

The logo for the PEITHO trial, featuring the word "PEITHO" in a stylized, blue, outlined font.An anatomical illustration of the human lungs and heart. A red, clotted mass representing a pulmonary embolism is shown blocking a branch of the pulmonary artery. The heart is shown in a cross-section, and the lungs are shown in a similar view. The overall color scheme is red and pink, highlighting the blood and the embolism.

***Medical treatment with impact
of thrombolytic therapy on
long-term outcome of patients
with intermediate risk PE:
PEITHO trial***

S. / Phototako

By***M.Wafaie aboleineen, MD, FACC***The logo for the PEITHO trial, featuring the word "PEITHO" in a stylized, blue, outlined font.

***The role of fibrinolytic
therapy in patients with
intermediate-risk
pulmonary embolism is
controversial***

Guy Meyer, M.D., et al, N Engl J Med 2014

OPÉITHO ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Rationale: risk-adjusted treatment of acute PE

PE-related early MORTALITY RISK	RISK MARKERS			Potential treatment implications
	CLINICAL (Shock or hypotension)	RV Dysfunction	Myocardial injury	
HIGH > 15%	+	(+)*	(+)*	Thrombolysis or Embolectomy
NON HIGH Inter mediate 3 - 15%	-	+	+	Thrombolysis? Hospital Admission
Low <1%	-	-	-	Early discharge or home treatment

www.escardio.org Guy Meyer, M.D., et al, N Engl J Med 2014.

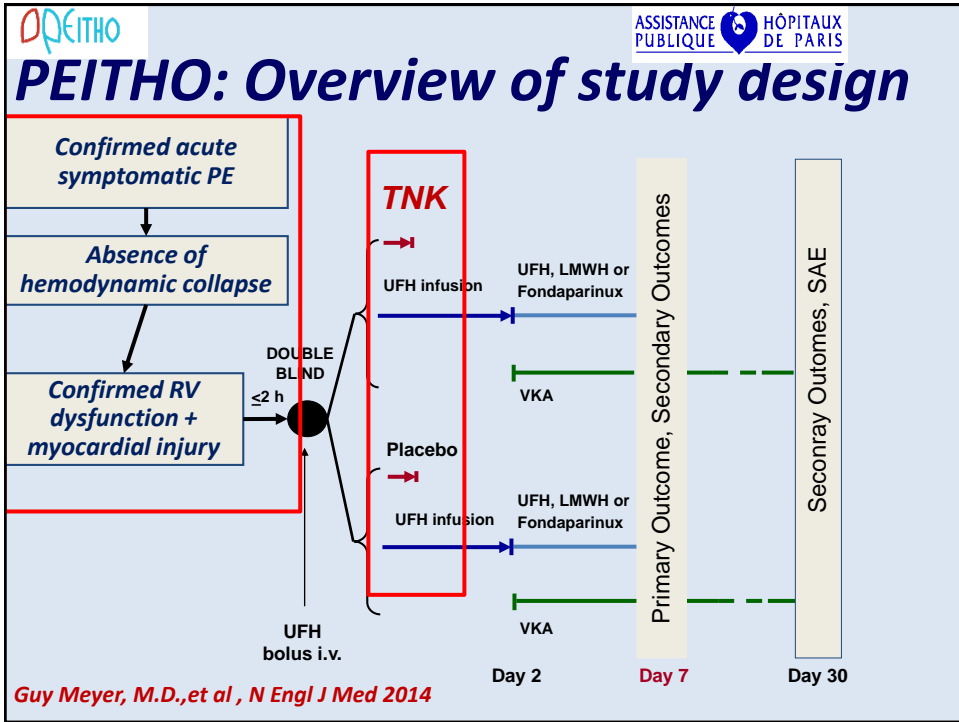
Pulmonary Embolism Thrombolysis Study

an investigator-initiated, investigator-sponsored trial

The **OPÉITHO** Investigators



Guy Meyer, M.D., et al, N Engl J Med 2014.



PEITHO: Primary efficacy outcome

	Tenecteplase (n=506)		Placebo (n=499)		P value
	n	(%)	n	(%)	
All-cause mortality or hemodynamic collapse within 7 days of randomization	13	(2.6)	28	(5.6)	0.015

Odds ratio: 0.23, 0.44, 0.88

Thrombolysis superior

Guy Meyer, M.D., et al, N Engl J Med 2014.

PEITHO: Analysis of primary efficacy outcome

	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		

Guy Meyer, M.D., et al, N Engl J Med 2014.

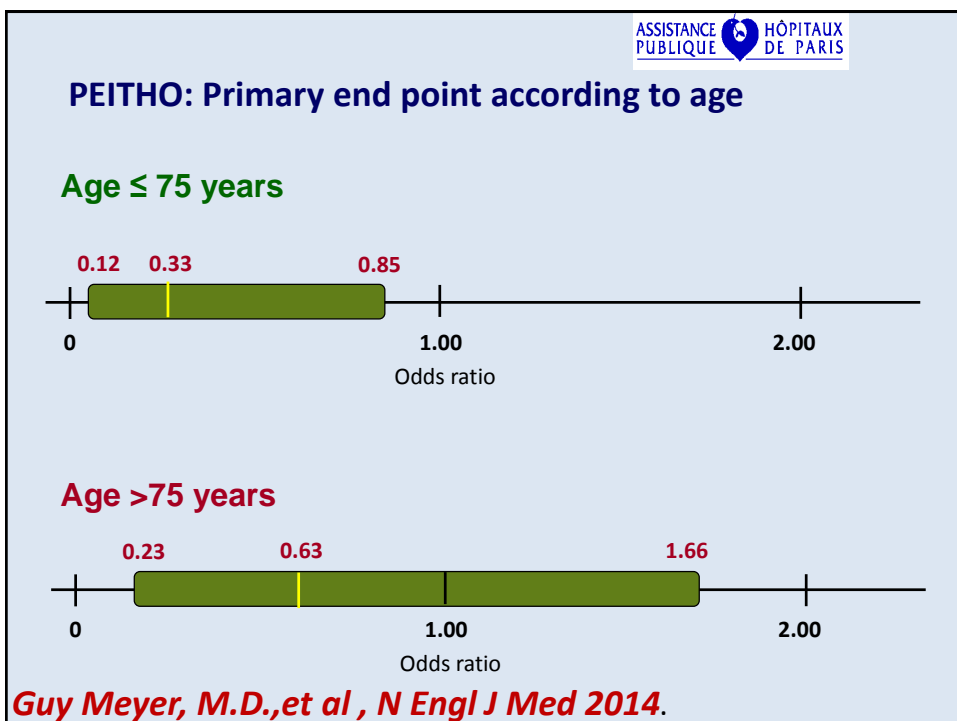
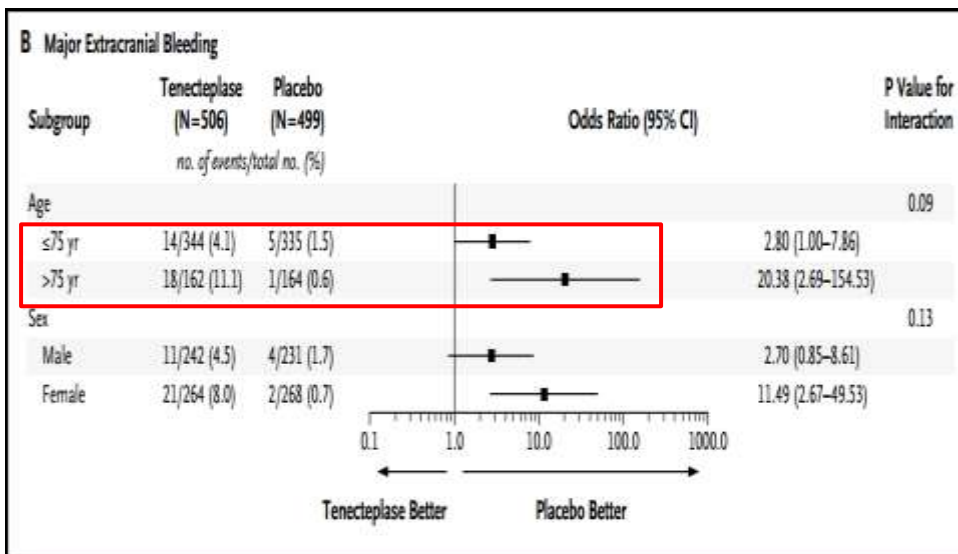


Table 4. Safety Outcomes in the Intention-to-Treat Population.^{a,b}

Outcome	Tenecteplase (N=506) no. (%)	Placebo (N=499) no. (%)	Odds Ratio (95% CI)	P Value
Bleeding between randomization and day 7				
Major extracranial bleeding	32 (6.3)	6 (1.2)	5.55 (2.3–13.39)	<0.001
Minor bleeding	165 (32.6)	43 (8.6)		
Major bleeding†	58 (11.5)	12 (2.4)		
Stroke between randomization and day 7	12 (2.4)	1 (0.2)	12.10 (1.57–93.39)	0.003
Ischemic stroke	2 (0.4)	0		
Hemorrhagic stroke‡	10 (2.0)	1 (0.2)		

Guy Meyer, M.D., et al, N Engl J Med 2014.

**Figure 1. Efficacy and Safety Outcomes in Prespecified Subgroups.**

Panel A shows the primary efficacy outcome (death or hemodynamic decompensation), and Panel B shows a safety outcome (major extracranial bleeding), both within 7 days after randomization.

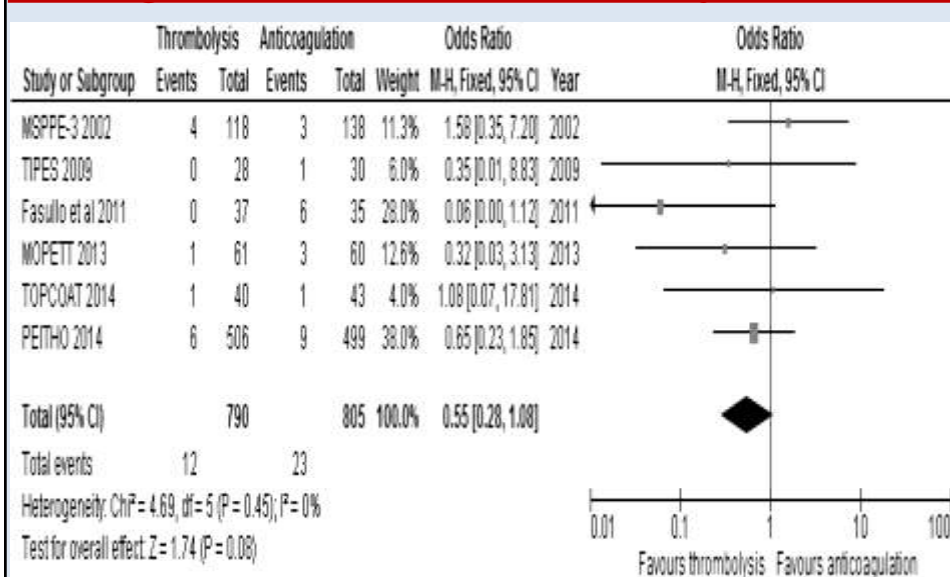
Guy Meyer, M.D., et al, N Engl J Med 2014.

PEITHO: Conclusions

- ❖ *In intermediate-risk PE, IV. tenecteplase reduced death or collapse.*
- ❖ *Benefits of thrombolysis came at the cost of increased risk of major, intracranial, hemorrhage.*
- ❖ *The patient's age should be taken into account when weighing the expected benefits versus risks of systemic thrombolysis.*

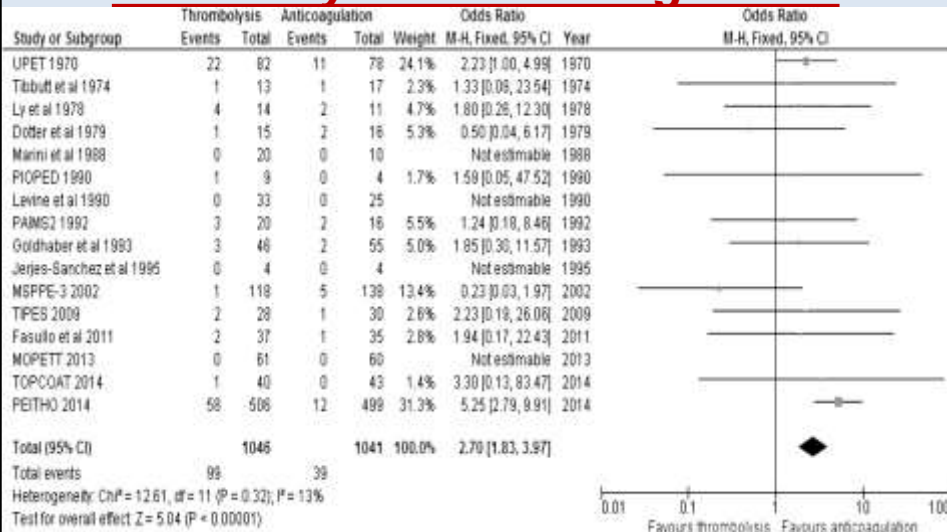
Guy Meyer, M.D., et al, N Engl J Med 2014.

OR of overall mortality comparing thrombolysis to anticoagulation in stable PE with clearly defined RVD.



Tzu-Fei Wang et al. Blood 2015

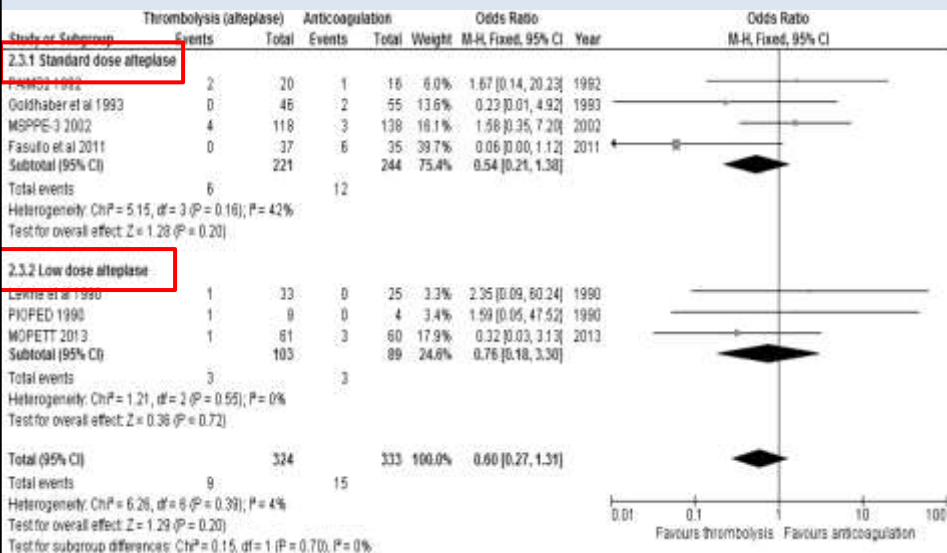
OR of major bleeding events comparing thrombolysis to anticoagulation.



Tzu-Fei Wang et al. Blood 2015

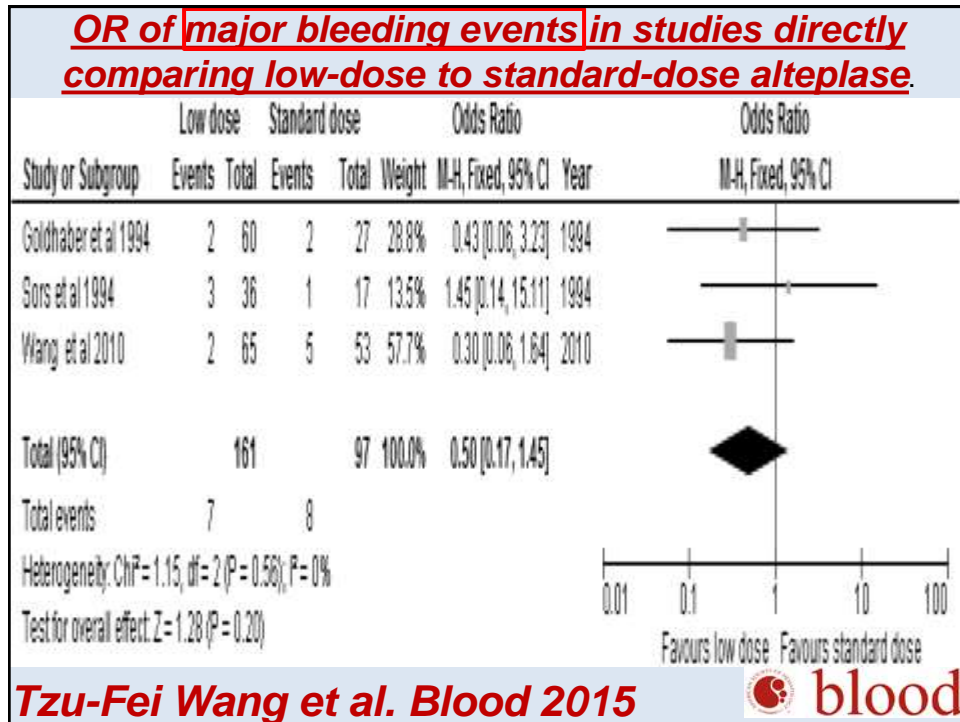


Overall mortality comparing alteplase to anticoagulation, subcategorized by standard-dose vs low-dose alteplase



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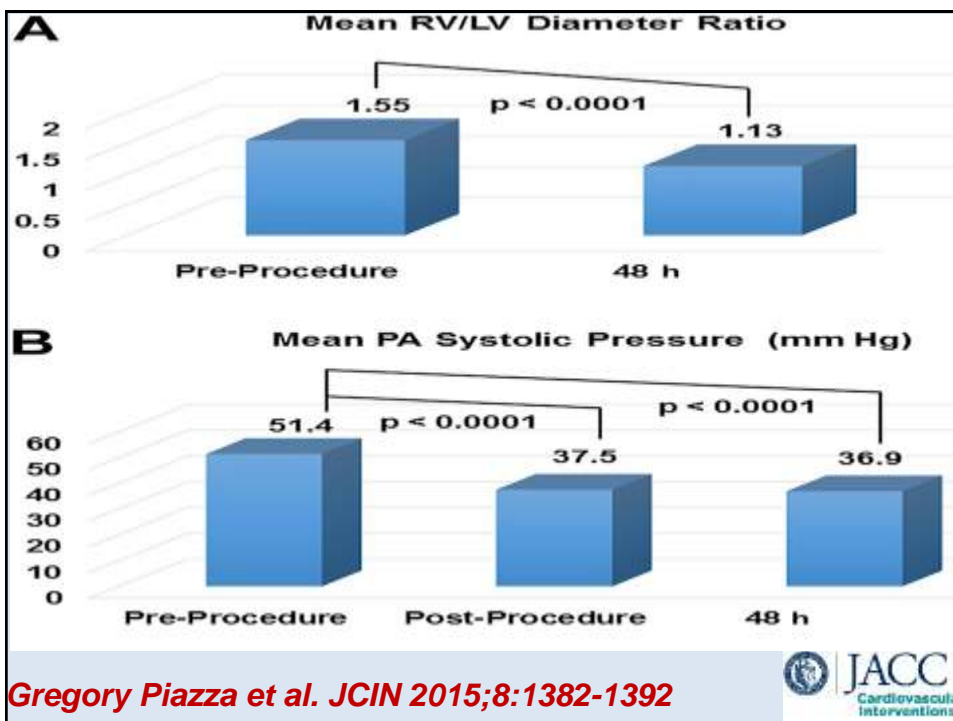
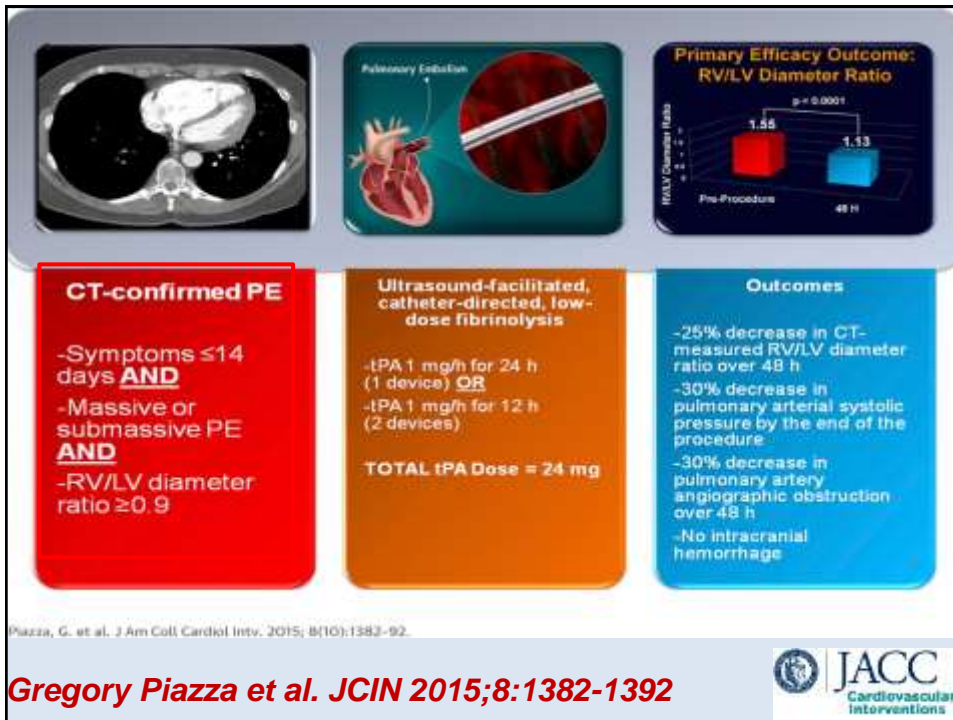




A Prospective, Single-Arm, Multicenter Trial of Ultrasound- Facilitated, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism (SEATTLE II)

***Gregory Piazza, MD, MS
 on behalf of the SEATTLE II Investigators
 March 30, 2014***





Clinical Outcomes

Clinical outcomes*	N = 150
<i>Mean length of stay ± SD, days</i>	8.8 ± 5
<i>In-hospital death, n (%)</i>	3 (2)
<i>30-day mortality**, n (%)</i>	4 (2.7)
<i>Serious adverse events due to device, n (%)</i>	2 (1.3)
<i>Serious adverse events due to t-PA, n (%)</i>	2 (1.3)
<i>IVC filter placed, n (%)</i>	24 (16)
<i>Major bleeding within 30 days**, n (%)</i>	17 (11.4)
<i>GUSTO moderate**</i>	16 (10.7)
<i>GUSTO severe**</i>	1 (0.7)
<i>Intracranial hemorrhage, n (%)</i>	0 (0)

*All death, serious adverse, and bleeding events were adjudicated by an independent safety monitor.

Overcoming the Hurdle of Intracranial Hemorrhage

Study	Intracranial Hemorrhage (Fibrinolysis Group)
ICOPER (Goldhaber SZ, et al. 1999)	9/304 (3%)
PEITHO (Meyer G, et al. 2014)	10/506 (2%)
SEATTLE II (Piazza G, et al. 2014)	0/150 (0%)

Conclusions

Ultrasound-facilitated catheter-directed low-dose fibrinolysis for acute PE improves RV function and decreases pulmonary hypertension and angiographic obstruction, minimizing intracranial bleed.

A potential “game-changer” in treatment of high-risk PE patients.

