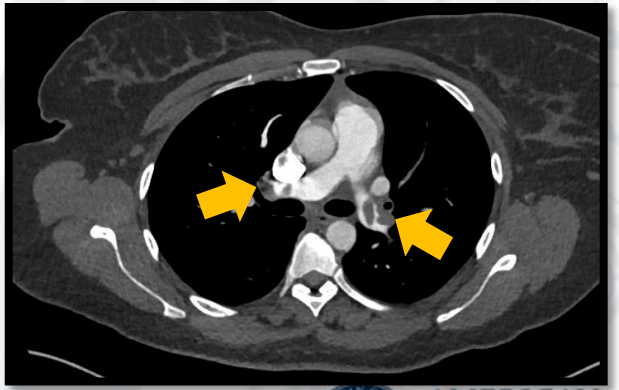
Critical Pathways for PE Diagnosis







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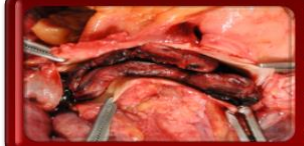
Spectrum of Disease

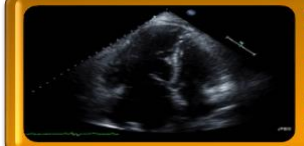


Massive PE (~5%)

- Hypotension, syncope, cardiogenic shock, cardiac arrest
- Respiratory failure
- Often fatal if aggressive care not instituted

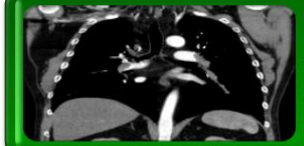
Catastrophic PE (<1%)

- "Super-massive PE"
- Refractory cardiogenic shock
- Ongoing CPR



Submassive PE (~25%)

- Normotensive
- Right ventricular (RV) dysfunction is present
- Increased risk of adverse outcomes



PE with normal BP and RV function (~70%)

- Normotensive
- Normal RV function
- Excellent prognosis with anticoagulation alone

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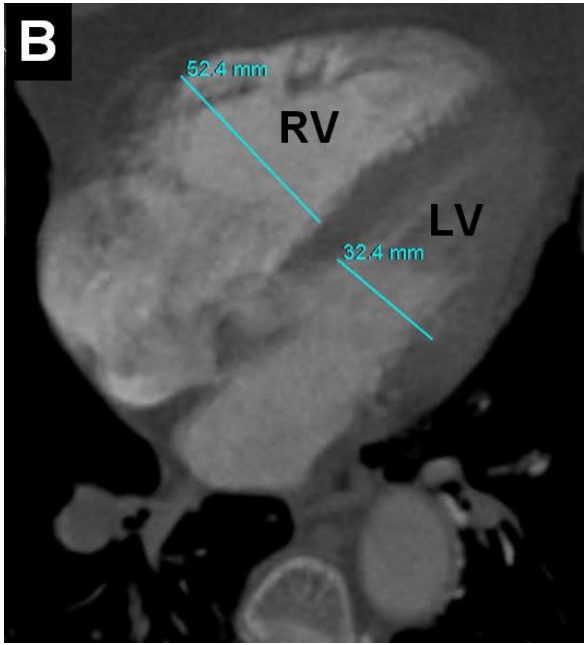
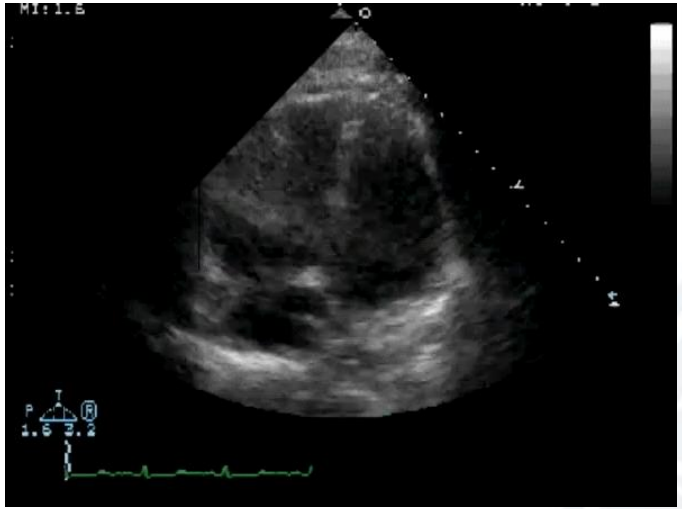
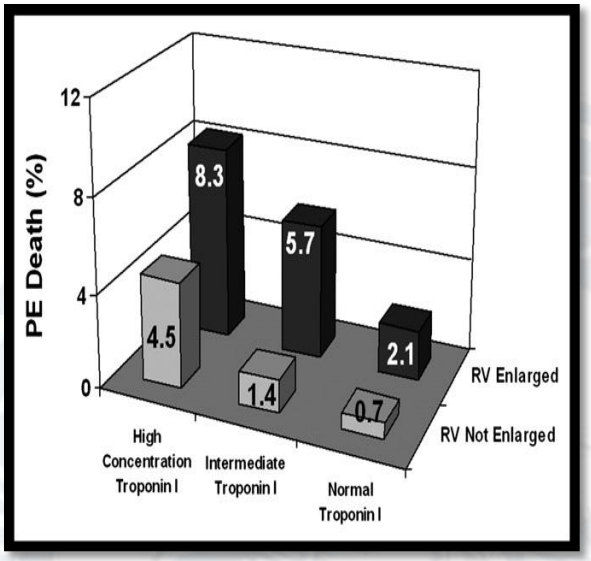
Risk Stratification Tools for PE



CT RV-to-LV Diameter Ratio



Echocardiography



Troponin

Trujillo-Santos J, et al. J Thromb Haemost 2013;11:1823
Stein PD, et al. Am J Cardiol 2010;106:558

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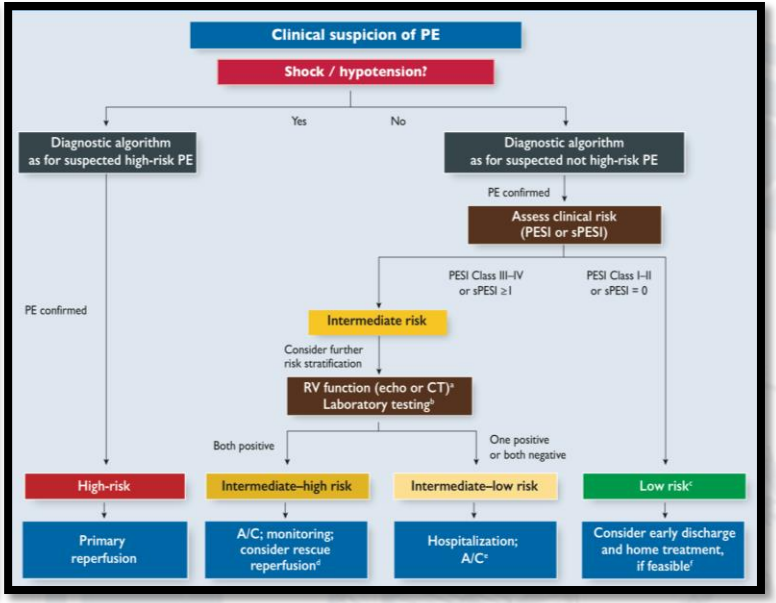
2014 ESC Guidelines: Risk Stratification of Acute PE

Table 9 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]	

PE = pulmonary embolism; PESI = Pulmonary embolism severity index; RV = right ventricular; sPESI = simplified Pulmonary embolism severity index.
[a]PESI Class III to V indicates moderate to very high 30-day mortality risk; sPESI ≥1 point(s) indicate high 30-day mortality risk.
[b]Echocardiographic criteria of RV dysfunction include RV dilation and/or an increased end-diastolic RV–LV diameter ratio (in most studies, the reported threshold value was 0.9 or 1.0); hypokinesia of the free RV wall; increased velocity of the tricuspid regurgitation jet; or combinations of the above. On computed tomographic (CT) angiography (four-chamber views of the heart), RV dysfunction is defined as an increased end-diastolic RV/LV (left ventricular) diameter ratio (with a threshold of 0.9 or 1.0).
[c]Markers of myocardial injury (e.g. elevated cardiac troponin I or -T concentrations in plasma), or of heart failure as a result of (right) ventricular dysfunction (elevated natriuretic peptide concentrations in plasma).
[d]Neither calculation of the PESI (or sPESI) nor laboratory testing are considered necessary in patients with hypotension or shock.
[e]Patients in the PESI Class I–II, or with sPESI of 0, and elevated cardiac biomarkers or signs of RV dysfunction on imaging tests, are also to be classified into the intermediate-low-risk category. This might apply to situations in which imaging or biomarker results become available before calculation of the clinical severity index.



Konstantinides SV, et al. Eur Heart J 2014;35:3033

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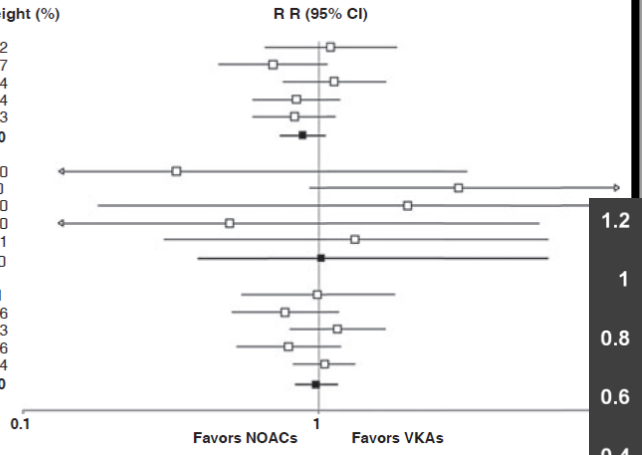
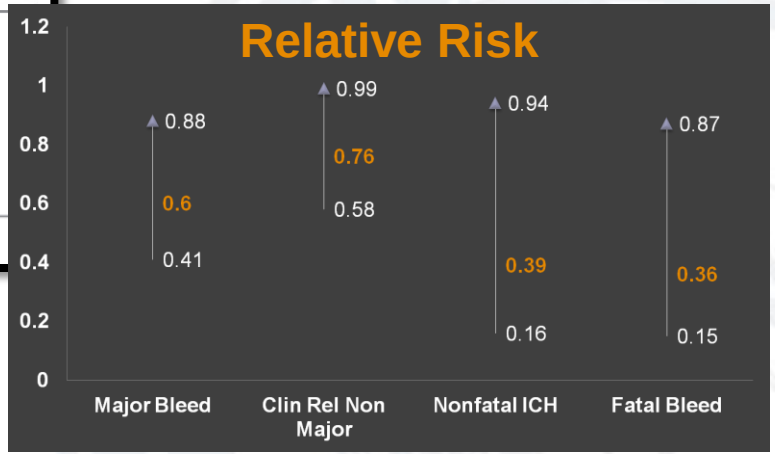
NOACs for VTE: Meta-Analysis

Outcome Study	R R	Lower limit	Upper limit	Weight (%)
Recurrent VTE				
Re-Cover (dabigatran)	1.10	0.66	1.84	11.2
Einstein-DVT (rivaroxaban)	0.70	0.46	1.07	16.7
Einstein-PE (rivaroxaban)	1.13	0.76	1.69	18.4
Amplify (apixaban)	0.84	0.60	1.18	25.4
Hokusai (edoxaban)	0.83	0.60	1.14	28.3
Subtotal (I^2 = 0%, P = 0.46)	**0.88**	**0.74**	**1.05**	**100**
Fatal PE				
Re-Cover (dabigatran)	0.33	0.03	3.18	18.0
Einstein-DVT (rivaroxaban)	2.98	0.12	73.04	9.0
Einstein-PE (rivaroxaban)	2.00	0.18	21.99	16.0
Amplify (apixaban)	0.50	0.05	5.57	16.0
Hokusai (edoxaban)	1.33	0.30	5.96	41.1
Subtotal (I^2 = 0%, P = 0.71)	1.02	0.39	5.96	100
Overall mortality				
Re-Cover (dabigatran)	0.99	0.55	1.81	7.1
Einstein-DVT (rivaroxaban)	0.77	0.51	1.17	14.6
Einstein-PE (rivaroxaban)	1.16	0.80	1.68	18.3
Amplify (apixaban)	0.79	0.53	1.19	15.6
Hokusai (edoxaban)	1.05	0.82	1.33	44.4
Subtotal (I^2 = 0%, P = 0.50)	**0.97**	**0.83**	**1.14**	**100**





van der Hulle T, et al. J Thromb Haemost. 2014;12:320

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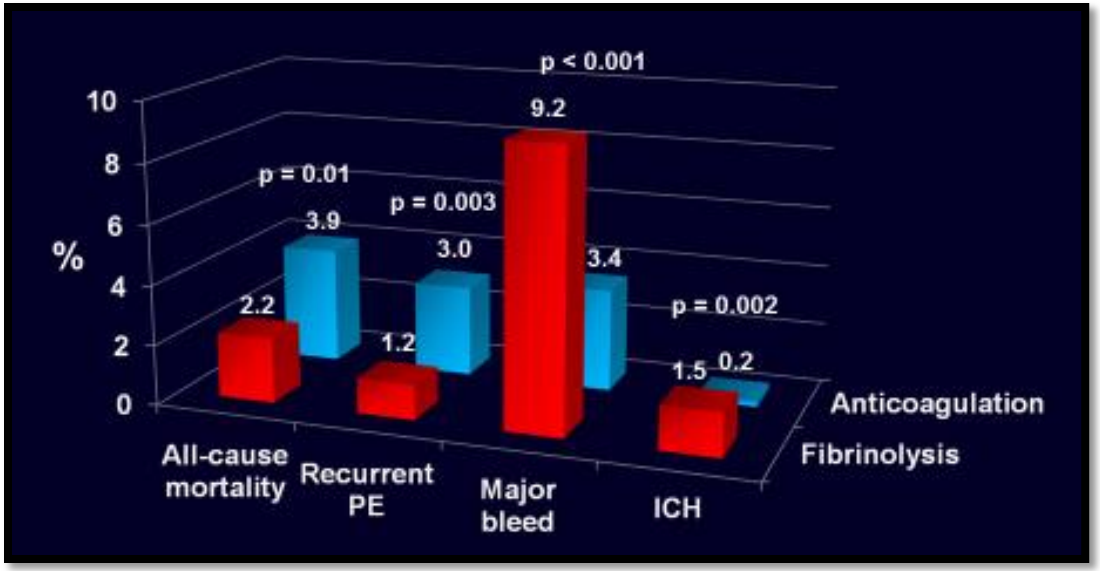
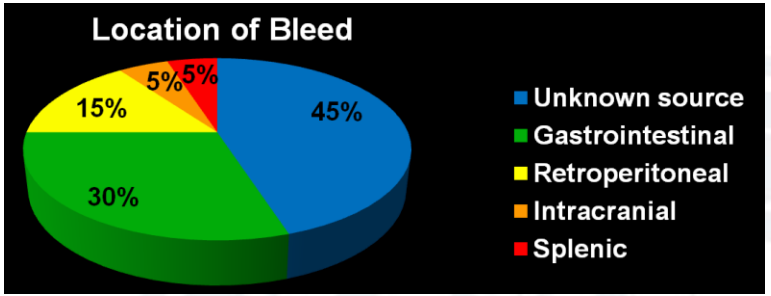
Systemic Fibrinolysis





In a series of 104 patients with acute PE treated with fibrinolysis:

- 20 patients had major bleeding
- 1 patient had a fatal bleed (intracranial hemorrhage)
- 1 patient required surgery to stop the bleeding
- 7 patients had bleeding >3 units

Chatterjee S, et al. JAMA 2014;311:2414
Fiumara K, et al. Am J Cardiol 2006;97:127

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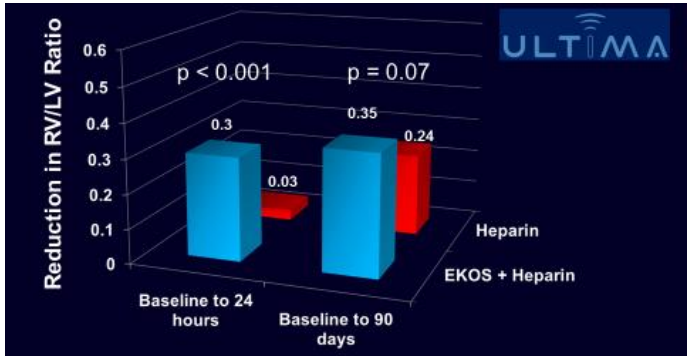
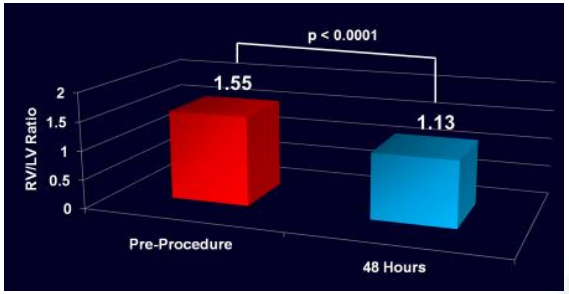
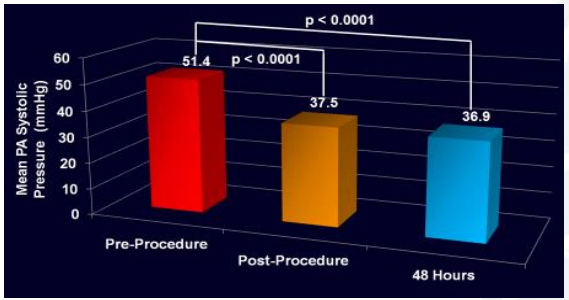
Ultrasound-Facilitated, Catheter-Directed Embolectomy



ULTIMA





SEATTLE II

Study	Intracranial Hemorrhage (Fibrinolysis)
ICOPER (Goldhaber SZ, et al. 1999)	9/304 (3.0%)
PEITHO (Meyer G, et al. 2014)	10/506 (2.0%)
ULTIMA (Kucher N, et al. 2014)	**0/30 (0%)**
SEATTLE II (Piazza G, et al. 2015)	**0/150 (0%)**

Kucher N, et al. Circulation 2014;129:479
Piazza G, et al. JACC Cardiovasc Interv. 2015;8:1382

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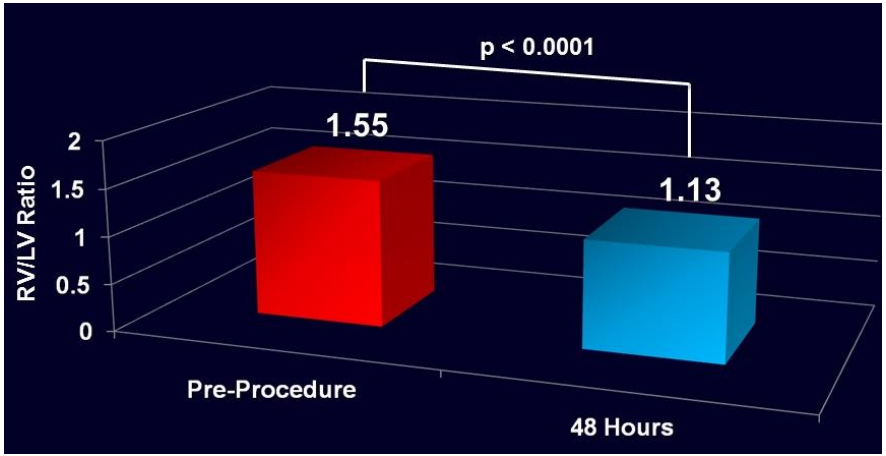
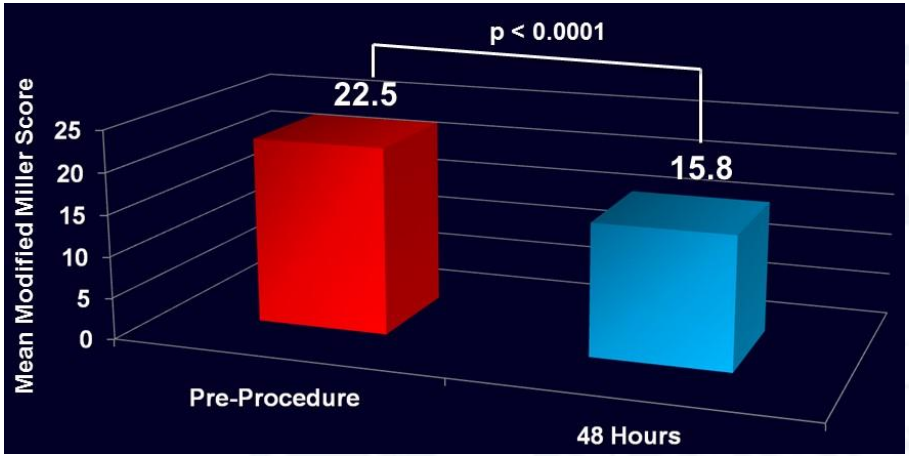
The SEATTLE II Paradox

Change in RV/LV Diameter Ratio



Change in Angiographic Obstruction



- While most patients have normalization of RV size on chest CT, the average observed reduction in angiographic obstruction (modified Miller score) is only 30%.
- This paradox suggests that symptomatic improvement and reduction in RV size may be achieved by mechanisms in addition to reduction in proximal pulmonary artery obstruction.

Piazza G, et al. JACC Cardiovasc Interv. 2015;8:1382

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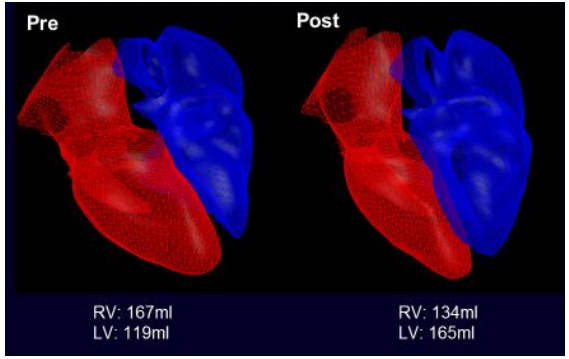
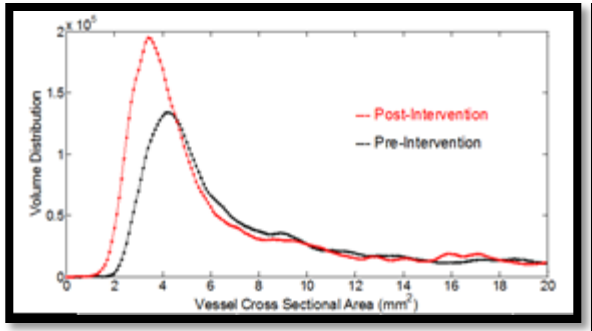
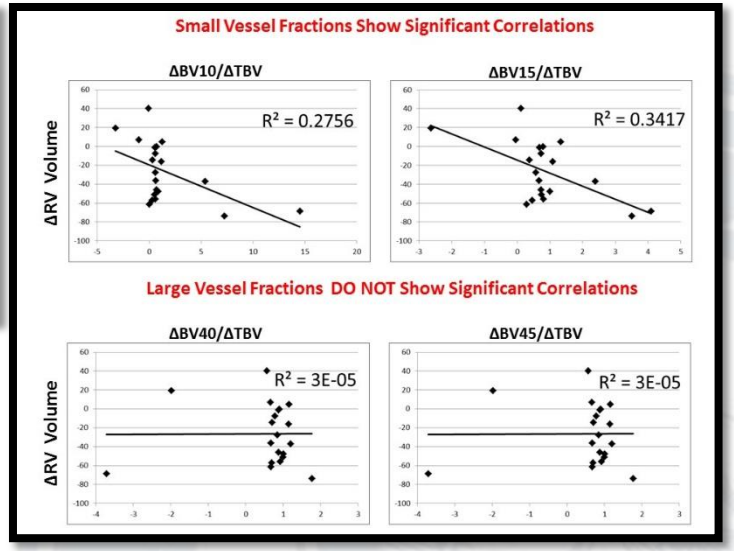
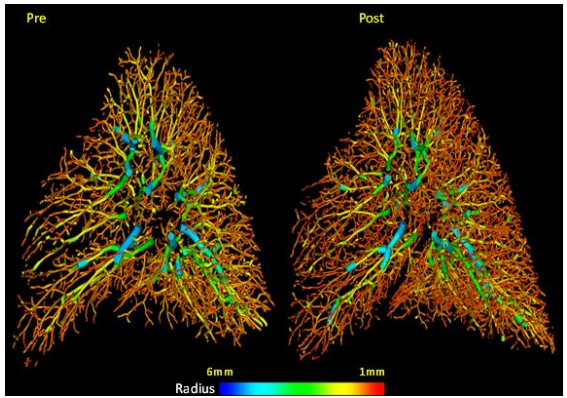
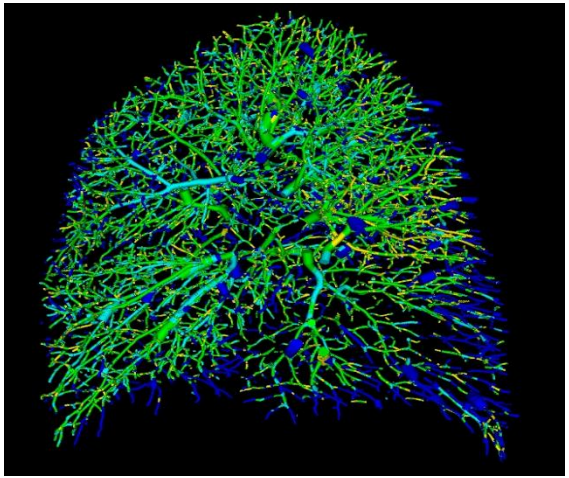
SEATTLE-3D: Small, Not Large Vessel Response Correlates with RV Recovery











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OPTALYSE PE: Optimizing US-Facilitated Catheter-Directed Fibrinolysis

Objective: Answer Questions from SEATTLE II and ULTIMA

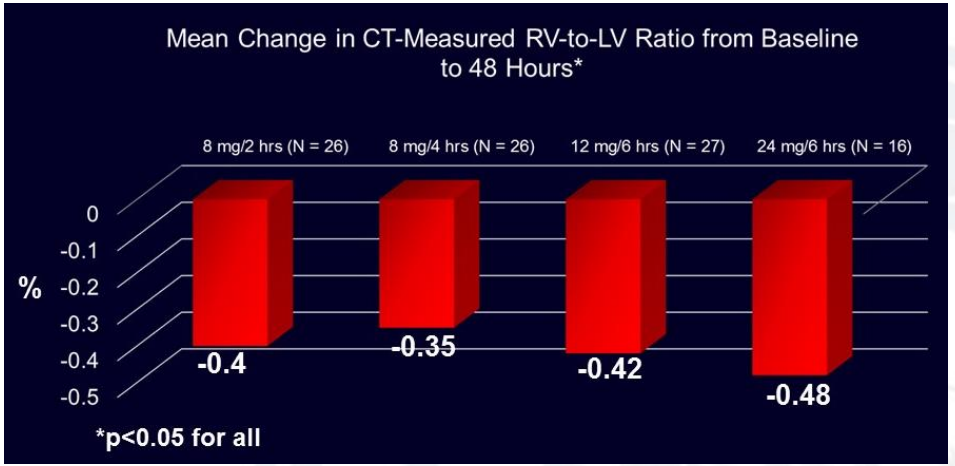
- Can we lower the fibrinolytic dose to improve safety without compromising efficacy?
- Can we improve efficiency and decrease cost by reducing infusion time?

Multi-Center, 100-Submassive PE Patient, Randomized, Controlled Trial

8 mg/2 hrs	8 mg/4 hrs	12 mg/6 hrs	24 mg/6 hrs

Study End Points

- Change in CT RV-to-LV ratio from baseline to 48 hours
- Change in Miller Index from baseline to 48 hours
- Treatment success (composite end point)
- Major bleeding at 72 hours



Overall Major Bleeding Rate = 3%
Intracranial Hemorrhage Rate = 2%

Presented at American Thoracic Society 2017

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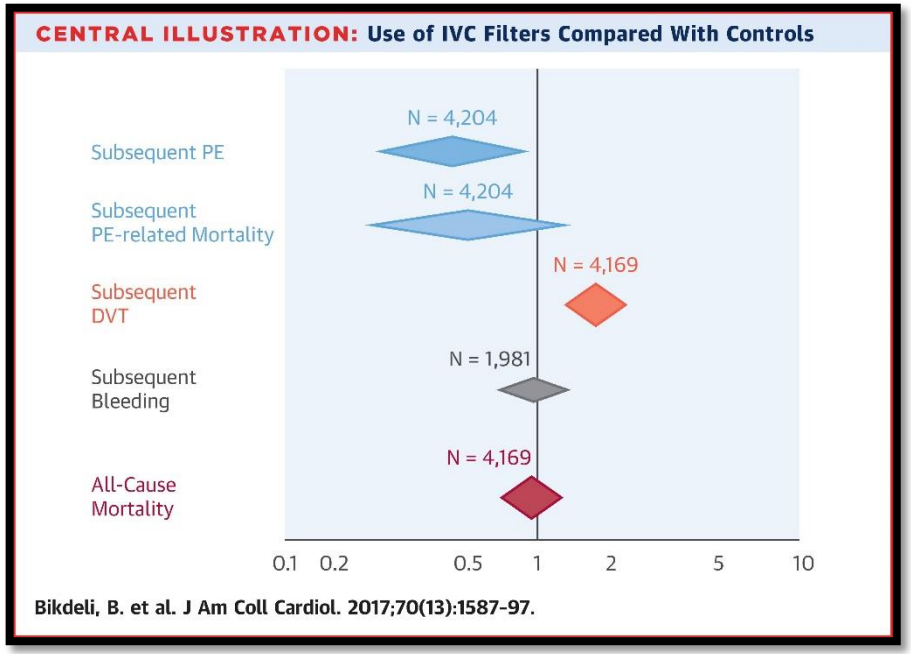
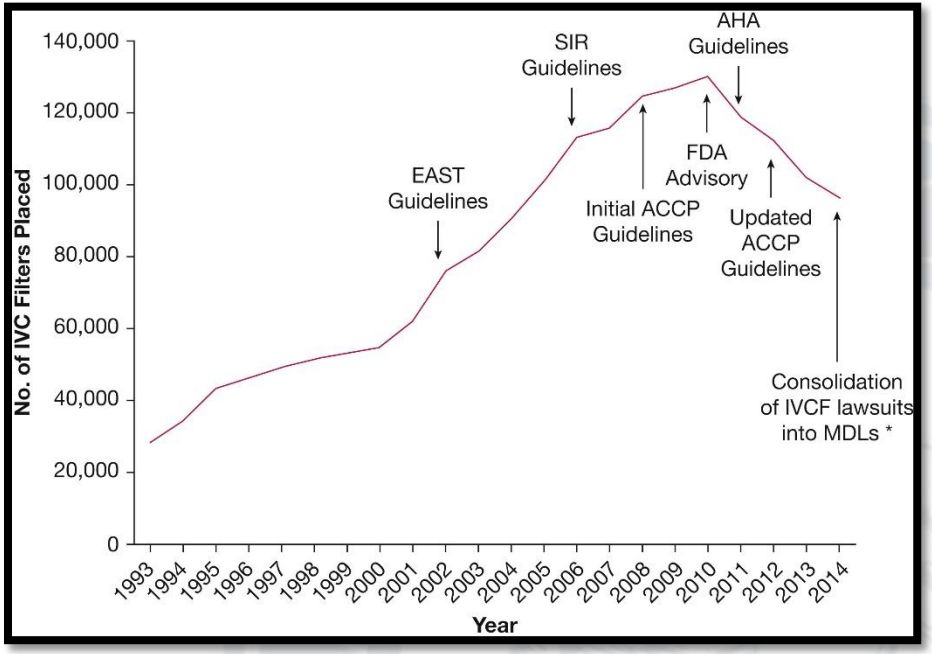
Inferior Vena Cava Filters





Bikdeli B, et al. J Am Coll Cardiol. 2017;70:1587
Ahmed O, et al. CHEST. 2017;151:1402

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PE Response Teams

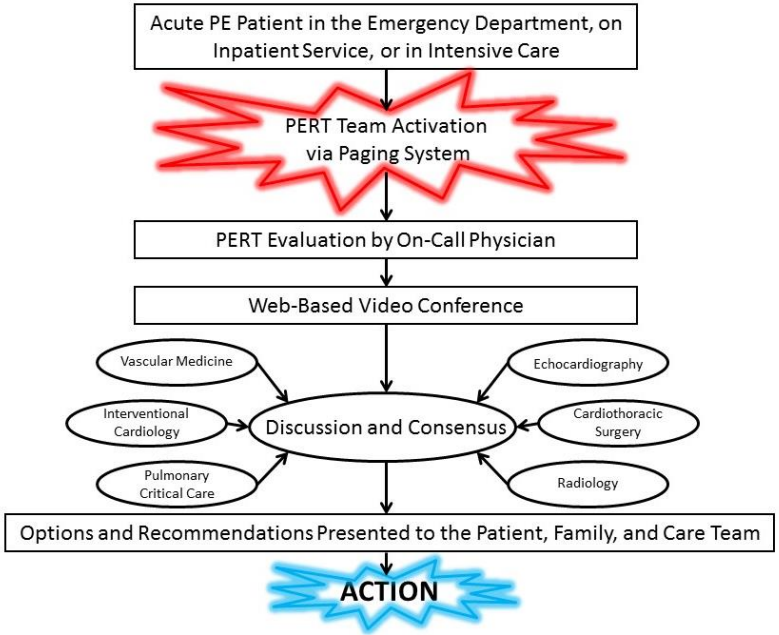

Table 1. Pulmonary embolism response team (PERT) midterm report card.

Outcome	Grade (yes, possibly, no, incomplete)	Comment
Reduced heterogeneity of PE care	Incomplete	No data available
Facilitate access to advanced therapies for those with increased risk of adverse outcomes	Possibly	Studies provide indirect evidence that PERTs increase access to advanced therapies such as systemic fibrinolysis, catheter-directed embolectomy, and mechanical circulatory support[7,8]
More appropriate use of interventional therapies for PE	Incomplete	No data available; however, the PERT model has been associated with increased utilization of interventional therapies for PE
Improved clinical outcomes	Incomplete	No data available
Reduced length of stay and costs associated with PE care	Incomplete	No data available
Overall	**Incomplete**	**Data beyond those from descriptive studies are required**

Dudzinski D and Piazza G. Circulation. 2016;133:98
Giri JS and Piazza G. Vasc Med. 2017; in press

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Summary Points

- Risk stratification is a critical component of PE diagnosis.
- Determining the optimal anticoagulation regimen should consider risk of recurrence, risk of bleeding, and patient preference.
- Selection of advanced therapies depends on assessment of the patient's risk of adverse outcomes and major bleeding.

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