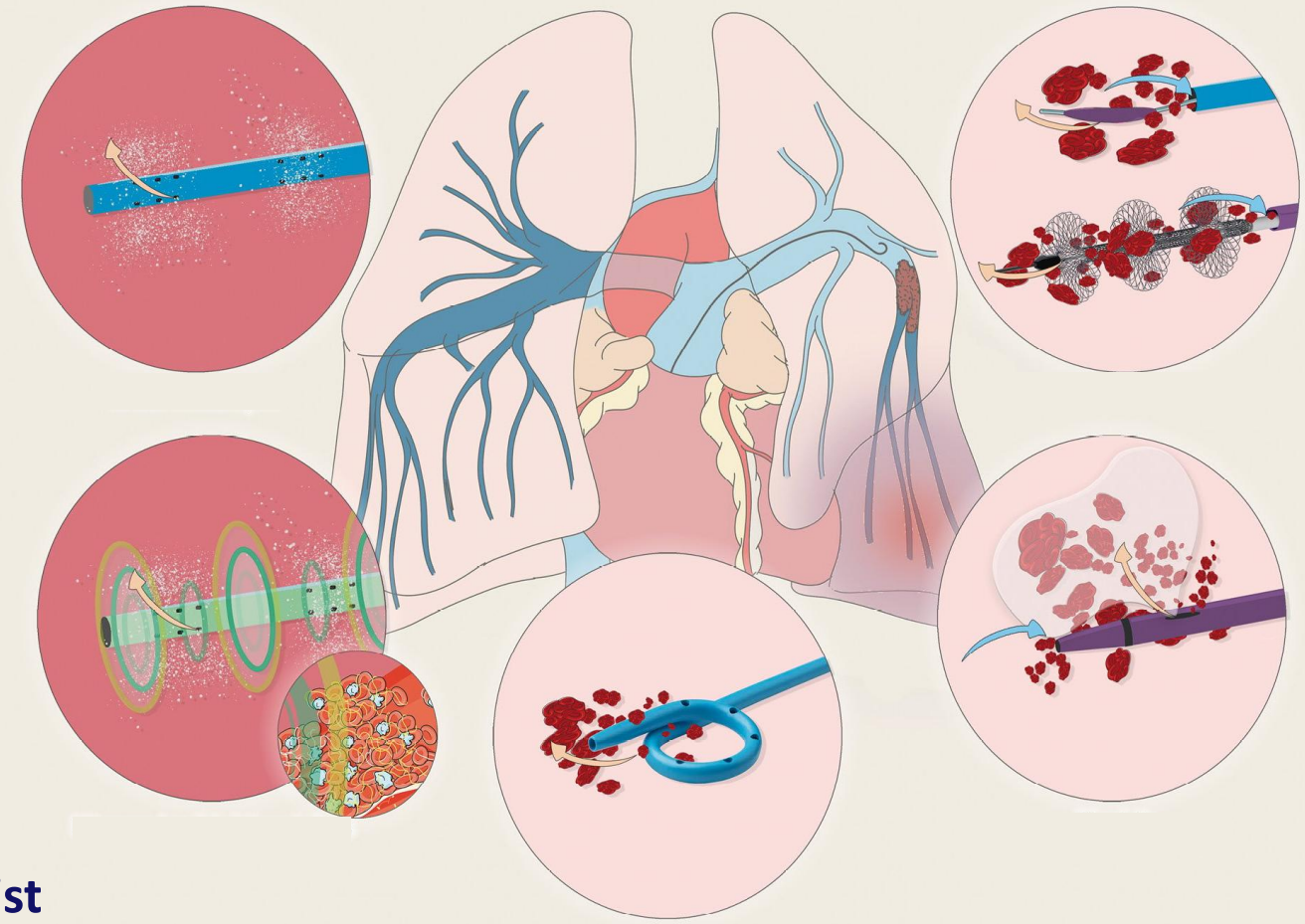
Broad implementation of percutaneous intervention for pulmonary embolism

Is it time?



I. Al Amri, MD, PhD

Interventional Cardiologist

Finocchiaro et al. EuroIntervention, 2024.

Disclosures

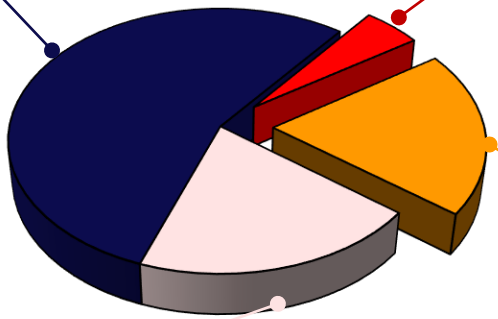
Nederlands Trombose Congres 16-05-2025

- Speakers fee Penumbra Inc.
- Speakers fee Medtronic

Current treatment landscape

Low risk PE
55%
Good prognosis
Low mortality risk <1%

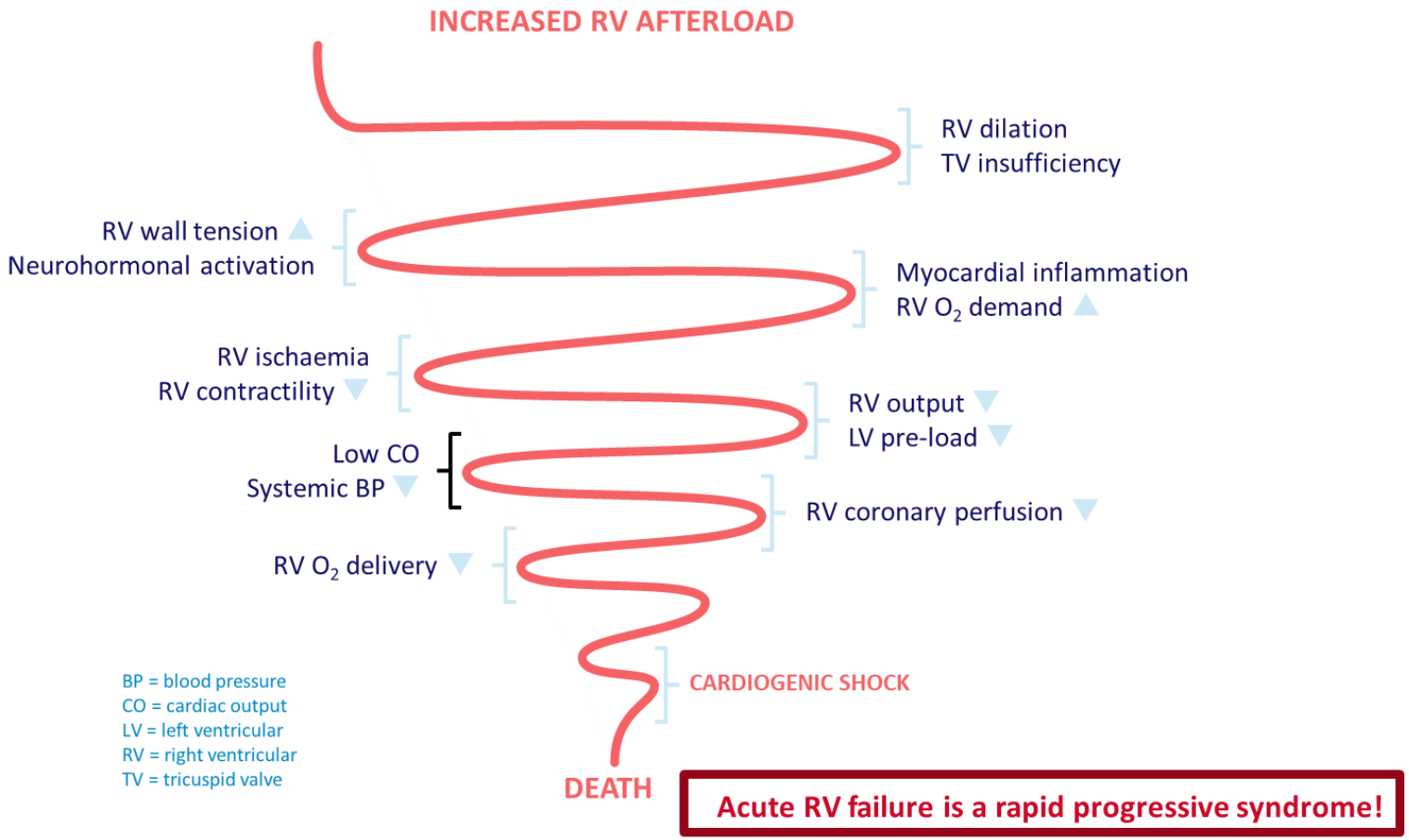
High-risk PE
5%
58% mortality at 3 months



Intermediate high-risk PE
20%
21-29% mortality at 3 months

Intermediate low risk PE
20%
3-15% mortality at 3 months

Identification of those at risk of HD collapse



Konstantinides SV et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism.

High-risk PE, but how high?

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]	+	(+)

59 years-old male

Collapse

CT: bilateral central PE, dilated RV

TnT 4000; Lactate 1

BP 90/60, HR 105/min

59 years-old male

Collapse

CT: bilateral central PE, dilated RV

TnT 5000; Lactate 4

BP 95/55, HR 135/min

Low dosis noradrenaline

59 years-old male

Collapse

Ongoing CPR due to PEA

POCUS: dilated RV

Current international guideline recommendations

High risk PE

IV thrombolytic therapy

- Recommended unless contra-indicated
- Class I/B (ESC/AHA), Grade 2C (ACCP)

Percutaneous mechanical thrombectomy

- Only if thrombolysis fails or contra-indicated
- Class IIa/C (ESC/AHA), Grade 2C (ACCP)

Intermediate risk PE

IV thrombolytic therapy

- Only if clinical/ HD deterioration on anticoagulation, unless contra-indicated
- Class I/A, ACCP no recommendation

Percutaneous mechanical thrombectomy

- Only if thrombolysis fails or contra-indicated
- Class IIa/B (ESC), IIb/C (AHA), ACCP: only in the setting of clinical trials

ESC Guidelines, Eur Heart J. 2024;45(19):1417–1527.
ACCP Guidelines, CHEST 2016;149(2):315–352.
AHA Statement, Circulation 2019;140(20):e774–e801.

Thrombolysis is the way to go in high-risk PE, right?

- Rapid clot resolution → improved RV function & perfusion
- Only proven reperfusion therapy with mortality benefit
- PEITHO sub-analyses + meta-analyses show hemodynamic stabilization

Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany

Karsten Keller [1†], Lukas Hobohm[1,2†], Matthias Ebner[3], Karl-Patrik Kresoja[3,4,5], Thomas Münzel[2,6], Stavros V. Konstantinides[1,7‡], and Mareike Lankeit[1,3,5*‡]

- Data from over 88,000 PE patients in Germany (2005–2015)
- Relative reduction of In-hospital mortality rates ~44%

It saves lives!

Keller K et al. European Heart Journal 2020

Thrombolysis is the way to go in high-risk PE, right?

Systemic thrombolysis was administered to only 23.1% of haemodynamically unstable patients!!

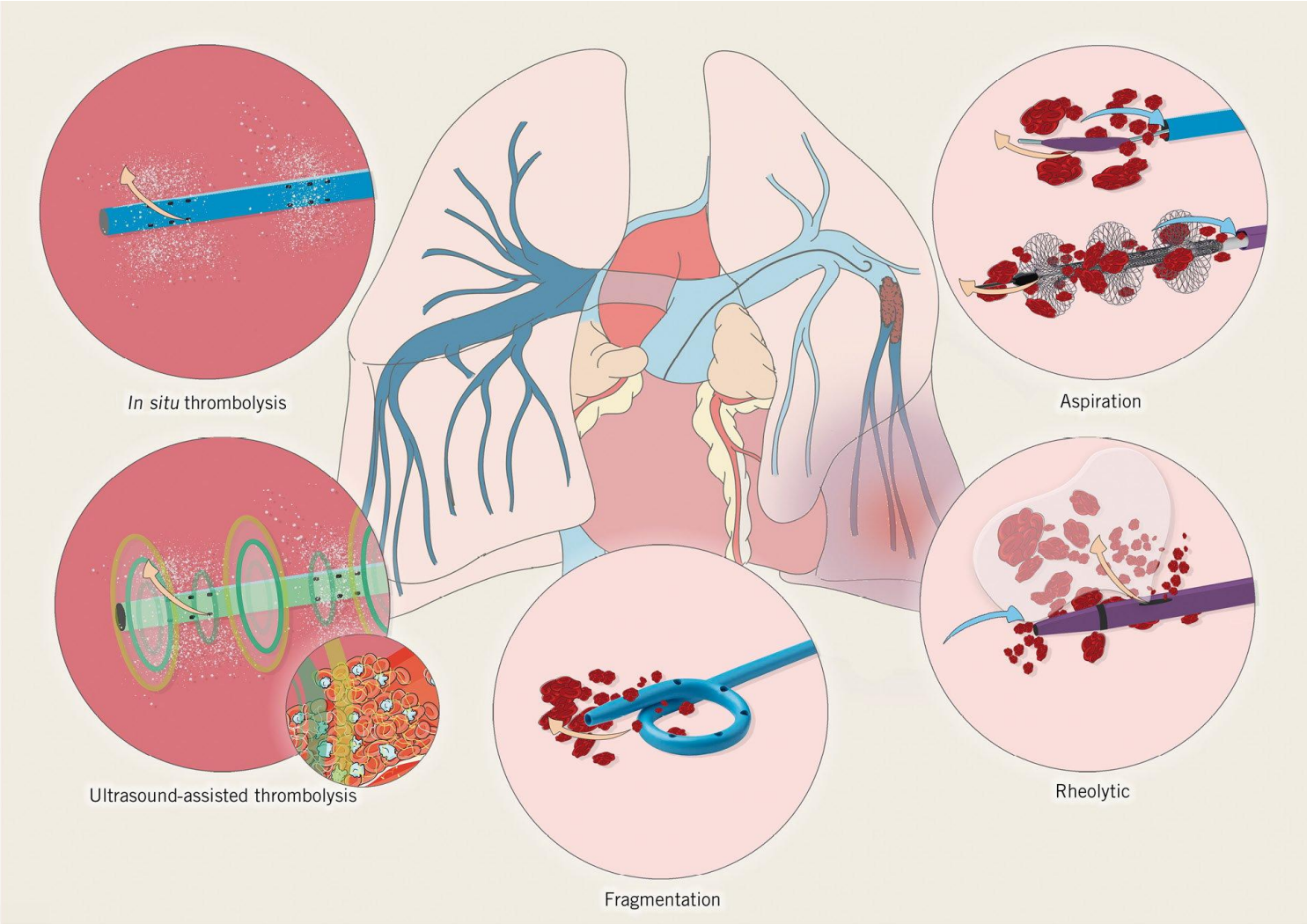
Major bleeding 10%

Intracranial hemorrhage 2-3%

Reluctance to apply thrombolysis despite guideline recommendations

Keller K et al., Eur Heart J. 2020;41(24):2515–2523.
Konstantinides SV et al. PEITHO trial, N Engl J Med. 2014;370(15):1402–1411.

Emerging catheter directed therapies



Finocchiaro et al. EuroIntervention, 2024.

Evolving landscape of clinical studies

- Exponential growth of evidence and experience over the last decade
- Multiple trials and real-world studies show safety and efficacy in expert centers

Safety in terms of low complication rates

Major bleeding 0-10%

Vascular access site 3-5%

Vascular injury, pseudoaneurysm, hematoma, arterial dissection

Other: rare

Hemoptysis, cardiac perforation, device embolization

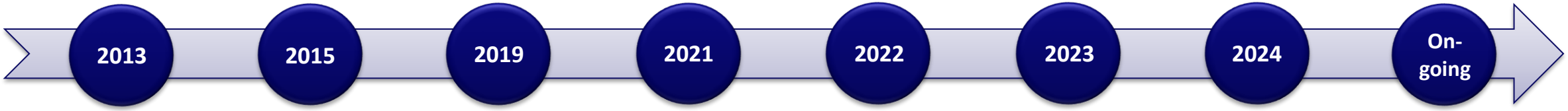
Giri J et al. AHA Scientific Statement, Circulation. 2019;140:e774–e801
Sista AK et al. JACC Cardiovasc Interv. 2016;9:1303–1313
ESC Guidelines, Eur Heart J. 2024;45:1417–1527

Efficacy in terms of rapid hemodynamic improvement

- Decrease in RV/LV diameter ratio as a marker of RV strain
- Reduction in mean pulmonary artery pressure
- Reduction in heart rate (tachycardia)
- Reduction in oxygenation and dyspnea scores

From ULTIMA, SEATTLE II, FLARE, EXTRACT-PE trials.

Evolving landscape of clinical studies – evidence gaps



2013 — **ULTIMA**
UACDT vs AC alone (RCT)

2015 — **SEATTLE II**
UACDT

2019 — **FLARE**
FlowTriever

2021 — **EXTRACT-PE**
Indigo

2022 — **RESCUE**
PM-CDT

2023 — **FLAME**
FlowTriever

2024 — **KNOCOUT PE**
USCDT

On-going — **STRIKE-PE**
Indigo

STORM-PE
Indigo vs AC alone (RCT)

15+ other studies

- No proven mortality or long-term functional benefit
- Unclear optimal patient selection criteria
- Absence of standardized operator training and credentialing
- Limited real-world data from non-tertiairy hospitals

Risks and safety concerns – real world reality

- Operator experience & center volume are key drivers of safety
- Complications underreported in trials from expert centers
- Real-world data shows higher variability in outcomes outside of trials

Giri J et al. AHA Scientific Statement, Circulation. 2019;140:e774–e801
Sista AK et al. JACC Cardiovasc Interv. 2016;9:1303–1313
ESC Guidelines, Eur Heart J. 2024;45:1417–1527

The promise of percutaneous interventions

- Exciting innovation, promising data
- Growing enthusiasm for PE interventions globally
- Enthusiasm does not equal readiness for broad adoption
- There is more needed than early success stories
- Caution, evidence and structured progress first

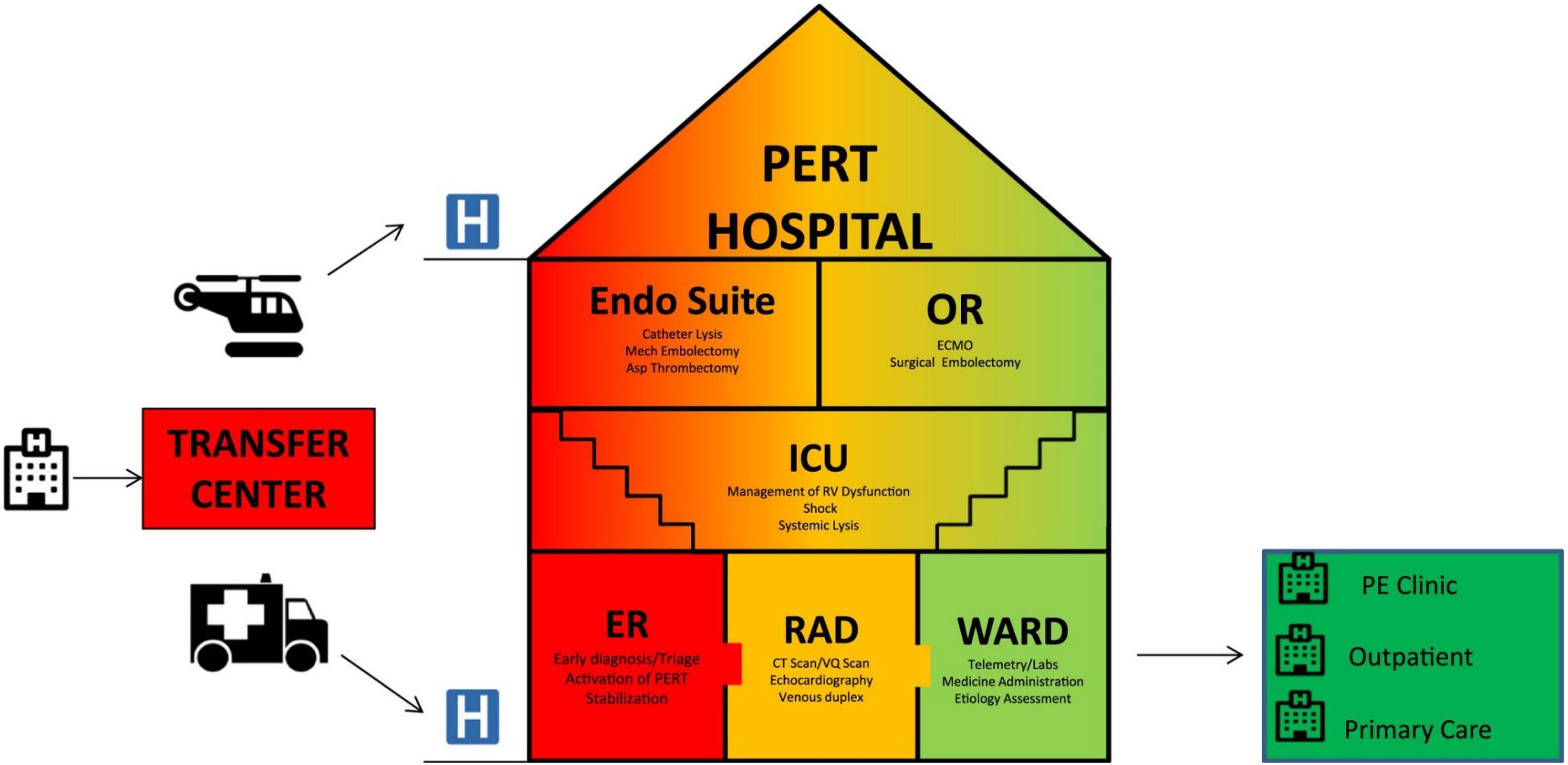
Many unresolved questions

- Which patients truly benefit?
- What is the optimal timing for intervention?
- Which device or technique should we use?
- How do we define treatment success?
- What are the long-term outcomes?
- How do we ensure operator experience and minimize risks?
- Logistics: hub and spoke model? 24/7 availability?

PERT/ EXPERT-PE teams; a game changing role

- **PERT CORE-GROUP**
- High team efficiency, collegiality
- Small team, representatives of key stakeholders
- Overview of logistics and activation of 2nd line actors
- Uniformity in care, predictability in decision making

PERT composition tailored to local logistics



Barnes at al. Chest 2016

Practical barriers

- Expertise concentrated in select high-volume centers
- Limited real-world data from smaller, non-tertiary hospitals
- Lack of structured operator training and credentialing
- High resource demands: devices, infrastructure, trained staff
- Cost-effectiveness remains unproven

Ethical and economical considerations

- High procedural costs with unclear long-term benefit
- Potential overuse of interventions in absence of strong evidence
- Risk of inequity: access limited to large, well-resourced centers
- Ethical dilemma: exposing patients to procedural risks for uncertain gains
- Need for responsible resource allocation and health system planning

What is needed before broad application?

- Large, well-designed randomized controlled trials
- Robust national and international registries
- Clear patient selection criteria and clinical pathways
- Consensus on operator training and center qualification
- Structured rollout: high-volume centers first

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Thrombectomy in high-Risk Pulmonary Embolism – Device versus thrombolysis Netherlands

Investigator-initiated, academically sponsored, multicentre, open-label, RCT

Catheter-directed thrombectomy (CDT) vs. systemic thrombolysis (2:1)

111 High-risk PE patients

15 participating centers

www.torpedo-NL.nl

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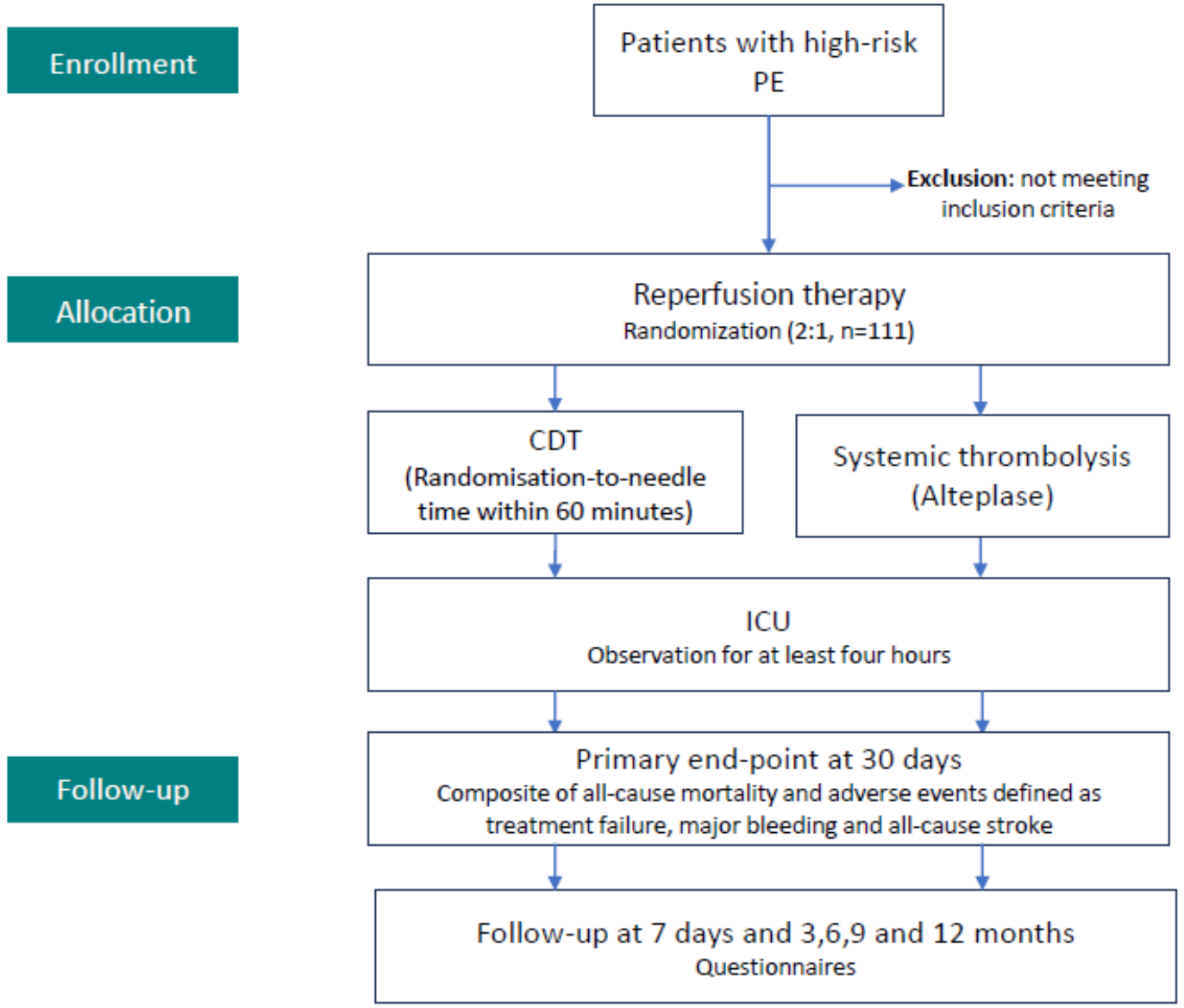

Note: PE: pulmonary embolism, CDT: Catheter-directed thrombectomy, ICU: intensive care unit

Leiden University Medical Center
alert acute longembolie response team
Leiden ECMO/SHOCK Team
HART LONG CENTRUM LEIDEN

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CDT	Systemic thrombolysis
Bolus 80 U/kg UFH (max 8000 U)	Bolus 80 U/kg UFH (max 8000 U)
Thrombectomy	Alteplase (LUMC) • Bolus 10mg • 90mg in 2h

Primary objective: 30-day composite incidence of:

1. All-cause mortality
2. Treatment failure
3. Major bleeding
4. All-cause stroke

Secondary Objective(s):

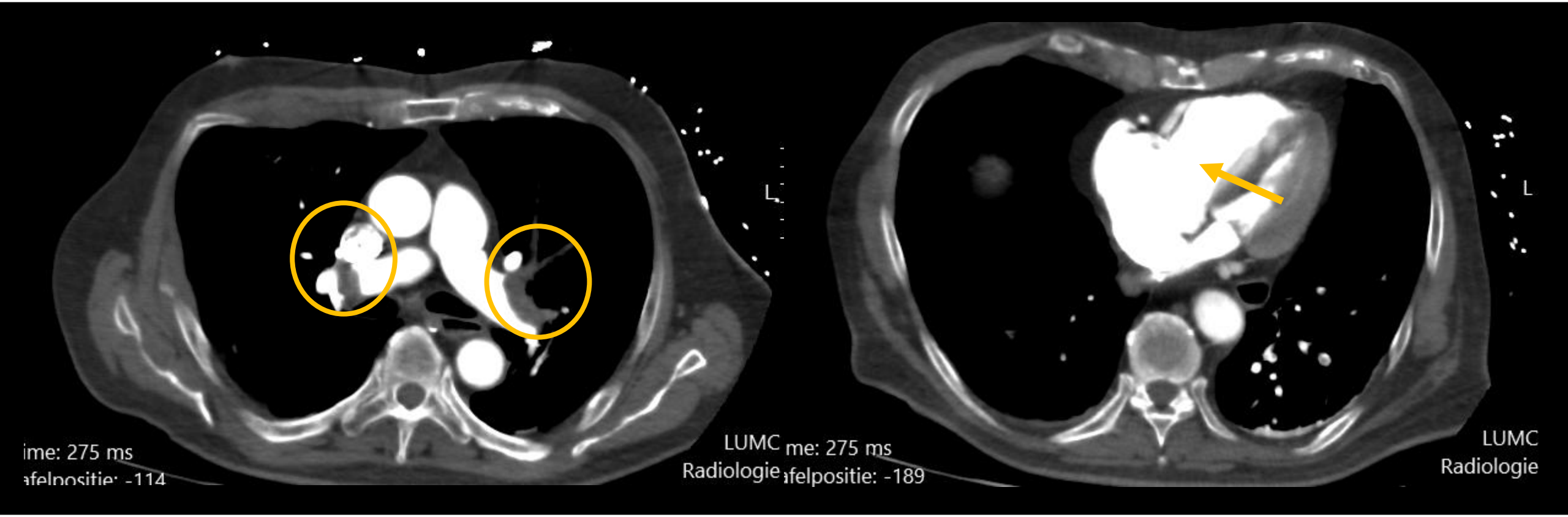
To evaluate whether CDT in high-risk PE patients relative to systemic thrombolysis is:

- associated with a better **survival** at day 7 and day 30
- associated with a lower incidence **of treatment failure** at day 7 and day 30
- associated with a lower incidence **of all-cause stroke** at day 7 and day 30
- associated with a lower incidence of **all-cause mortality** at day 7, 30 and 90
- associated with a lower incidence of **BARC3b and BARC3c bleeding**, at day 7 and day 30
- associated with a lower incidence **of ISTH major and non-major** clinically relevant bleeding at day 7 and day 30
- Primary objective at day 7
- associated with a better **Desirability of Outcome Ranking (DOOR)** at day 7
- associated with a lower level of **oxygen supplementation at 48 hours**
- associated with shorter **LOS** at the ICU and in hospital
- associated with better **patient-relevant outcomes**
- **cost-effective** after a time horizon of a year
- associated with an impact on **budget**

Case 76 y/o male patient

- DM type II, hypertension, dyslipidemia
- Chest pain, dyspnea and syncope
- Awake at arrival ED
- Signs of HD instability (tachycardia, hypotension)
- When transferred to the emergency bed low output state, 1 block of resuscitation

Case of high-risk pulmonary embolism

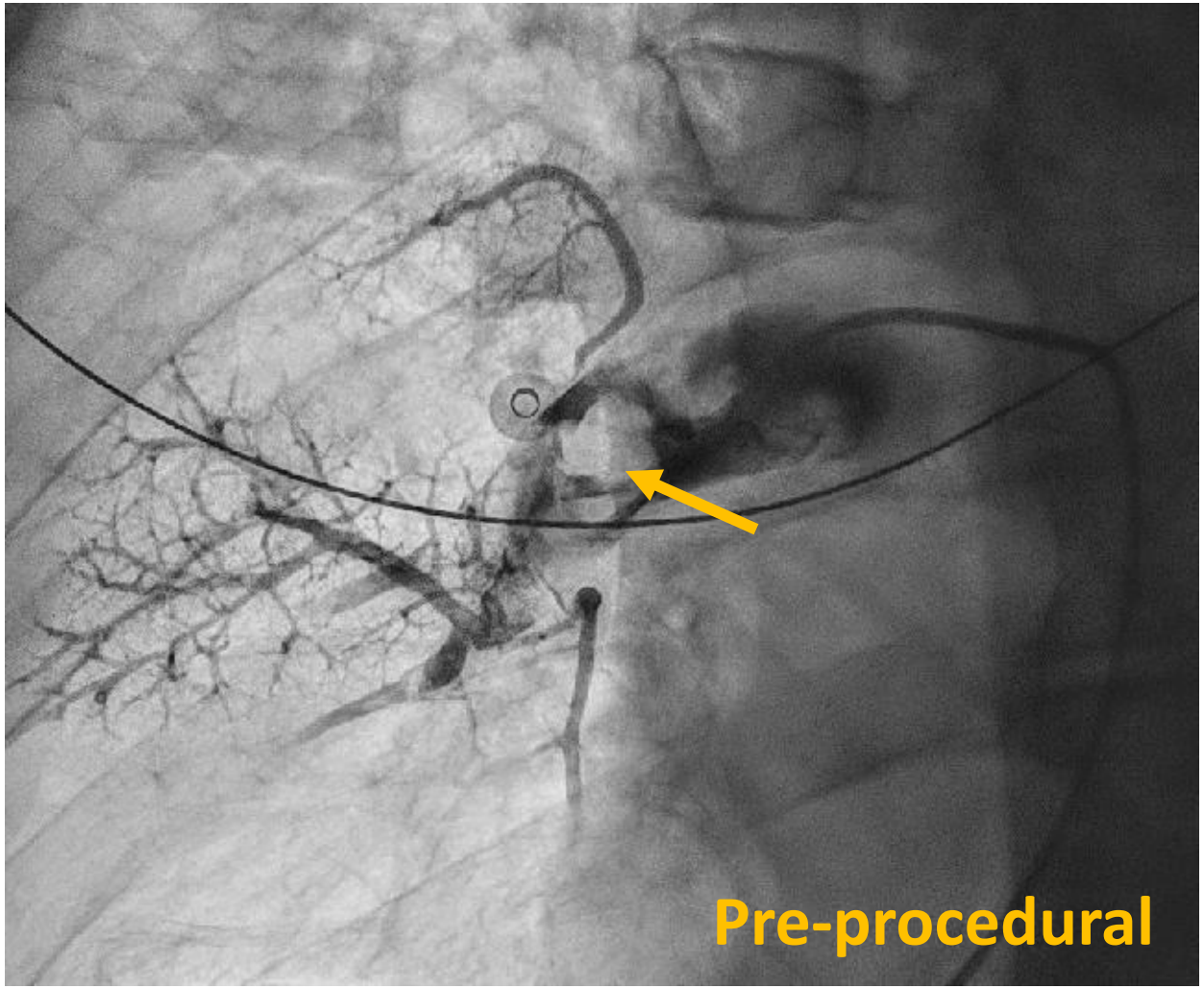


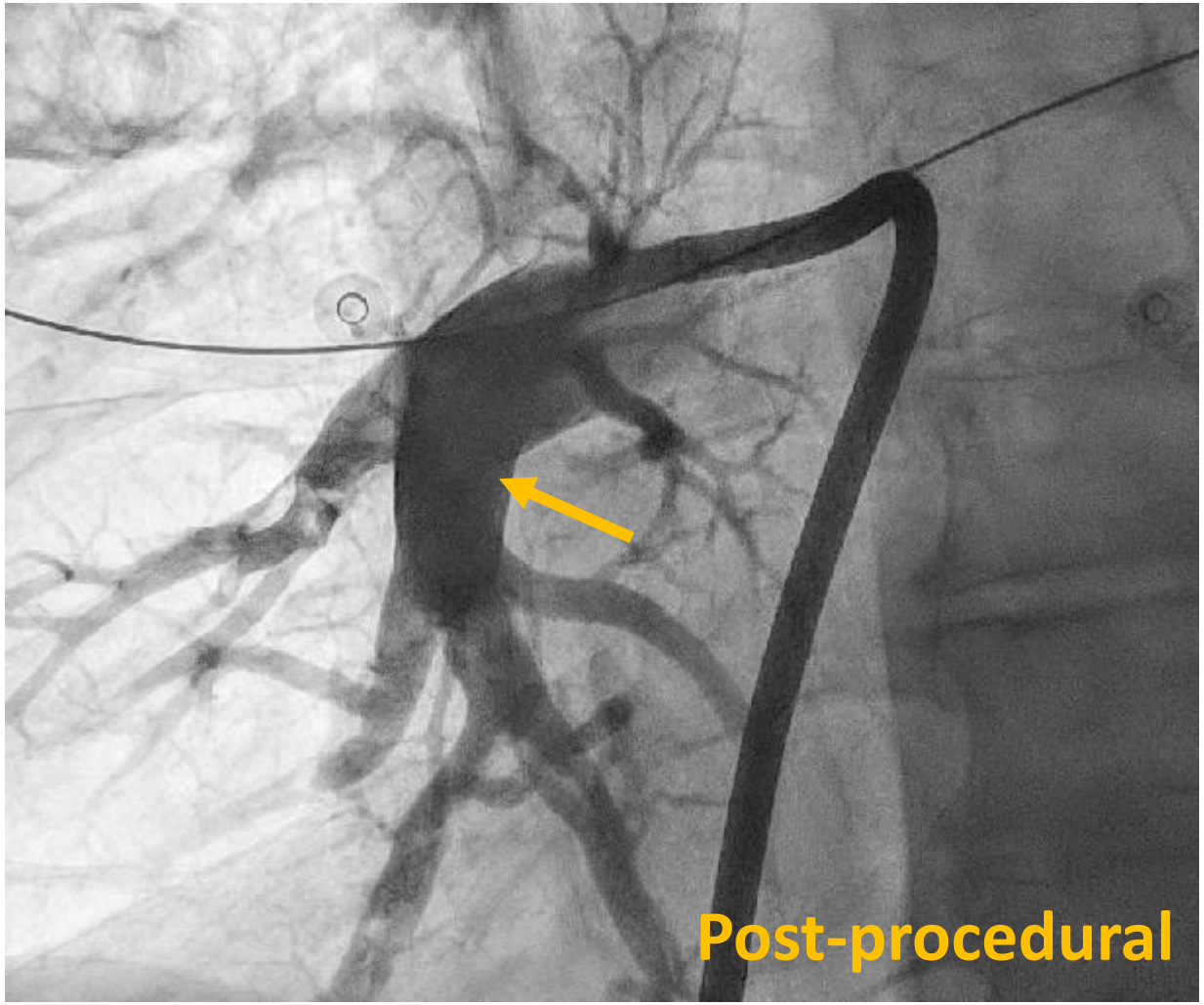
Case of high-risk pulmonary embolism

- After CT scan further HD deterioration; adrenalin i.v.
- ECMO cannulation first, thrombectomy second at the cathlab

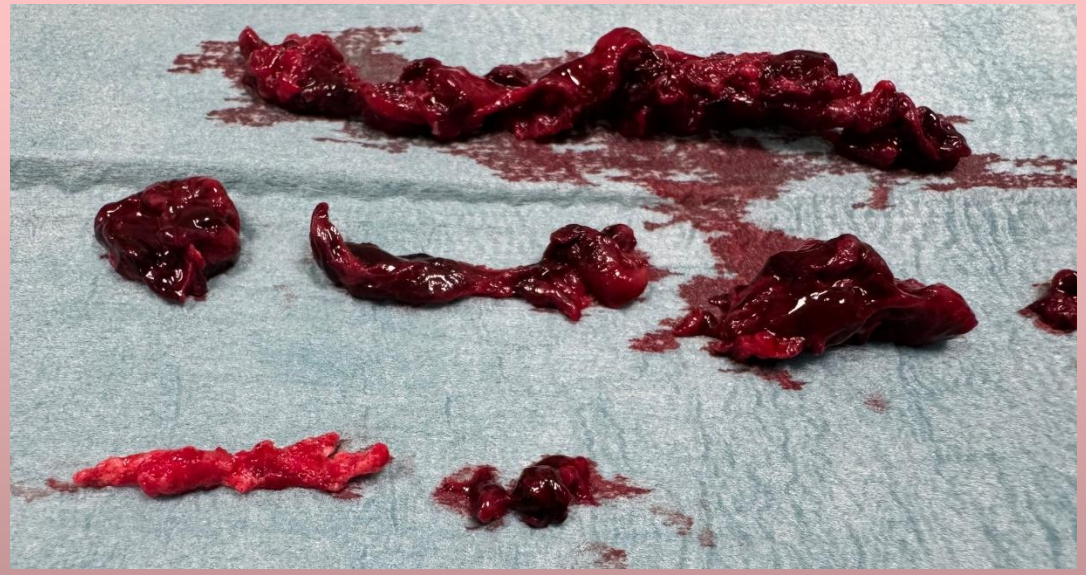
Case of high-risk pulmonary embolism

Case 76 y/o male patient





Case of high-risk pulmonary embolism



Parameters

	PRE	POST
mPAP (mmHg)	28	15
RA (mmHg)	10	8
HR (bpm)	117	118
BP (mmHg)	82/45	ECMO

Procedural device related blood loss 150cc

Case of high-risk pulmonary embolism

- Persistent HD instability
- Bleeding leg ECMO cannula insertion site → Emergency vascular surgery
- Dislocation of distal peripheral canula → Surgical bleeding control
- Transfer to the ICU, removal of ECMO 2 days postop

Case of high-risk pulmonary embolism

- Life-saving potential of percutaneous interventions
- The risk isn’t in the procedure, it’s in the patient
- Real and serious access site risks, even in experienced centers
- The importance of structured training, teamwork and center expertise

Conclusions – is it time for broad implementation?

- Percutaneous interventions offer promising tools to improve acute care
  - Optimal patient selection?
  - Timing and type of intervention?
  - Safety across different settings and operators?
  - Long-term outcomes and mortality benefit?

- The field is evolving rapidly—we are close, but not quite there yet

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Inclusion criteria
Adults with confirmed acute PE: • Contrast filling defect in lobar/ more proximal PA on CTPA and/ or • Obstructive shock with TTE signs of PE (RV dilatation, VCI congestion) This can be with or without ultrasound signs of clot in transit (heart) or DVT (leg)
High risk for mortality, i.e. • Post cardiac arrest (but ROSC at presentation) OR • Obstructive shock (SBP <90mmHg + signs of end organ hypoperfusion (lactate >2mmol/l) or the need for vasopressors ((nor)adrenaline) to maintain adequate BP OR • Persistent hypotension (SBP <90 mmHg or a drop ≥ 40mmHg for at least 15 min) not caused by new onset arrhythmia, hypovolemia or sepsis OR • Abnormal RV function on TTE or CTPA AND elevated CTpn AND respiratory failure (SaO2 <90%) refractory to O2 suppletion (100% FiO2), high flow nasal O2 or (N)IMV
CDT available and technically feasible to allow for a randomization-to-needle time of 60 min or less

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Exclusion criteria
"**Catastrophic PE**": ongoing cardiac arrest and/or ECPR and/or immediate indication for VA-ECMO
GCS <8 following CPR
Alternative diagnosis than acute PE contributing to the acute hemodynamic and/or respiratory failure, e.g. **sepsis, COPD** GOLD 3 or 4, or known **heart failure with NYHA 4**
A known "**do not admit to the ICU**" or "**do not resuscitate**" directive
An absolute **contraindication to systemic thrombolysis**, i.e. • History of hemorrhagic stroke • Ischemic stroke in past 6 months • Central nervous system neoplasm • Major trauma, major surgery or major head injury in past 3 weeks • Active bleeding, life-threatening or into a critically organ/area; OR known severe bleeding diathesis with previous bleeding fulfilling these criteria

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Exclusie
Reperfusion therapy or placement of a non-retrieved **inferior vena cava filter** in the past 3 months
Thrombus in transit through a patent foramen ovale.
Known **CTEPH** (or strong suspicion of CTEPH)
Known hypersensitivity to systemic thrombolysis, heparin, or to any of the excipients
If, in the Investigator's opinion, or after consultation with the local PERT-team or EC-members, the **patient is not appropriate for thrombectomy**
Chronic use of full-dose oral or parenteral anticoagulation before presentation.
Pregnancy
Current participation in another study that would interfere with participation in this study
Previous enrolment in this study
Refusal of deferred consent by the next of kin or by the patient himself to use the data. Deferred consent will not be asked to relatives of **patients who die in scene**, but are included in the study.