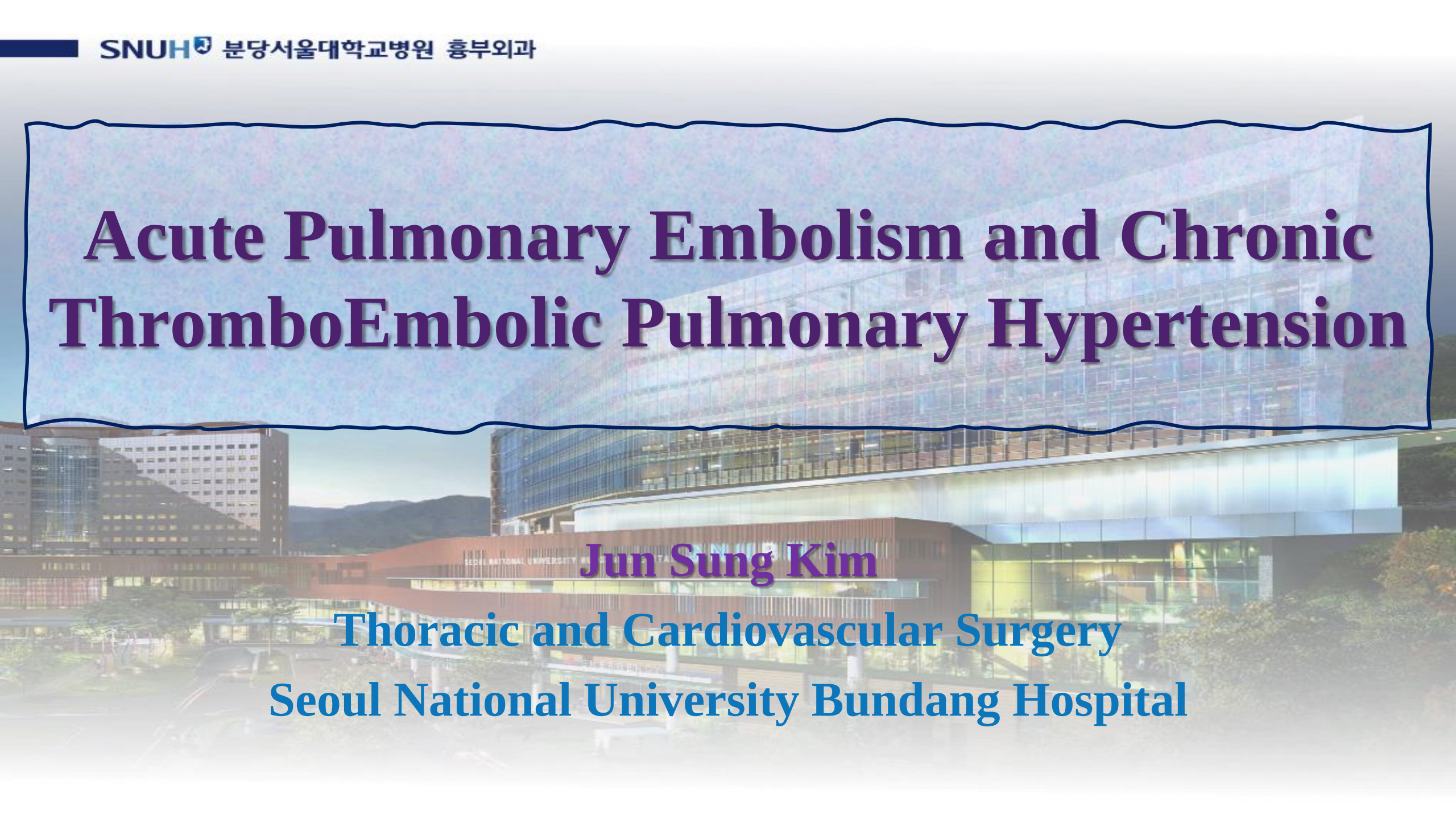
Acute Pulmonary Embolism and Chronic ThromboEmbolic Pulmonary Hypertension



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Seoul National University Bundang Hospital

Contents

- Acute PE
- CTEPH

History

- Trendelenburg, 1908, 1st pulmonary embolectomy
- Ochsner & DeBakey, 1932, IVC ligation
- Gibbon, 1953, 1st successful operation with CPB
- **Cooley, 1961**, 1st successful surgical embolectomy using CPB
- 1984, 1st percutaneous IVC filter

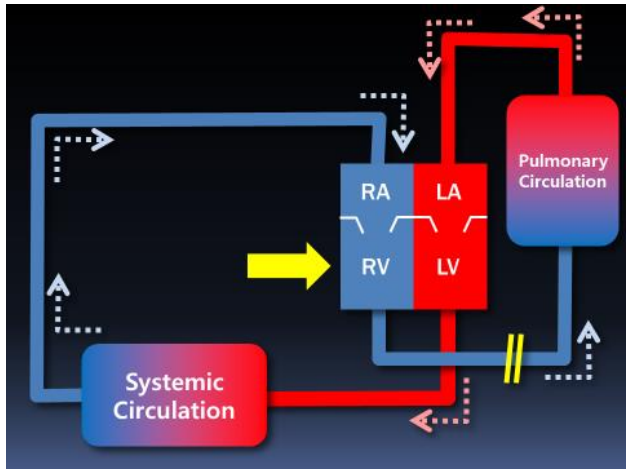
Epidemiology

- 1.5 / 1000 person-year
- $\propto$ age
- Male $\fallingdotseq$ Female
- Half idiopathic,
  - Trauma
  - Surgery
  - Immobilization
  - Cancer

- Risk factors for PE
  - Age, HT
  - Obesity, DM, Dyslipidemia
  - Cigarette smoking
  - Hypercoagulability
    - Antithrombin def
    - Protein C, S def
    - Antiphopholipid AB synd

Pathophysiology

- Hypercoagulable states
- RV dysfunction leading shock
- Hypoxemia



Pulmonary embolism

Anatomical obstruction

Neurohumoral effects

↑PA pressure
↑RV afterload

↑RV wall tension

↑RV O_2 demand

RV dilation/dysfunction

RV ischemia

↓RV output

Interventricular septal shift to LV

↓RV O_2 supply

↓Coronary perfusion

↓LV preload

↓LV output

↓Systemic perfusion

↓Systemic perfusion

Hypotension

Clinical Presentation

- Symptoms
  - Unexplained dyspnea
  - Chest pain (pleuritic / atypical)
  - Anxiety, Cough

- Signs
  - Tachypnea
  - Tachycardia
  - Low-grade fever
  - Hemoptysis, leg edema
  - TR murmur

TABLE 77-6	Differential Diagnosis of Pulmonary Embolism
Anxiety, pleurisy, costochondritis	
Pneumonia, bronchitis	
Myocardial infarction	
Pericarditis	
Congestive heart failure	
Idiopathic pulmonary hypertension	

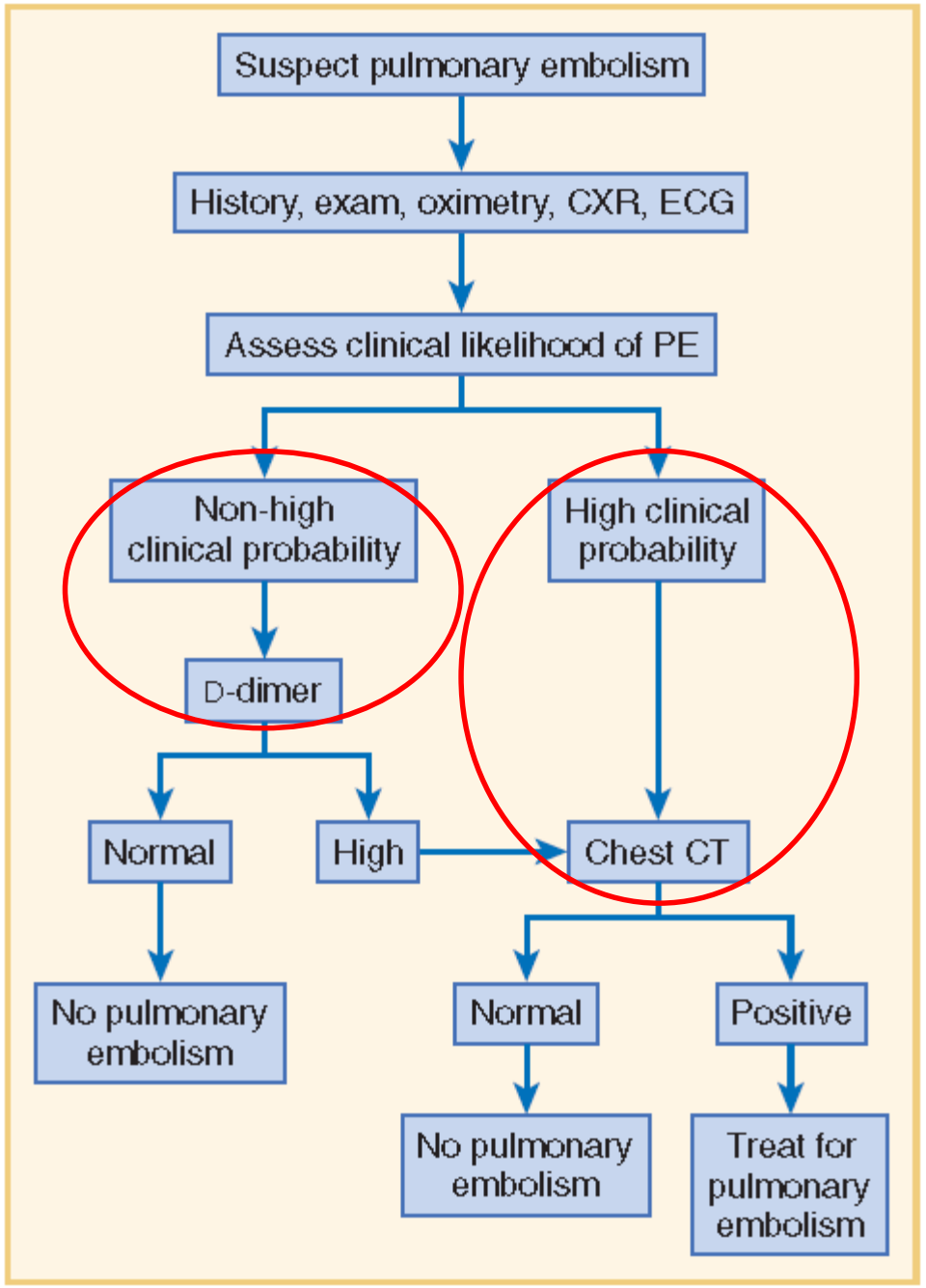
Diagnosis

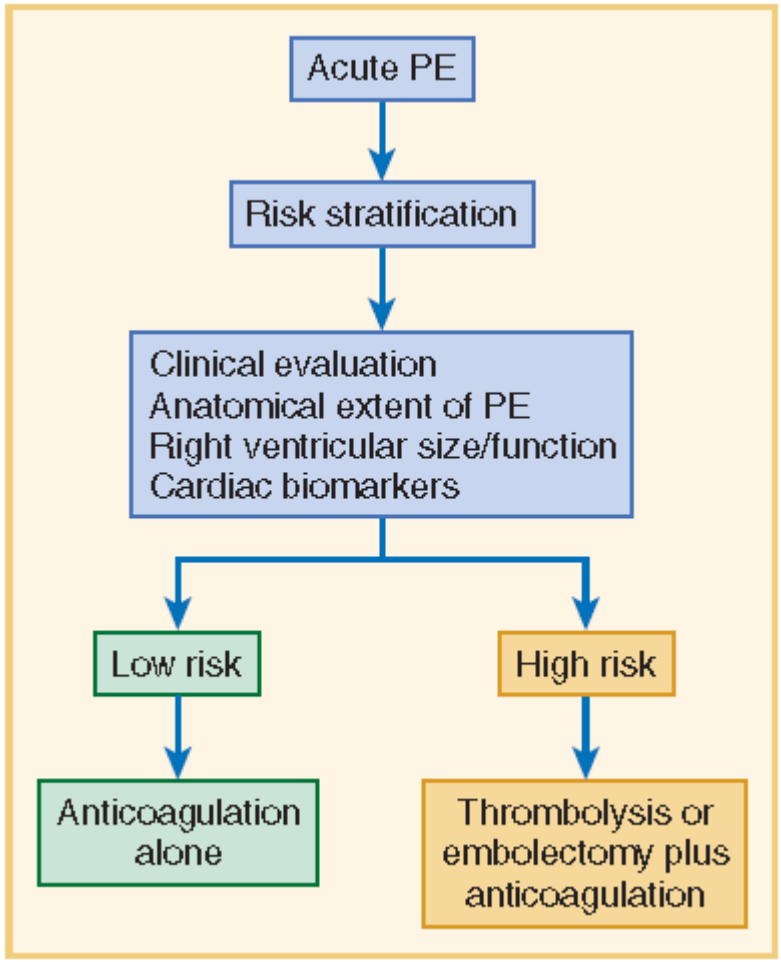
- Lab : D-dimer, ABGA, pro-BNP…
- EKG : Tachycardia, RBBB, T-wave inversion, Afib…
- EchoCG
  - McConnell sign : RV free wall hypokinesia
  - D-shape LV
  - TR, elevated PAP

Diagnosis - CT

- In suspected high-risk PE (Class I, LOE C)

- Size, location, and extent of thrombus
- Pulmonary artery enlargement
- Age of thrombus
  - Acute / Subacute / Chronic
- Location of thrombus
  - PA, pelvic veins, DVT
- Right ventricular enlargement
  - Contour of the interventricular septum


Suspect pulmonary embolism
History, exam, oximetry, CXR, ECG
Assess clinical likelihood of PE
Non-high clinical probability
High clinical probability
D-dimer
Normal
High
Chest CT
No pulmonary embolism
Normal
Positive
No pulmonary embolism
Treat for pulmonary embolism


Acute PE
Risk stratification
Clinical evaluation
Anatomical extent of PE
Right ventricular size/function
Cardiac biomarkers
Low risk
High risk
Anticoagulation alone
Thrombolysis or embolectomy plus anticoagulation

Classification of Acute PE

Classification	Presentation	Therapy
Massive PE	Systolic BP <90 MOF plus main pulmonary artery clot	Thrombolysis or embolectomy or IVC filter plus anticoagulation
Submassive PE	Hemodynamic stable with RV dysfunction	Thrombolysis or embolectomy or IVC filter controversial
Small to moderate PE	Normal hemodynamics and normal RV function	Anticoagulation

TABLE 77-14 Predictors of Increased Mortality

Hemodynamic instability
Right ventricular hypokinesis on echocardiogram
Right ventricular enlargement on echocardiogram or chest CT scan
Right ventricular strain on electrocardiogram
Elevated cardiac biomarkers

Tx - Anticoagulation

- Cornerstone for Tx (Class I, LOE A)

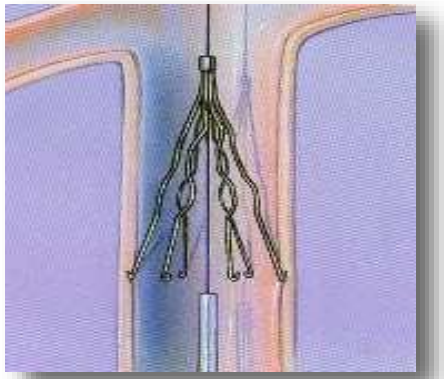
- UFH
- LMWH
  - Enoxaparin
  - Dalteparin
  - Nadroparin
- WFR
- NOAC (I, B)

TABLE 77-15 Intravenous Unfractionated Heparin "Raschke Nomogram"

VARIABLE	ACTION
Initial heparin bolus	80 units/kg bolus, then 18 units/kg/hr
aPTT <35 seconds (<1.2 times control)	80 units/kg bolus, then increase by 4 units/kg/hr
aPTT 35 to 45 seconds (1.2 to 1.5 times control)	40 units/kg bolus, then increase by 2 units/kg/hr
aPTT 46 to 70 seconds (1.5 to 2.3 times control)	No change
aPTT 71 to 90 seconds (2.3 to 3 times control)	Decrease infusion rate by 2 units/kg/hr
aPTT >90 seconds (>3 times control)	Hold infusion 1 hr, then decrease infusion rate by 3 units/kg/hr

From Raschke RA, Reilly BM, Guidry JR, et al: The weight-based heparin dosing nomogram compared with a "standard care" nomogram: A randomized controlled trial. Ann Intern Med 119:874, 1993.

Tx – IVC filter



- Ix
  - Major bleeding risk (precluding anticoagulation) (Class IIA, LOE C)
  - Recurrent PE despite anticoagulation
  - Routine use is not recommended (Class III, LOE A)

- After 80years RCTs,
  - ↓risk of PE, ↑risk of DVT
  - ≒ long term survival

Celect (Cook), 2007

Gunther Tulip (Cook), 2000

Titanium Greenfield (Boston Sci), 1989

OptEase (Cordis), 2002

Tx - Thrombolysis

- Advantages
  - Lessen thrombus burden
  - Better hemodynamics
  - Lessen the chance of CTEPH

Streptokinase	250 000 IU as a loading dose over 30 min, followed by 100 000 IU/h over 12–24 h
	Accelerated regimen: 1.5 million IU over 2 h
Urokinase	4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg/h over 12–24 h
	Accelerated regimen: 3 million IU over 2 h
rTPA	100 mg over 2 h
	or 0.6 mg/kg over 15 min (maximum dose 50 mg)

- Disadvantages
  - Risk of major bleeding : ICH, in women
  - 13% major bleeding, 1.8% ICH

Outcomes of Thrombolysis

- In many RCTs,
  - Embolic burden reduction & hemodynamic improvement
  - 92% response (~till 2weeks)
- rTPA is slightly better than others
- Local direct infusion of rTPA ≒ systemic infusion

Outcomes of Thrombolysis

Outcome	Trials that included patients with massive PE			Trials that excluded patients with massive PE		
	Thrombolysis (n/N)	Heparin (n/N)	OR	Thrombolysis (n/N)	Heparin (n/N)	OR
Recurrent PE or death	12/128 (9.4%)	24/126 (19.0%)	0.45 (0.22–0.92)	13/246 (5.3%)	12/248 (4.8%)	1.07 (0.50–2.30)
Recurrent PE	5/128 (3.9%)	9/126 (7.1%)	0.61 (0.23–1.62)	5/246 (2.0%)	7/248 (2.8%)	0.76 (0.28–2.08)
Death	8/128 (6.2%)	16/126 (12.7%)	0.47 (0.20–1.10)	8/246 (3.3%)	6/248 (2.4%)	1.16 (0.44–3.05)
Major bleeding	28/128 (21.9%)	15/126 (11.9%)	1.98 (1.00–3.92)	6/246 (2.4%)	8/248 (3.2%)	0.67 (0.24–1.86)

Wan S, et al. Thrombolysis compared with heparin for the initial treatment of pulmonary embolism: a meta-analysis of the randomized controlled trials, Circulation, Vol. 110, 744–749.

Indication of Thrombolysis

- 1st line therapy in high-risk PE with cardiogenic shock (Class I, LOE B)

- Absolute Contraindication of thrombolysis
  - Haemorrhagic stroke at any time
  - Ischaemic stroke in 6 months
  - CNS damage or neoplasms
  - Recent major trauma/surgery/head injury (within 3 weeks)
  - GI bleeding within the last month

Catheter Embolectomy

- Mechanical fragmentation
- PA balloon dilatation and stenting

- + catheter directed thrombolysis

As an alternative to surgery in patients with high-risk PE if thrombolysis is absolutely contraindicated or has failed (Class IIA, LOE C)

Surgical Embolectomy

- Traditionally,
  - Rare rescue operation : CPR,
  - CIx or failure of thrombolysis
  - PFO / intracardiac thrombus

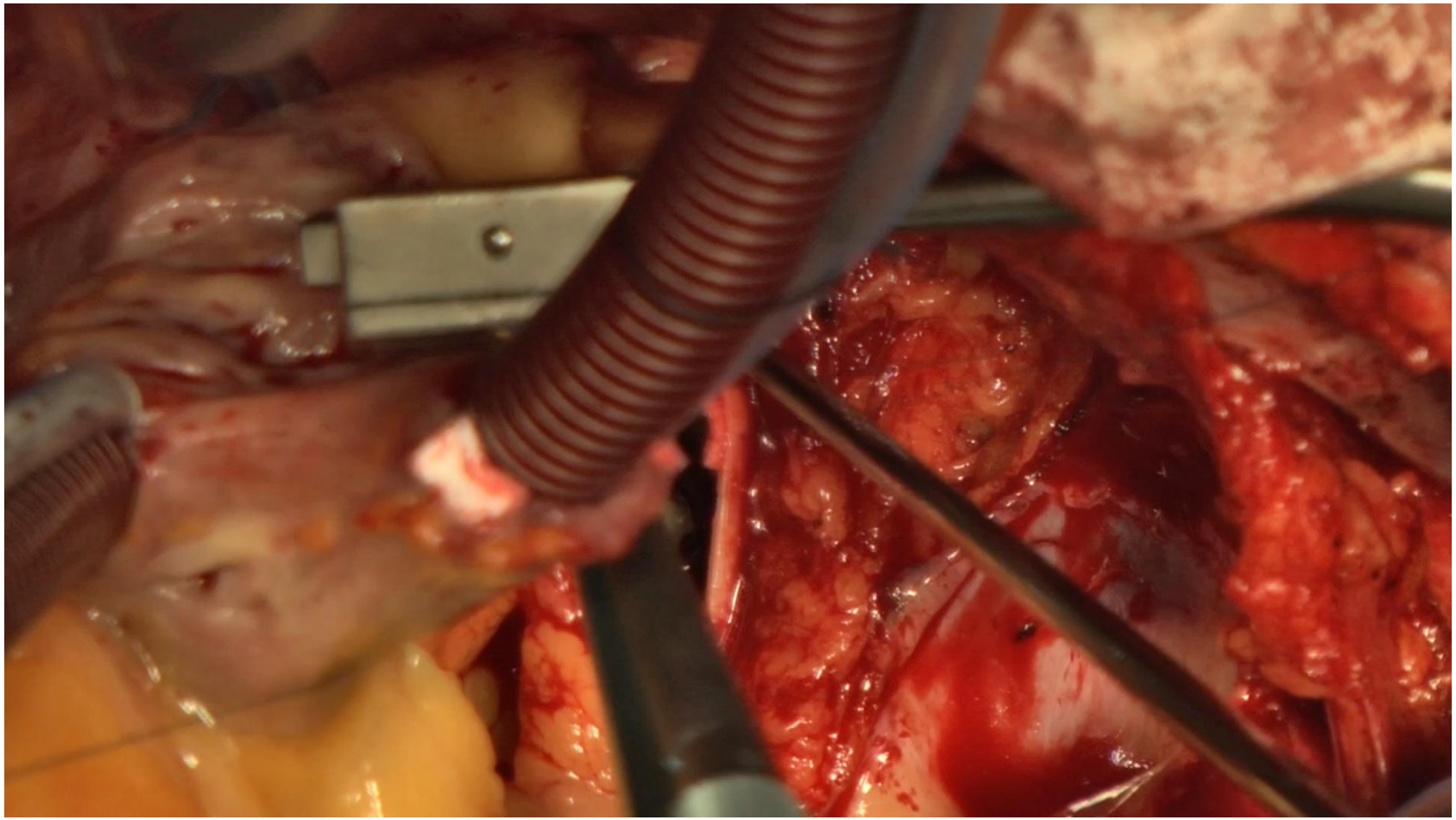
  - High mortality approaching 30~40%

In patients with high-risk PE in whom thrombolysis is absolutely contraindicated or has failed (Class I, LOE C)

Surgical Embolectomy

- CPB
- Norm
- No A
  Fibri

Operation Video : Acute PE



Acute Pulmonary Embolectomy

A Contemporary Approach

Lishan Aklog, MD; Christopher S. Williams, PhD; John G. Byrne, MD; Samuel Z. Goldhaber, MD

Circulation. 2002;105:1416-1419.

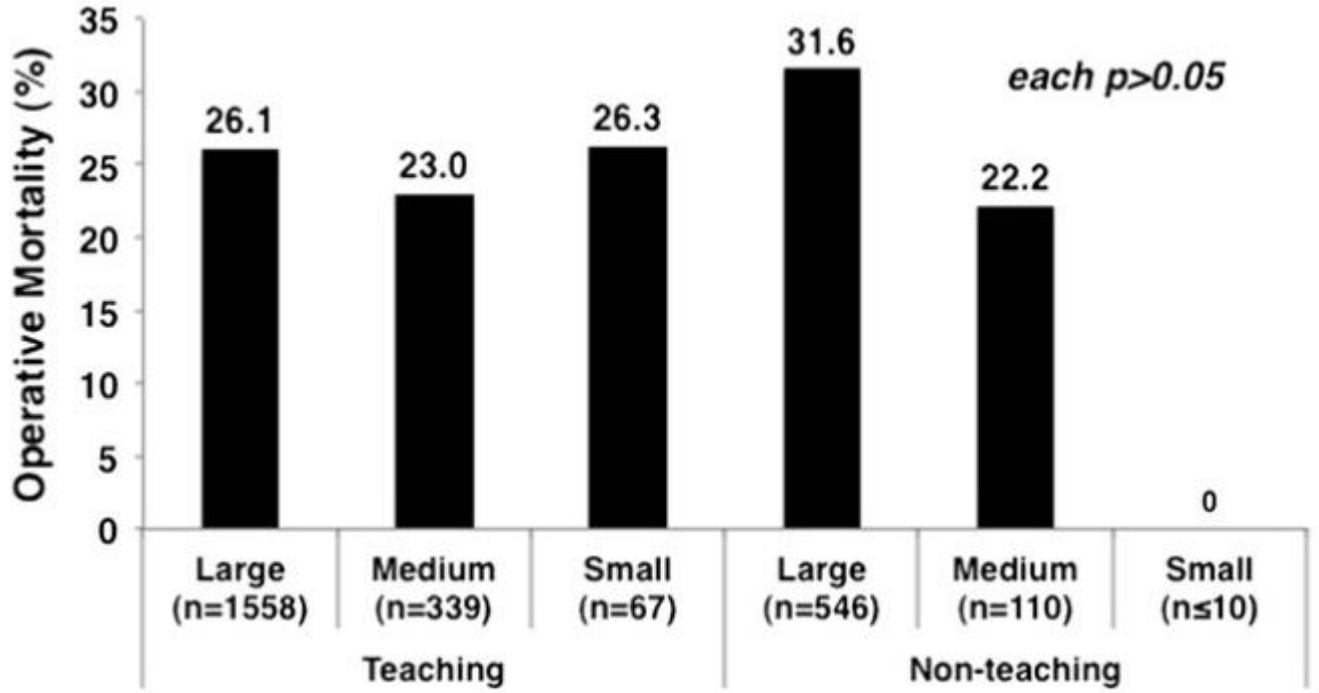
- October 1999 ~ October 2001
- 29 (17 men and 12 women)
- 11% 30-day mortality
- Brigham and Women's Hospital

Nationwide outcomes of surgical embolectomy for acute pulmonary embolism

Arman Kilic, MD,[a] Ashish S. Shah, MD,[a] John V. Conte, MD,[a] and David D. Yuh, MD[b]

J Thorac Cardiovasc Surg 2013;145:373-7

- 2709, 57.0±16.0 years
- Overall inpatient mortality 27.2%



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Management of acute massive pulmonary embolism: Is surgical embolectomy inferior to thrombolysis?☆

Yang Hyun Cho [a,1], Kiick Sung [a,1], Wook Sung Kim [a,*], Dong Seop Jeong [a], Young Tak Lee [a], Pyo

[a] Depa
[b] Depa

Analysis of predictors of cardiac death.

	Univariate	Multivariate	
	P value	HR (95% CI)	*P* value
Age	0.106	1.005 (0.956–1.055)	0.856
Female gender	0.046	9.263 (0.982–23.702)	0.05
Diabetes mellitus	0.448		
Hypertension	0.752		
Cardiopulmonary resuscitation	0.715		
Malignancy	0.745		
Recent pregnancy	0.486		
Recent major surgery	0.53		
ECMO	0.958		
Thrombolysis only	0.038	4.798 (1.161–19.829)	0.03

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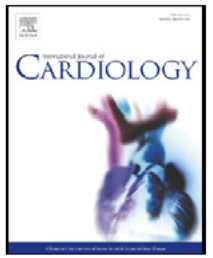


Management of acute massive pulmonary embolism: Is surgical embolectomy inferior to thrombolysis?☆

Yang Hyun Cho [a,1], Kiick Sung [a,1], Wook Sung Kim [a,*], Dong Seop Jeong [a], Young Tak Lee [a], Pyo Won Park [a], Duk-Kyung Kim [b]

[a] *Department of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea*
[b] *Department of Internal Medicine, Division of Cardiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea*

- Surgical embolectomy is associated with lower cardiac mortality risk than thrombolysis

- First-line treatment option for acute massive PE for patients.

- **Regardless of Tx for massive PE,**
- **Hemodynamic Instability is major risk factor for massive PE !!!**
- **Use of ECMO is important !!!**

VA ECMO in acute PE

- ECMO not in guidelines and no RCT

- But, most deaths occur in first 2.5hrs
- Major cause is shock (>30% mortality vs 5% without)
- Average survival in surgery is only 70%.
- Surgery not always immediately available.
- Thrombolysis takes time to be effective.

VA ECMO in acute PE

- As part of CPR
- To allow stabilization prior to surgery or intervention/thrombolysis
- For post embolectomy RV failure or reperfusion lung injury
- Acute PE might be self-limiting

Take Home Messages

- Low risk PE : D-dimer & Anticoagulation
- Submassive/Massive PE : CT/EchoCG & Thrombolysis/Op/Intervention

- **High risk PE**, hemodynamic status is most important factor for survival.
- ECMO support is mandatory for life-saving!!!
- Surgical embolectomy is not inferior to Thrombolysis Tx.

Contents

- Acute PE
- CTEPH

University of California SD

- UCSD, 190
- 1966, medi
- 3rd of 10 U
- 59th in worl
- 20 winners

TS of UCSD

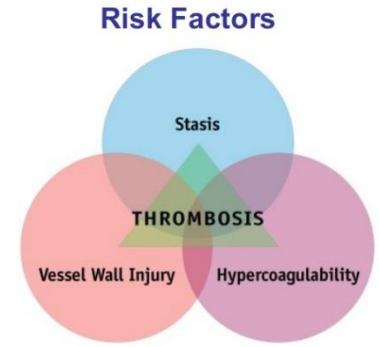
- Specialized center for PEA
- 3 OR + 1 Hybrid OR
- Annual 500 cases of OHS
  - **~250 PEA**
  - ~40 LVAD surgery
  - ~150 CABG
  - ~100 Valve
  - ~50 TAVI

Diagnosis of CTEPH

- Pulmonary hypertension : mean PAP > 25mmHg (not all patients have PH)

- Persistent perfusion defect despite therapeutic anticoagulation

Natural Hx of CTEPH



Genetic

Medical Condition (infection and inflammation)

Prothrombotic tendency

Recurrent TE events/In-situ thrombosis

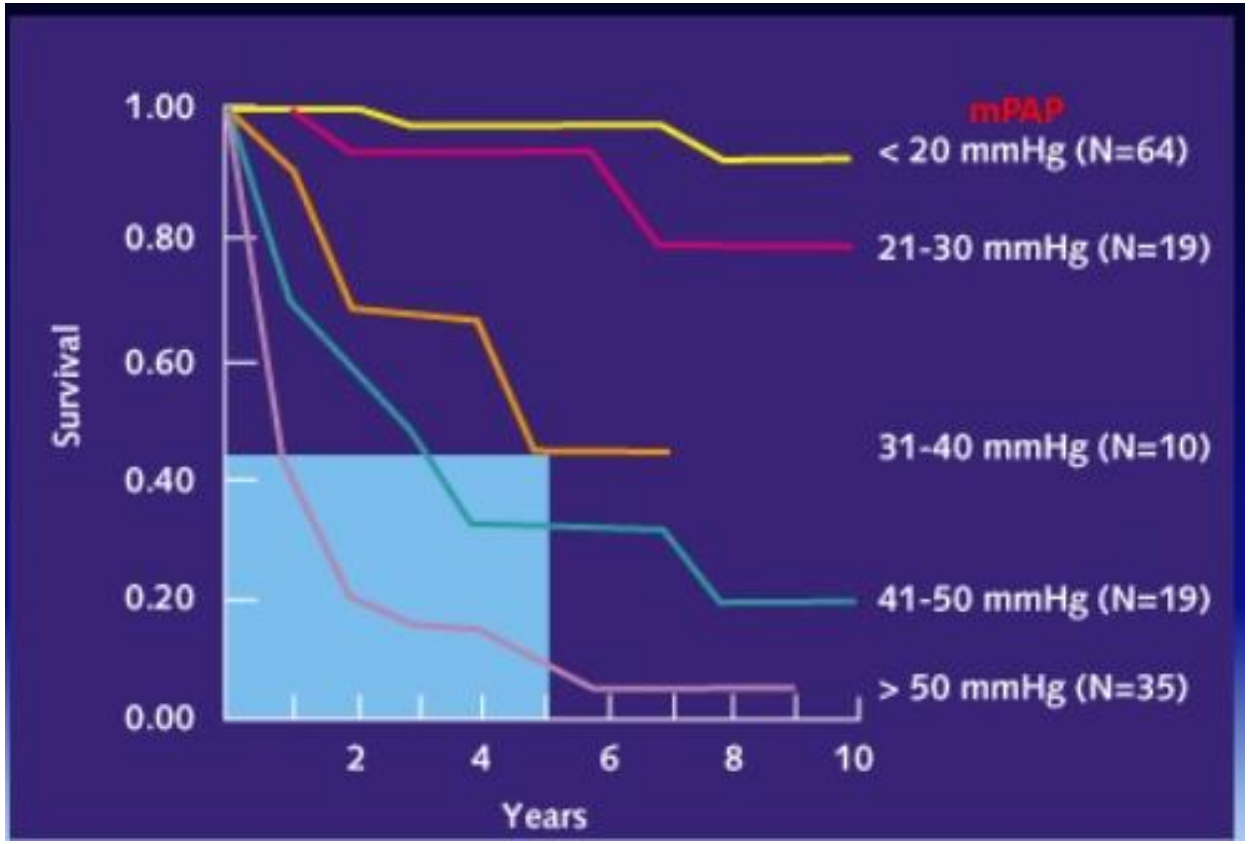
Acute PE → **CTEPH**

Resolution
(96~99%)

Small Vessel Changes

Natural Course of CTEPH

- Riedel M et al. Chest 1982;81:151-8



Incidence & Prevalence

- More prevalent than recognized
  - Acute PE : Estimated 1 in 1,000 population
  - About 1~5% risk of CTEPH from acute PE
  - Estimated 3,000~15,000 new cases annually in the U.S

  - Perhaps about ~250-300 endarterectomy performed

  - Where are these patients ?

Clinical Presentation

- Symptoms
  - Progressive dyspnea
  - Chest pain, hemoptysis, recurrent thrombophlebitis, chronic non-productive cough, palpitation

- Sign
  - Signs of RHF and severe PHT
  - Bruit over lung field

CTE Disease and CTEPH

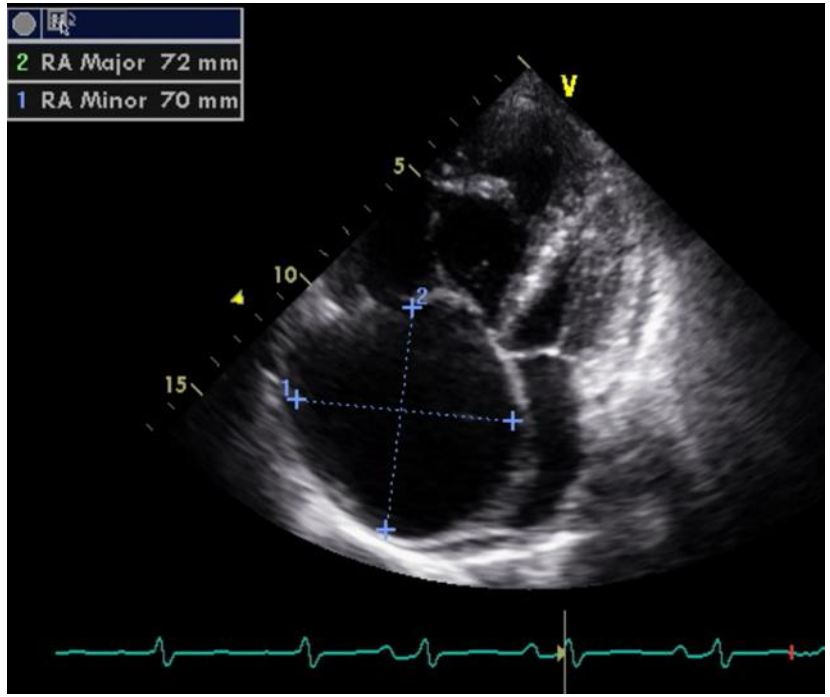
- High index of suspicion in patients who have unexplained exertional dyspnea
- Absence of a known history of DVT does not exclude CTEPH
- DDx : COPD, Asthma, Deconditioning…
- Dx of PH should be considered in all patients with unexplained dyspnea… and CTEPH in all patients with PH

Diagnostic Evaluation : SCAR

- Suspect
  - Echo : Assess for PH
  - V/Q scan : detect of vascular occlusion
- Confirm
  - Right Heart Cath : Assess for PH
  - Pulmonary Angiography (CT or MRI, invasive) : detect of vascular occlusion
- Assess Risk
  - Hemodynamics, comorbidities, suegeon/CTEPH team experience

TTE

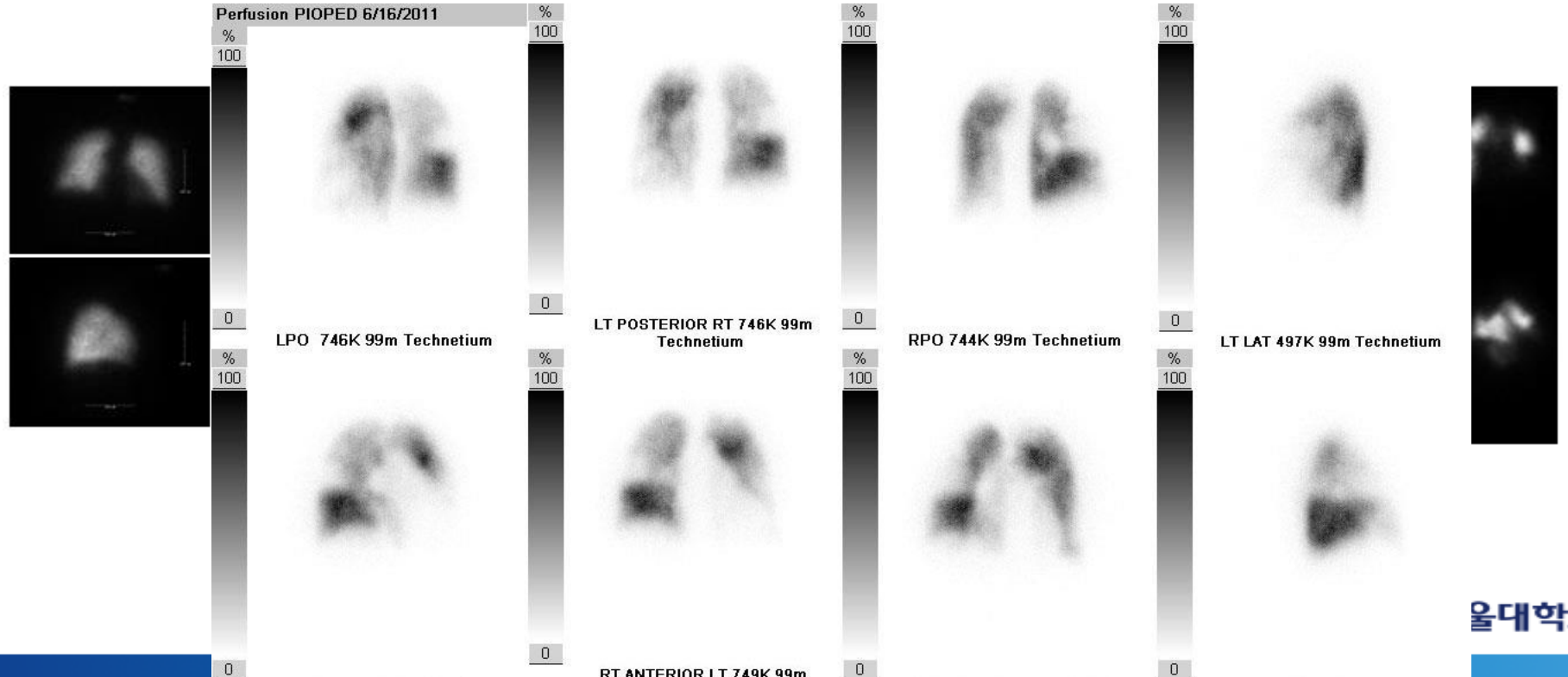
- Hemodynamics
  - Indirect PA pr
  - RV function
  - TR grading



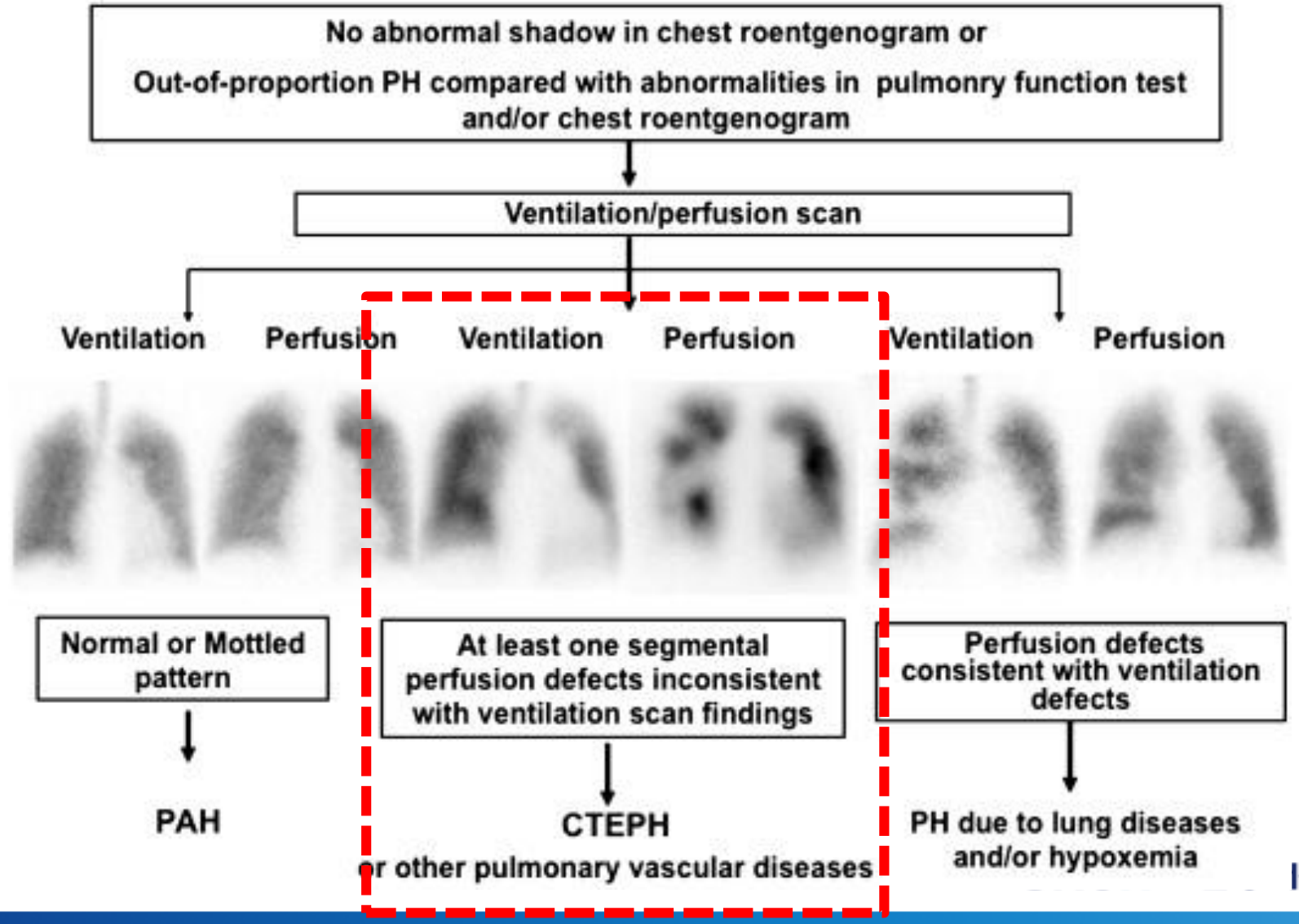
- Structural Assess
  - D shaped LV
  - Intracardiac shunt : ASD/PFO…
  - R/O Left heart problem causing PH

VQ scan

- High sensitivity >96% (CTPA 51%)
- Normnal VQ scan can R/O CTEPH

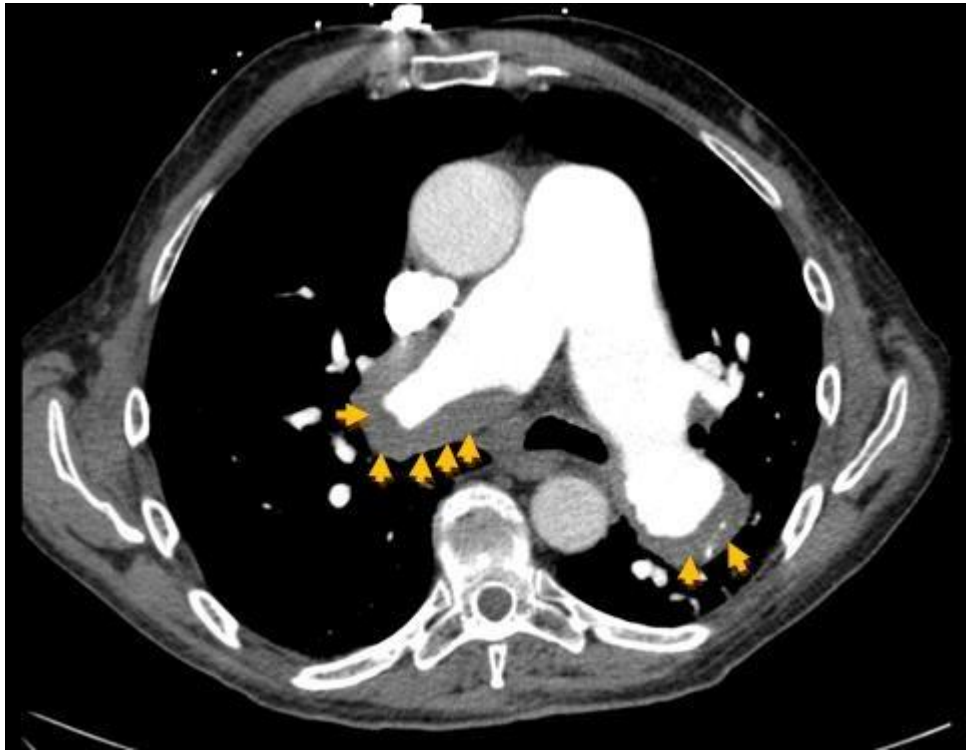


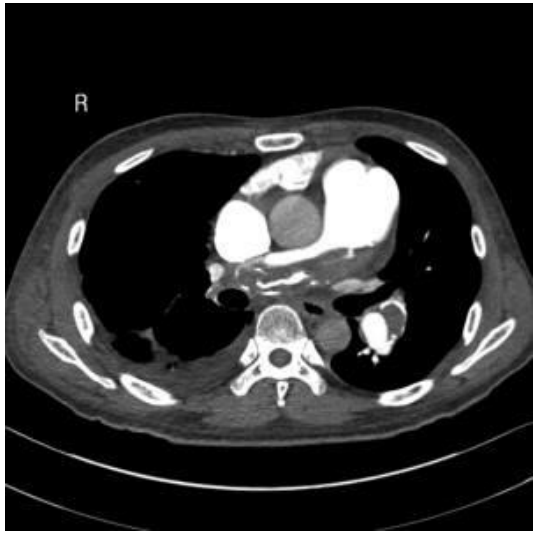
D/D of VQ scan


No abnormal shadow in chest roentgenogram or
Out-of-proportion PH compared with abnormalities in pulmonry function test and/or chest roentgenogram
Ventilation/perfusion scan
Ventilation
Perfusion
Ventilation
Perfusion
Ventilation
Perfusion
Normal or Mottled pattern
At least one segmental perfusion defects inconsistent with ventilation scan findings
Perfusion defects consistent with ventilation defects
PAH
CTEPH
or other pulmonary vascular diseases
PH due to lung diseases and/or hypoxemia

CT findings

- Eccentric thrombus
- Lining thrombus
- Enlarged PA

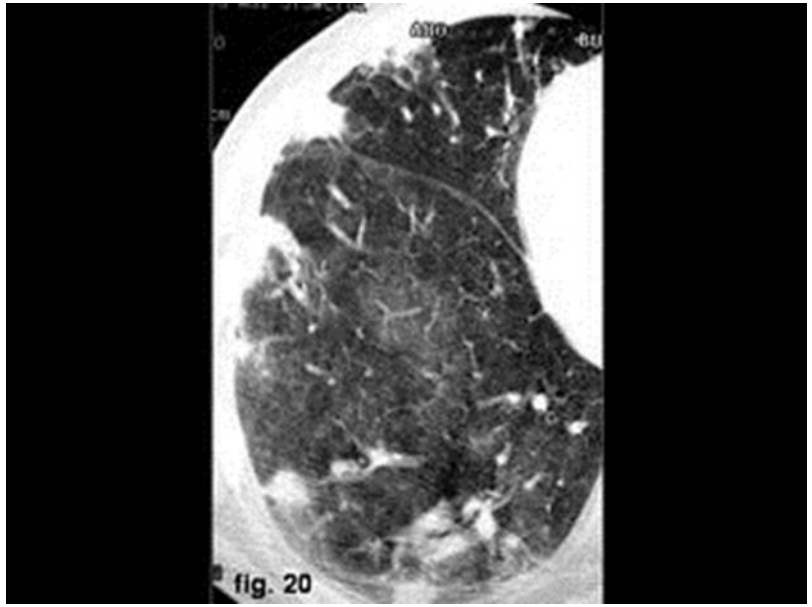


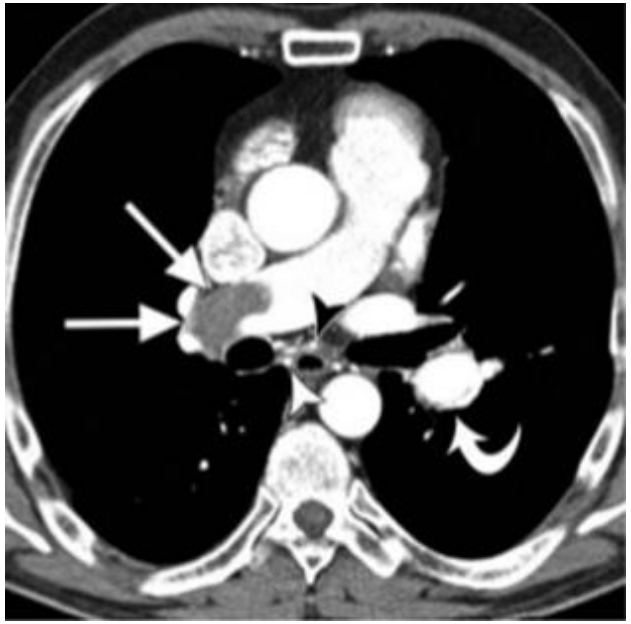


- Recanalization

CT findings

- Mosaic perfusion





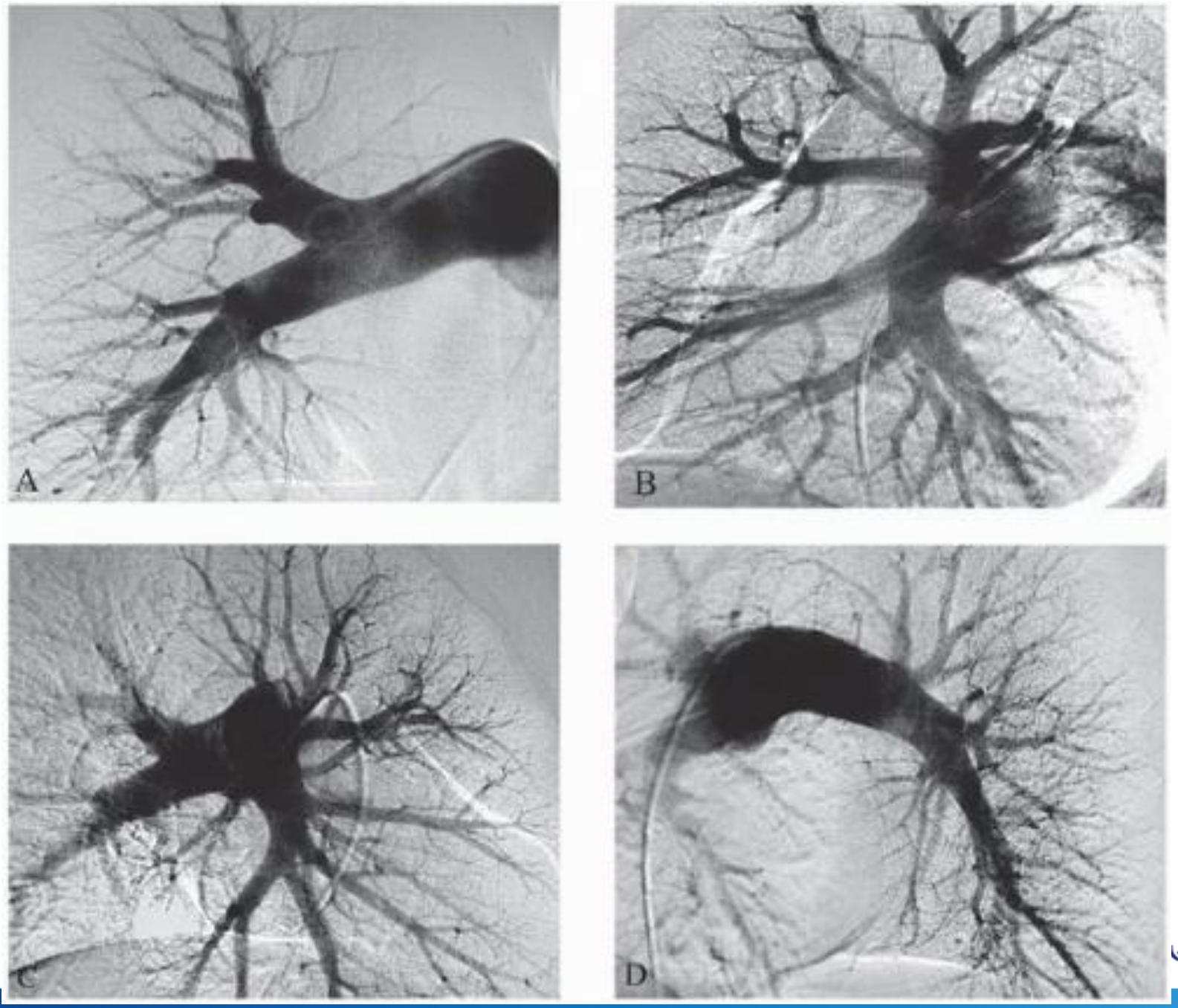
- Bronchial artery collaterals

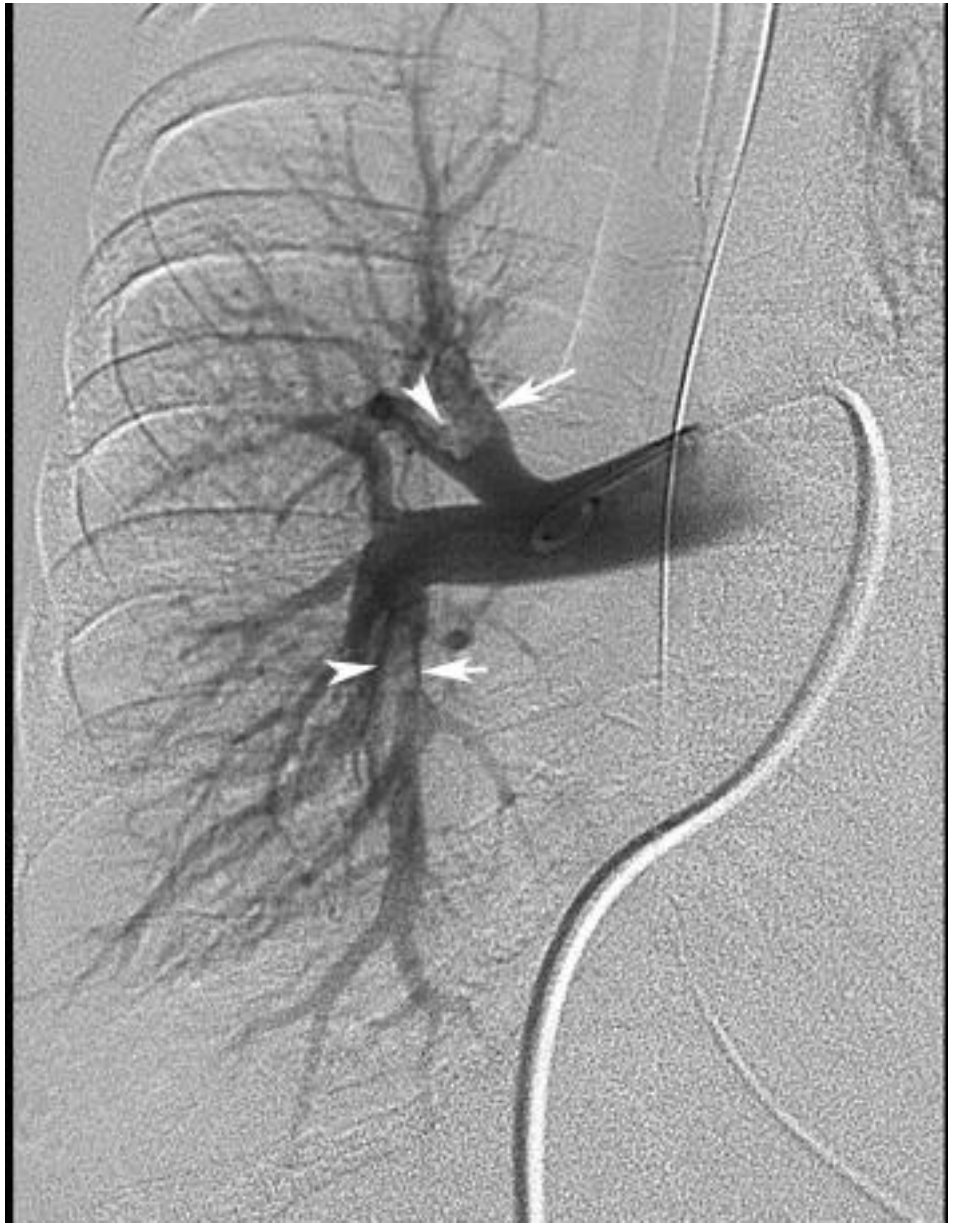
Pulmonary Angiography

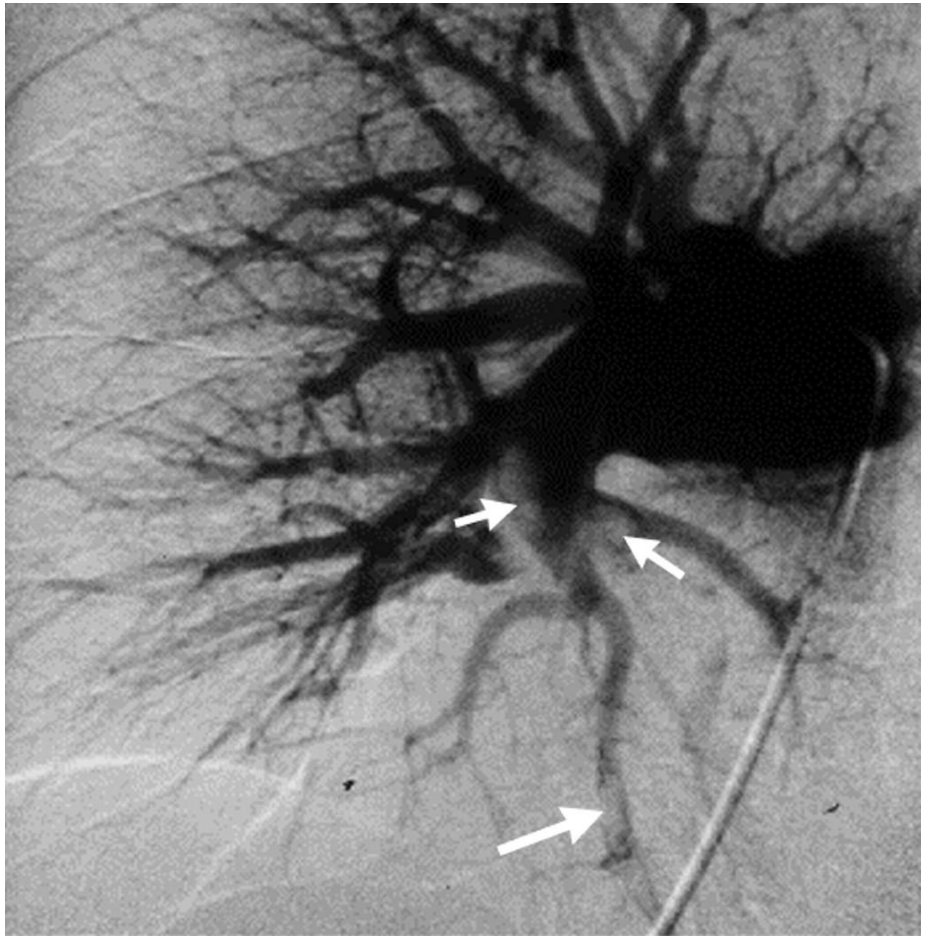
- ‘Gold Standard’
- Essential to establish operability for more distal CTE disease

  - Single injection : Rt and Left
  - Biplane study : PA and Lateral

  - ‘Pouch’ defects
  - Webs and bands
  - Intimal irregularity
  - Abrupt vascular narrowing
  - Complete obstruction at main. Lobar or segmental levels

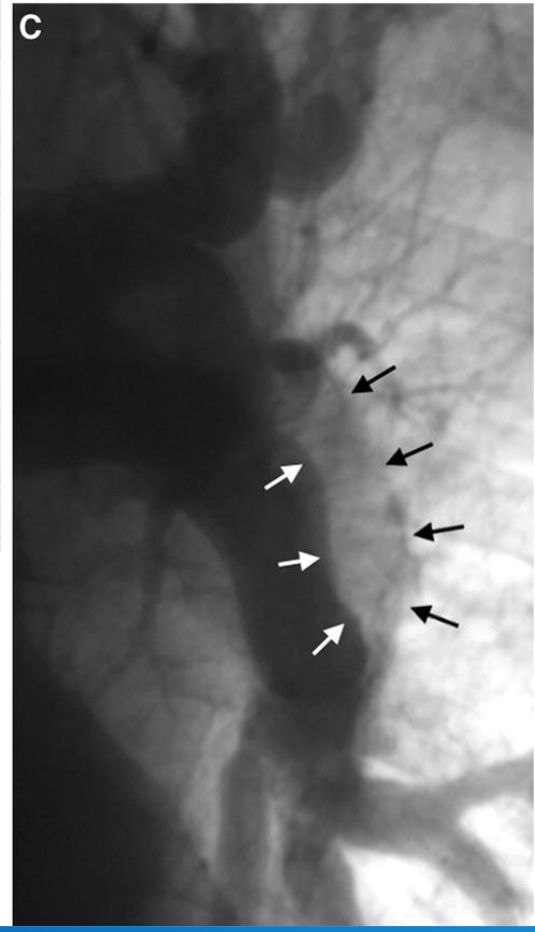

A
B
C
D

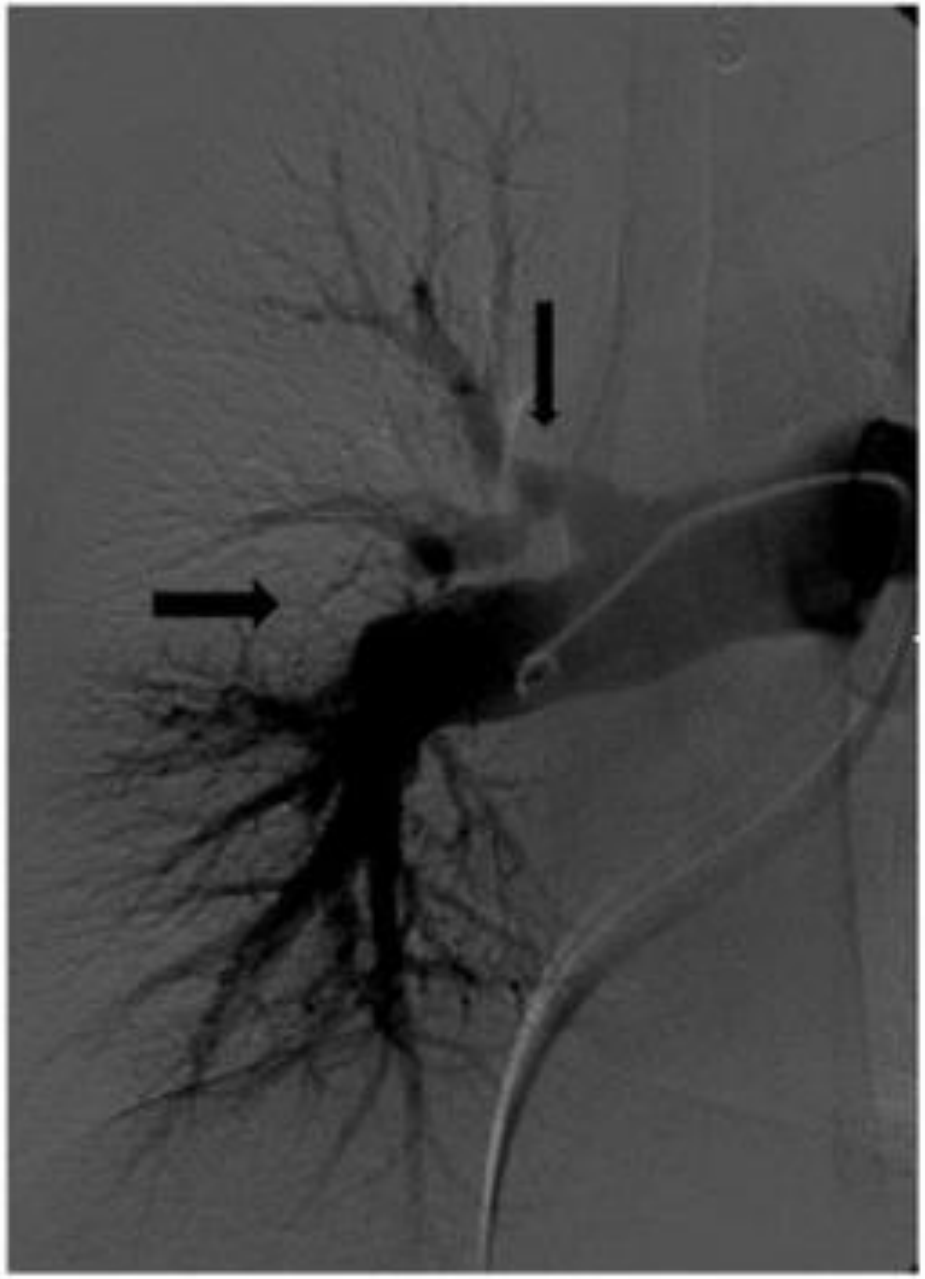


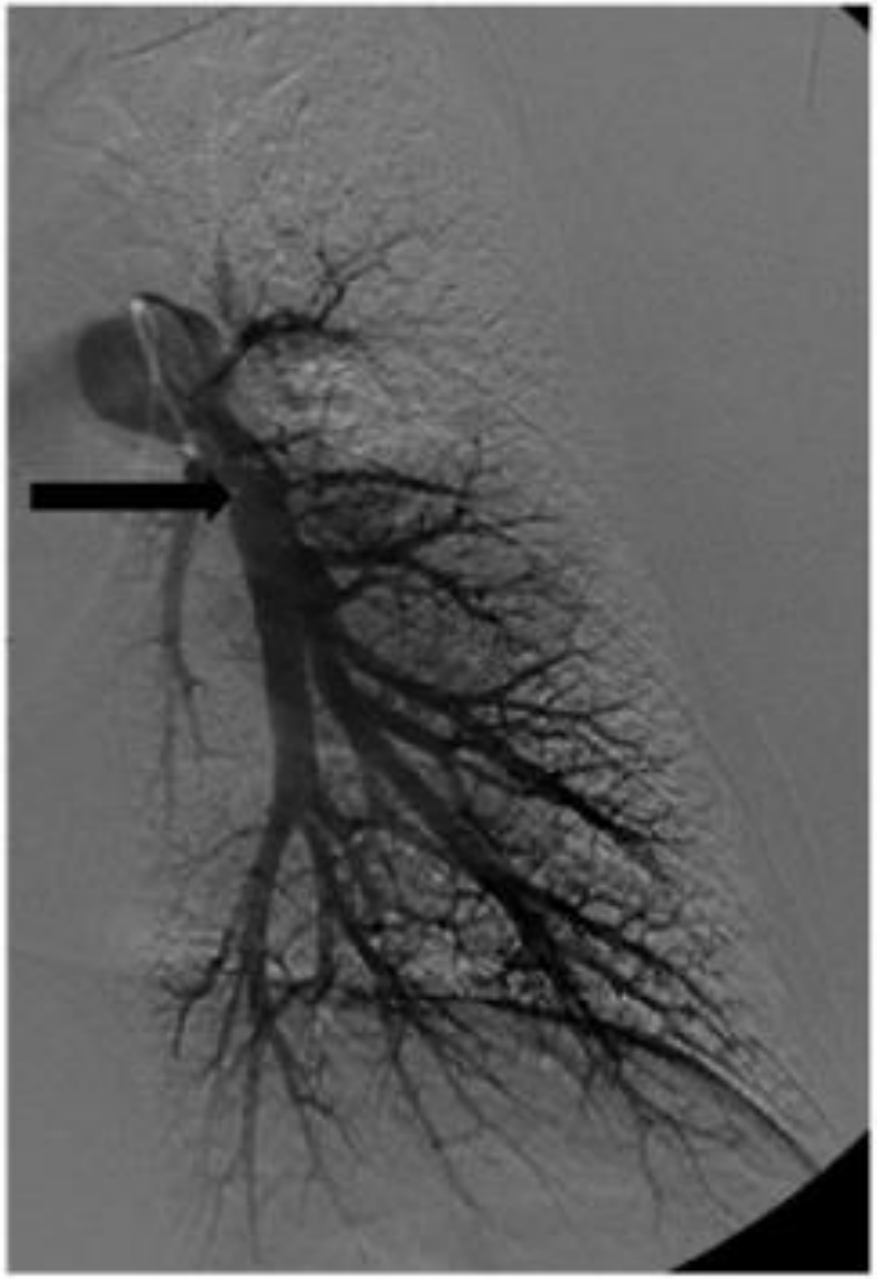


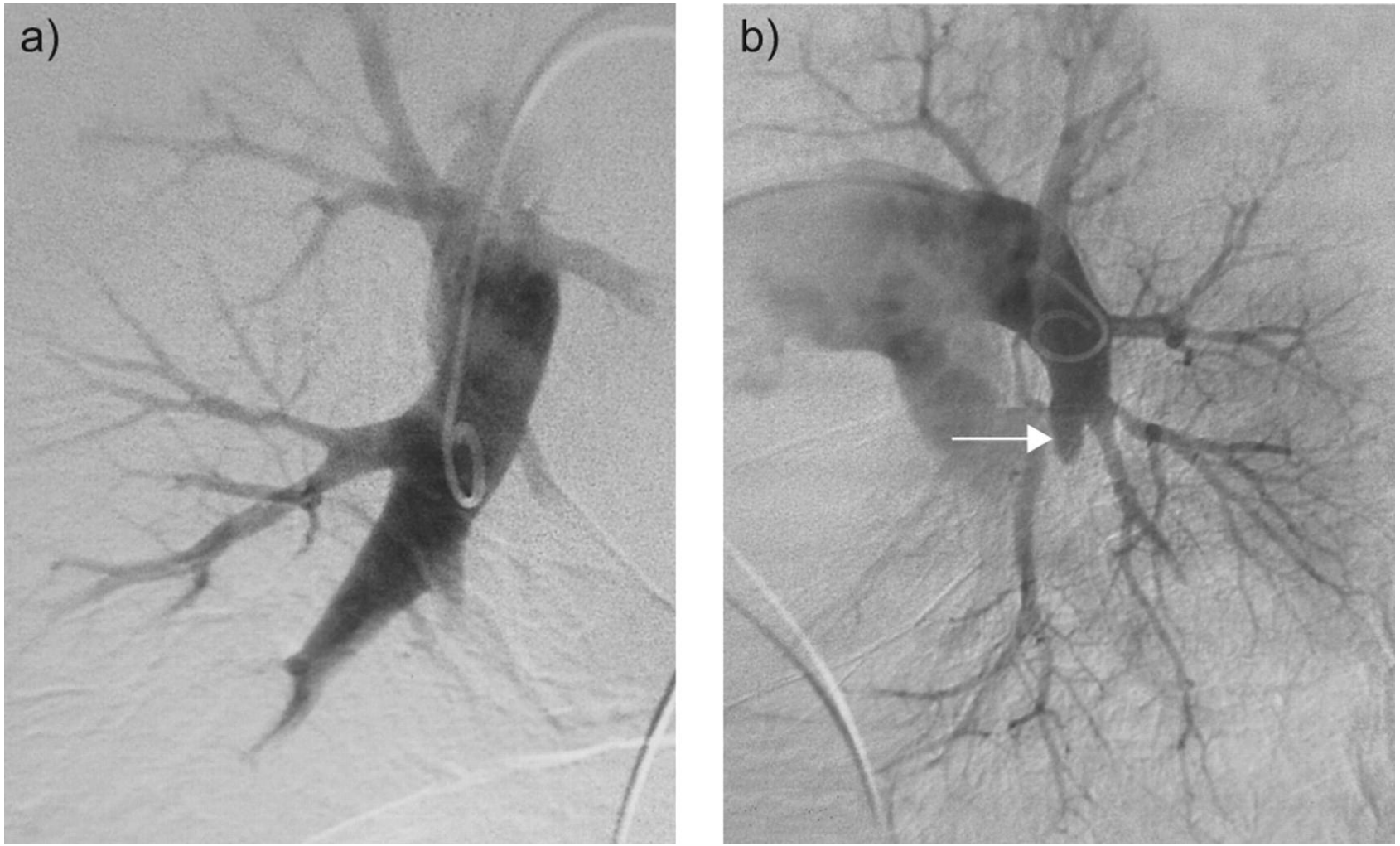

A


B


C






a)
b)

Pulmonary Angiography : Rt Ht Cath

- Hemodynamic assessment : PCWP, sPAP, RVP, PVR…

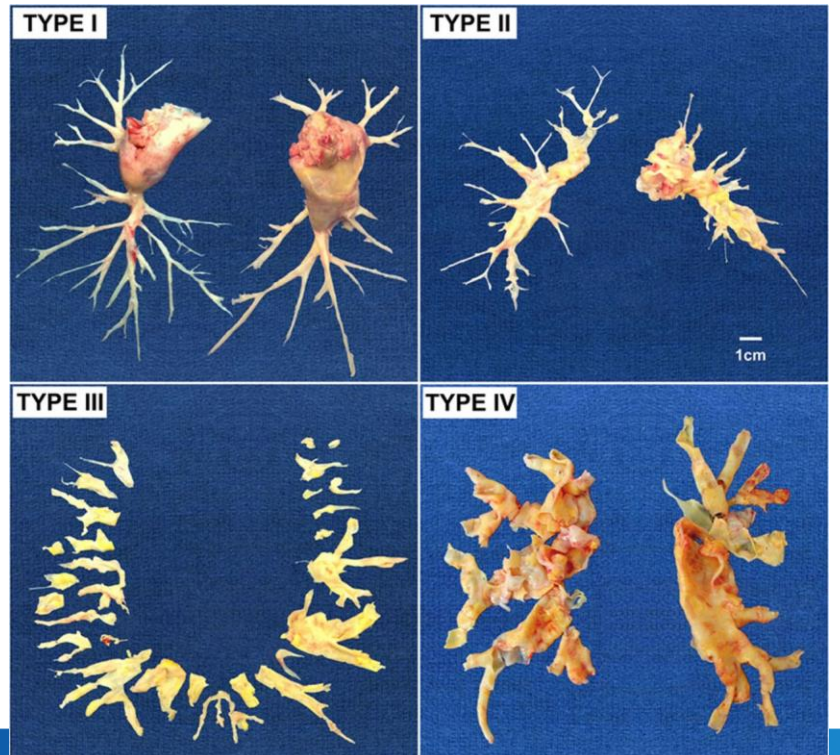
- Complete assessment process for surgical candidacy

Measurement	Normal Range
Right atrial pressure	0-5 mmHg
Right ventricular pressure, systolic	15-25 mmHg
Right ventricular pressure, diastolic	0-10 mmHg
Pulmonary artery pressure, systolic	15-25 mmHg
Pulmonary artery pressure, diastolic	6-12 mmHg
Mean pulmonary artery pressure	<25 mmHg
Pulmonary artery wedge pressure	≤12 mmHg
Cardiac output	>5 L/min
Cardiac index	>2.4 L/min/m^2
Transpulmonary gradient	≤12 mmHg
Pulmonary vascular resistance	≤240 dyn-sec-cm^{-5}

Surgical Classification of CTEPH

Type 1	Fresh thrombus in main-lobar PA
Type 2	Intimal thickening and fibrosis proximal to segmental arteries
Type 3	Disease within distal segmental arteries
Type 4	Distal arteriolar vasculopathy without thromboembolic disease

20%

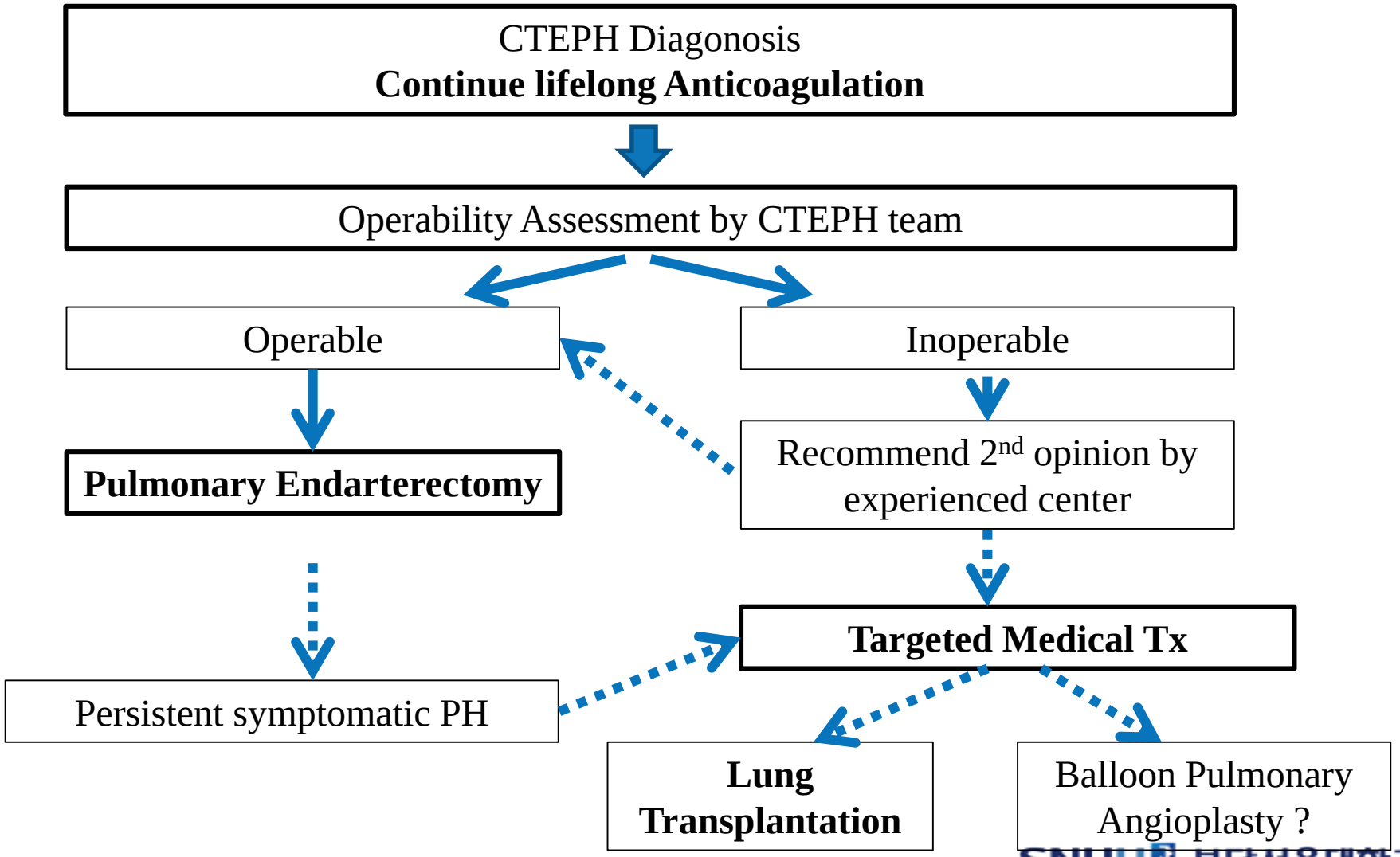


60%

20%

<5%

Treatment Algorithm for CTEPH



Operable vs Inoperable CTEPH

- Is there CTED that matches PH ?
  - PA angiography
  - What is the PVR ?
- Is there microvascular disease(inoperable) ?
  - Type IV
  - Expert opinion
- Surgical expertise
- Co-morbidities

Thrombo-

endo-

Artery

-ectomy

Thromboendarterectomy

Surgical Considerations

- Median sternotomy
- **CPB with DHCA under 18~20 ° C**
- LV venting
- Circulatory arrest

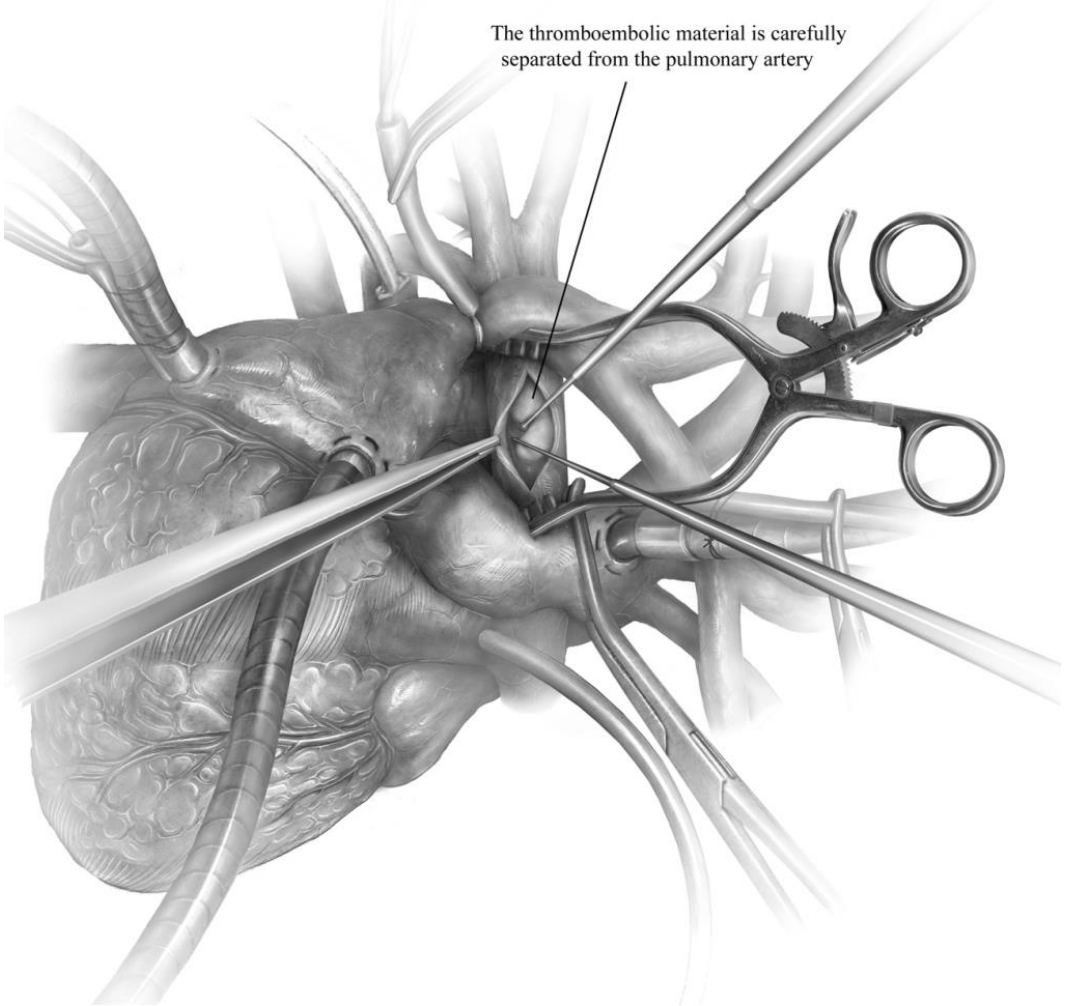
} Collateral flow

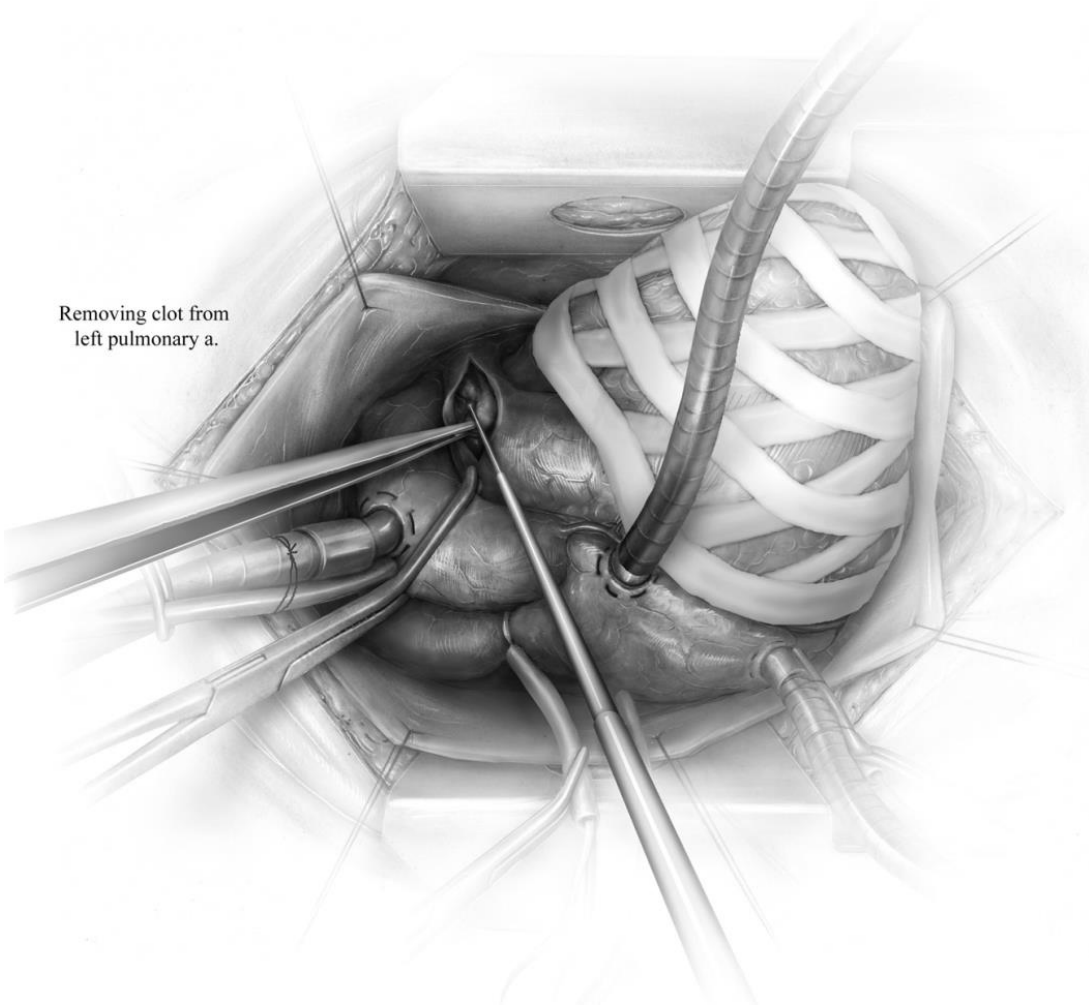
- **Complete bilateral endarterectomy, NOT embolectomy**
- **Identification of the plane : media**
    - Too superficial : risk of persistent pulmonary hypertension
    - Too deep : risk of vessel wall perforation that difficult to repair
- Functional TR : no correction!

Profound Hypothermia and TCA

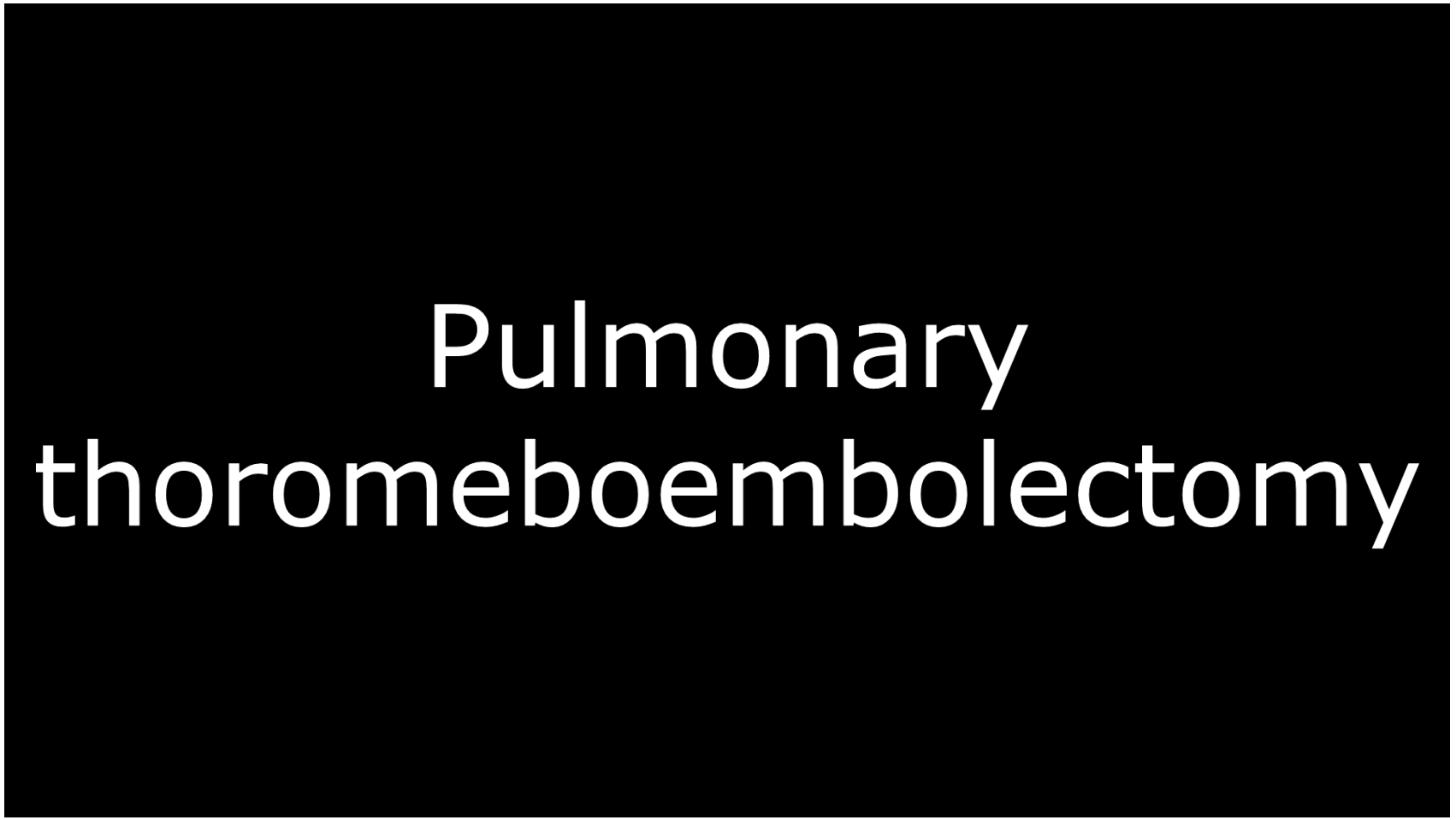
- Excellent visibility and a bloodless field are required.
  - To define an adequate endarterectomy plane
  - To follow the pulmonary endarterectomy specimen deep into the subsegmental vessels
  - To stop copious bronchial blood flow from aortic perfusion
- “Complete” endarterectomy is possible only with transient TCA.
- TCA periods are limited to 20 min, with restoration of flow between each arrest: intermittent TCA
- The endarterectomy usually can be performed with a single period of circulatory arrest on each side.

- Jamieson sucker tip
- Double action long forcep

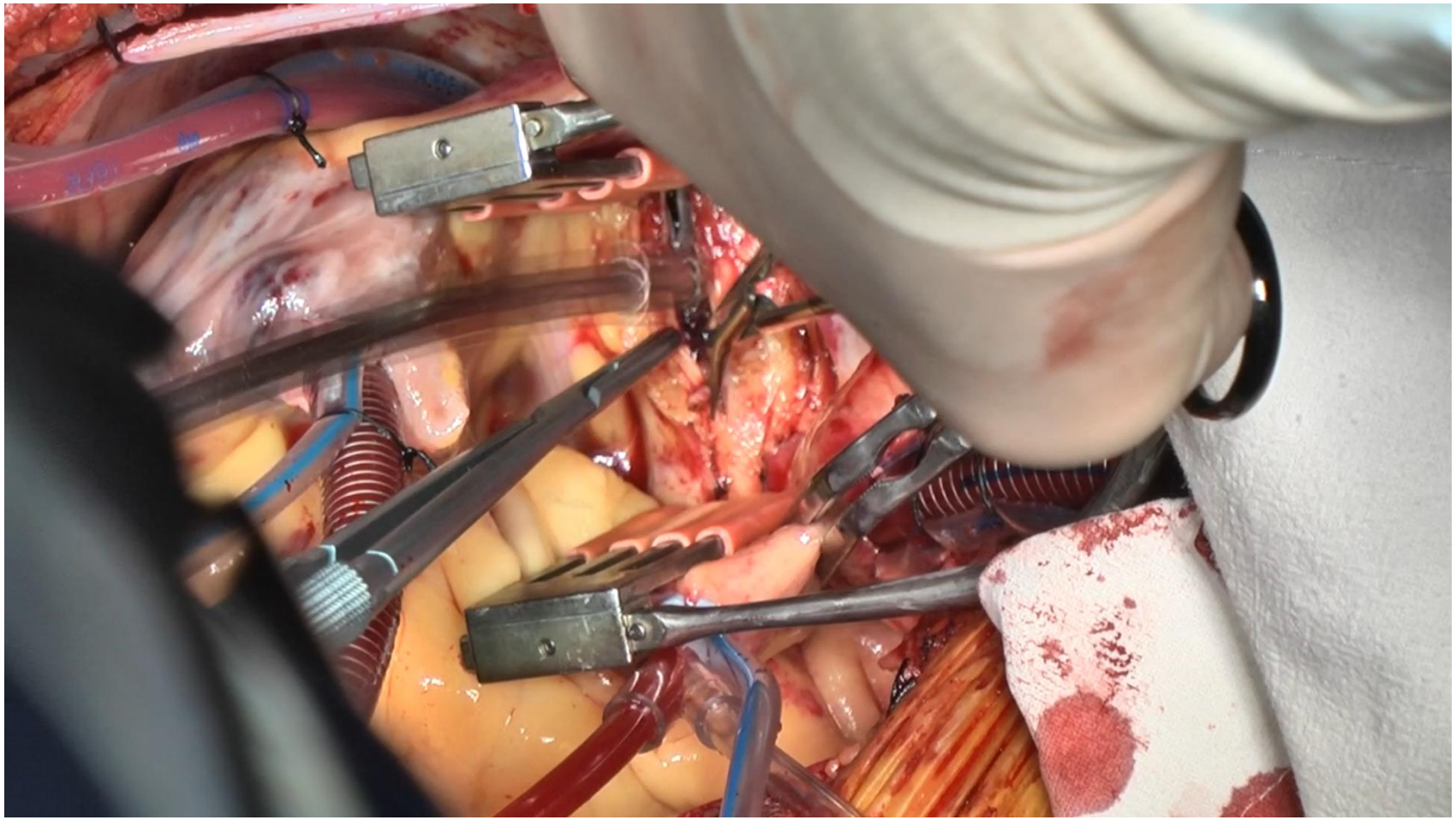




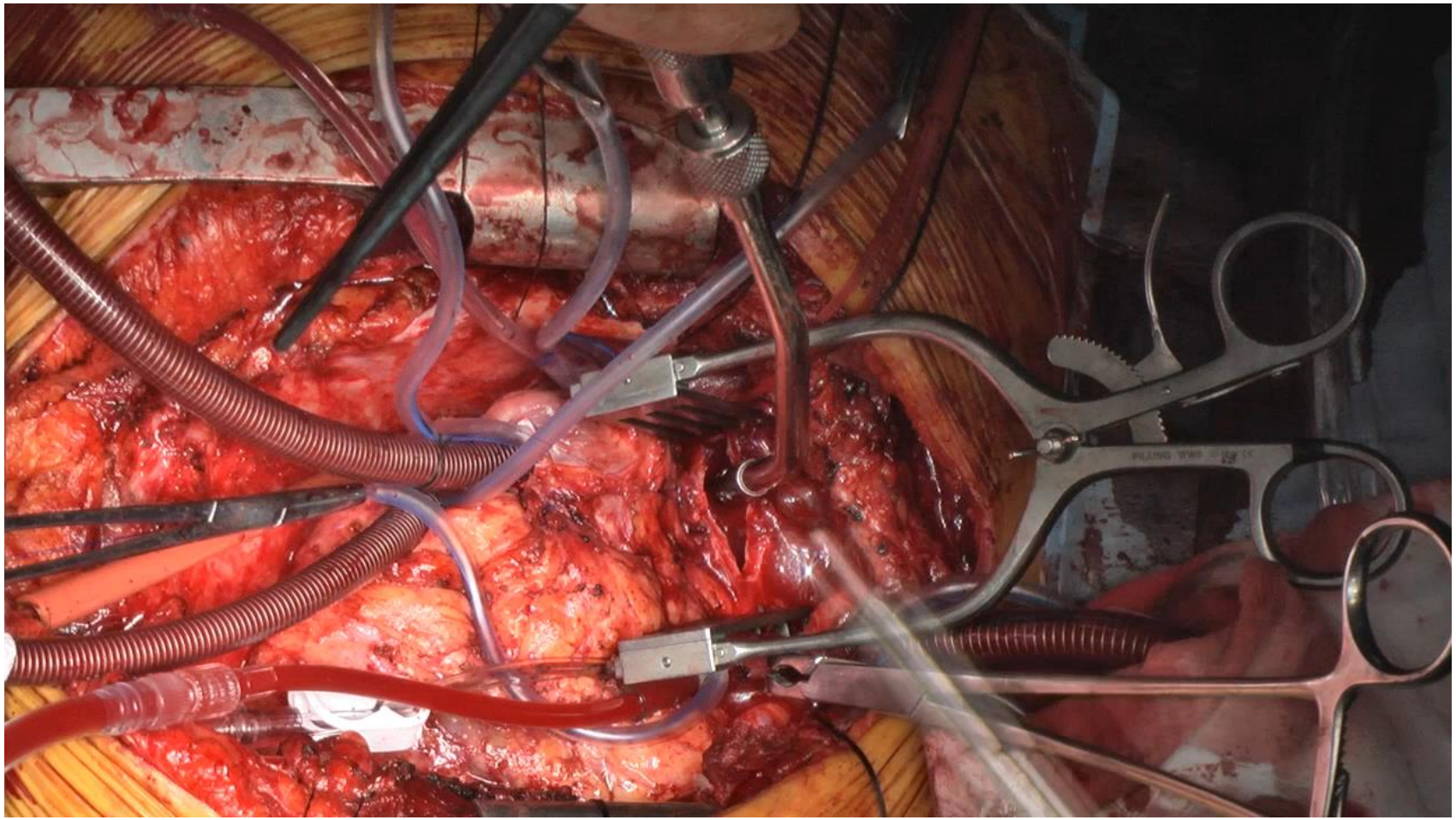
Operation Video : Type II CTEPH



Operation Video : Type I Subacute on CTEPH



Operation Video : redo Type II CTEPH



Operation Video : Type III CTEPH

Postoperative Care

- Early extubation
- AC ASAP
- Diuresis
- Persistent PH
- Reperfusion injury
- “Steal” phenomenon
- Re-exploration for bleeding
- Neurological deficits

Postop. Serious Complications

- “Reperfusion Response”
  - Localized pulmonary edema
  - Definition: Radiologic opacitiy seen in the lungs within 72 hours of pulmonary endarterectomy
  - True reperfusion injury : up to 10% of pts.
  - Symptoms & signs
    - Profound desaturation
    - Edema-like fluid (bloody tinge) is suctioned from the endotracheal tube.
  - Management
    - Minimize the development of pulmonary edema with diuresis
    - Maintenance of Hct levels
    - Early use of peak end-expiratory pressure
    - Careful management of ventilation and fluid balance
    - Inhaled NO at 20~40ppm can improve the gas exchange

Causes of Death

- **Residual PH** and RV failure
  - Inoperable case selection, PAH/type 4 disease
- Reperfusion lung injury
- Multi-organ failure
- Intra-operative hemorrhage from technical error

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Results : UCSD

- Over 3400 cases at UCSD medical center
  - Mean age 53 (7 to 88)
  - One third had at least one additional cardiac procedure…

  - Average operation time : about 7 hours
  - Mean CPB time : 218 ± 41 min
  - Mean ACC time : 88 ± 25 min
  - Mean TCA time : 37 ± 12 min

Pre & Post hemodynamics

- PVR : 897 → 245 (dynes/sec/cm-5)
- Mean PAP : 45.9 → 26 (mmHg)
- SPAP : 79 → 45 (mmHg)
- C.O : 3.6 → 5.8 (L/min)

Reduction of PVR is Key

- 500 patients Oct 2006 ~Dec 2010
- Postop PVR > 500 dsc-5
  - 10.3% mortality
- Postop PVR < 500 dsc-5
  - 0.9% mortality

Madani MM Ann Thorac Surg 2012

Overall Mortality by Era

- Before 1990 : 17%
- 1990~1998 : 8%
- 1998~2006 : 4.1%
- 2006~2010 :2.2%
- 2010~2014 : 1%

The volume–outcome relationship for pulmonary endarterectomy in chronic thromboembolic pulmonary hypertension

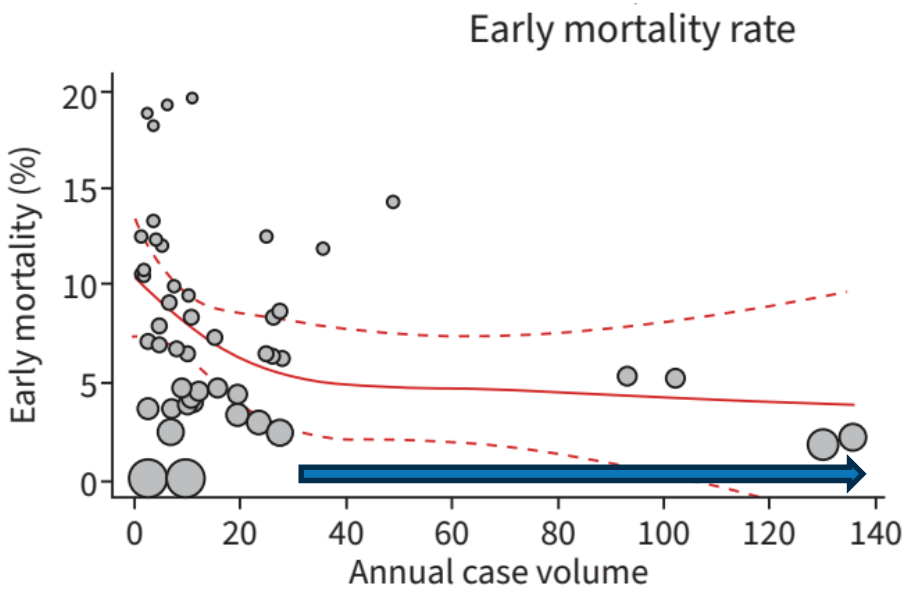
Samuel Heuts, Michal J. Kawczynski, Arthur Leus, Laurent Godinas, Catharina Belge, Vanessa van Empel, Bart Meyns, Jos G. Maessen, Marion Delcroix and Tom Verbelen

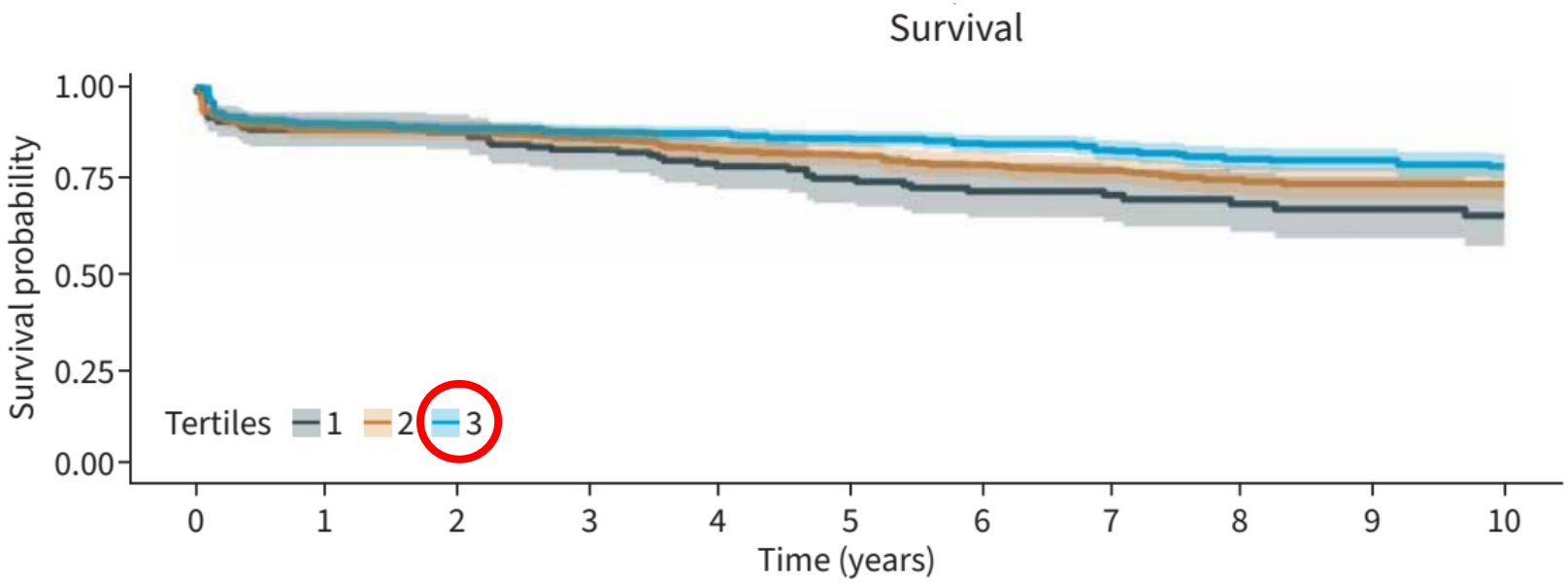
Eur Respir J 2025; 65: 2401865

Pulmonary endarterectomy
n=11 345 patients

52 unique cohorts
25 countries
4 continents

High volume center (>33 cases per year) showed better early and long term survival.



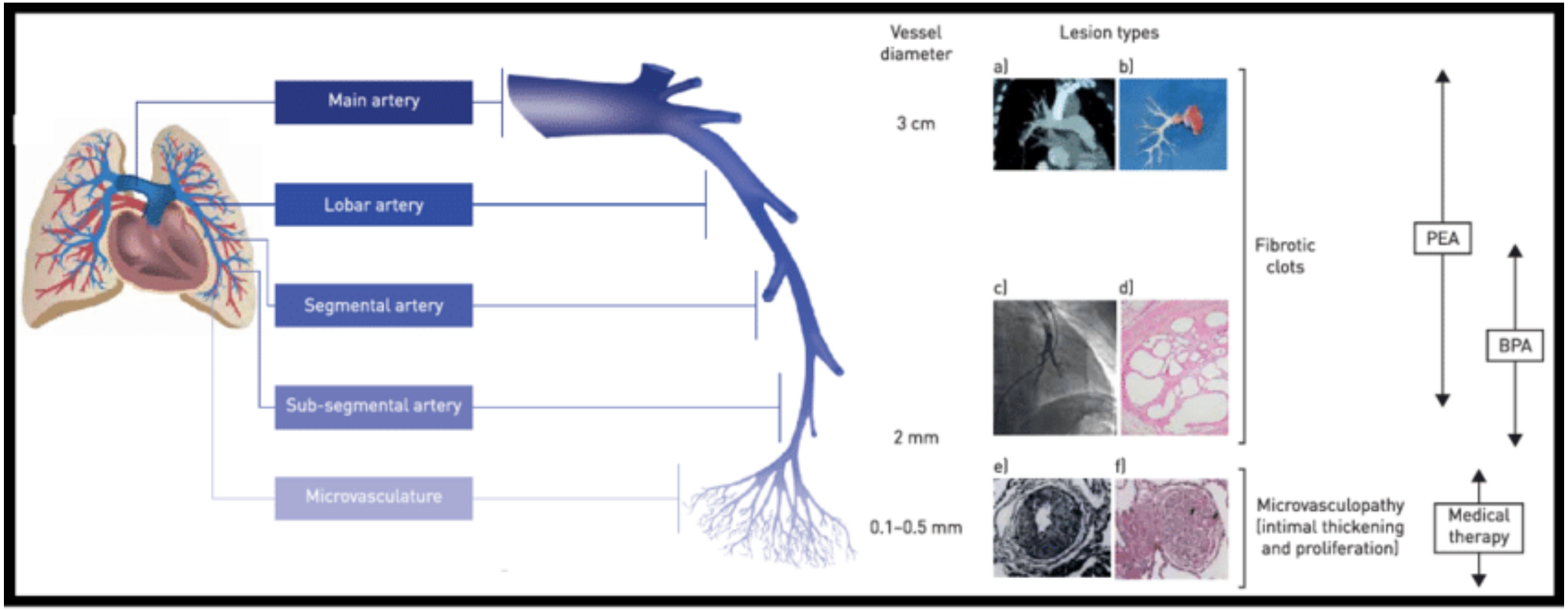


Hybrid Approach : PEA+BPA

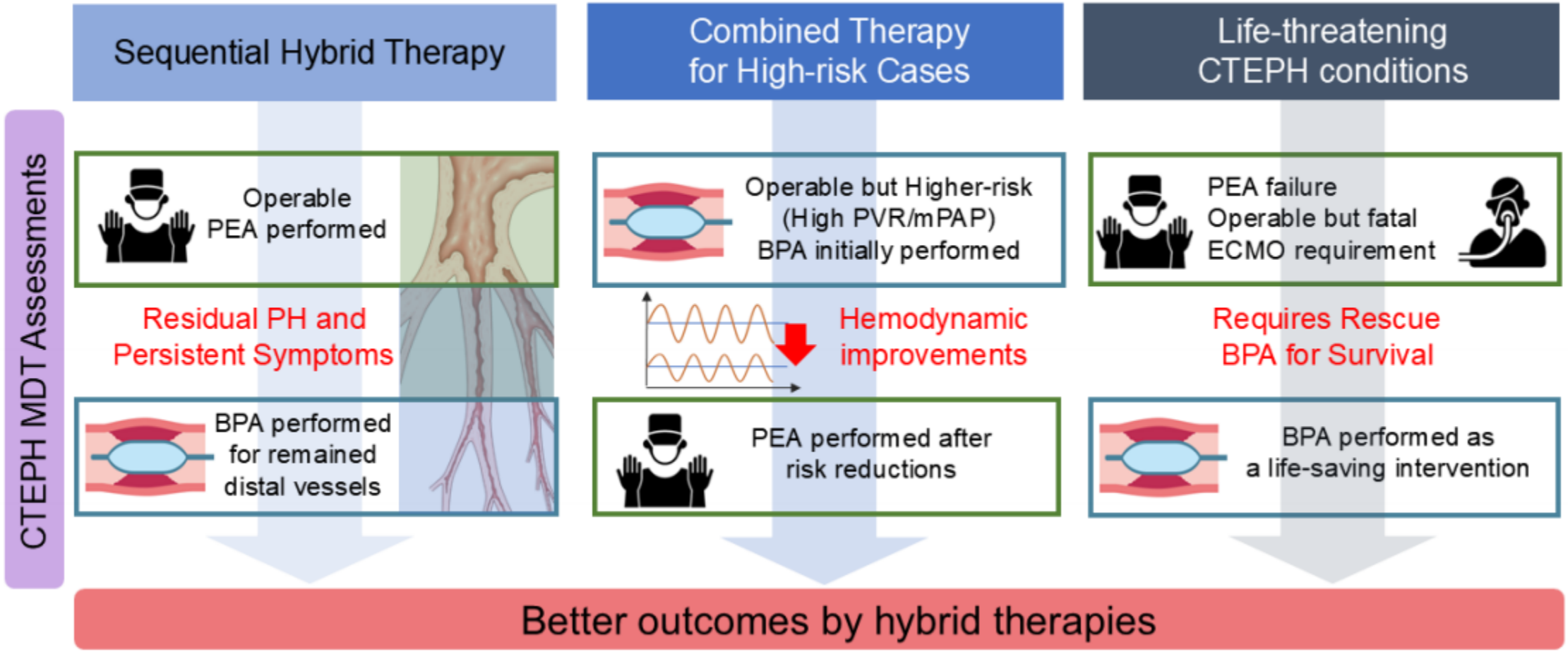
Supplementary file 1. Summary of the findings of studies on the use of additional BPA after PEA, including the number of patients, timing after PEA, haemodynamic improvements, and complication rates

Authors	Year	Patients (n)	Period from PEA to 1st BPA (months)	PVR before BPA (dyne/sec/cm^{-5})	PVR after BPA (dyne/sec/cm^{-5})	ΔPVR	Severe haemoptysis*	Mechanical ventilation or ECMO
Shimura et al.	2015	9	4.1 (2.7 –7.9)	648 (488–984)	336 (224384)	-48 %	2.30 %	0 %
Yanaka et al.	2018	10	7.3 ± 2.3	386 ± 42	242 ± 39	-37 %	8.30 %	0 %
Araszkiewicz et al.	2019	15	28.1 ± 25.8	552 ± 184	348 ± 126	-37 %	2.80 %	0 %
Ito et al.	2021	25	unknown	392 ± 160	296 ± 40	-24 %	16.80 %	0 %
Kirkby et al.	2023	20	unknown	532 ± 172	454 ± 182	-15 %	unknown	unknown

Hybrid Approach : PEA+BPA



Hybrid Approach : PEA+BPA



Conclusions

- PEA remains the definitive and curative Tx for CTEPH.
- Successful PEA requires precise identification and dissection of organized thrombus plane under hypothermic circulatory arrest.
- Complete bilateral endarterectomy and avoiding residual PH are key to optimizing postoperative hemodynamics.

Conclusions

- Hybrid strategy (PEA+BPA) is optimal Tx for high risky patients.

- Surgical success depends on experience and multidisciplinary evaluation.

Thank you for your Attention !!!

Any Questions ?