

PE INTERVENTIONS: PATIENT AND DEVICE SELECTION

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DISCLOSURES

- None



OBJECTIVES

- To discuss the **different interventions** in the management of pulmonary embolism (**PE**), with focus on **catheter-directed therapies (CDT)**
- To review rationale behind patient selection for different interventions in PE, with emphasis on **CDT**
- To discuss the **existing evidence** for the use of **CDT** in PE
- To review some **considerations for device selection** when opting for **CDT**

PE INTERVENTIONS

- Anticoagulation alone
- Systemic thrombolysis (ST)
- **Catheter-directed therapies (CDT)**
 - Thrombolysis, Thrombectomy, Thrombolysis + Thrombectomy
- Surgical thrombectomy

- Additional interventions
 - IVC filter placement

PATIENT SELECTION FOR PE INTERVENTIONS

- High-risk PE (Massive PE):
 - **Systemic thrombolysis (ST)**
 - +/- **CDT** if contraindication to ST or ST failure
- Low-risk PE:
 - **Anticoagulation (AC) alone**
- Intermediate-risk PE (Submassive PE):
 - **Optimal therapy controversial (ST vs CDT vs AC alone)**

SYSTEMIC THROMBOLYSIS (ST) IN MASSIVE PE

Stein PD, Matta F. Thrombolytic therapy in unstable patients with acute pulmonary embolism: saves lives but underused. The American journal of medicine 2012;125:465-70.
National Database 1999 - 2008

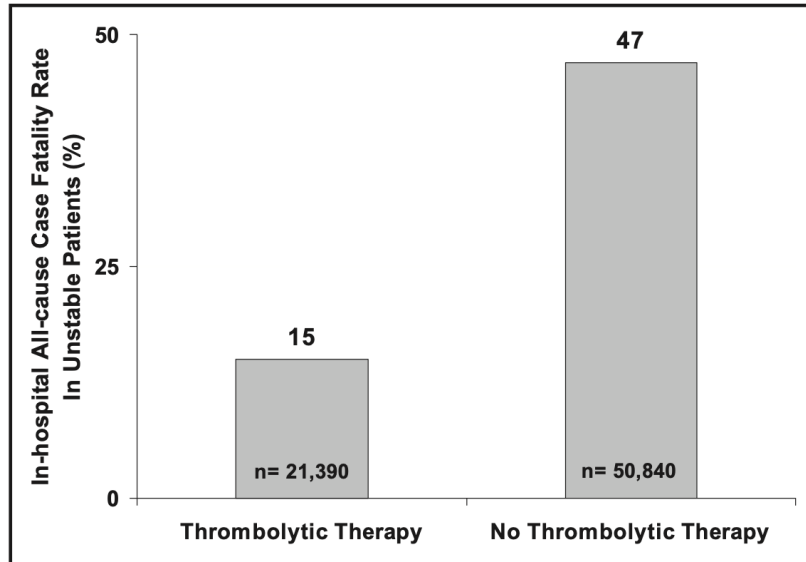
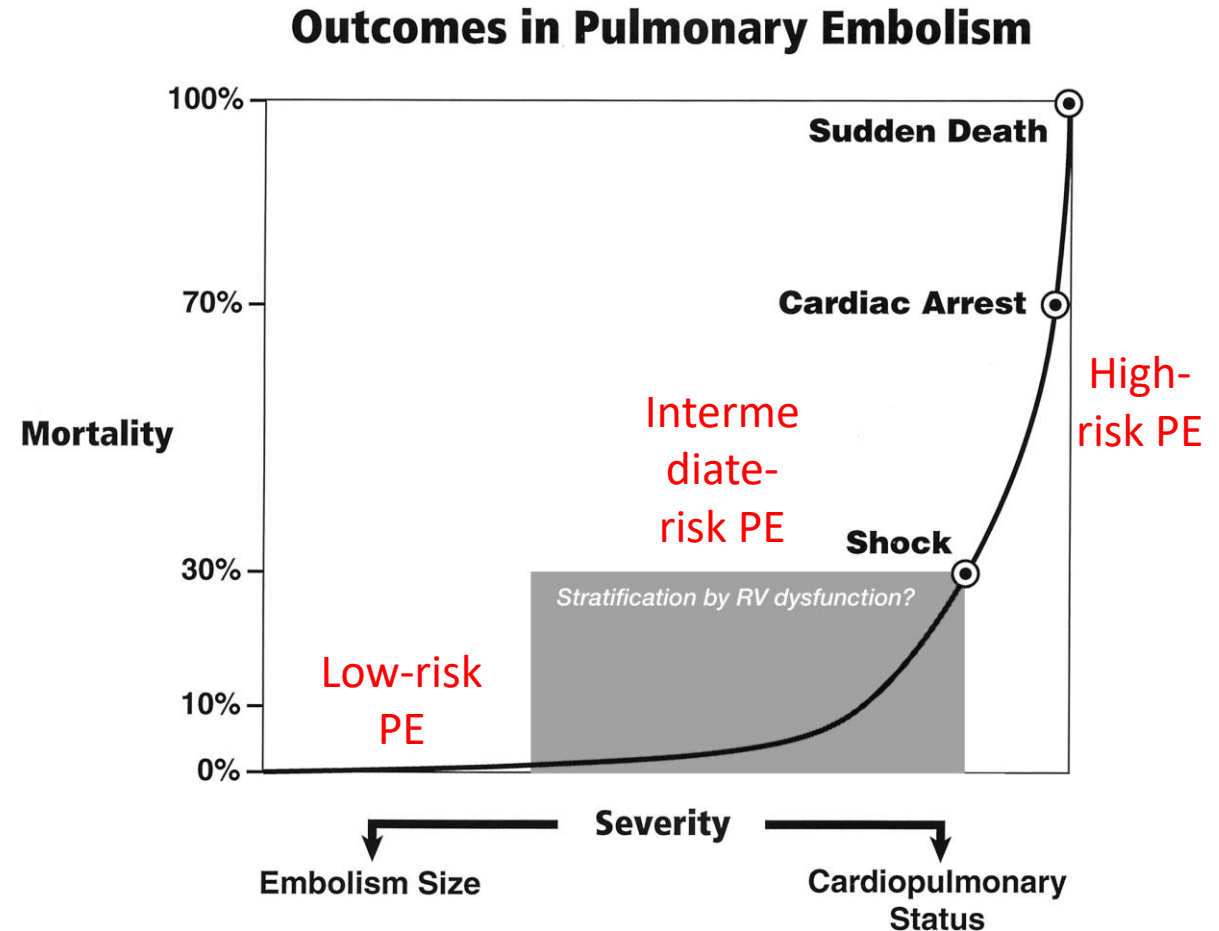


Figure 2 In-hospital all-cause case fatality rate in unstable patients with pulmonary embolism who received thrombolytic therapy and in those who did not. The number (n) in both groups is shown within the bar. Difference of mortality, $P < .0001$.



Wood KE. Major pulmonary embolism: review of a pathophysiologic approach to the golden hour of hemodynamically significant pulmonary embolism. Chest 2002;121:877-905.

ANTICOAGULATION ALONE IN **SUBMASSIVE PE**

- **Most patients do well with AC alone:**
 - **Mortality** relatively low in submassive PE (1.8-17% AC alone)
 - **2.9%** mortality (AC alone) in largest MA

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		
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

Chatterjee S, Chakraborty A, Weinberg I, et al. Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding, and intracranial hemorrhage: a meta-analysis. *Jama* 2014;311:2414-21.

Mean f/u ~81 days for all studies

THROMBOLYTICS (ST or CDT) IN SUBMASSIVE PE

• Challenging patient selection

- Different methods of administration (ST vs CDT) and dosing (full vs reduced dose) is available
- Submassive PE group very heterogeneous
- Current studies with important limitations
- Patient selection best made in consultation with multidisciplinary (PERT) team
 - *For best risk stratification and risk/benefit discussion*

CDT IN PE: PATIENT SELECTION

- Routine use in **submassive PE** likely not supported by evidence (IIIB ESC)

- *Pts with the highest risk of death due to RV failure probably will benefit the most*
 - Signs of significant RV dysfunction
 - ST (full or reduced dose) alternative to CDT

- Should be considered in **massive PE** with: (IIaC: ESC)

- *Modest to high risk of bleeding*
- *Hemodynamic instability despite ST*

CDT USE IN SUBMASSIVE PE

Table 2. Echocardiographic Core Laboratory Data

	Baseline		24 h		90 days	
	USAT	Heparin	USAT	Heparin	USAT	Heparin
RV/LV ratio, mean±SD	1.28±0.19	1.20±0.14	0.99±0.17	1.17±0.20	0.92±0.15	0.96±0.16
n	26	29	28	28	26	27
Between-group comparison	<i>P</i> =0.07		<i>P</i> =0.001		<i>P</i> =0.36	

(ULTIMA 2014)
Kucher N,
Boekstegers P,
Müller OJ, et al.
Randomized,
controlled trial of
ultrasound-assisted
catheter-directed
thrombolysis for
acute intermediate-
risk pulmonary
embolism.
Circulation
2014;129:479-86.

- Short-term improvement in RV/LV or PA pressures in CDT studies not validated as marker of improved clinical outcomes

THROMBOLYTICS VS AC ALONE IN SUBMASSIVE PE

- No mortality difference between ST vs AC alone
- No mortality difference between CDT vs AC alone
- Increased bleeding risk with ST/CDT
- Similar CTEPH rates (~3.2%)
- Similar persistent symptoms/functional impairment at 2 yrs (ST)
- **Prospective, randomized studies needed to determine the long-term effect of CDT on mortality, functional status, rates of CTEPH**

(PEITHO 2014)
 Meyer G, Vicaut
 E, Danays T, et
 al. Fibrinolysis for
 patients with
 intermediate-risk
 pulmonary
 embolism. N Engl
 J Med
 2014;370:1402-
 11.

Table 3. Efficacy Outcomes.*

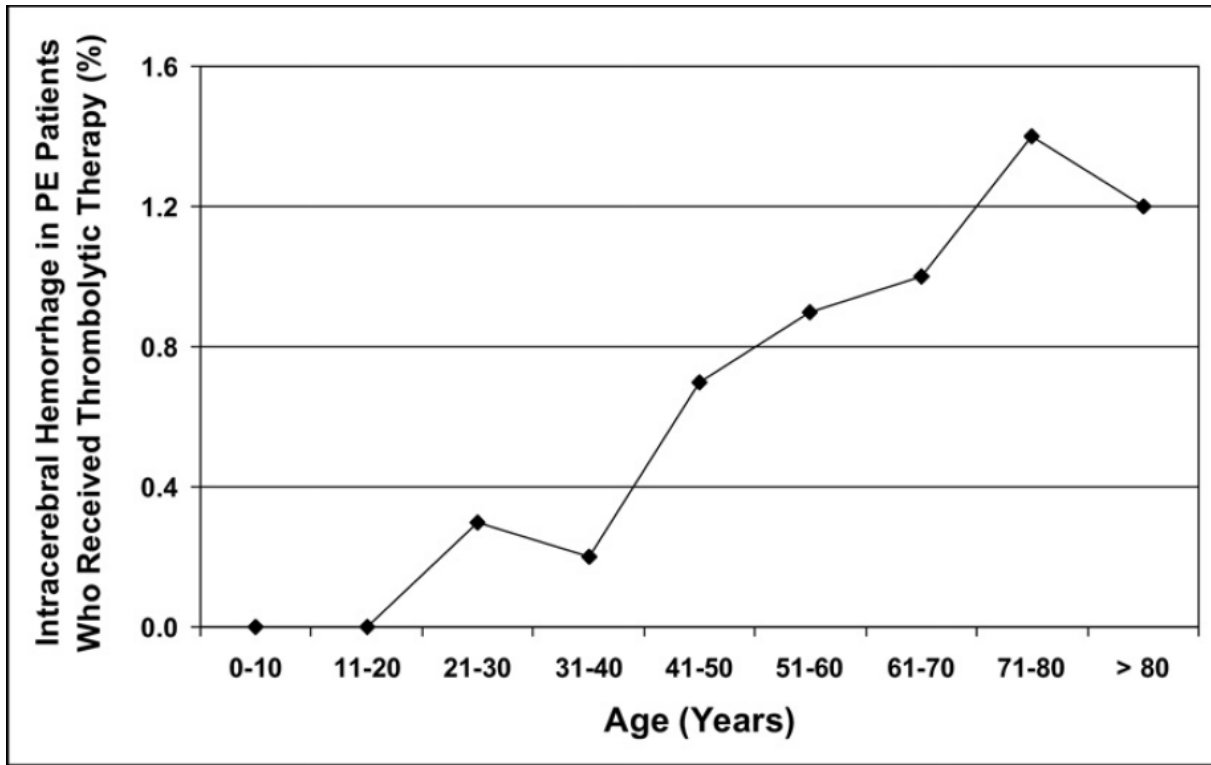
Outcome	Tenecteplase (N = 506)	Placebo (N = 499)	Odds Ratio (95% CI)	P Value
Primary outcome — no. (%)	13 (2.6)	28 (5.6)	0.44 (0.23–0.87)	0.02
Death from any cause	6 (1.2)	9 (1.8)	0.65 (0.23–1.85)	0.42
Hemodynamic decompensation	8 (1.6)	25 (5.0)	0.30 (0.14–0.68)	0.002
Death from any cause between randomization and day 30 — no. (%)	12 (<u>2.4</u>)	16 (<u>3.2</u>)	0.73 (0.34–1.57)	<u>0.42</u>

TABLE 5 Safety Outcomes (N = 150)

Length of stay, SD, days	8.8 ± 5
In-hospital death	3 (2)
30-day mortality*	4 (2.7)

(SEATTLE II 2015, CDT) Piazza G, Hohlfelder B, Jaff MR, et al. A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism: The SEATTLE II Study. JACC Cardiovasc Interv 2015;8:1382-92

- Long-term PEITHO follow-up (2017):
 - CTEPH rates 2.1% ST vs 3.2% AC alone, P= 0.79



Stein PD, Matta F, Steinberger DS, Keyes DC. Intracerebral hemorrhage with thrombolytic therapy for acute pulmonary embolism. *The American journal of medicine* 2012;125:50-6.

National Database 1998 – 2008, n = 49,500

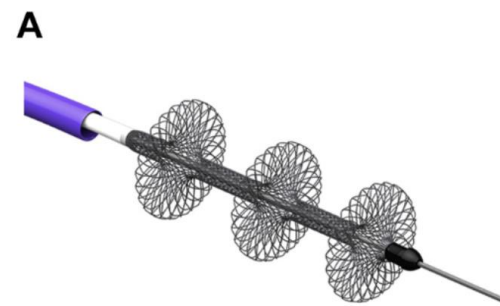
- PEITHO 2014 (ST vs AC alone):
 - X10 ICH (2% vs 0.2%)
 - x5 major hemorrhage (6.3% vs 1.2%)
- ULTIMA 2014 (CDT vs AC alone) and PERFECT 2015 (CDT): No major bleeding
- SEATTLE II 2015 (CDT): 10% major bleeding

CDT IN PE: PATIENT SELECTION

- **Insufficient data in PE without clear signs of RV dysfunction with:**
 - Severe isolated hypoxemia
 - Extensive clot burden
 - Clot in transit
 - Pregnancy

CDT: SOME CONSIDERATIONS FOR DEVICE SELECTION

- Current device selection:
 - **Operator dependent**
 - Expertise
 - Clot characteristics
 - Hospital specific
- **Limited studies with side-to-side comparisons (SUNSET trial 2021)**



CDT: SOME CONSIDERATIONS FOR DEVICE SELECTION

- Catheter-guided thrombolysis
 - **Standard vs USAT:**
 - Similar bleeding (~2-4% at 48hrs) and complication profiles
 - No difference in PA pressure change (at 24-48 hrs)
 - No change in infusion times (~14 hrs)
 - No change in thrombolytic dose (USAT 19 vs CDT 18 mg tPA)
 - No difference in thrombus reduction

CDT: SOME CONSIDERATIONS FOR DEVICE SELECTION

- Catheter-guided thrombectomy
 - +/- thrombolytic
 - Operator variability
 - **FlowTrievers** (16-24F) vs **Indigo** (up to 8-12F):
 - Similar mean RV/LV reduction at 48 hrs (0.38 Flowt vs 0.43 Ind)
 - Similar major adverse events similar, major bleeding (2.5-3.8% and 0.9-1.7%, respect) and blood loss
 - Mean proc time 94 min (FlowTrievers) vs median proc time 37 min (Indigo)



Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. JACC Cardiovasc Interv 2021;14:319-29.

Tu T, Toma C, Tapson VF, et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. JACC Cardiovasc Interv 2019;12:859-69

CONCLUSION

- Multiple interventions available in PE, including CGT
- ST saves lives in massive PE
- Most patients with non-massive PE do well on AC alone
- CDT could benefit a subgroup of patients at high risk of death from RV failure, but more studies with patient-centered outcomes are needed
- Patient selection for ST/CDT is complex and best done in consultation with a multidisciplinary (PERT) team
- Once decision made to go ahead with CDT, device selection is based at this time on operator preferences, expertise, hospital availability

THANK YOU

- Questions?



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