Hemodynamic collapse - is your gestalt good enough to empirically lyse?

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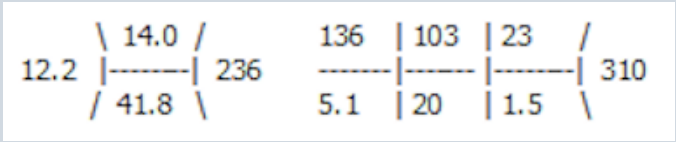
Case

- 43 year-old M brought in by EMS after found down in the street
- v/s: BP 95/55, HR 105, O2 93% 8L
- Labs:
  - Trp 0.18 ng/mL (Nm < 0.1 ng/mL)
  - Utox + cocaine



- CXR: RLL aspiration pneumonia
- Started on IVFs, Antibiotics
- Admitted to MICU
- 2 hours later, BP 80/40, HR 130, O2 90% 12L

Questions:

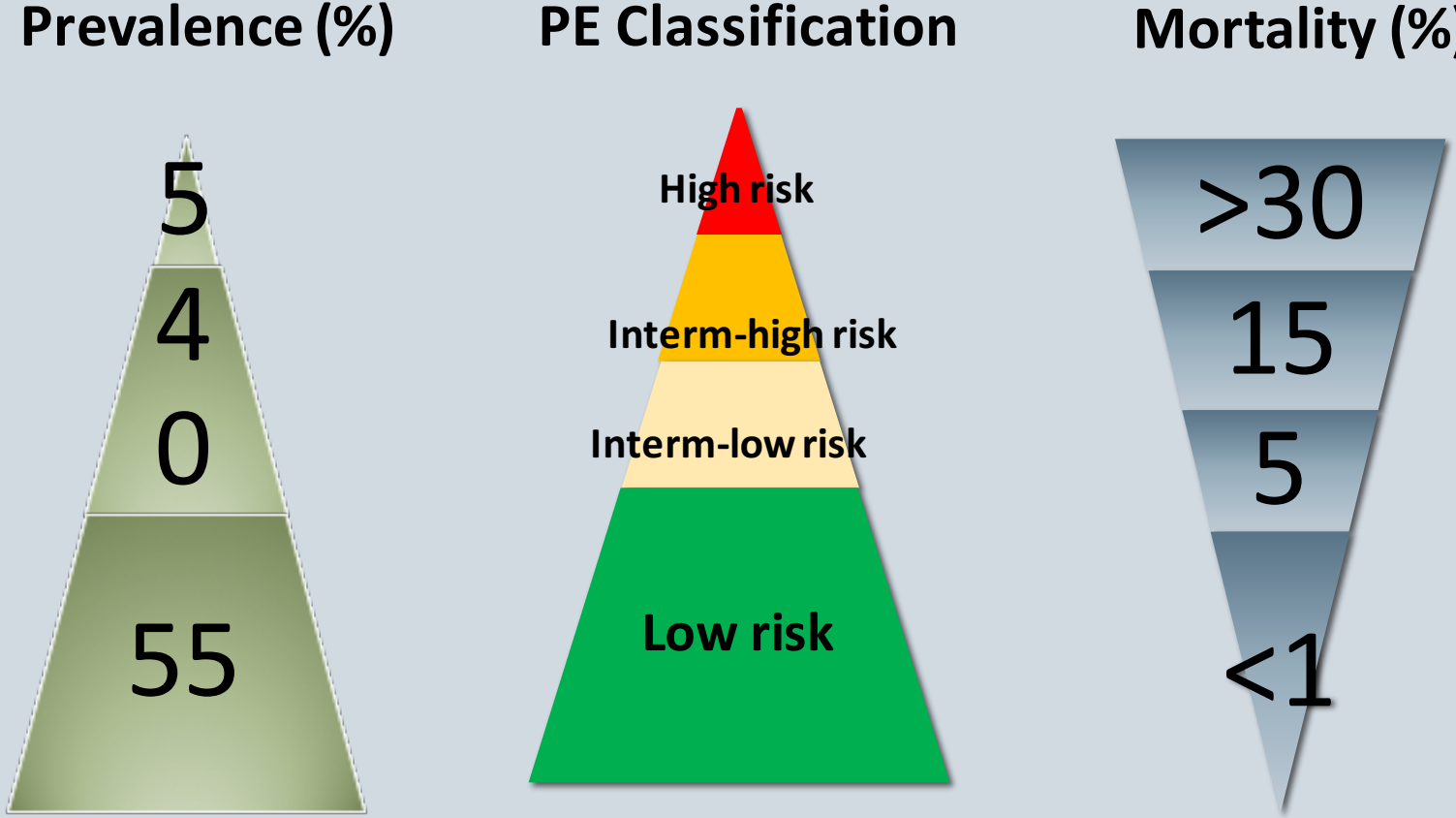
Is this a PE?

Would you empirically lyse this patient?

American Classification of PE (AHA)

Low Risk	Submassive (Intermediate Risk)	Massive (High Risk)
Normotensive No RV dysfunction Normal biomarkers	• Normotensive • **RV strain** (CTA/TTE) – RV dilation – RV dysfunction – **BNP** > 90 pg/mL, pro-BNP > 500 pg/mL – **Trop** I > 0.4 ng/mL, Trop T > 0.1 ng/mL	• **Hypotension** (SBP < 90 for >15 min) • **Shock** (on pressor) • **Pulselessness**

Jaff. Circ 2011



Adapted from Dudziski

How to *diagnose* PE in a unstable patient?

Step 1: Clinical Probability

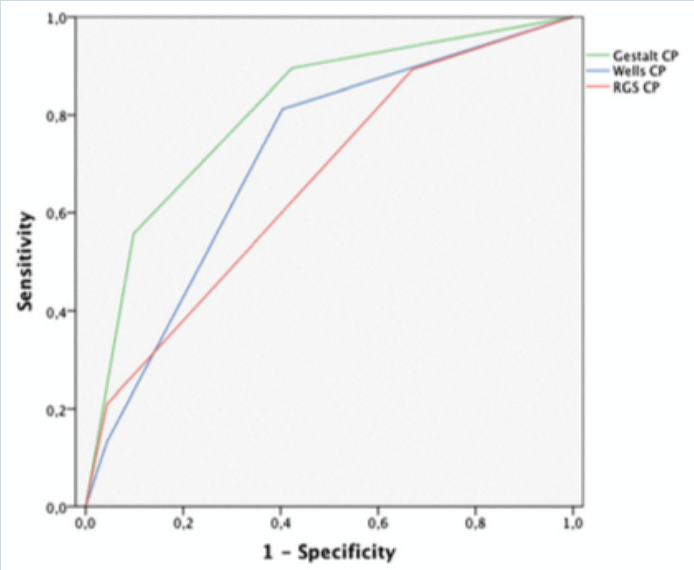
Wells score		Revised Geneva score	
Variable	**Points**	**Variable**	**Points**
Previous DVT or PE	1.5	Age >65 years	1
Recent surgery or immobilization	1.5	Previous DVT or PE	3
Cancer	1	Surgery or fracture within 1-month	2
Hemoptysis	1	Active malignancy	2
Heart rate >100 beats/min	1.5	Unilateral lower limb pain	3
Clinical signs of DVT	3	Hemoptysis	2
Alternative diagnosis less likely than PE	3	Heart rate 75–94 beats/min	3
		Heart rate ≥95 beats/min	5
		Pain on lower limb deep vein at palpation and unilateral edema	4
Clinical probability (3 levels)	Total	Clinical probability (3 levels)	Total
Low	0–1	Low	0–3
Intermediate	2–6	Intermediate	4–10
High	≥7	High	≥11
Clinical probability (2 levels)		Clinical probability (2 levels)	
PE unlikely	0–4	PE unlikely	0–3
PE likely	>4	PE likely	>3

DVT: Deep vein thrombosis; PE: Pulmonary embolism.

Wells. Thromb Haemost. 2000
Le Gal. Ann Int Med. 2006

Scores vs. Gestalt

	Wells score	Revised Geneva
Shen et al. **J Thromb Thrombolysis 2016**	AUC 0.78 (CI 0.74-0.81)	AUC 0.69 (CI 0.65-74)



Shen. J Thromb Thrombolysis 2016

Penaloza. Ann Emerg Med 2013

Clinical Probability of PE-Cardiac Arrest

- Clinical decision rule derived from 44 subjects witnessed PEA arrest
- Triad: **respiratory distress**, **altered mental status**, and **shock**

Clinical features observed prior to cardiac arrest

Feature	PE ($N=18$)	%	Non-PE ($N=15$)	%
Respiratory distress	14	77.8	10	66.7
Alteration of mental status	13	72.2	7	46.7
Shock index >0.8	14	77.8	4	26.7
2 of 3	15	83.3	5	33.3
3 of 3	8	44.4	2	13.3

- Sudden Death Expertise Center Registry – Paris, France
- 8294 out-of hospital cardiac arrest (CA)
- 82/2926 had PE-related CA (2.8%)
- Predictors of PE-related CA
  - **Initial nonshockable rhythm** (OR 12.4, CI 4.9-31)
  - **Previous VTE** (OR 10.4, CI 5.6-19.4)
  - **Absence of known heart disease** (OR 3.8, CI 2-7.3)
  - **Female** sex (OR 1.9, CI 1.2-3.0)

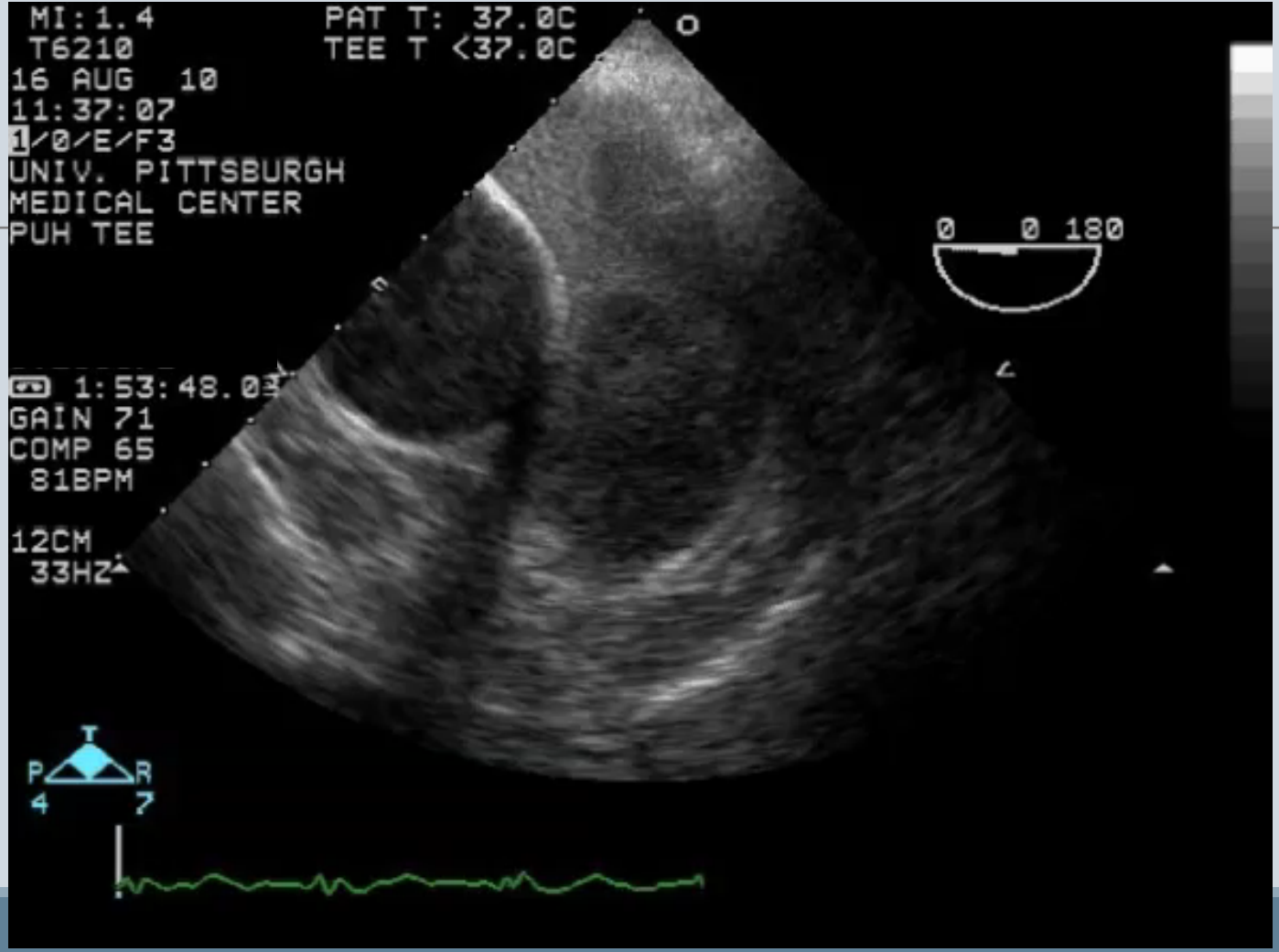
Courtney, Kline. Resuscitation 2005

Bougouin. Circulation 2016

Step 2: Alternative Imaging

Imaging	Sensitivity % (CI)	Specificity % (CI)	Pros	Cons
TTE	74 (61-84)	54 (51-56)	RV dil, RV dysf, clot-in-transit	Availability, Use during CPR
TEE	76	100	Clot in PA, Use during CPR	Availability
Bedside Cardiac US	91 (80-97)	87 (80-91)	Readily available	Expertise
Bedside Leg Venous US	56 (45-60)	95 (88-99)	DVT	Does not rule out PE

Coutance. Crit Care 2011
Pruszczyk. 2001. Heart
Nazerian. Intern Emerg Med 2017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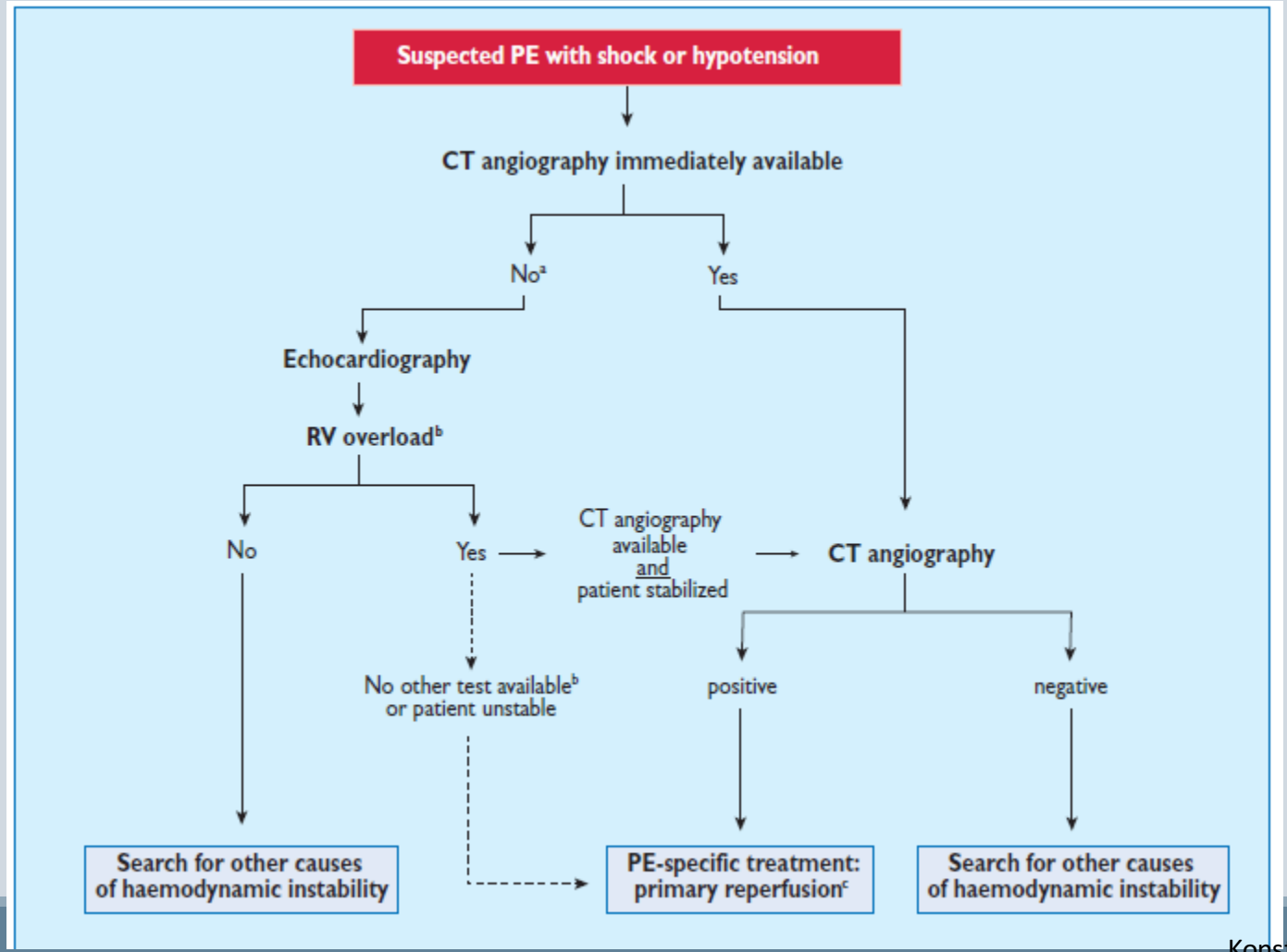
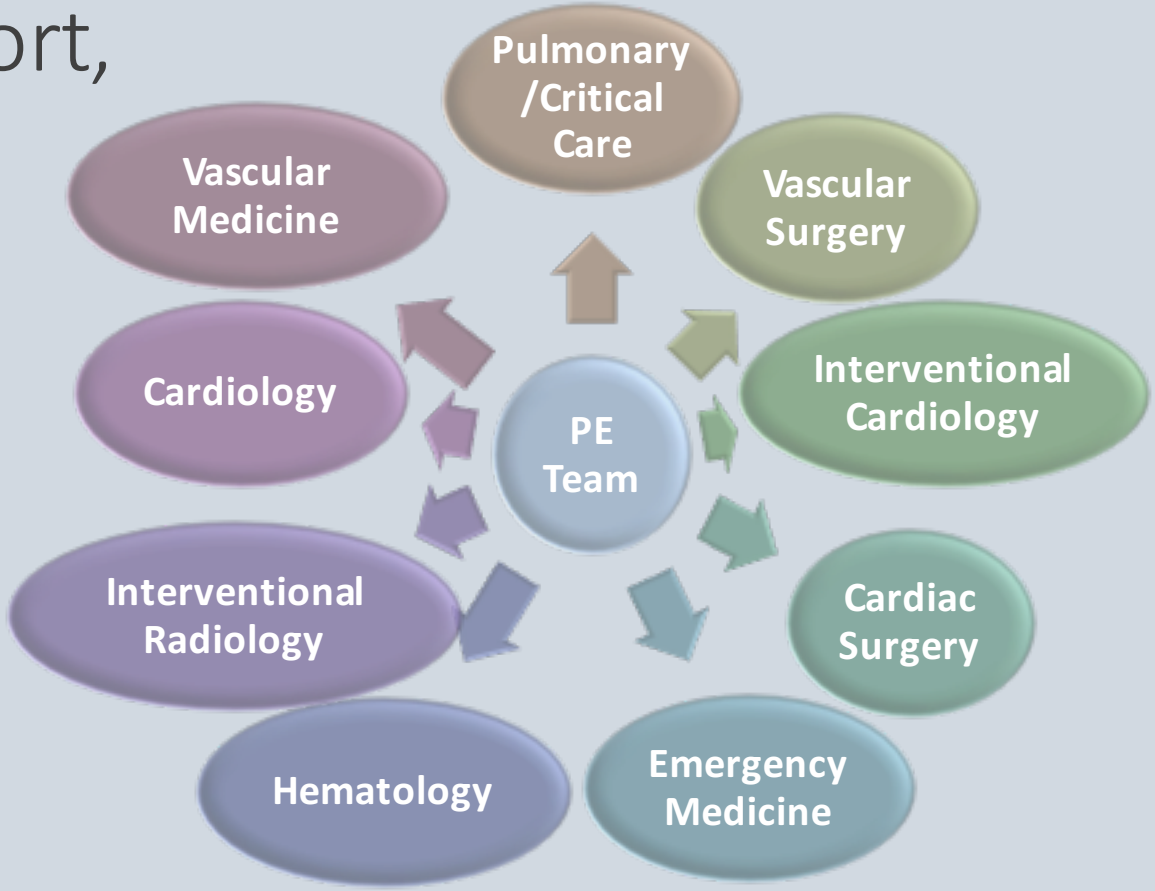


Konstantinides. Eur Heart J 2014

Step 3: Get support, share decision making
Call PERT!

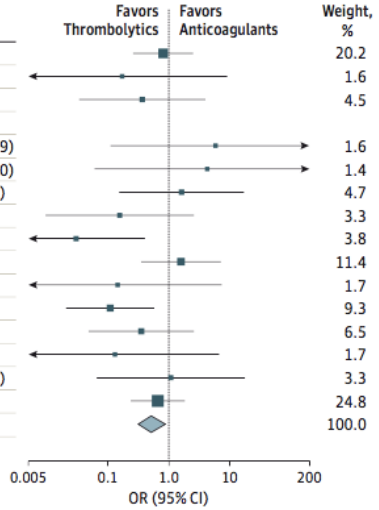


Step 4: Determine Risk-Benefit of Thrombolysis

Figure 2. Odds of Mortality in Patients With Pulmonary Embolism Treated With Thrombolytic Therapy vs Anticoagulation

Source	Thrombolytics No. of Events	Thrombolytics No. of Patients	Anticoagulants No. of Events	Anticoagulants No. of Patients	OR (95% CI)	Weight, %
UPETSG,[31] 1970	6	82	7	78	0.80 (0.26-2.49)	20.2
Tibbutt et al,[28] 1974	0	13	1	17	0.17 (0.00-8.94)	1.6
Ly et al,[25] 1978	1	14	2	11	0.37 (0.03-3.96)	4.5
Marini et al,[26] 1988	0	20	0	10	Not estimable	
Levine et al,[22] 1990	1	33	0	25	5.80 (0.11-303.49)	1.6
PIOPED,[27] 1990	1	9	0	4	4.24 (0.06-296.20)	1.4
Dalla-Volta et al,[23] 1992	2	20	1	16	1.61 (0.15-16.82)	4.7
Goldhaber et al,[2] 1993	0	46	2	55	0.16 (0.01-2.57)	3.3
Jerges-Sanchez et al,[24] 1995	0	4	4	4	0.03 (0.00-0.40)	3.8
Konstantinides et al,[3] 2002	4	118	3	138	1.58 (0.35-7.09)	11.4
TIPES,[29] 2010	0	28	1	30	0.14 (0.00-7.31)	1.7
Fasullo et al,[11] 2011	0	37	6	35	0.11 (0.02-0.58)	9.3
MOPETT,[10] 2012	1	61	3	60	0.35 (0.05-2.57)	6.5
ULTIMA,[30] 2013	0	30	1	29	0.13 (0.00-6.59)	1.7
TOPCOAT,[9] 2014	1	40	1	43	1.08 (0.07-17.53)	3.3
PEITHO,[8] 2014	6	506	9	499	0.66 (0.24-1.82)	24.8
Total	23	1061	41	1054	0.53 (0.32-0.88)	100.0

Heterogeneity: $\chi^2_{14} = 16.51$; $P = .28$; $I^2 = 15\%$
Overall effect: $z = 2.45$; $P = .01$



Chatterjee. JAMA 2014

Thrombolysis

Table 2. Absolute Risk Metrics of Outcomes of Major Interest

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

Chatterjee. JAMA 2014

Guidelines	AHA 2011	ESC 2014	ACCP 2016
Systemic thrombolysis			
High-risk PE and low bleeding risk	X	X	X
Intermediate-risk PE with severe RV dysfunction and respiratory insufficiency	X		
Intermediate-risk PE with severe symptoms and cardiopulmonary impairment			X
Deterioration after starting AC without hypotension			X
Catheter-directed thrombolysis			
High-risk PE and high bleeding risk	X	X	X
Failed systemic thrombolysis	X		X
Intermediate-risk PE with severe RV dysfunction and respiratory insufficiency	X		
Intermediate-risk PE when systemic thrombolysis is contraindicated		X	

Thrombolysis in **Unstable Massive PE**

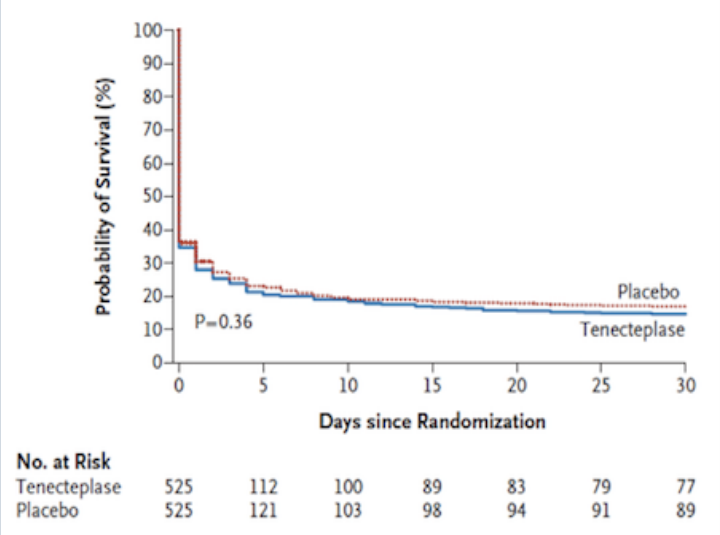
- Prospective RCT of 8 patients with massive PE and cardiogenic shock
  - Streptokinase vs Heparin
  - 100% survival in lysis group vs 0% survival in heparin ($p = 0.02$)
  - Ethics committee stopped trial early

- Retrospective review of Nationwide Inpatient Sample
  - 72,230 hemodynamically unstable patients (shock or ventilator)
  - 30% received thrombolytics
  - Mortality: 15% in lysis group vs 47% no lysis ($p < 0.001$)

Jerjes-Sanchez. J Thromb Thrombolysis 1995
Stein and Matta. Am J Med 2012

Thrombolysis in (All) Cardiac Arrest

- Prospective, multicenter, placebo RCT of 1050 witnessed, out-of-hospital cardiac arrest due to presumed cardiac causes
- 30 day survival: 14.7% thrombolytics vs 17% placebo (p = 0.36)
- No difference in survival to admission, 24-h survival or ROSC
- Confirmed PE subgroup: 2/15 (13.3%) thrombolytics vs 0/22 placebo (p = 0.31)
- 2.7% ICH with lytics



Bottiger. NEJM 2008

Thrombolysis in PE-Cardiac Arrest

Author	Year	Study type	Lytics	Results	Bleeding
Janata et al	2003	Retrospective	30/60 (50%)	**ROSC**: 67% vs 43% (p=0.06) **Survival at 24h**: 53% vs 23% (0.01) **Survival at discharge**: No diff	No diff major/minor bleeding

Take Home Points

- 3 steps to determine empiric lysis:
  - **Step 1**: Rely on clinical judgement (combined history and physical exam)
  - **Step 2**: Bedside diagnostic tools (TTE, TEE, bedside cardiac or LE US)
  - **Step 3**: Activate PERT! (share decision making)
  - **Step 4**: Estimate risk-benefit ratio for administering thrombolytics
- *Easier said than done!*