What's New in Intermediate Risk Pulmonary Embolism

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Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

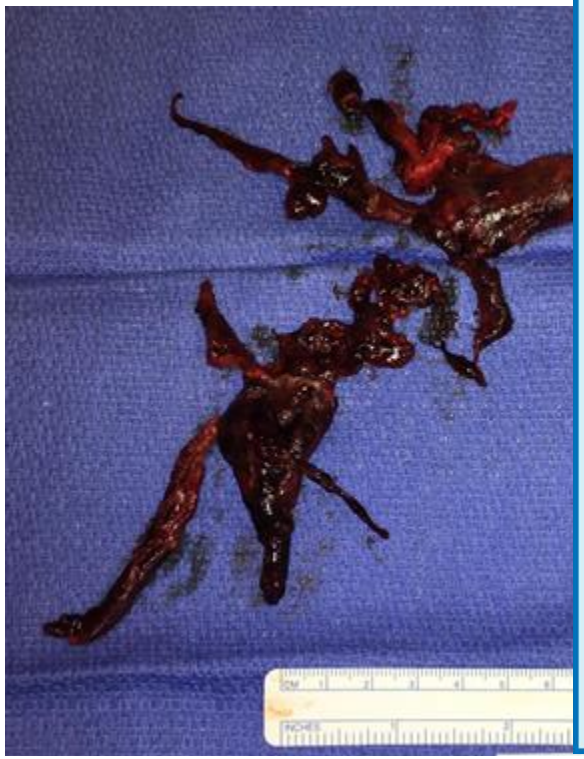
Nature of Financial Relationship	Ineligible Company
Grant/Research Support	
Consultant Fees/Honoraria/Speaker's Bureau	Inari Medical
Individual Stock(s)/Stock Options	
Royalties/Patent Beneficiary	
Executive Role/Ownership Interest	
Other Financial Benefit	

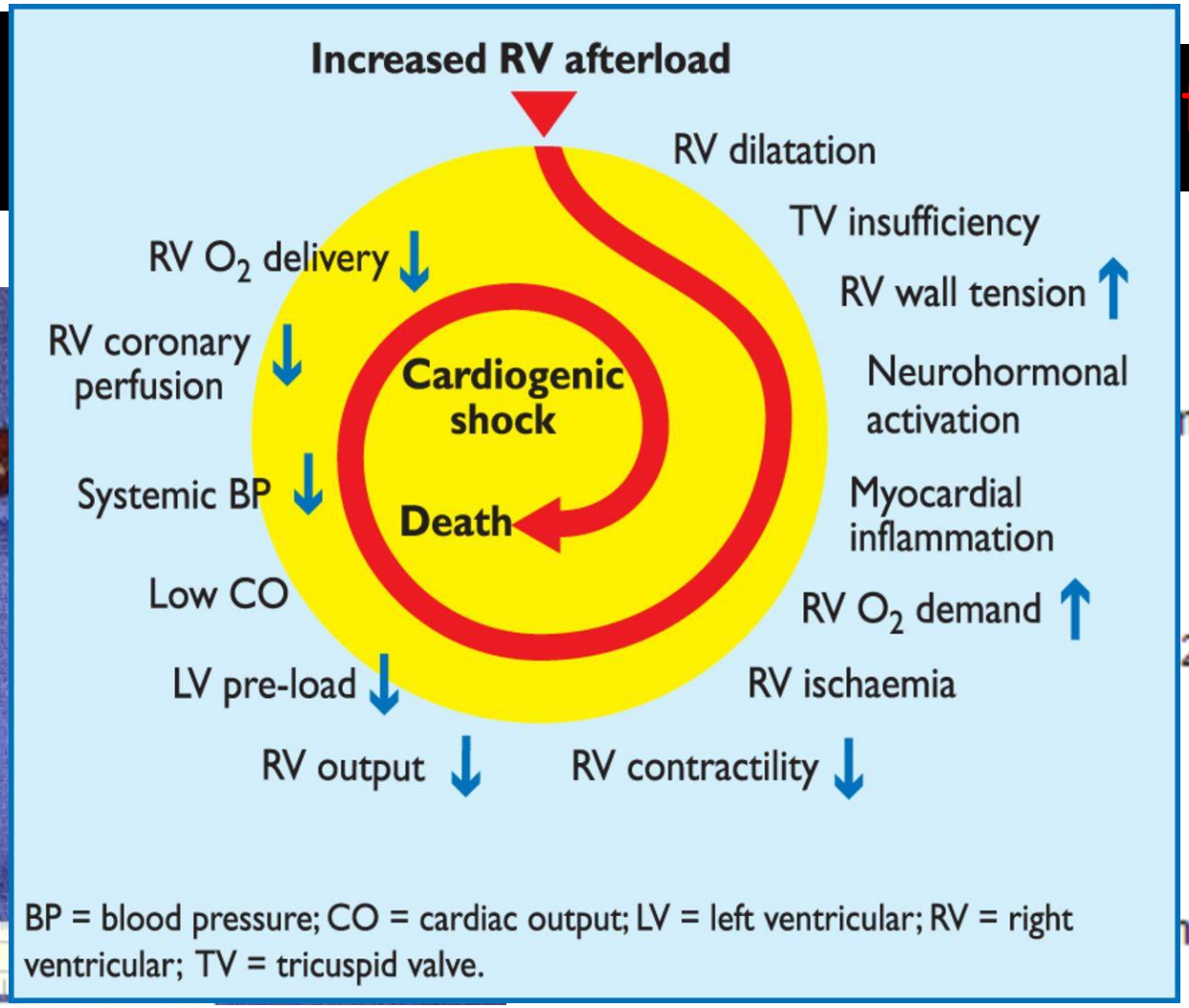
Objectives

1. Risk Stratification in Acute PE
2. Problems with Current Management Strategy
3. Trial Updates
4. Future directions

RV Failure IS the Pathophysiology of PE

CVP 18 mmHg
PASP 51 mmHg





BP = blood pressure; CO = cardiac output; LV = left ventricular; RV = right ventricular; TV = tricuspid valve.

fterload

ned showed the following:

2

n2

Current Risk Stratification

Table 8 **Classification of pulmonary embolism severity and the risk of early (in-hospital or 30 day) death**

Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥I	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

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Not all Sub-massive PE is created equally.

Case

64-year-old woman with a history of HTN, presented to an OSH ER with complaints of chest pain, dyspnea, and palpitations and episode of syncope

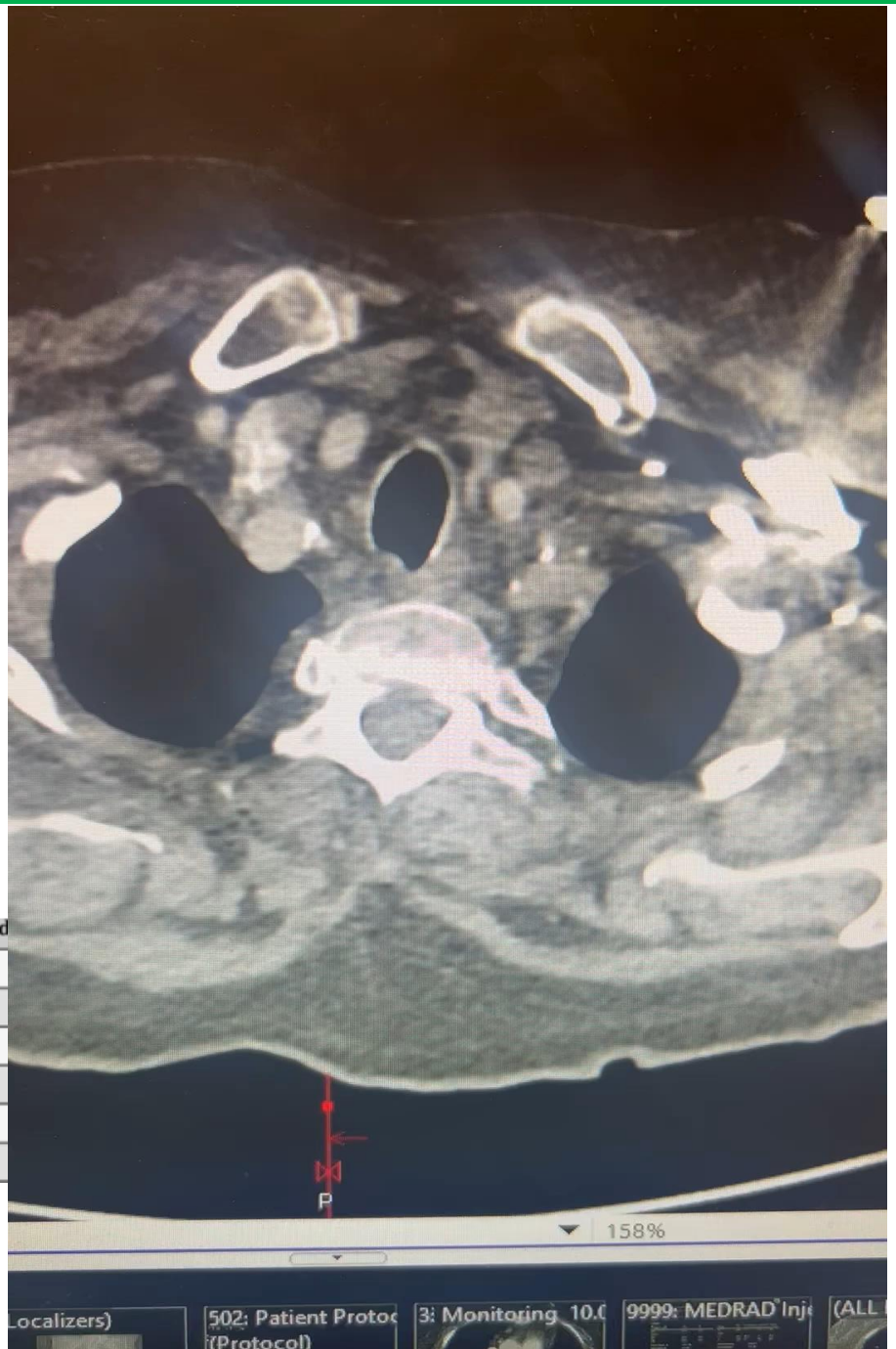
VS in ER: HR 160s, BP 100/80, RR 25, 88% SaO2 on room air.

PERT Patient

Labs

- hsTroponin → 83 → 167 → 149 → 172 (6PM)
- Lactic Acid 3.7
- NT-proBNP 1138

Parameters	Points assigned
Age > 80 years	+1
History of cancer	+1
History of chronic cardiopulmonary disease	+1
Pulse rate ≥ 110/min	+1
Systolic blood pressure < 100 mmHg	+1
Arterial blood oxygen saturation < 90%	+1



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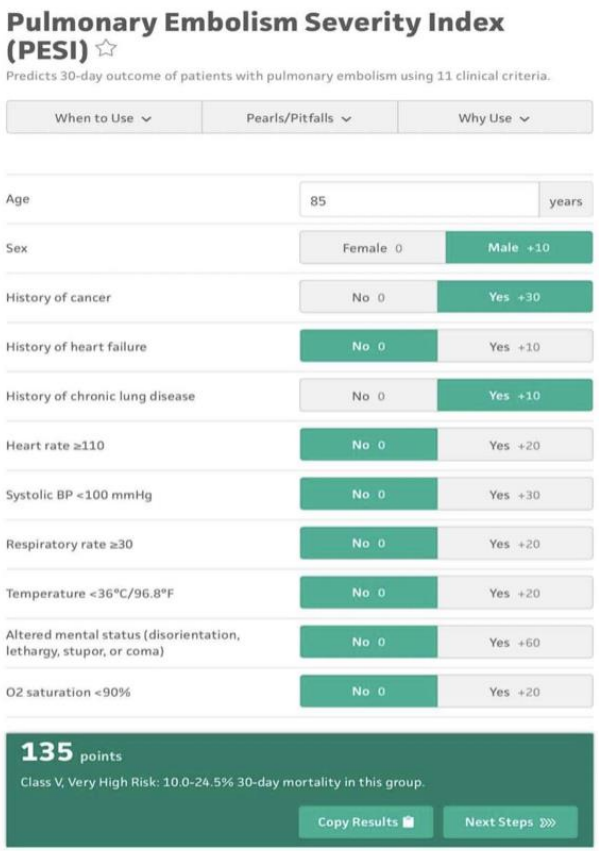
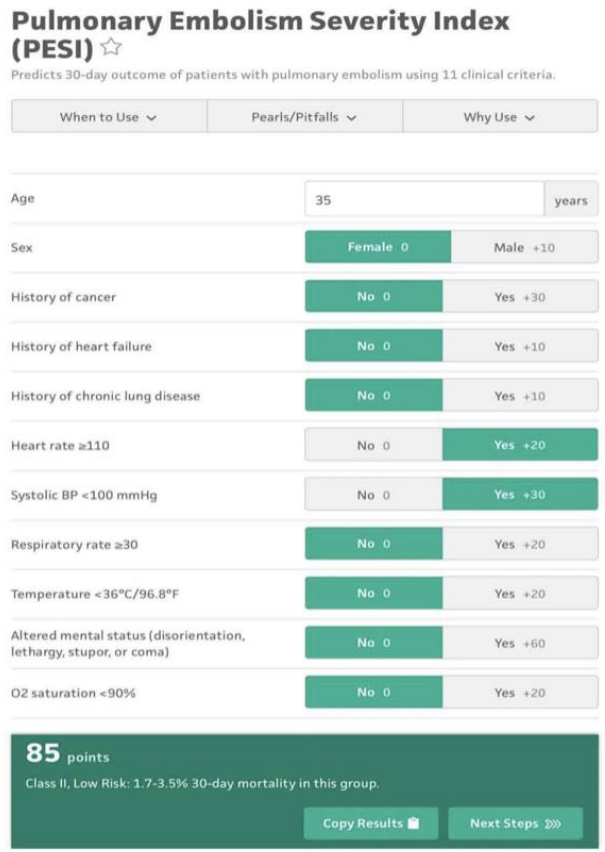
Current Risk Stratification

1. **PESI Score**
   - Designed to predict 30 day all cause mortality.
   - Heavy focus on epidemiological data

2. **BOVA Score**
   - Easy to use
   - Validated for hemodynamically stable patients
   - Does not stratify etiology of instability

Examples of how the PESI score fails in acute prognosis of PE





PESI score fails because it was designed to detect 30-day all-cause mortality (not short-term PE-related mortality).

- **Left panel**: PESI may categorize elderly patients with comorbidities as "very high risk" - even if they have a tiny pulmonary embolism and have no acute physiologic abnormality at all.
- **Right panel**: PESI may categorize young patients without comorbidities as "low risk" - even if they have hemodynamic instability.

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ACC/AHA Guidelines = Way behind

FIGURE 2 Risk Categories for Patients Presenting With Acute PE

Guidelines	Category	Hemodynamic Status	PE Severity Index (PESI) (or Simplified PESI)	Evidence of RV Dysfunction
American Heart Association (AHA, 2011)	Massive	Unstable	High	Typically Abnormal RV on Imaging, Elevated Troponin, OR Both
	Submassive	Stable	High	May Have Abnormal RV on Imaging OR Elevated Troponin OR Both
	Low Risk	Stable	Typically Low	None
European Society of Cardiology (ESC, 2019)	High Risk	Unstable	High	Typically Abnormal RV on Imaging, Elevated Troponin, OR Both
	Intermediate-High Risk	Stable	High	Abnormal RV on Imaging, AND Elevated Troponin
	Intermediate-Low Risk	Stable	High	May Have Abnormal RV on Imaging OR Elevated Troponin But Not Both
	Low Risk	Stable	Low	None

Although terminology may differ, risk stratification strategies are consistent in considering hemodynamics, clinical presentation, and evidence of RV dysfunction.
PESI = Pulmonary Embolism Severity Index; RV = right ventricular.

2020 JACC State of the Art Review: Advanced Management of Intermediate and High-Risk Pulmonary Embolism

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What percentage of PE presentations fall into Massive/Sub-massive category?

TABLE 84.1 Classification of Acute Pulmonary Embolism

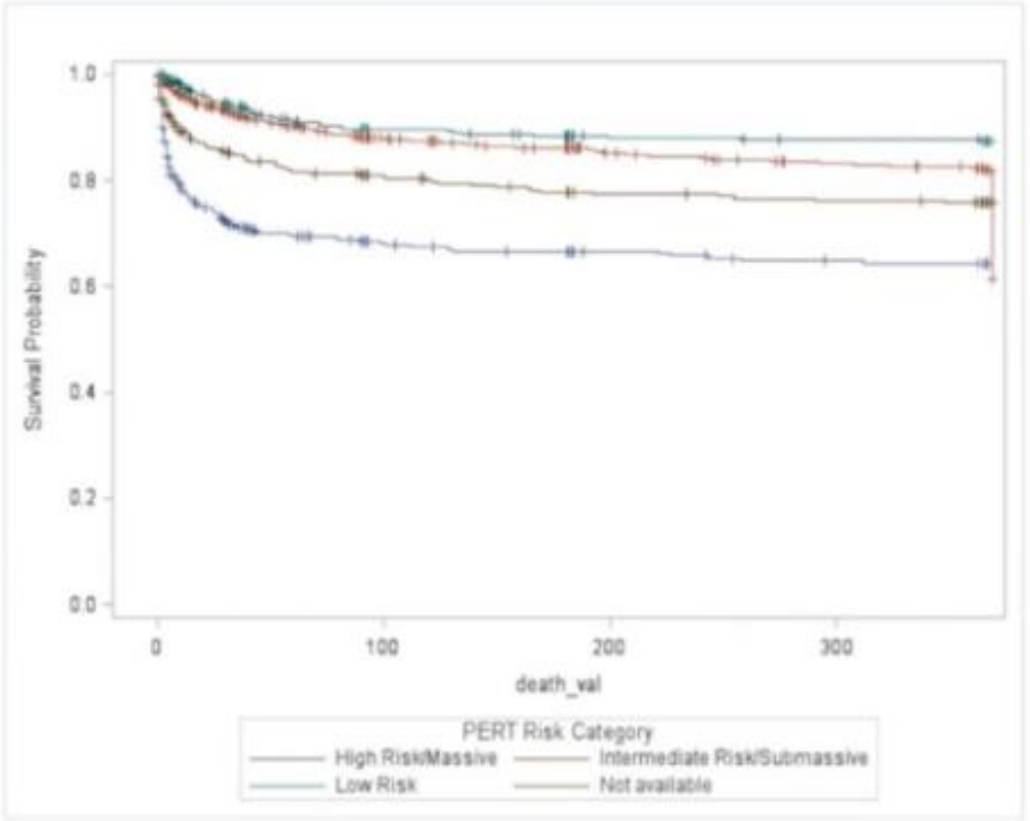
CATEGORY (FREQUENCY)	PRESENTATION	THERAPY
Massive PE (5% to 10%)	Systolic blood pressure < 90mmHg or poor tissue perfusion or multisystem organ failure plus extensive thrombosis, such as "saddle" PE or right or left main pulmonary artery thrombus	Anticoagulation (usually with high-dose intravenous UFH), plus advanced therapy: systemic thrombolysis, pharmacomechanical catheter–directed therapy, surgical embolectomy, and/or inferior vena cava (IVC) filter
Submassive PE, high risk (15%)	Hemodynamically stable but moderate or severe RV dysfunction or enlargement, coupled with biomarker elevation indicative of RV microinfarction and/or RV pressure overload	Anticoagulation until decision made regarding implementation of advanced therapy; controversy centers on this group. For systemic thrombolysis, reducing the rate of cardiovascular collapse and death must be balanced against the increased rate of hemorrhagic stroke.
Submassive PE, low risk (5% to 10%)	Hemodynamically stable with RV dysfunction or biomarker elevation, but not both	Anticoagulation followed by "watch and wait." Implement advanced therapy if there is clinical deterioration.
Small to moderate PE (70%)	Normal hemodynamics and normal RV size and function	Anticoagulation and consider brief hospital stay or entirely home therapy.

RV, right ventricular; *UFH*, unfractionated heparin.

PERT Consortium Data

Survival of PERT PE Patients

	All patients	PERT Risk Category		
		High Risk	Intermediate Risk	Low Risk
30 day mortality	10.2%	27.7%	6.7%	5.2%
1 year mortality	20.1%	35.6%	17.7%	12.5%



Role of Systemic Thrombolytics

1. Thrombolytic therapy in patients with hemodynamic instability (massive PE) is considered standard of care……based on very little RCT data

2. What remains controversial is the use of thrombolytic therapy in patients who are hemodynamically stable at the time of presentation.

Role of Systemic Thrombolytics

In patients who are hemodynamically stable, what does administration of thrombolytics do?

1. Prevent death?

2. Prevent Chronic thromboembolic pulmonary hypertension (CTEPH)?

3. Improve symptoms?

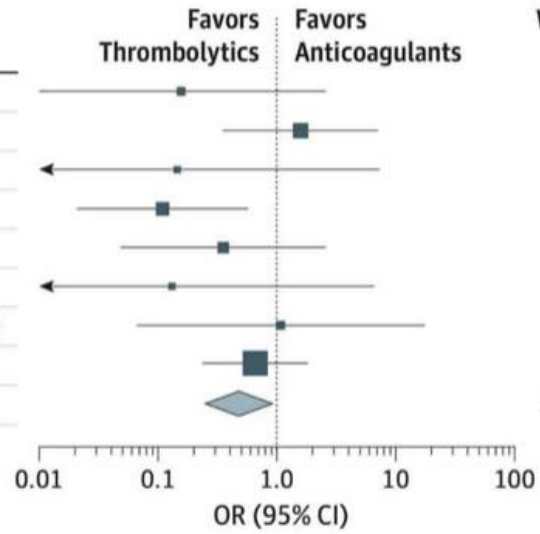
4. Prevent hemodynamic collapse?

Role of Systemic Thrombolytics

Figure 3. Odds of Mortality in Patients With Intermediate-Risk 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, %
Goldhaber et al,[2] 1993	0	46	2	55	0.16 (0.01-2.57)	5.3
Konstantinides et al,[3] 2002	4	118	3	138	1.58 (0.35-7.09)	18.4
TIPES,[29] 2010	0	28	1	30	0.14 (0.00-7.31)	2.7
Fasullo et al,[11] 2011	0	37	6	35	0.11 (0.02-0.58)	15.1
MOPETT,[10] 2012	1	61	3	60	0.35 (0.05-2.57)	10.5
ULTIMA,[30] 2013	0	30	1	29	0.13 (0.00-6.59)	2.7
TOPCOAT,[9] 2014	1	40	1	43	1.08 (0.07-17.53)	5.3
PEITHO,[8] 2014	6	506	9	499	0.66 (0.24-1.82)	40.0
Total	12	866	26	889	0.48 (0.25-0.92)	100.0

Heterogeneity: $\chi^2_7 = 7.63$; $P = .37$; $I^2 = 8\%$
Overall effect: $z = 2.22$; $P = .03$



Meta-analyses disagree about whether thrombolysis improves mortality in sub-massive PE. This analysis in JAMA found a mortality benefit, but other meta-analyses have not (Chatterjee S et al. JAMA 311:2414). *Any* evidence of benefit here (whether or not statistically significant) suggests that benefit exists for patients with *high-risk submassive PE* (because patients in the high-risk subgroup would be expected to have greater benefit than the entire pool of patients with both low-risk submassive PE and high-risk submassive PE).

Chatterjee S et al. JAMA 2014; 8(10);1382-1392

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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 mortal			64	.07
Major bleeding (			11	<.001
Age ≤65 y				
All-cause mortal			51	.09
Major bleeding (			176	.89
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

Major Bleeding: 10%+

ICH: 3%+

Chatterjee, et al. JAMA 2014

Impact of Thrombolytic Therapy on the Long-Term Outcome of Intermediate-Risk Pulmonary Embolism

5 year follow up from original PEITHO trial (NEJM 2014)

•Patients with sub-massive PE treated with UFH
•administration of tenecteplase reduced a composite outcome of all cause mortality and hemodynamic decompensation* at 7 days.

Tenecteplase was associated with increased rate of bleeding.

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Konstantinides, S et al. JACC 2016.12.039

ABSTRACT

BACKGROUND The long-term effect of thrombolytic treatment of pulmonary embolism (PE) is unknown.

OBJECTIVES This study investigated the long-term prognosis of patients with intermediate-risk PE and the effect of thrombolytic treatment on the persistence of symptoms or the development of late complications.

METHODS The PEITHO (Pulmonary Embolism Thrombolysis) trial was a randomized (1:1) comparison of thrombolysis with tenecteplase versus placebo in normotensive patients with acute PE, right ventricular (RV) dysfunction on imaging, and a positive cardiac troponin test result. Both treatment arms received standard anticoagulation. Long-term follow-up was included in the third protocol amendment; 28 sites randomizing 709 of the 1,006 patients participated.

RESULTS Long-term (median 37.8 months) survival was assessed in 353 of 359 (98.3%) patients in the thrombolysis arm and in 343 of 350 (98.0%) in the placebo arm. Overall mortality rates were 20.3% and 18.0%, respectively ($p = 0.43$). Between day 30 and long-term follow-up, 65 deaths occurred in the thrombolysis arm and 53 occurred in the placebo arm. At follow-up examination of survivors, persistent dyspnea (mostly mild) or functional limitation was reported by 36.0% versus 30.1% of the patients ($p = 0.23$). Echocardiography (performed in 144 and 146 patients randomized to thrombolysis and placebo, respectively) did not reveal significant differences in residual pulmonary hypertension or RV dysfunction. Chronic thromboembolic pulmonary hypertension (CTEPH) was confirmed in 4 (2.1%) versus 6 (3.2%) cases ($p = 0.79$).

CONCLUSIONS Approximately 33% of patients report some degree of persistent functional limitation after intermediate-risk PE, but CTEPH is infrequent. Thrombolytic treatment did not affect long-term mortality rates, and it did not appear to reduce residual dyspnea or RV dysfunction in these patients. (Pulmonary Embolism Thrombolysis study [PEITHO]; NCT00639743) (J Am Coll Cardiol 2017;69:1536–44) © 2017 by the American College of Cardiology Foundation.

Thrombolytics Not Used in Most Unstable PE Patients

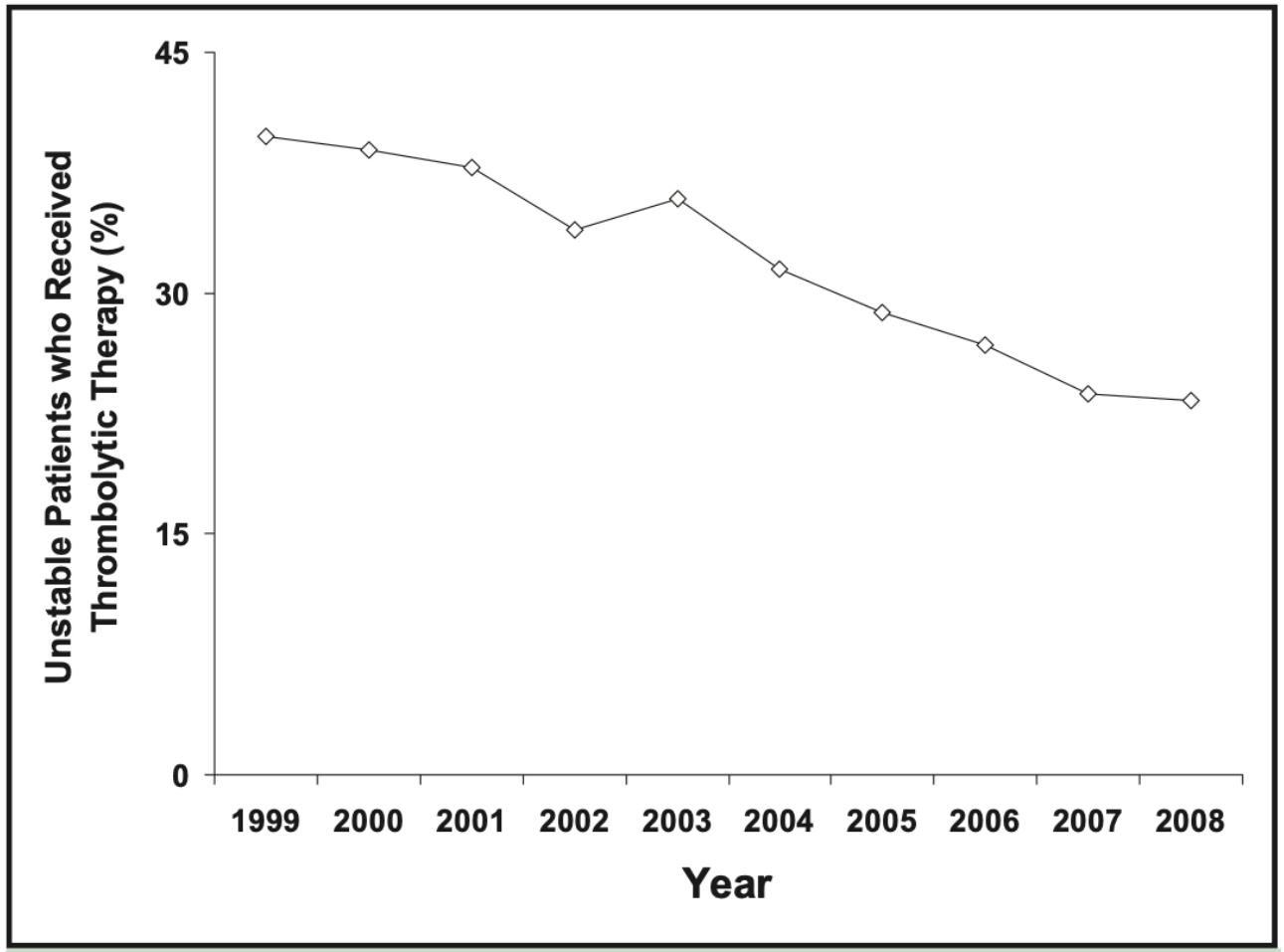
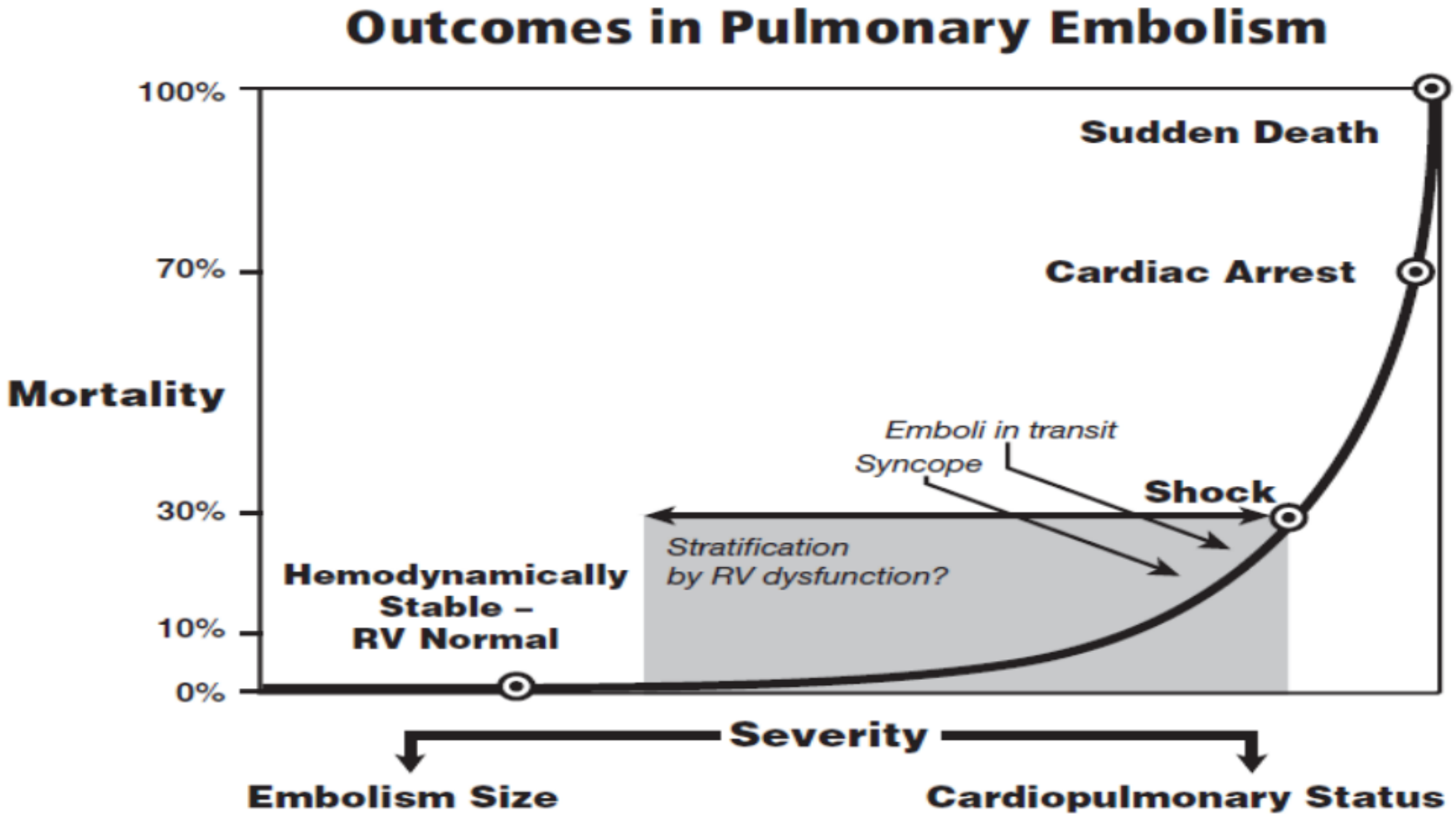


Figure 1 Proportion of unstable patients with pulmonary embolism who received thrombolytic therapy. The proportion decreased linearly from 1999 to 2008 ($r = -0.9797$, slope -1.1998 %/year, $P < .0001$).

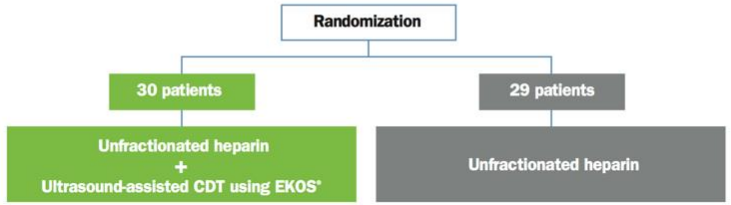
Stein et al., Am J Med 2012

Rationale for Advanced Therapy



Nils Kucher, MD et al. Circulation 2014; 129: 479-486

Patients: Acute PE with RV/LV ratio ≥ 1.0

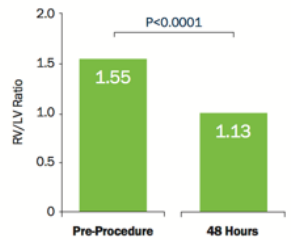


ULTIMA: EKOS vs. UFH

ULTIMA confirme
using EKOS® regi
at

Acute massive and submassive PE patients treated with EKOS® showed:

25% decrease in RV/LV ratio over 48 hours



Minimized risk 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. 2015)	0/150 (0%)

SEATTLE II: EKOS single arm trial
(n=150; 22 centers)

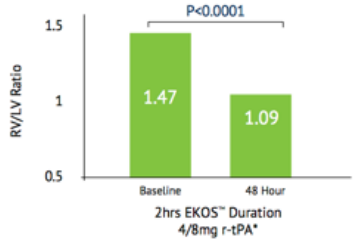
sis for acute PE improves
angiographic obstruction.
potential "game-changer"
nts.

OPTALYZE PE: EKOS 4 Cohorts
(n= 101; 17 centers across US)

Acute PE patients treated with EKOS™ showed the following improvements:

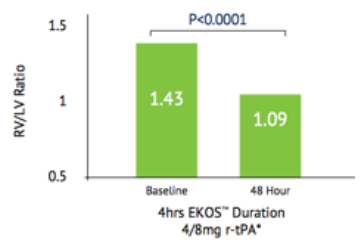
- **Significant reduction in RV/LV ratios in all cohorts at 48 hours post initiation of procedure**
- **RV/LV ratio reduced by 24% (P<0.0001) for the two-hour cohort using only 4mg of r-tPA per catheter**
- **All cohorts had zero to very low bleeding rates[1]**

Cohort 1
24% Reduction in RV/LV Ratio



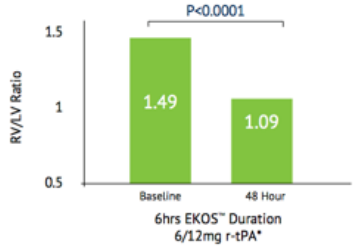
2hrs EKOS™ Duration
4/8mg r-tPA*

Cohort 2
23% Reduction in RV/LV Ratio



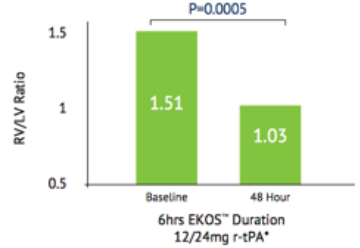
4hrs EKOS™ Duration
4/8mg r-tPA*

Cohort 3
26% Reduction in RV/LV Ratio



6hrs EKOS™ Duration
6/12mg r-tPA*

Cohort 4
26% Reduction in RV/LV Ratio



6hrs EKOS™ Duration
12/24mg r-tPA*

CONCLUSION

The EKOS™ system's very-low-dose and short-duration regimens in the OPTALYSE PE trial appear to be as acutely effective as the regimens in other EKOS™ studies (ULTIMA & SEATTLE II), pointing to a paradigm-changing approach for PE treatment. These results offer physicians a new treatment standard for proven PE clinical efficacy and safety.

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PA Catheter Directed Thrombolysis Devices

Cragg-McNamara
- 4-5 F
- 100 cm catheter length
- 5-10 cm infusion length

Unifuse
- 4-5 F
- 100 cm catheter length
- 5-10 cm infusion length

EKOS
- 5F
- 100 cm catheter length
- 5-10 cm infusion length

Thrombolex
- 7F
- Nitinol Expandable Basket

STANDARD

SPECIALIZED

HI-PEITHO

The Higher-risk Pulmonary Embolism Thrombolysis Study

- Prospective multicenter, **randomized controlled trial** - 1:1 randomization
- Multicenter, multinational - up to **65 sites in the US and Europe**
- Patients - **Acute intermediate-high-risk pulmonary embolism**
- Treatment arms
  - **EkoSonic® Endovascular System and Best Medical Therapy**
  - **Control: Best Medical Therapy (systemic anticoagulation)**
- Primary endpoint - **Safety** - composite of PE-related mortality, cardiorespiratory decompensation or collapse, non-fatal PE recurrence within 7 days
- 1-Year follow up

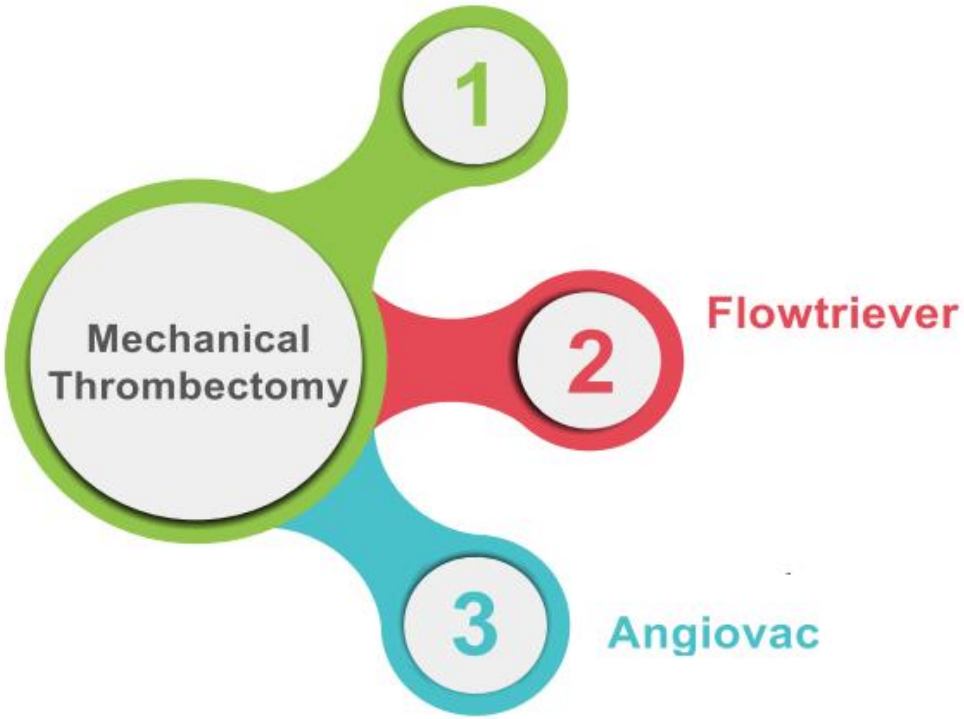
PIs: Stavros Konstantinides, MD | Kenneth Rosenfield, MD

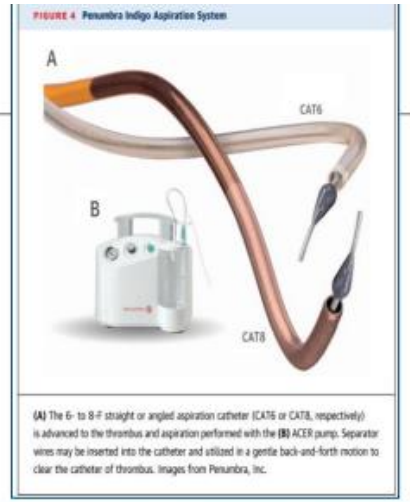
3-way Partnership

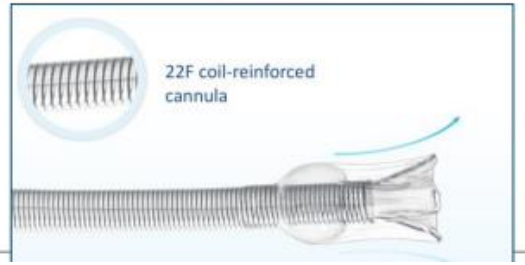
PERT Consortium | University Mainz/PEITHO Network | Boston Scientific Corporation

FI-P003104-A

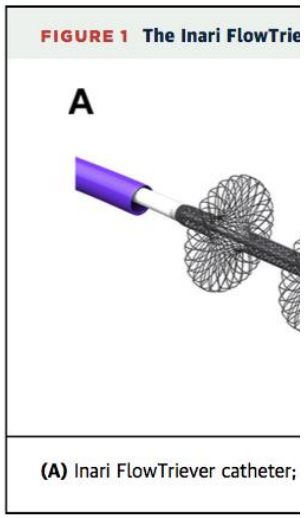
Mechanical Thrombectomy Options



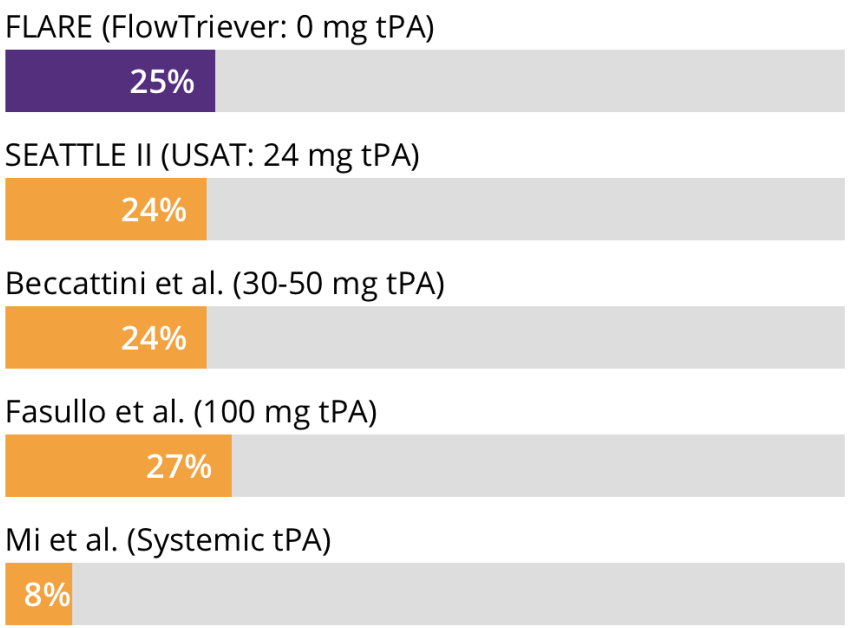




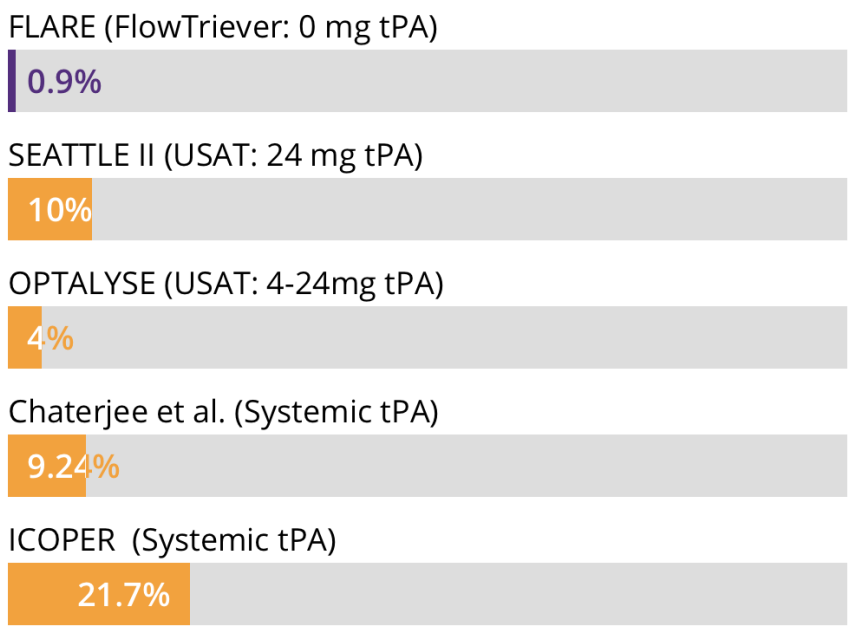
FLARE in Context[1]



Reduction in RV/LV Ratio at 48 hours



Major Bleeding Rates



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SAFETY RESULTS

FLASH

Mortality through 48 hours: 0/230 (0%)
Mortality through 30 days: 1/227 (0.4%)*

**3 patients lost to f/u. 80-year-old female experienced fatal cardiac arrest due to septic shock and ischemic bowel 12 d post-procedure.*

Primary Endpoint 48h MAE: 3/230 (1.3%)

- 0 device-related deaths
- 3 major bleeds (non-ICH)
- 0 intraprocedural device or procedure-related AEs
  - 0 clinical deteriorations
  - 0 device-related pulmonary vascular injuries
  - 0 device-related cardiac injuries

Total readmissions through 30 days: 14/209 (6.7%)
PE-related readmissions through 30 days: 1/209 (0.5%)

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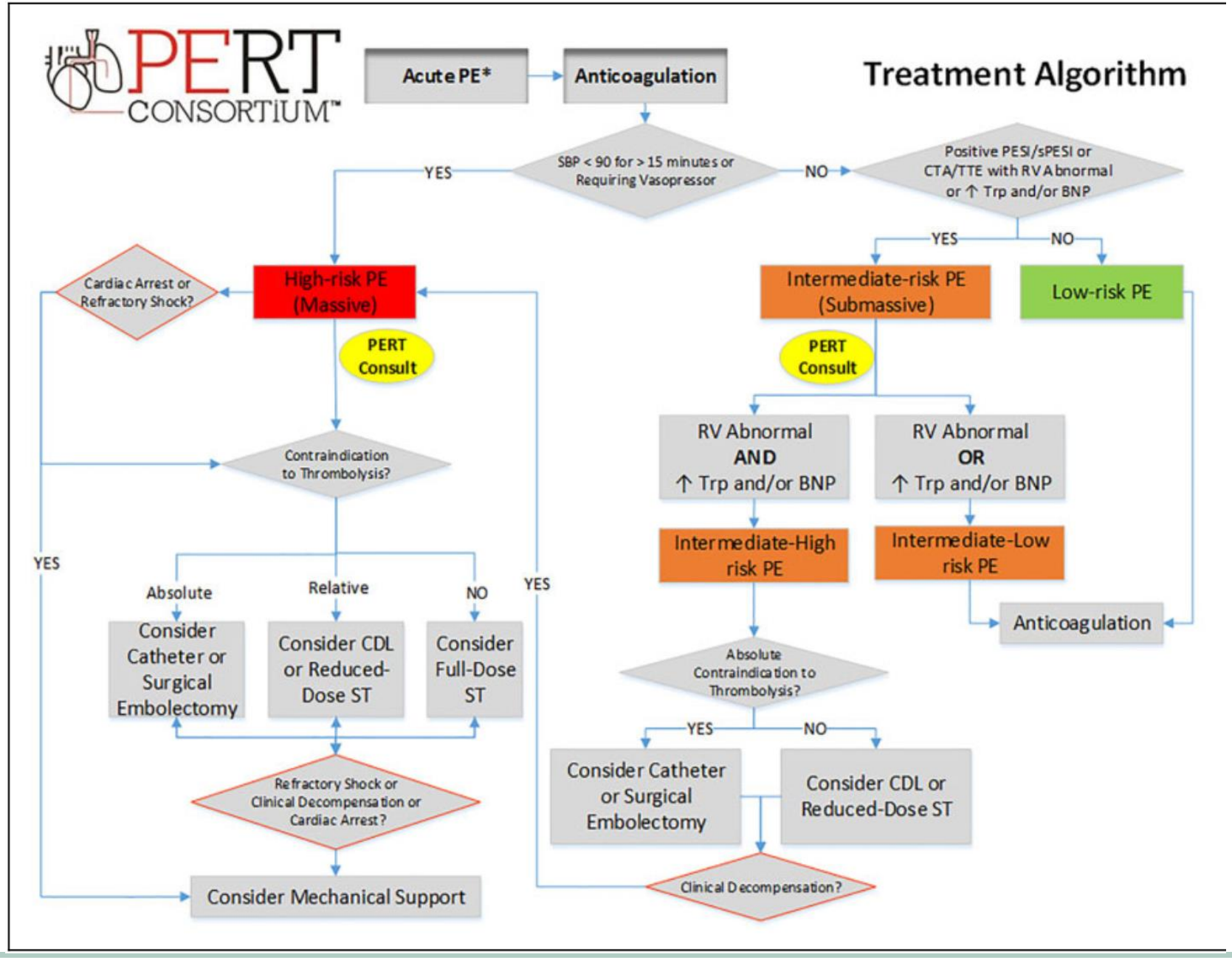
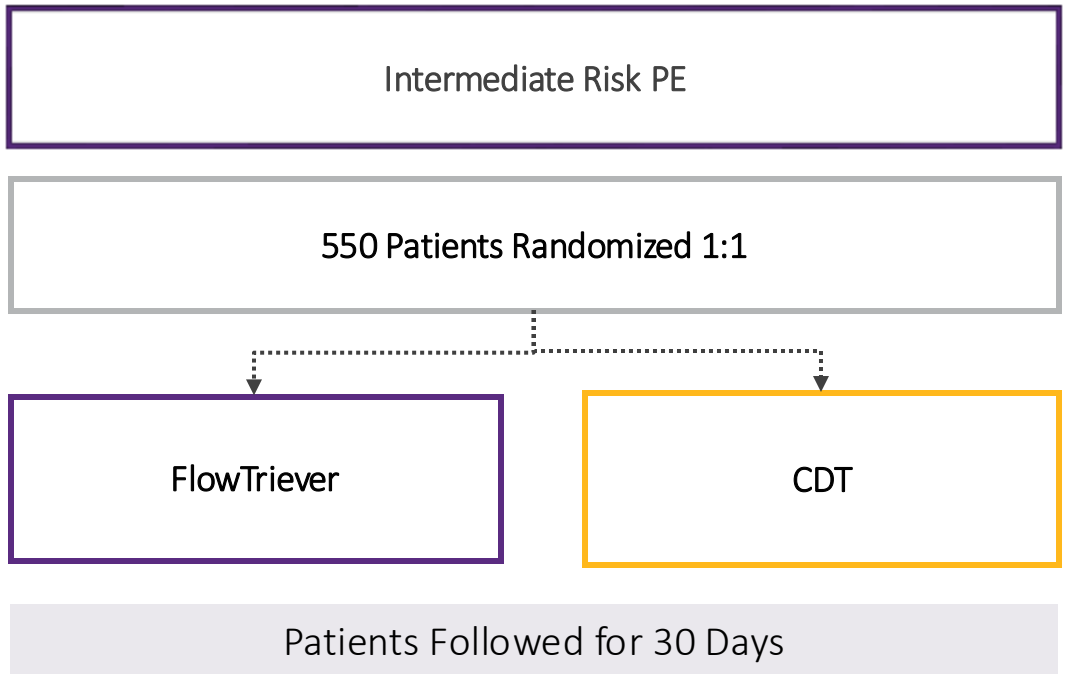

PERT CONSORTIUM™
Treatment Algorithm
Acute PE*
Anticoagulation
SBP < 90 for > 15 minutes or Requiring Vasopressor
YES
NO
Positive PESI/sPESI or CTA/TTE with RV Abnormal or ↑ Trp and/or BNP
YES
NO
Cardiac Arrest or Refractory Shock?
High-risk PE (Massive)
PERT Consult
Intermediate-risk PE (Submassive)
PERT Consult
Low-risk PE
Contraindication to Thrombolysis?
YES
Absolute
Relative
NO
Consider Catheter or Surgical Embolectomy
Consider CDL or Reduced-Dose ST
Consider Full-Dose ST
Refractory Shock or Clinical Decompensation or Cardiac Arrest?
Consider Mechanical Support
YES
RV Abnormal AND ↑ Trp and/or BNP
RV Abnormal OR ↑ Trp and/or BNP
Intermediate-High risk PE
Intermediate-Low risk PE
Anticoagulation
Absolute Contraindication to Thrombolysis?
YES
NO
Consider Catheter or Surgical Embolectomy
Consider CDL or Reduced-Dose ST
Clinical Decompensation?

PEERLESS: RCT of FlowTriever vs. CDT in PE

PEERLESS

Superiority RCT of FlowTriever vs. CDT in PE



Currently, Catheter Directed Thrombolysis (CDT) is used in nearly half of interventions commercially*

Primary endpoint via win ratio:

- All-Cause Mortality
- Intracranial Hemorrhage
- ISTH Major Bleeding
- Clinical Deterioration/Bailout
- ICU Admission & ICU LOS

Definitive advanced therapy treatment trial for PE

*Based on third party data and Inari management estimates.

Circulation

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LARGE-BORE MECHANICAL THROMBECTOMY VERSUS CATHETER-DIRECTED THROMBOLYSIS IN THE MANAGEMENT OF INTERMEDIATE-RISK PULMONARY EMBOLISM: PRIMARY RESULTS OF THE PEERLESS RANDOMIZED CONTROLLED TRIAL

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CIRCULATION

HTTPS://WWW.AHAJOURNALS.ORG/DOI/10.1161/CIRCULATIONAHA.124.072364

SCAN TO VIEW

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Trial design

Eligibility criteria

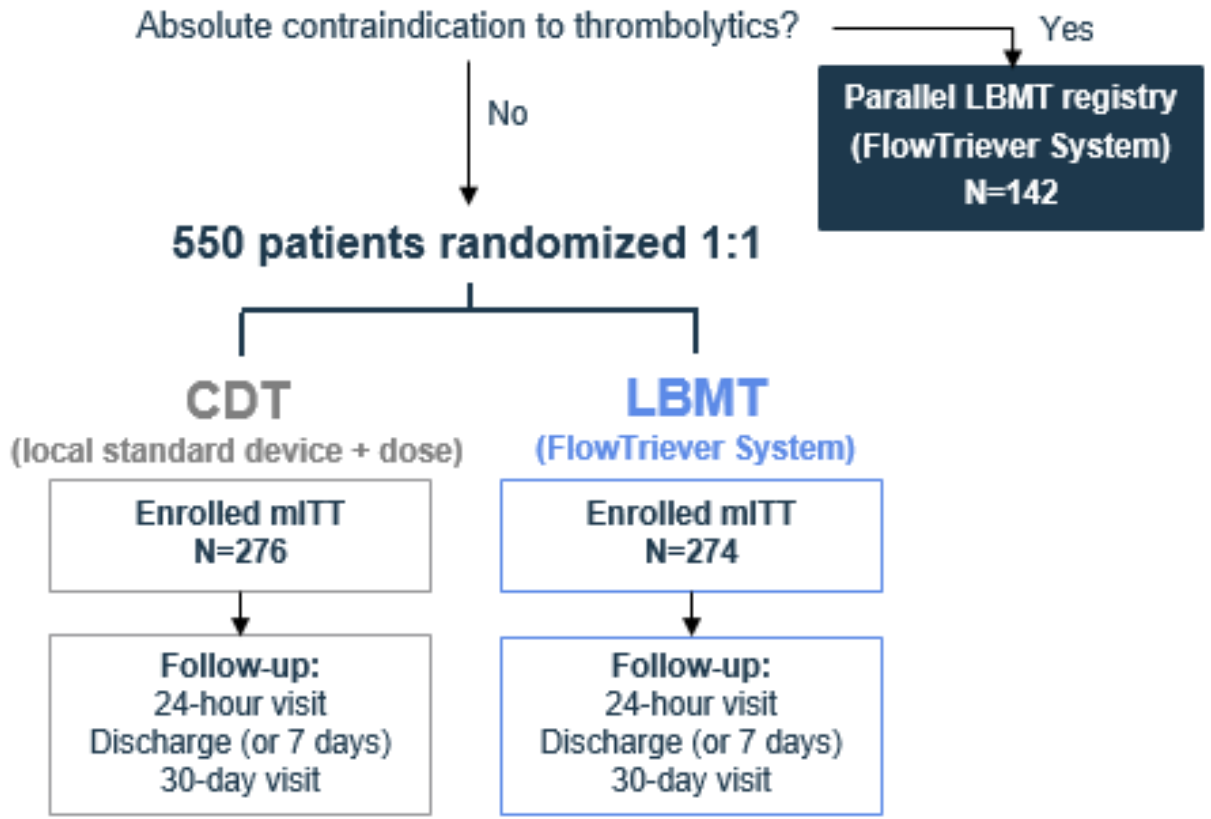
Inclusion

- SBP > 90 mmHg + central clot + RV dysfunction
- Symptom onset within 14 days
- Intervention planned within 72 hours
- + ≥ 1 additional clinical risk factor
  - Elevated cardiac troponin
  - History of heart failure
  - History of chronic lung disease
  - Heart rate ≥ 110 bpm
  - SBP < 100 mmHg
  - RR ≥ 30 breaths per min
  - Oxygen saturation < 90%
  - Syncope related to PE
  - Elevated lactate

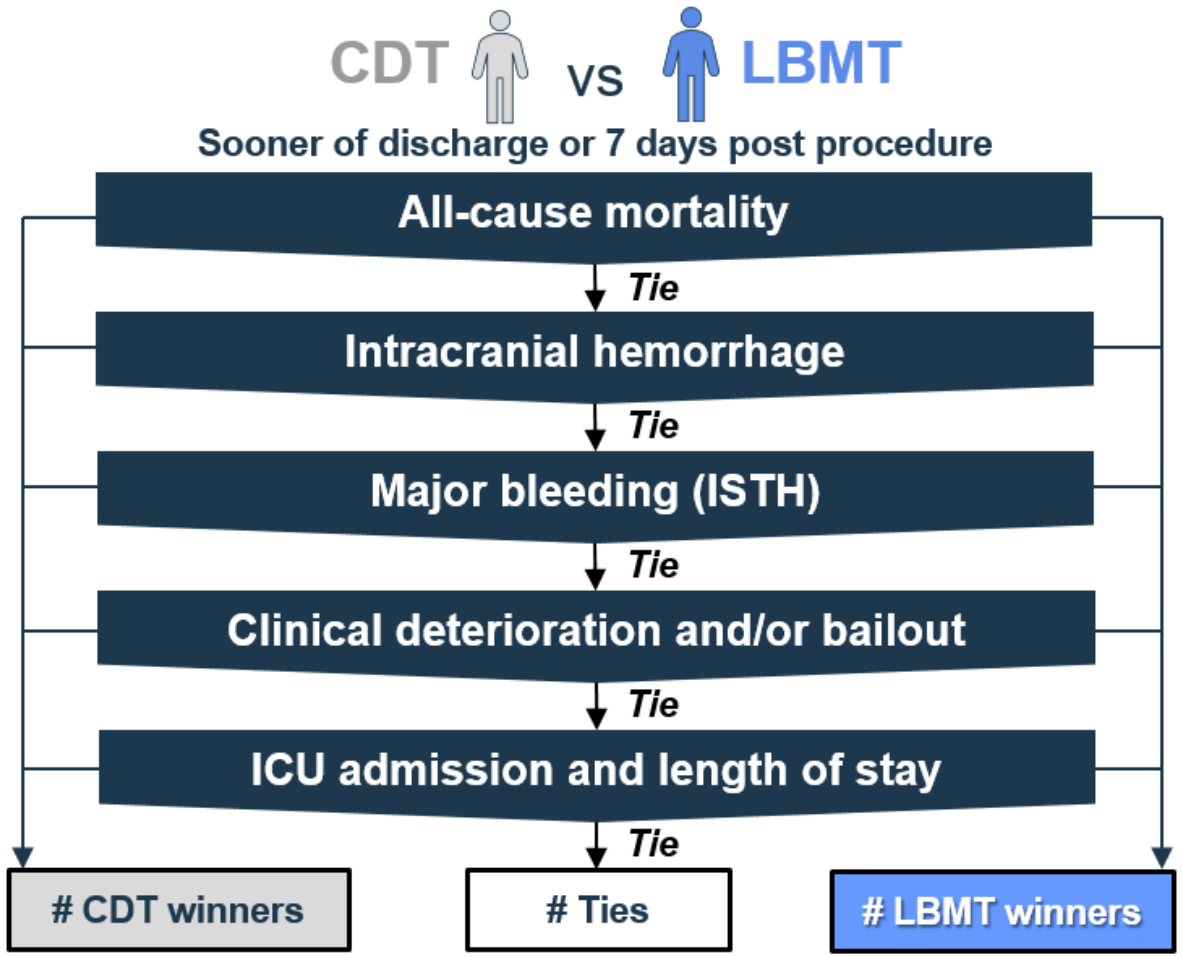
Exclusion

- Unable to receive AC
- Right heart clot in transit
- Life expectancy < 30 days
- CTEPH/CTED
- sPAP ≥ 70 mmHg on invasive hemodynamics

Treatment and follow-up



Primary



Secondary

Win ratio components assessed individually Win ratio of first 4 components of primary endpoint Clinically relevant non-major and minor bleeding	Discharge (or 7 days)
Change in RV/LV ratio from baseline Dyspnea score (mMRC and Borg*) RV function* (echo) Respiratory rate* NYHA classification*	24h visit
All-cause mortality All-cause and PE-related readmissions Hospital length of stay Dyspnea score (mMRC and Borg*) PEmb-QOL and EQ-5D-5L NYHA classification* Device- or drug-related SAEs	30 days or 30d visit

All safety endpoints were adjudicated by an independent CEC

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Patient population

Enrollment:

57 sites in the USA, Germany, and Switzerland

February 2022 to February 2024

Baseline Characteristics	CDT N = 276	LBMT N = 274
Age, years	61.2 ± 14.8	63.7 ± 13.0
Female sex	134 (48.6)	125 (45.6)
Race and ethnicity		
White	193 (74.5)	184 (72.4)
Black or African American	56 (21.6)	67 (26.4)
Other	10 (3.9)	3 (1.2)
Hispanic or Latino	27 (10.8)	13 (5.2)
Relative contraindication to lytics	11 (4.0)	12 (4.4)
VTE-BLEED score ≥ 2	77 (27.9)	68 (24.8)
BMI, kg/m^2	36.3 ± 9.4	34.5 ± 8.6
Active cancer	17 (6.2)	13 (4.7)
Concomitant DVT	168 (60.9)	178 (65.0)
Saddle PE	109 (39.5)	104 (38.0)
Elevated cardiac troponin	265 (96.0)	256 (93.4)
RV/LV ratio (CTPA or echo)	1.31 ± 0.27	1.27 ± 0.26
Mean PA pressure, mmHg	31.1 ± 7.2	30.0 ± 7.6

Values reported as mean ± SD or n (%). Other race category includes patients self-reporting as American Indian or Alaska Native, Asian, "Other" race, or multiple races. Sample size: N=259-276 for CDT, N=254-274 for LBMT.

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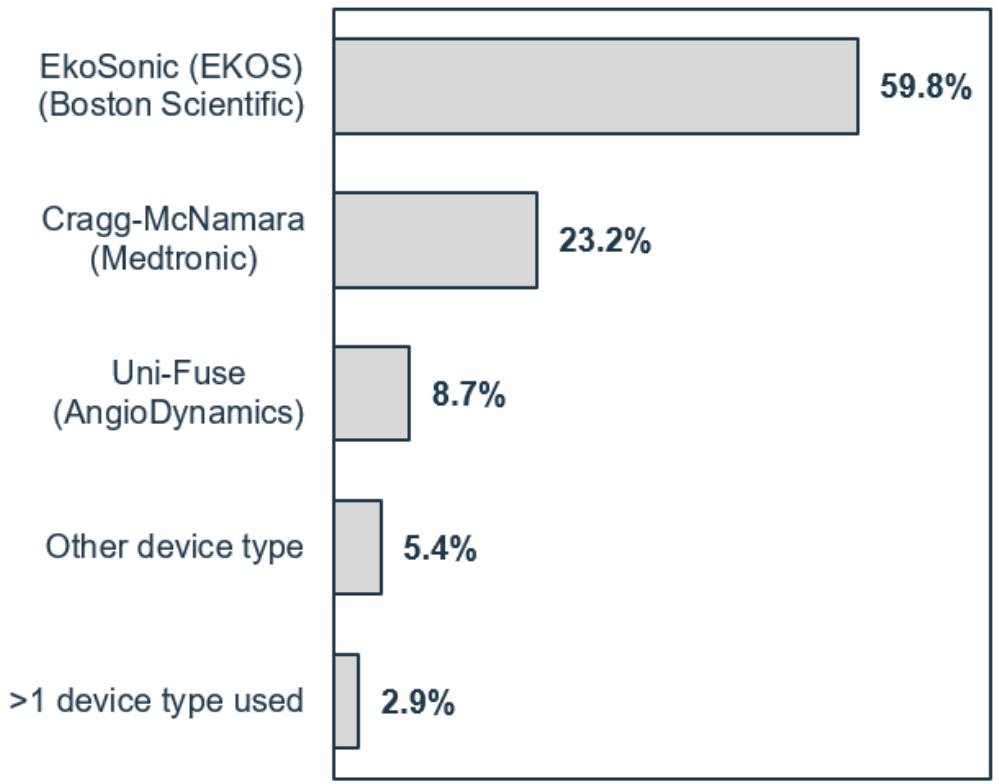
Device and procedure information

CDT device used



	CDT N = 276
tPA infusion rate per lung, mg/hour	1.0 [0.5, 1.0]
tPA infusion duration per lung, hours	12.0 [6.0, 15.6]
Total tPA dose per patient, mg	16.0 [12.0, 24.0]

Values reported as median [IQR].
tPA infusion rate and duration per lung: N=242.
Total tPA dose: N=261.

	CDT N = 276	LBMT N = 274
Procedure time, minutes	65.3 ± 42.5	93.2 ± 36.1
Treatment catheter dwell time, minutes	915.7 ± 464.7	47.9 ± 27.2
Estimated blood loss, mL	14.4 ± 22.2	87.7 ± 87.6
Time from admission to therapy, hr	22.3±17.7	24.8±19.6

Values reported as mean ± SD.
Procedure time: N=274 CDT, N=272 LBMT.
Treatment catheter dwell time: N=269 CDT, N=272 LBMT.
Estimated blood loss: N=228 CDT, N=245 LBMT.

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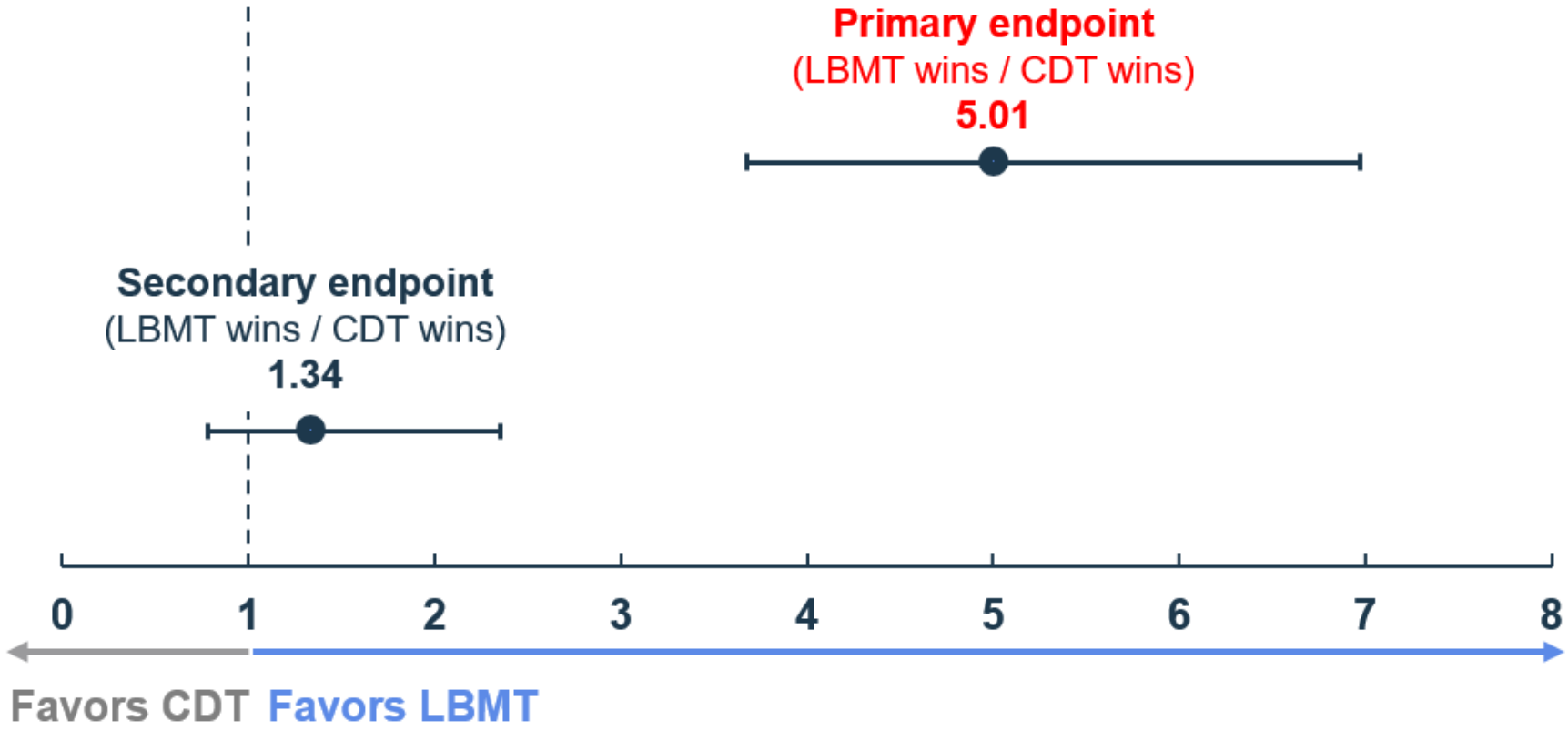
Results: Win ratio endpoints

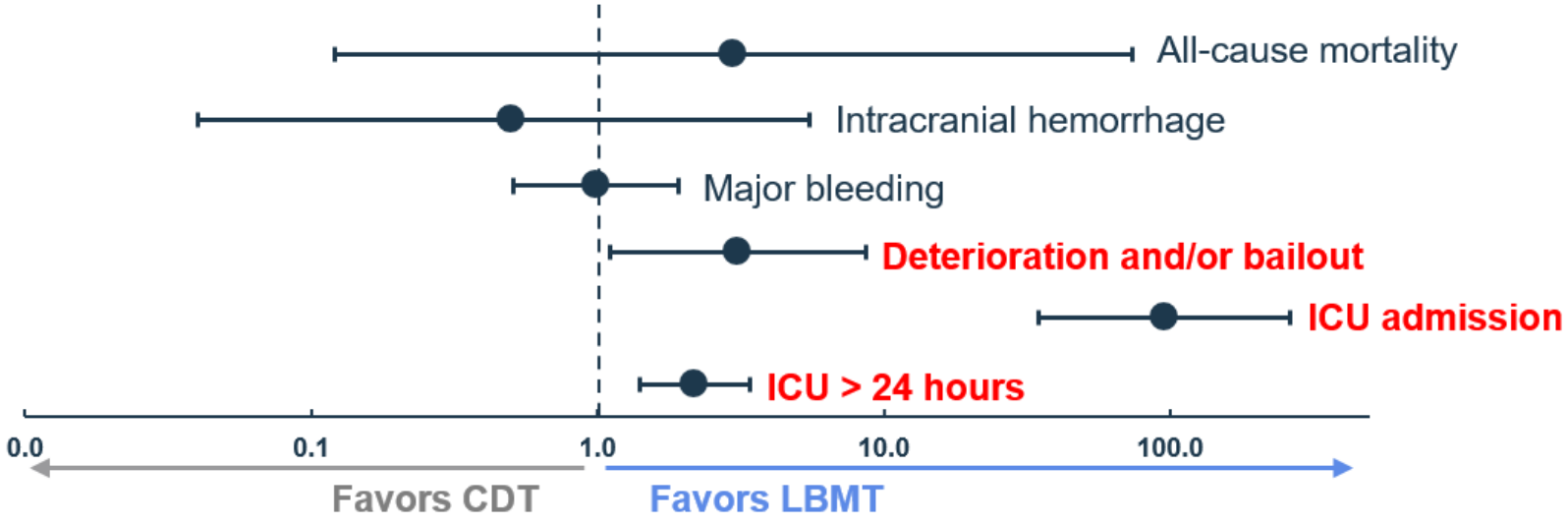


	Win ratio [95% CI]	*P* value
Primary Endpoint: 5-component win ratio*	5.01 [3.68 – 6.97]	**<0.001**
Secondary Endpoint: 4-component win ratio†	1.34 [0.78 – 2.35]	0.30

*Primary endpoint components:
1) all-cause mortality, 2) intracranial hemorrhage, 3) major bleeding, 4) clinical deterioration and/or escalation to a bailout therapy, and 5) ICU admission and length of stay.

†Secondary endpoint components:
1) all-cause mortality, 2) intracranial hemorrhage, 3) major bleeding, and 4) clinical deterioration and/or escalation to a bailout therapy.

Results: Win ratio components



	CDT events	LBMT events	Odds ratio [95% CI]	*P* value
All-cause mortality	1 (0.4)	0 (0.0)	2.99 [0.12–73.70]	1.00
Intracranial hemorrhage	1 (0.4)	2 (0.7)	0.50 [0.04–5.51]	0.62
Major bleeding	19 (6.9)	19 (6.9)	0.99 [0.51–1.92]	1.00
Clinical deterioration and/or escalation to bailout therapy	15 (5.4)	5 (1.8)	3.09 [1.11–8.63]	**0.038**
Postprocedural ICU admission	272 (98.6)	114 (41.6)	95.4 [34.6–263.6]	**< 0.001**
ICU stay > 24 hours*	178 (65.4)	53 (46.5)	2.18 [1.40–3.40]	**< 0.001**

Values reported as n (%) or OR [95% CI]. *P* values calculated using two-sided Fisher's exact test. ICH: N=275 CDT. *Percentages reported out of patients with postprocedure ICU admission.

Bleeding events through discharge / 7 days

	CDT N = 276	LBMT N = 274	*P* value
Major bleeding (ISTH)	**19 (6.9)**	**19 (6.9)**	1.00
Adjudicated reasons for major bleeding			
Fatal bleeding*	1 (0.4)	0 (0)	
Symptomatic bleeding in a critical area or organ‡	2 (0.7)	2 (0.7)	
Intracranial hemorrhage†	1	2	
Hemarthrosis	1	0	
Hgb drop ≥ 2 g/dL (1.24 mmol/L) and/or transfusion ≥ 2 units	16 (5.8)	17 (6.2)	
Access site source	10	8	
Transfusions administered	8	1	
# units transfused	3.3 ± 1.8	2.0	
Clinically relevant non-major bleeding events‡	9 (3.3)	7 (2.6)	0.80
Minor bleeding events‡	1 (0.4)	6 (2.2)	0.07

Values reported as n (%) or mean ± SD. *P* values calculated using two-sided Fisher's exact test. *CDT fatal bleeding involved thrombolytic- and anticoagulation-related intra-abdominal hematomas leading to hemorrhagic shock and death on postprocedural Day 5. †CDT ICH involved thrombolytic- and anticoagulation-related cerebral hemorrhage on Day 1 (n=1); LBMT ICH involved anticoagulation-related cerebral hemorrhage on Day 1 in a patient who had a fall with minor head trauma prior to treatment (n=1) and anticoagulation-related ischemic stroke with hemorrhagic conversion on Day 2 (n=1). ‡N=275 CDT.

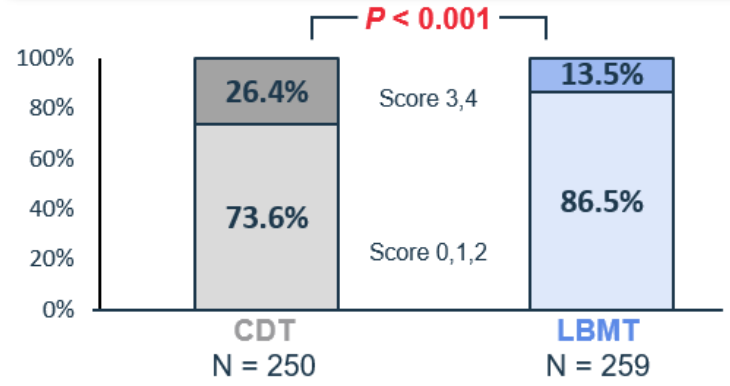
Clinical deterioration and therapy escalation events through discharge / 7 days

	CDT N = 276	LBMT N = 274	*P* value
Clinical deterioration and/or escalation to bailout	**15 (5.4)**	**5 (1.8)**	**0.038**
Patients with clinical deterioration	10 (3.6)	4 (1.5)	
Cardiac arrest	2 (0.7)	0 (0.0)	
High-grade atrioventricular block	1 (0.4)	0 (0.0)	
Respiratory failure	3 (1.1)	0 (0.0)	
Increased oxygen requirement	0 (0.0)	1 (0.4)	
Hypotension	4 (1.4)	3 (1.1)	
Patients with escalation to bailout	6 (2.2)	1 (0.4)	
Successful bailout†	5 (1.8)	0 (0.0)	
Unsuccessful bailout‡	1 (0.4)	1 (0.4)	

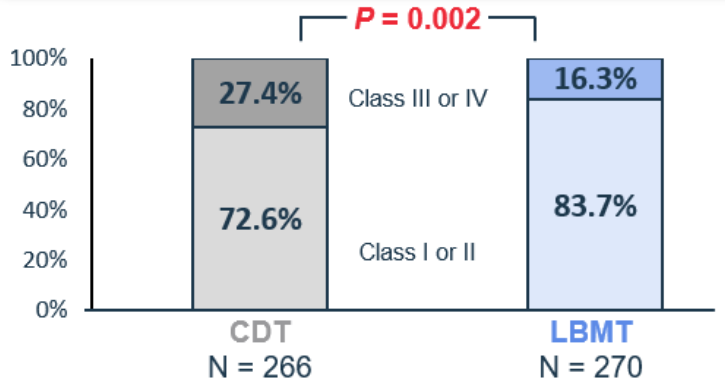
Values reported as n (%). *P* value calculated using two-sided Fisher's exact test. Bailout: N=275 CDT. †5 CDT patients underwent LBMT bailout procedure without adverse event, experienced postprocedural improvement, and were discharged without further intervention. ‡1 patient in each arm had a PE that could not be treated after multiple bailout attempts (systemic tPA, LBMT, CDT) and ultimately died after >7 days.

Clinical and imaging outcomes at 24-hour visit

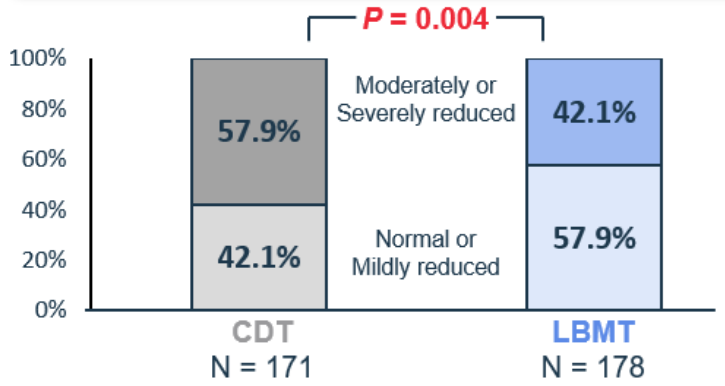
mMRC dyspnea score



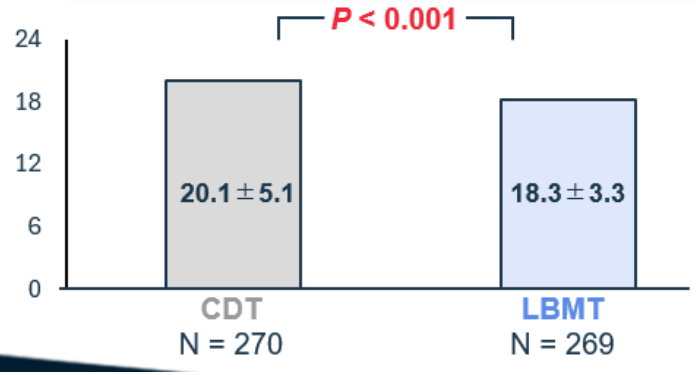
NYHA classification



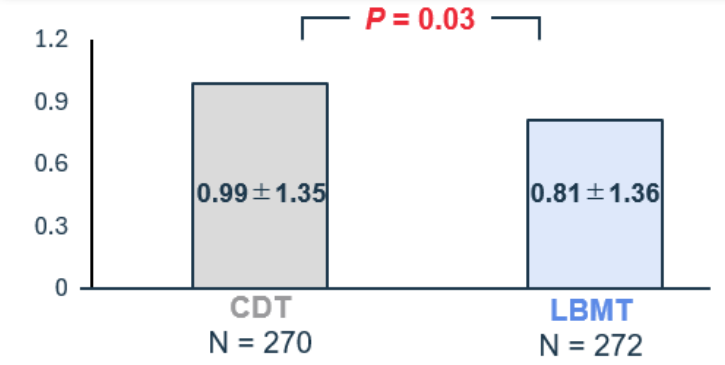
RV function (echo)



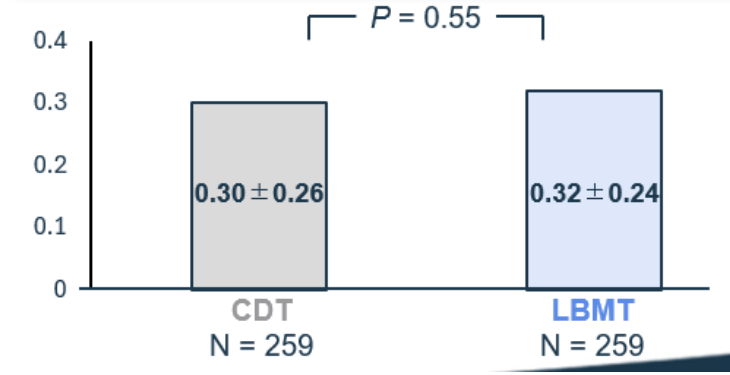
Respiratory rate (breaths/min)



Modified Borg dyspnea score at rest



Reduction in RV/LV ratio from baseline



Hospital length of stay and 30-day readmissions

	CDT N = 276	LBMT N = 274	*P* value
Total hospital LOS, days	5.3 ± 3.9	4.5 ± 2.8	**0.002**
Postprocedure LOS, days	4.0 ± 3.7	3.2 ± 2.7	**< 0.001**
Postprocedure ICU admission	272 (98.6)	114 (41.6)	**< 0.001**
stay ≤ 24 hours	94 (34.1)	61 (22.3)	**< 0.001**
stay > 24 hours	178 (64.5)	53 (19.3)	
Postprocedure ICU LOS, hours	39.3 ± 28.0	14.2 ± 25.4	**< 0.001**
30-day all-cause readmission†	19 (7.9)	8 (3.2)	**0.03**
30-day PE-related readmission†	2 (0.8)	0 (0.0)	0.237

Values reported as n (%) or mean ± SD. †30-day readmission: N=239 CDT, N=251 LBMT. Total and postprocedure hospital stay reported through 30 days. Postprocedure ICU stay reported through discharge / 7 days. *P* values calculated using two-sided Fisher's exact test or two-sided Wilcoxon rank sum test with continuity correction.

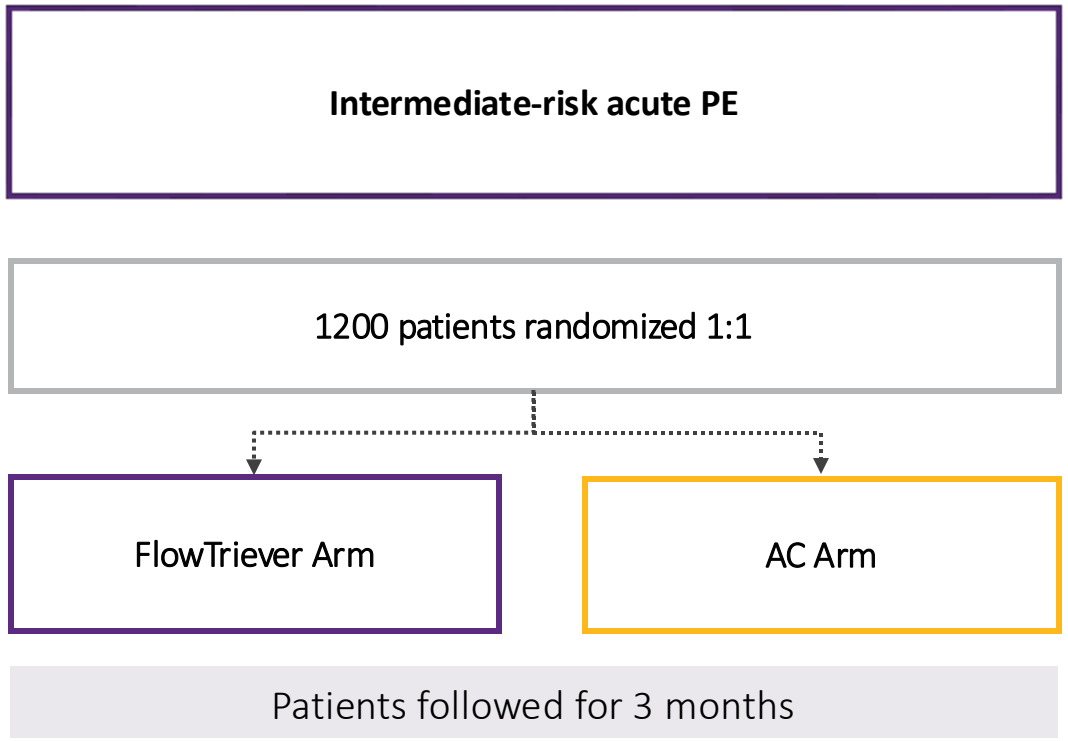
Conclusions

- PEERLESS met its primary endpoint, demonstrating superiority of LBMT compared to CDT in the treatment of acute intermediate-risk PE
- There was no difference between groups in:
  - mortality (very low in both arms), ICH, or major bleeding
- Compared to CDT, LBMT was associated with:
  - Less clinical deterioration or escalation of therapy
  - Faster clinical and hemodynamic improvement at 24 hours
  - Less ICU use and shorter hospital length of stay
  - Fewer readmissions through 30 days

PEERLESS II: RCT of FlowTriever vs. anticoagulation alone in acute PE

PEERLESS II

RCT of FlowTriever vs. anticoagulation alone in pulmonary embolism



Designed to evaluate whether anticoagulation alone or large-bore volume-controlled aspiration thrombectomy should be standard of care for intermediate-risk PE

Primary endpoint hierarchy (win ratio):

- All-cause mortality by 30 days
- Clinical deterioration and/or bailout by 30 days
- All-cause hospital readmission by 30 days
- Dyspnea score at 48-hour visit

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EU Principal Investigators:

Bernhard Gebauer, MD
Interventional Radiology
Charité University Hospital Berlin

Felix Mahfoud, MD
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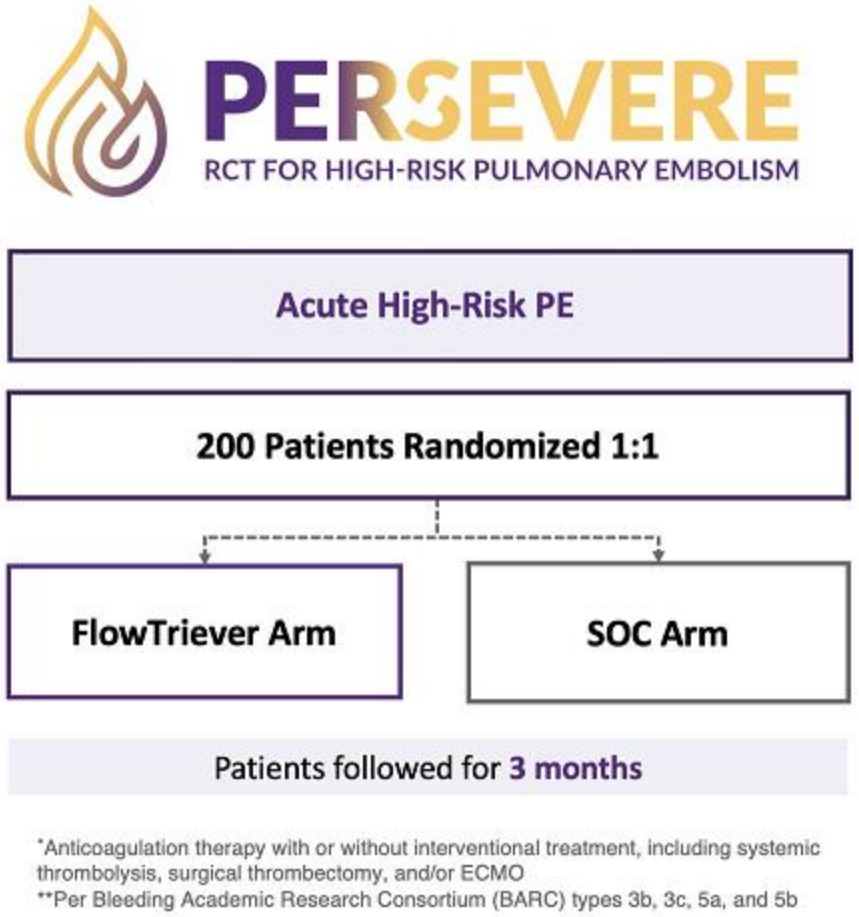
Saarland University Hospital Homburg

Indications for Use: The FlowTriever Retrieval/Aspiration system is indicated for (1) the non-surgical removal of emboli and thrombi from blood vessels; and (2) the injection, infusion, and/or aspiration of contrast media and other fluids into or from a blood vessel. The FlowTriever Retrieval/Aspiration system is intended for use in the peripheral vasculature and for the treatment of pulmonary embolism. The Triever catheters are also intended for use in treating clot in transit in the right atrium, but not in conjunction with FlowTriever catheters. Refer to IFU for complete indications for use, contraindications, warnings, and precautions. Caution: Federal (USA) law restricts this device to sale distribution and use by or on order of a physician.

Finally, some RCT data in High-Risk PE!



Designed to evaluate whether large-bore volume-controlled mechanical thrombectomy vs SOC* should be the guideline-recommended first-line therapy for high-risk PE

Composite Primary Endpoint

Through the earlier of initial hospital discharge or 7 days:

- All-cause mortality
- Cardiac arrest with loss of consciousness requiring CPR
- Bailout to an alternate therapeutic strategy
- Major bleeding**
- Persistent need for ECMO

Thank you

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