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National Blood Clot Alliance

Stop The Clot®

Navigating Post-Thrombotic Syndrome, Chronic Thromboembolic Pulmonary Hypertension and Chronic Thromboembolic Disease

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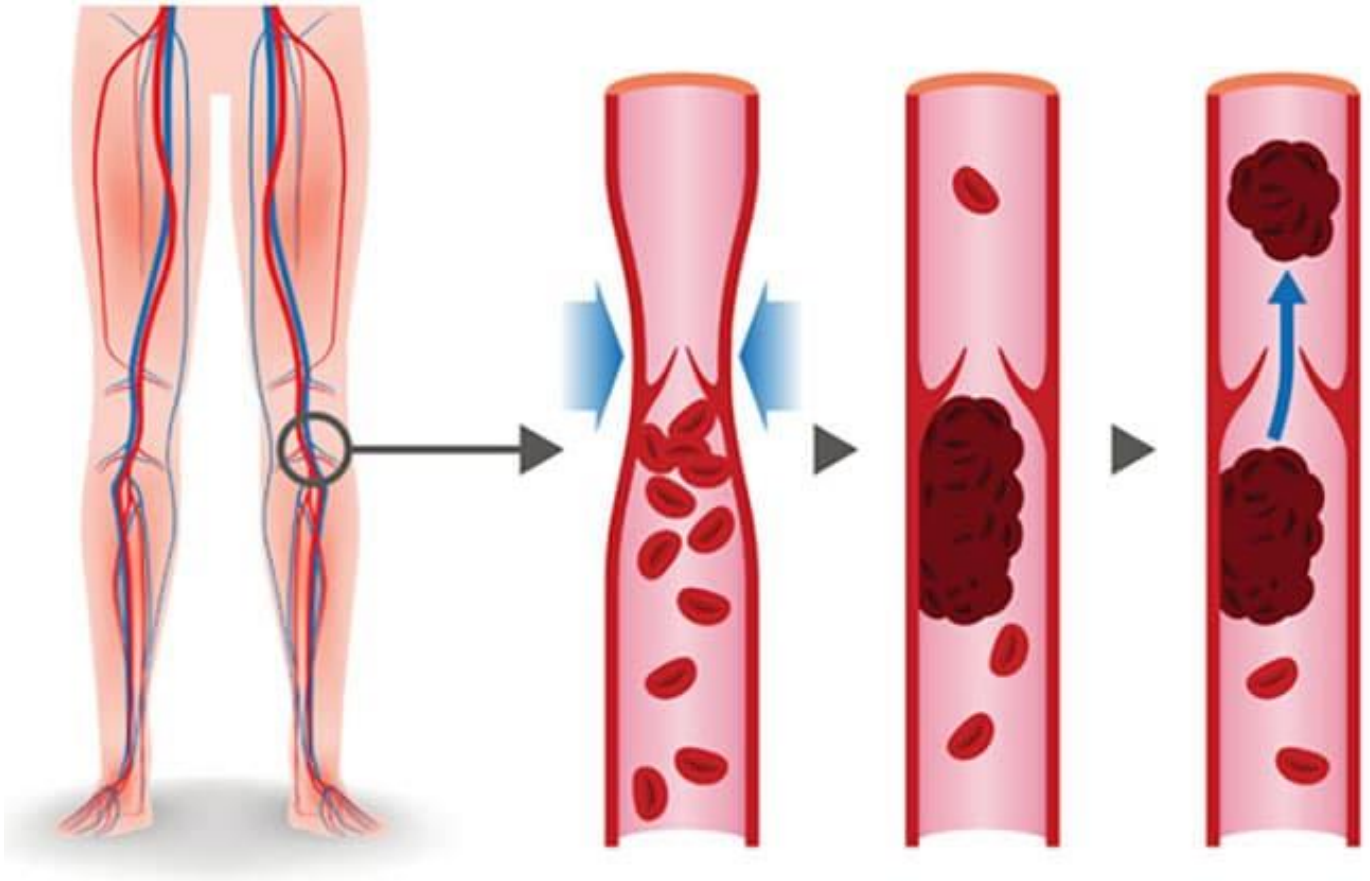
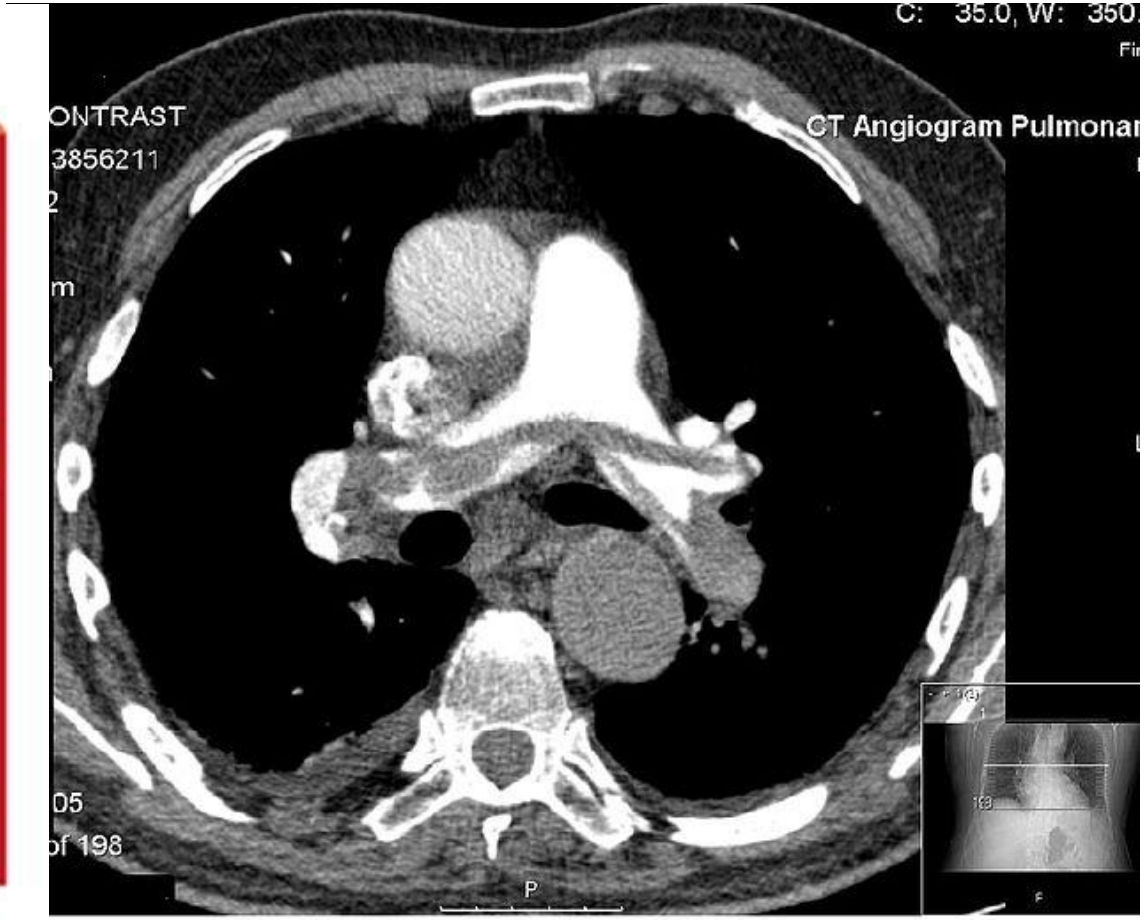
  - UT
  - Janssen

Acute Deep Vein Thrombosis and Pulmonary Embolism: The Race Begins…





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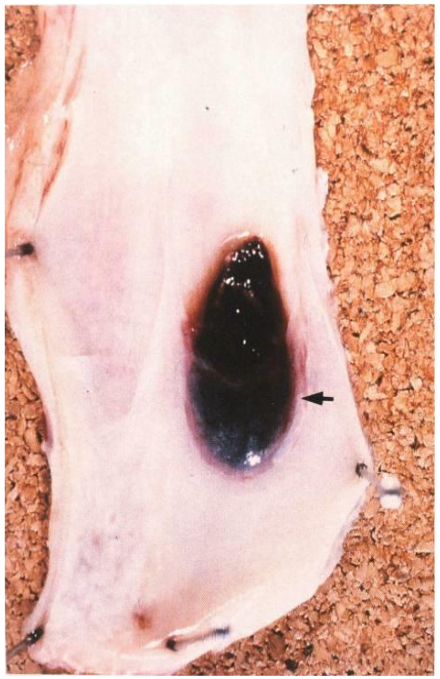
DVT Disease Progression to Post-Thrombotic Syndrome

Acute → **Subacute** → **Chronic**

Acute thrombus in a CFV valve

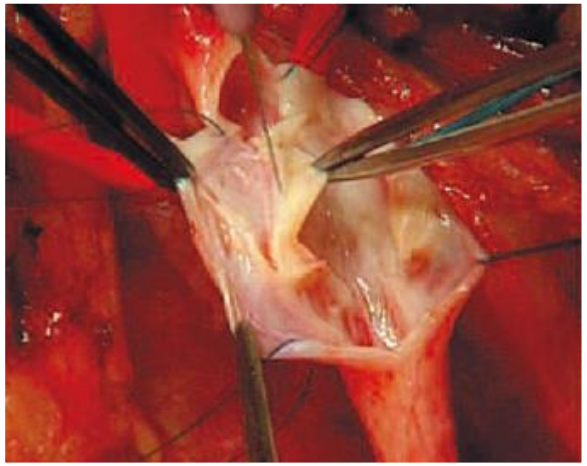




PTS damage in a CFV valve



Thrombus conversion to collagen “Chronic DVT”: Chronic Fibrosis



Post-thrombotic luminal changes

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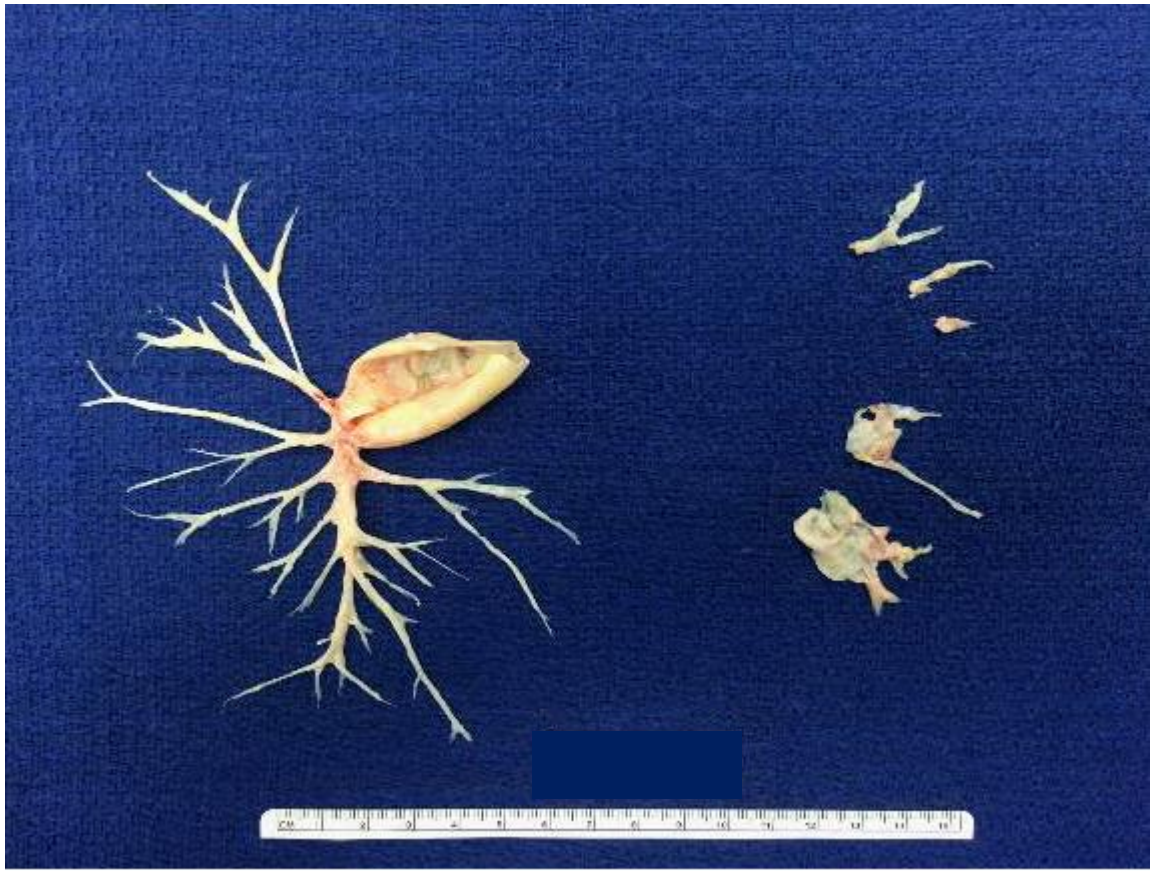
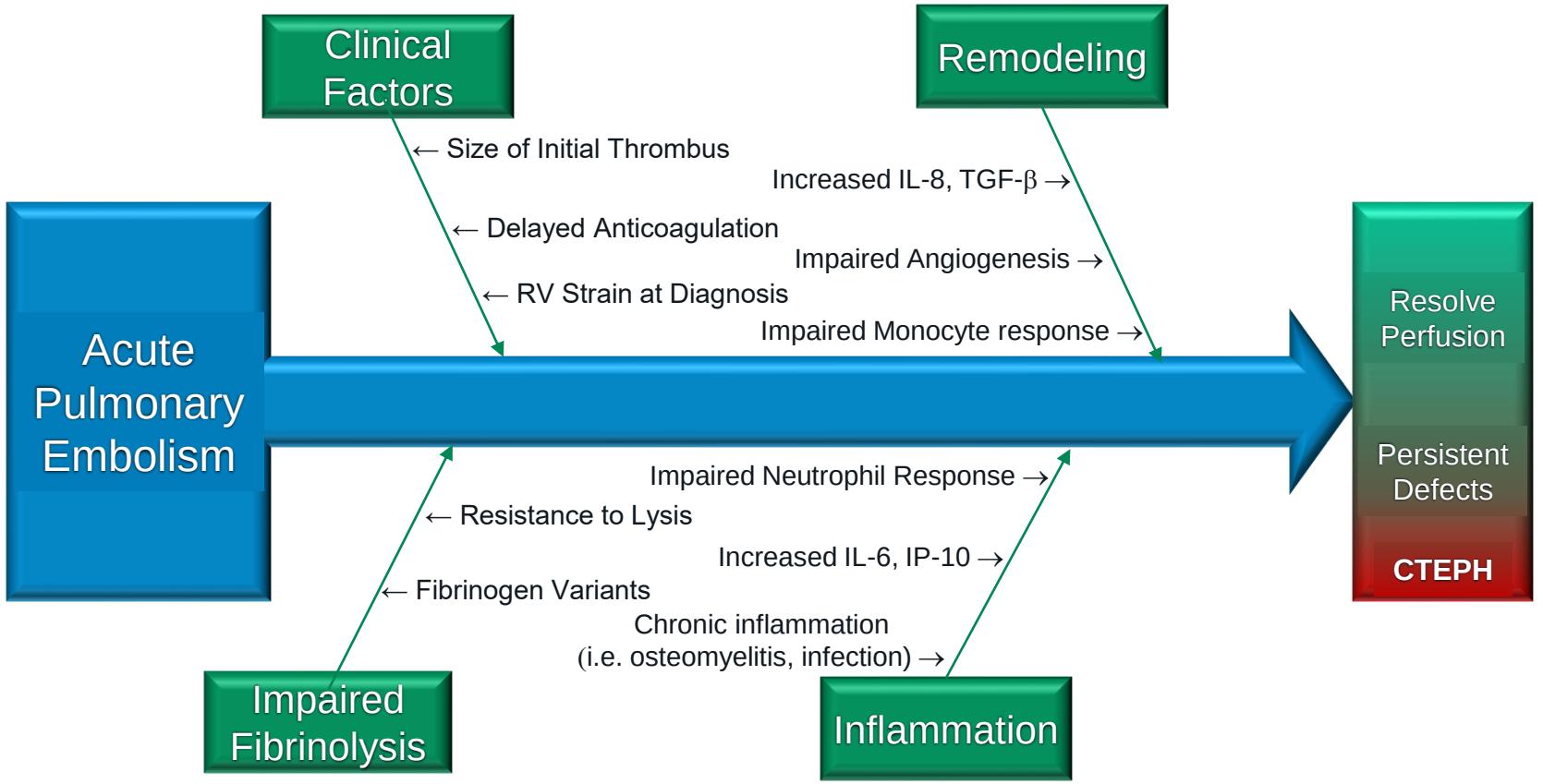
Slide content provided by Dr. Antonios P. Gasparis of Stony Brook Medicine, consultant to Penumbra. Procedural and operative techniques and considerations are illustrative examples from physician experience. Physicians' treatment and technique decisions will vary based on their medical judgment.

Acute PE May Fail to Resolve Leading to Chronic Clot (CTEPH or CTED)





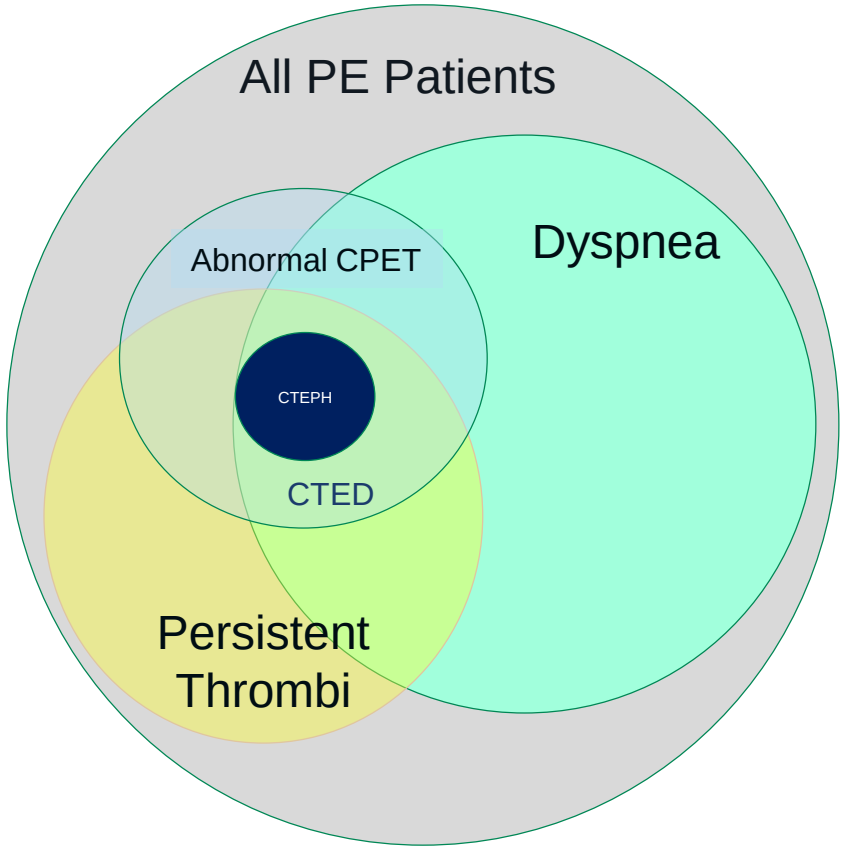
Acute PE May Fail to Resolve, Leading to CTEPH



The Post-PE Syndrome

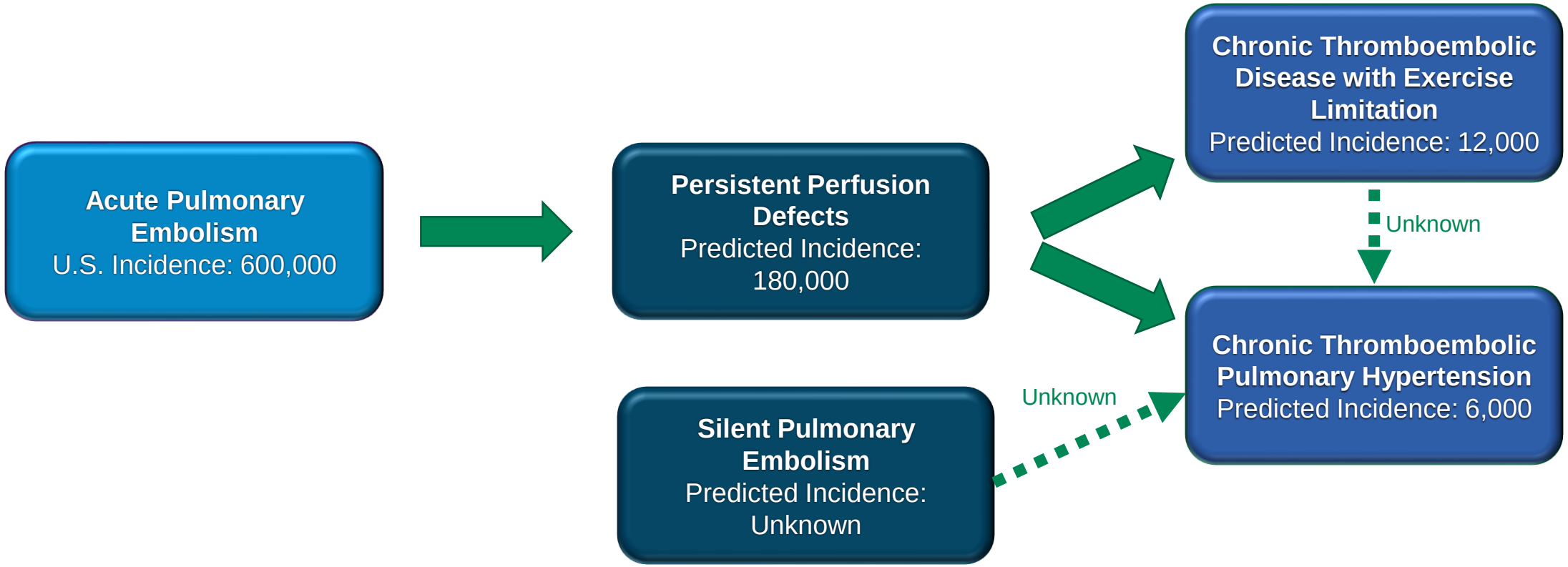
Modified from F.A. Klok et al. / Blood Reviews 28 (2014) 221–226

- Dyspnea Never returned to Pre-PE Baseline (50% of PE patients)
- Persistent Thrombi on Imaging (30-50% of PE patients)
- Measureable Cardiopulmonary Limitations
- Chronic Thromboembolic Pulmonary Hypertension (~3% of PE survivors)
- Chronic Thromboembolic _____ (~10% of PE survivors)

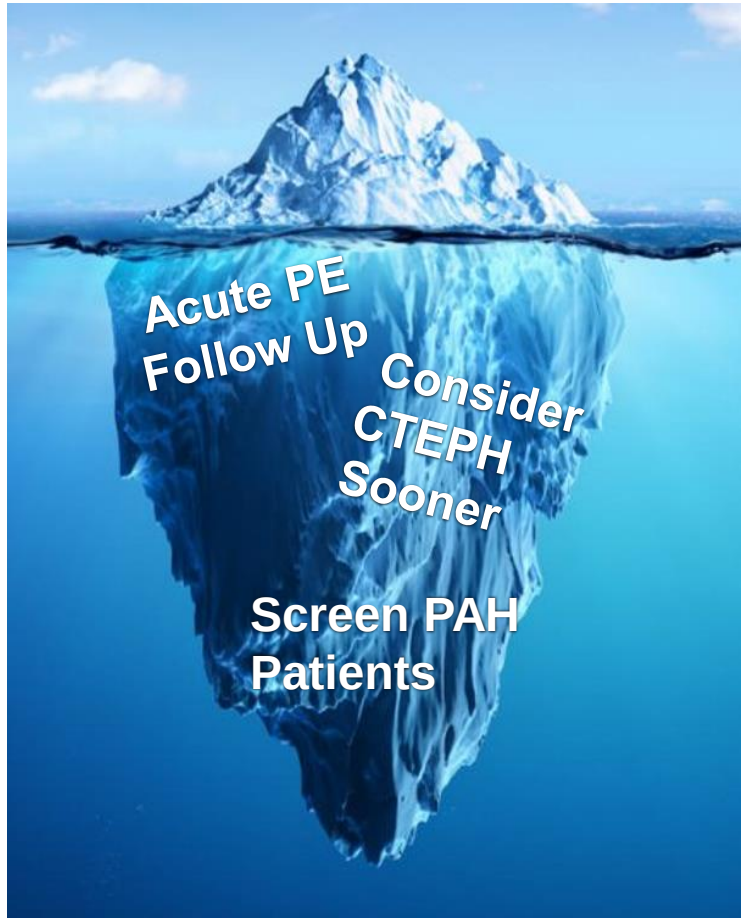


Mcguire WC, Alotaibi M, Morris TA, Kim NH, Fernandes TM. Chronic Thromboembolic Disease: Epidemiology, Assessment with Invasive Cardiopulmonary Exercise Testing, and Options for Management. *Structural Heart* 2021;5:120-127.

Annual CTEPH Incidence…the tip of the Iceberg



So where are all the CTEPH patients?



- INFORM Study[1] – 7068 incident PE
  - 87% had a claim for a PH-related symptom within 2 years
  - Only 55% had any diagnostic procedures
- Misdiagnosis and delay[2]
  - Median time from symptoms to CTEPH diagnosis: **21 months** (IQR 12-49 months)
  - Median saw 4 doctors; 13 visits
- PAH-QUERI
  - 43% of PAH patients did not have a screening V/Q scan

1. Tapson VF, *et al*. *Am J Med,* 2016;129:978-85.
2. Ende-Verhaar YM *et al. J Thromb Haemost,* 2018;16:2168–74

Screening for CTEPH and CTED

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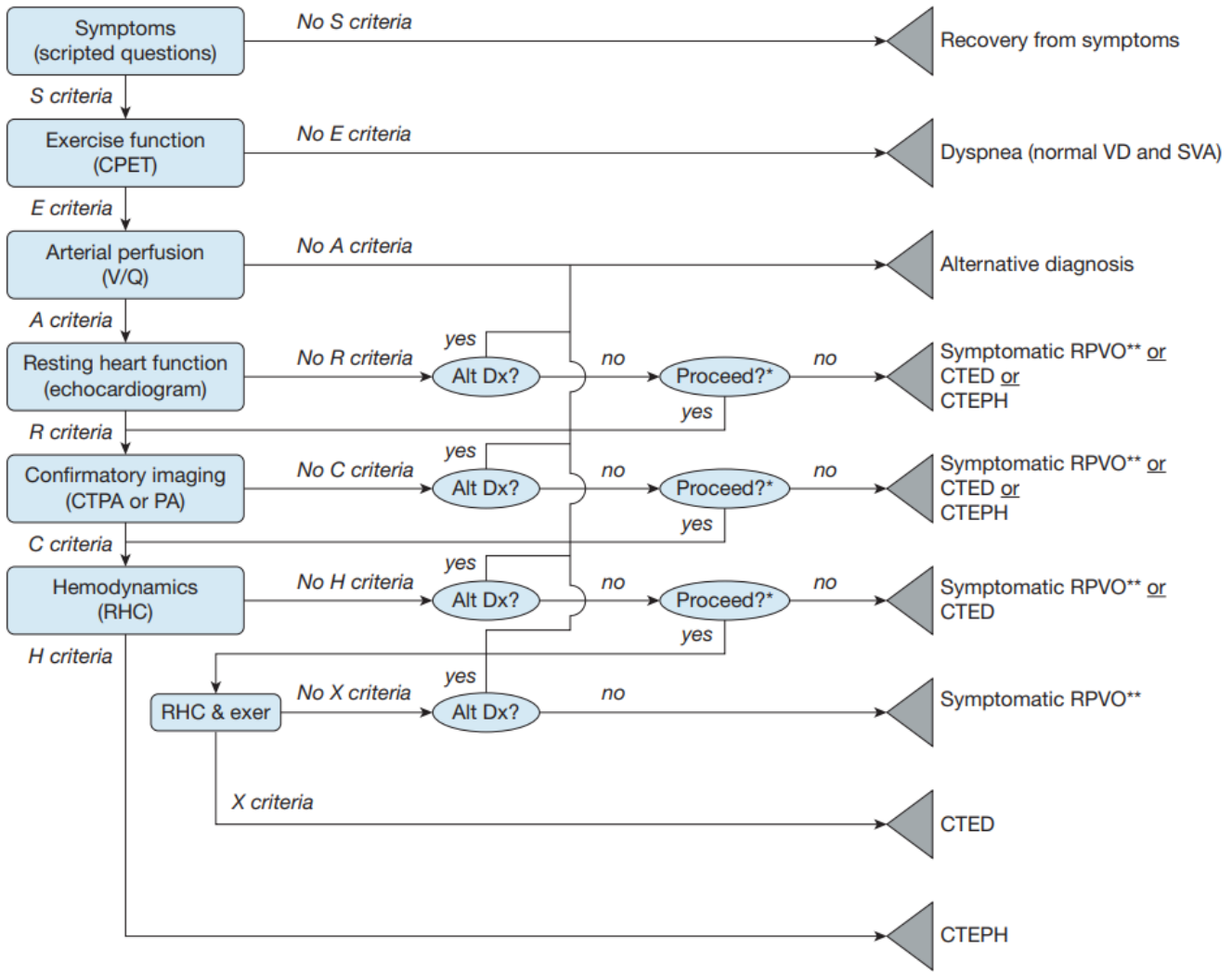
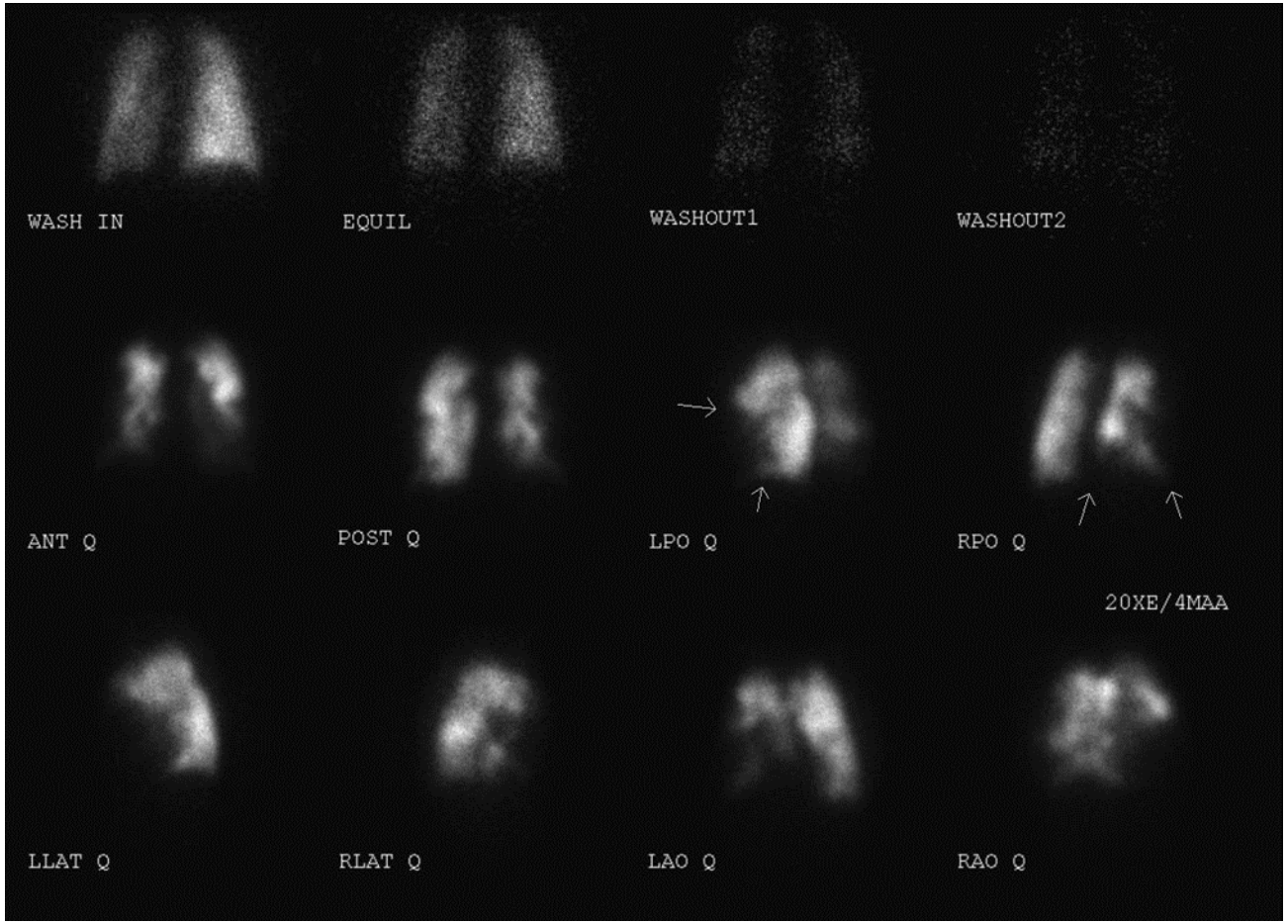
Are you back to your pre-pulmonary embolism baseline?

SEARCH Algorithm to Evaluate Post-PE Dyspnea

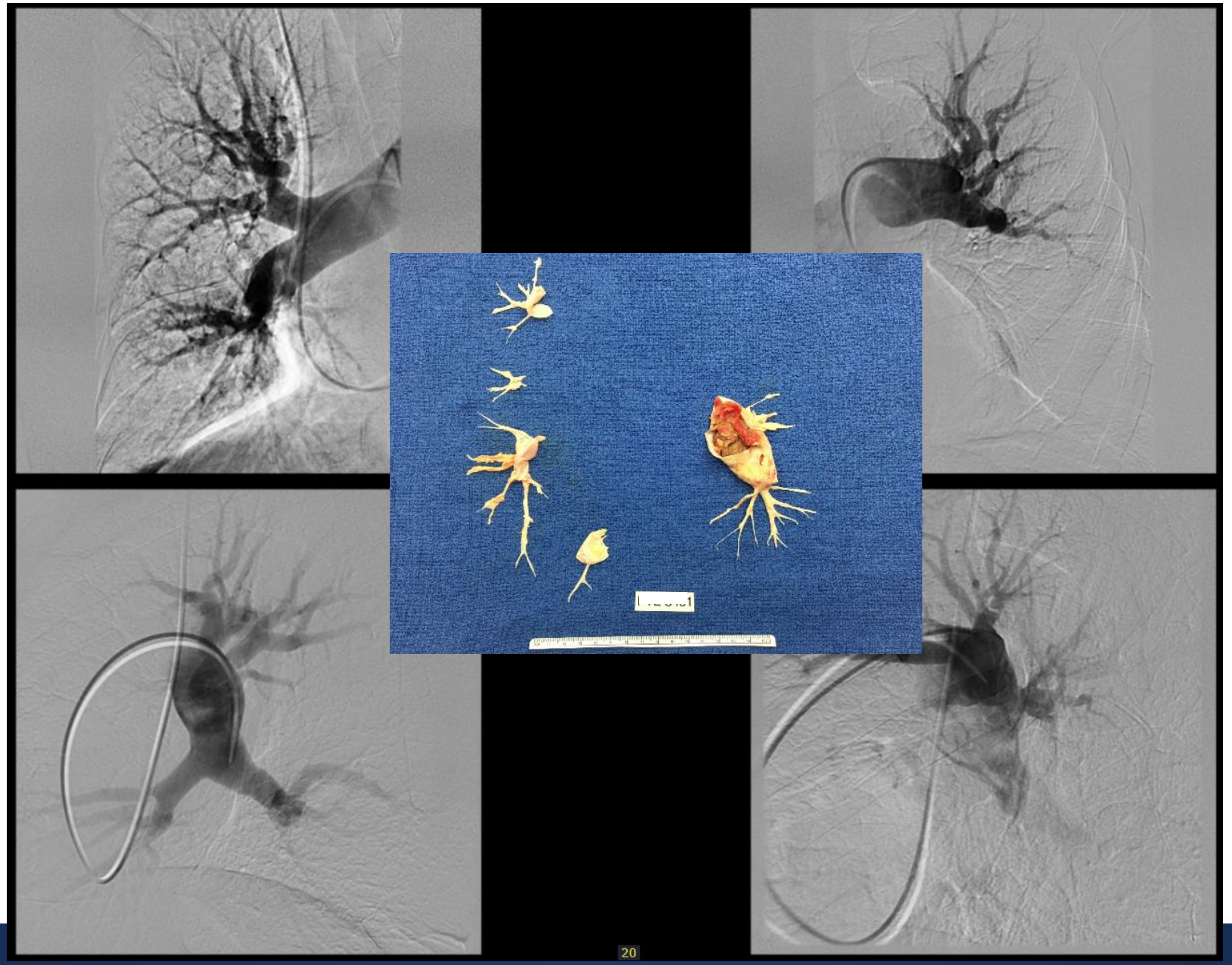




VQ scan remains screening test of choice



Pulmonary Angiogram: Gold Standard



Invasive Cardiopulmonary Exercise Testing

- Right heart catheterization in cath lab
- Exercise
  - Upright bicycle
- Measurement of exhaled gases to determine VO_2
- Continuous measurement of $p_{tc}CO2$
- Calculation of direct Fick cardiac output (ABG & VBG)
  - Direct PVR
  - Derive stroke volumes
  - Calculated Pulmonary Arterial Compliance



Chronic Thromboembolism with …

Ventilatory Insufficiency

- Increased dead space
- Regional perfusion defects
- Inefficient ventilation
- Increased ventilatory demand with exercise

Small Stroke Volume Augmentation

- Decrease pulmonary artery compliance
- Poor right ventricular reserve with inability to augment stroke volume
- May result in exercise-induced pulmonary hypertension

Management of CTEPH and CTED

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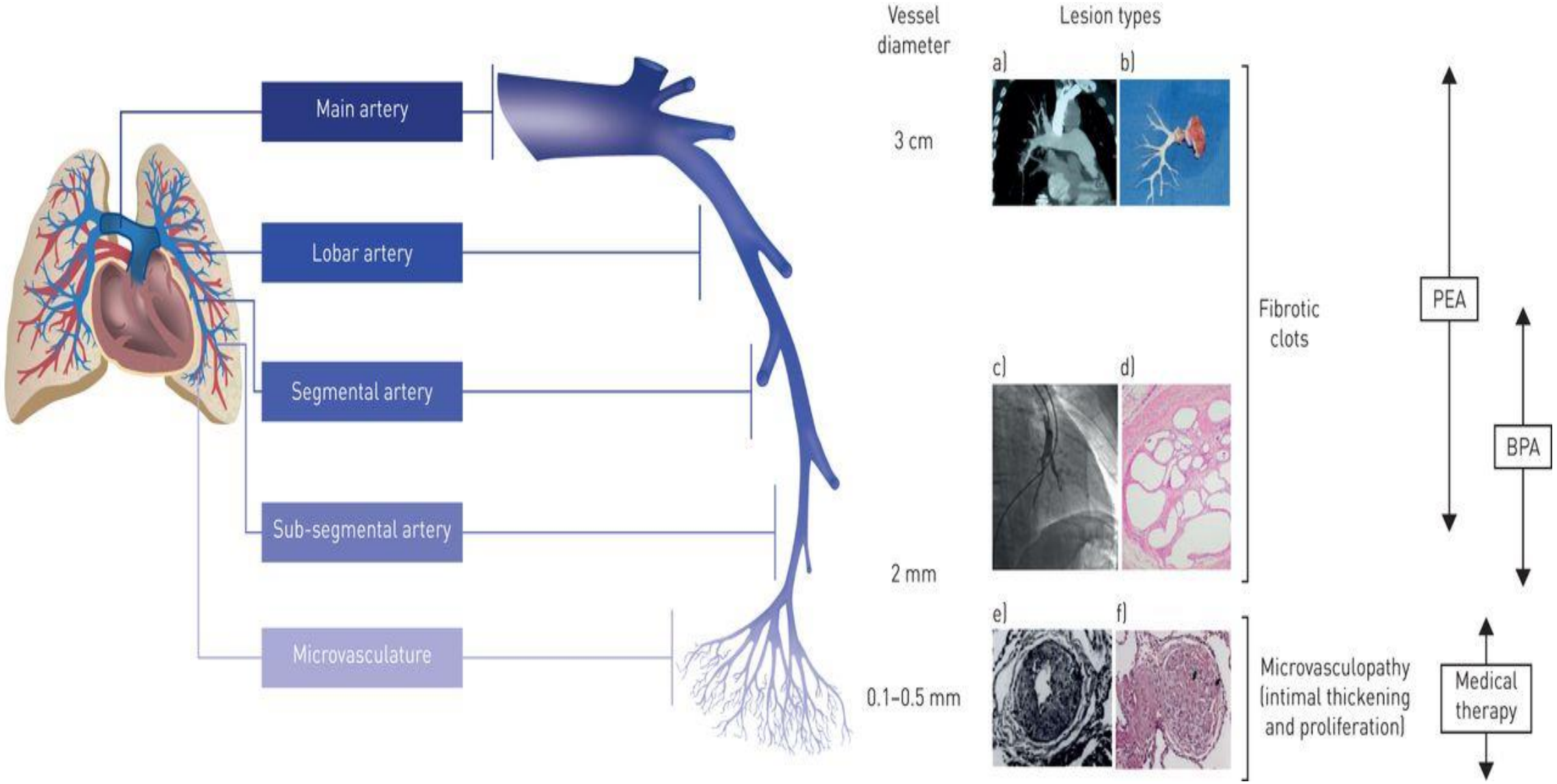
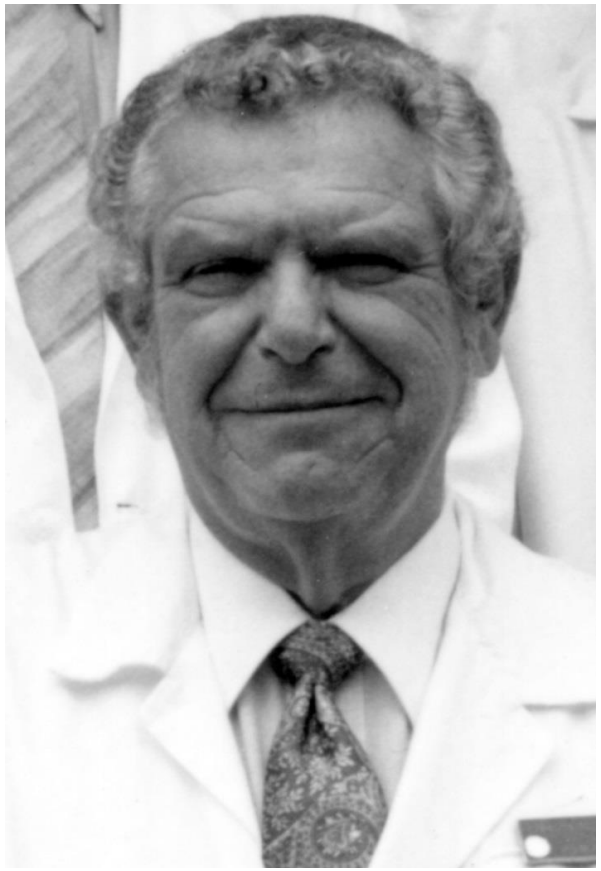
Etiology of Residual Pulmonary Hypertension



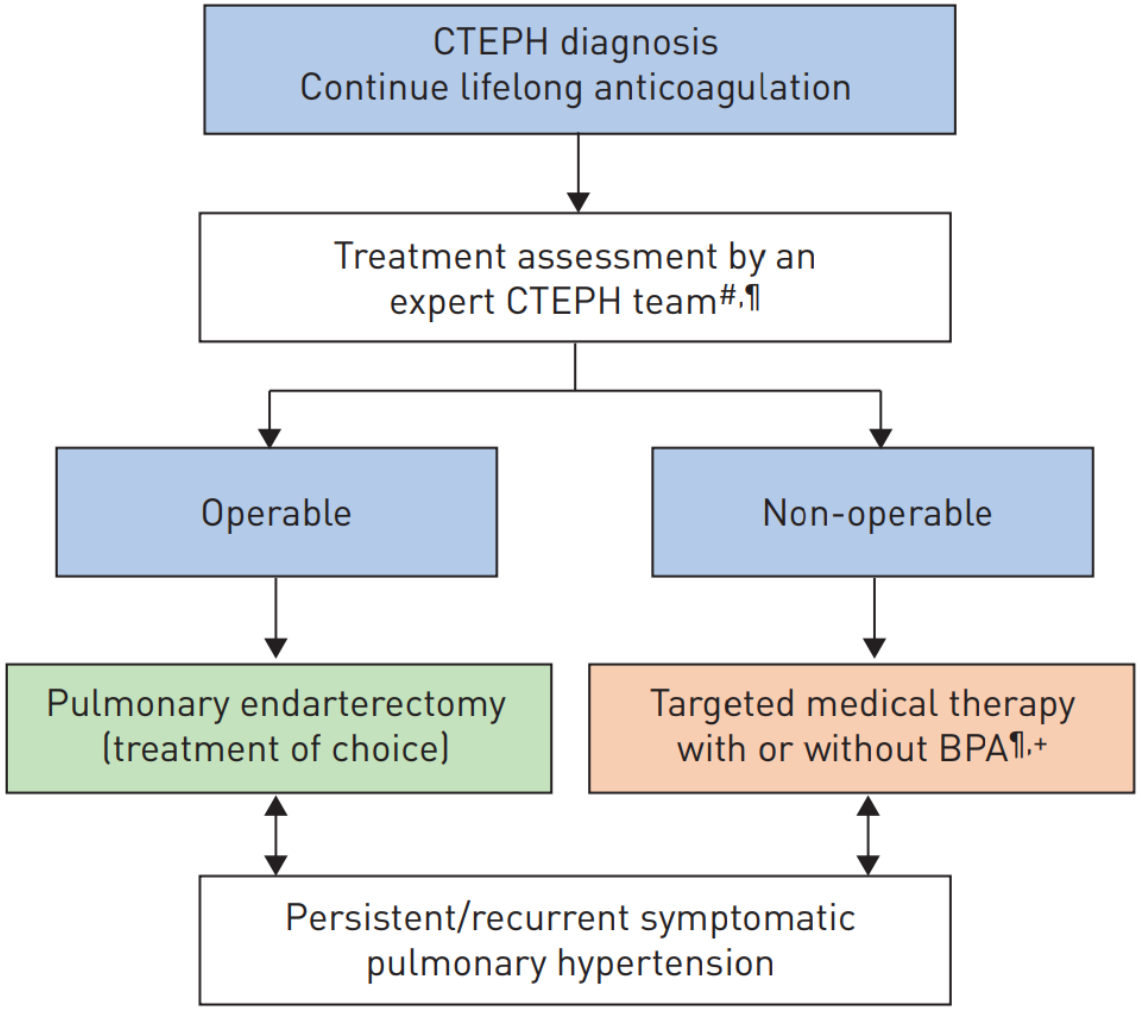
Successful Surgical Intervention in Severe Chronic Thromboembolic Pulmonary Hypertension

Kenneth M. Moser, M.D., F.C.C.P.,° and Nina S. Braunwald, M.D.°°



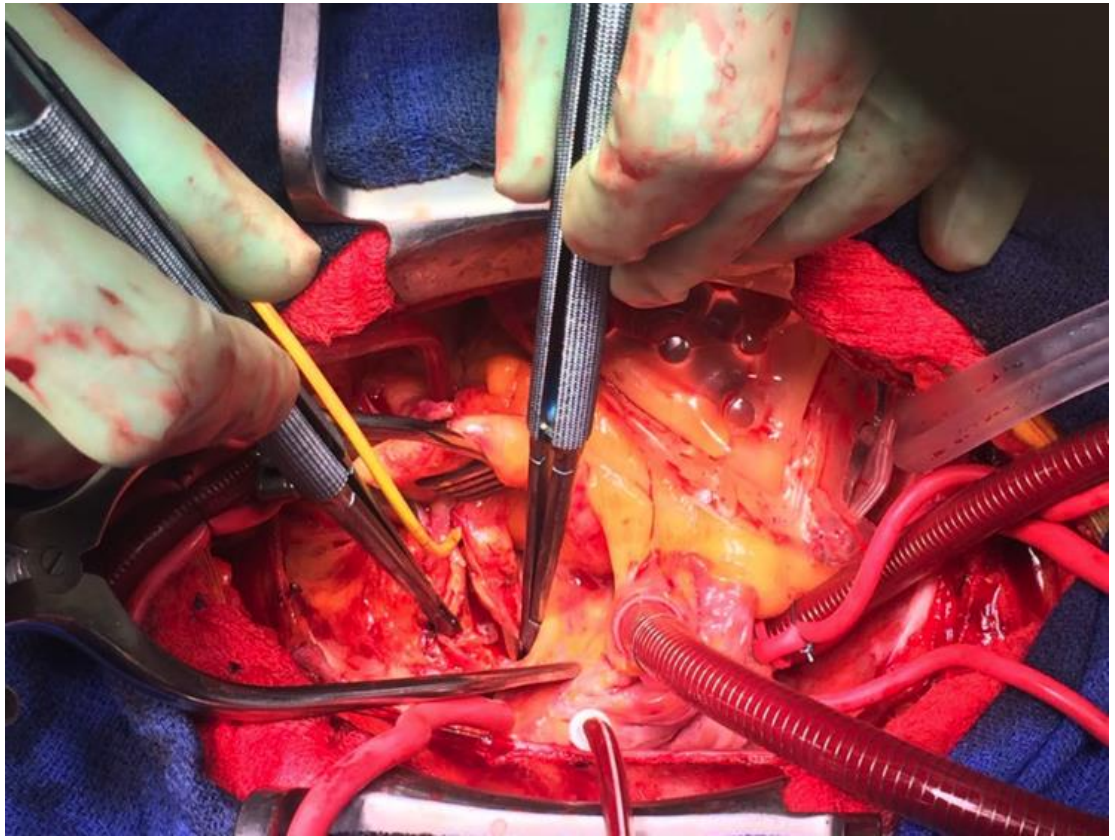


CTEPH Treatment 2018 Guidelines



PTE: Tools and Technique



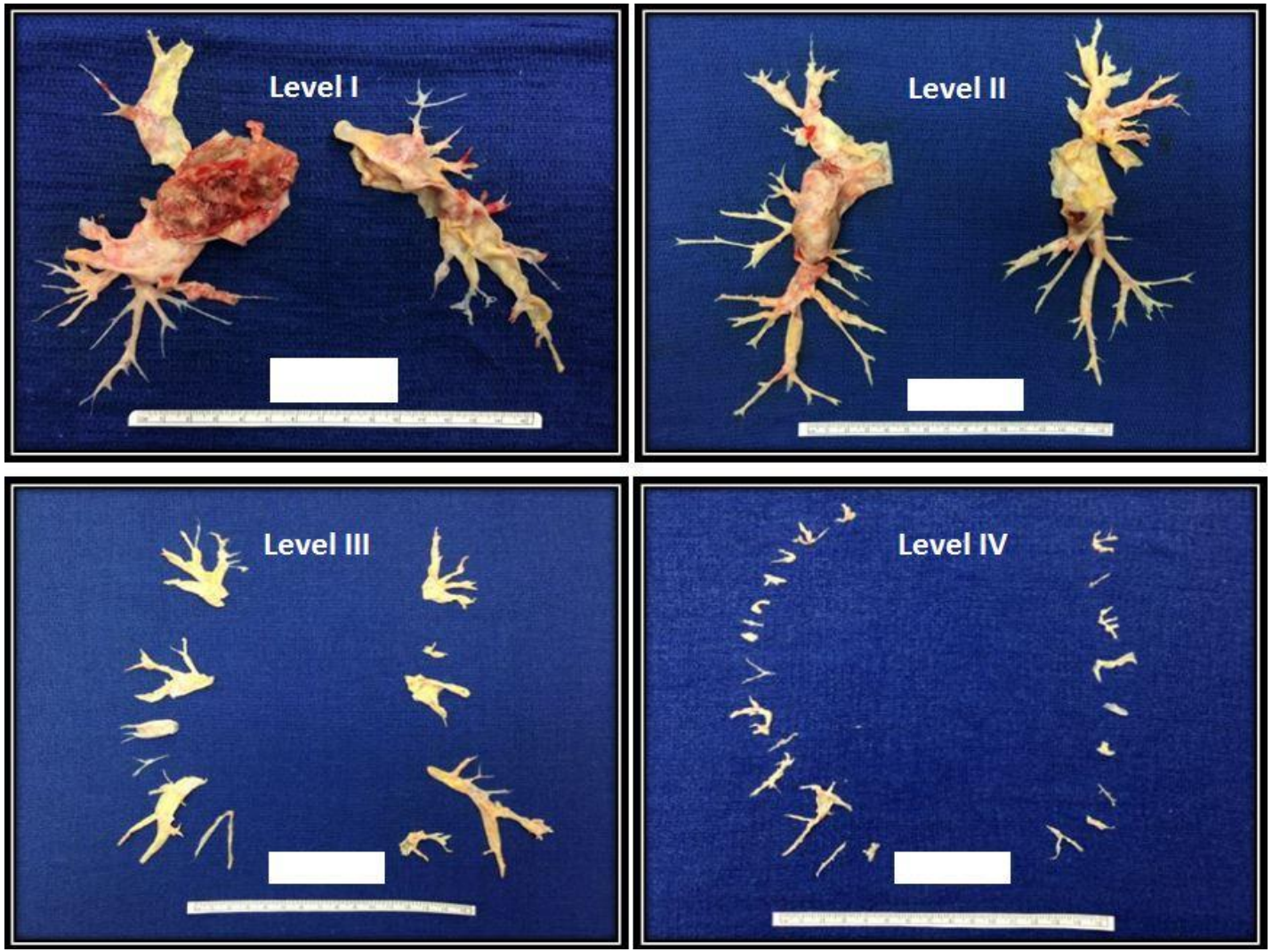


CTEPH: Surgical Approach

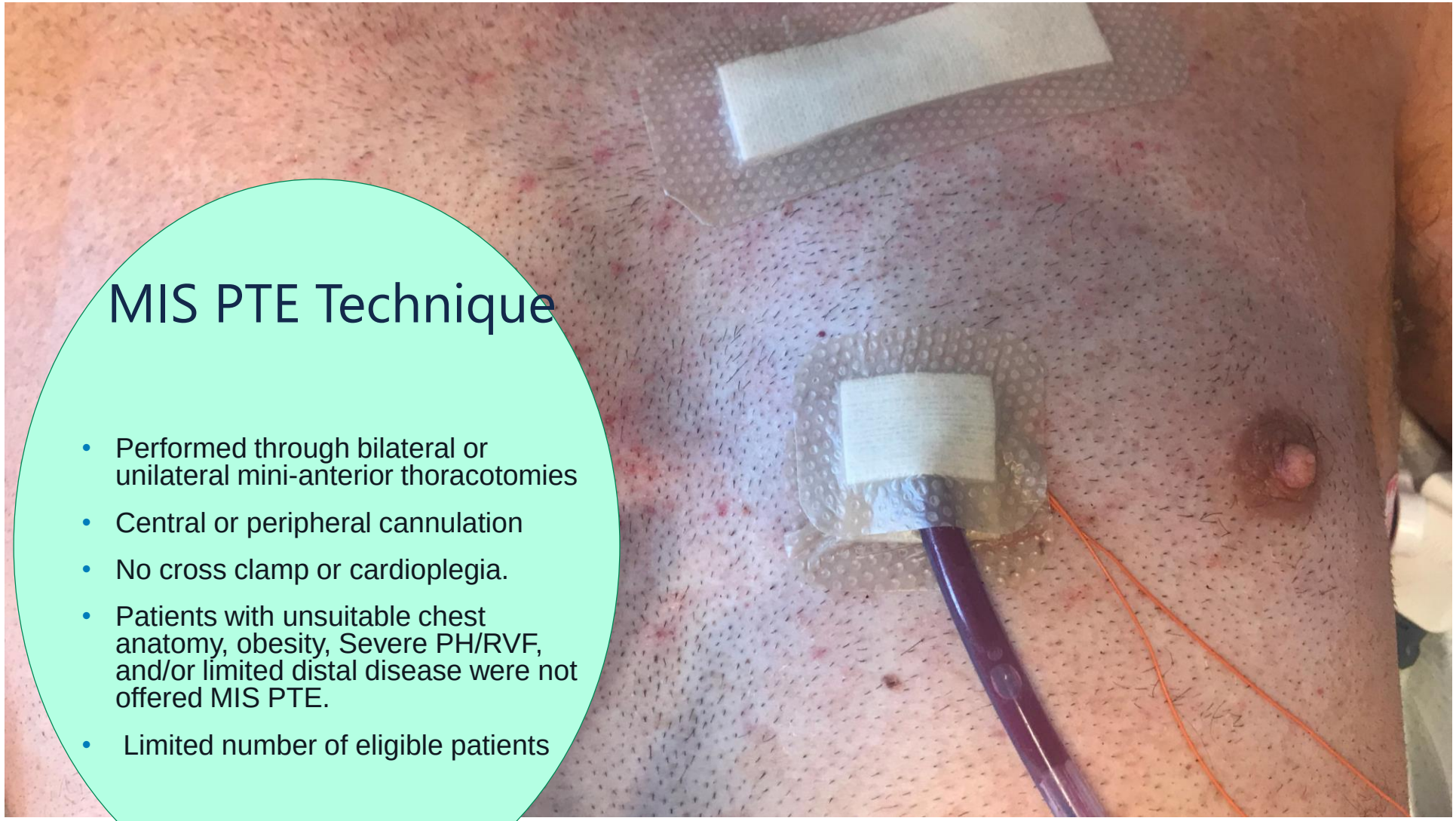
- Median Sternotomy (not thoracotomy)
- Cardiopulmonary bypass
- Deep hypothermia (18-20°) → Circulatory arrest
- True endarterectomy → Not embolectomy



UCSD Disease Level



MIS PTE Technique



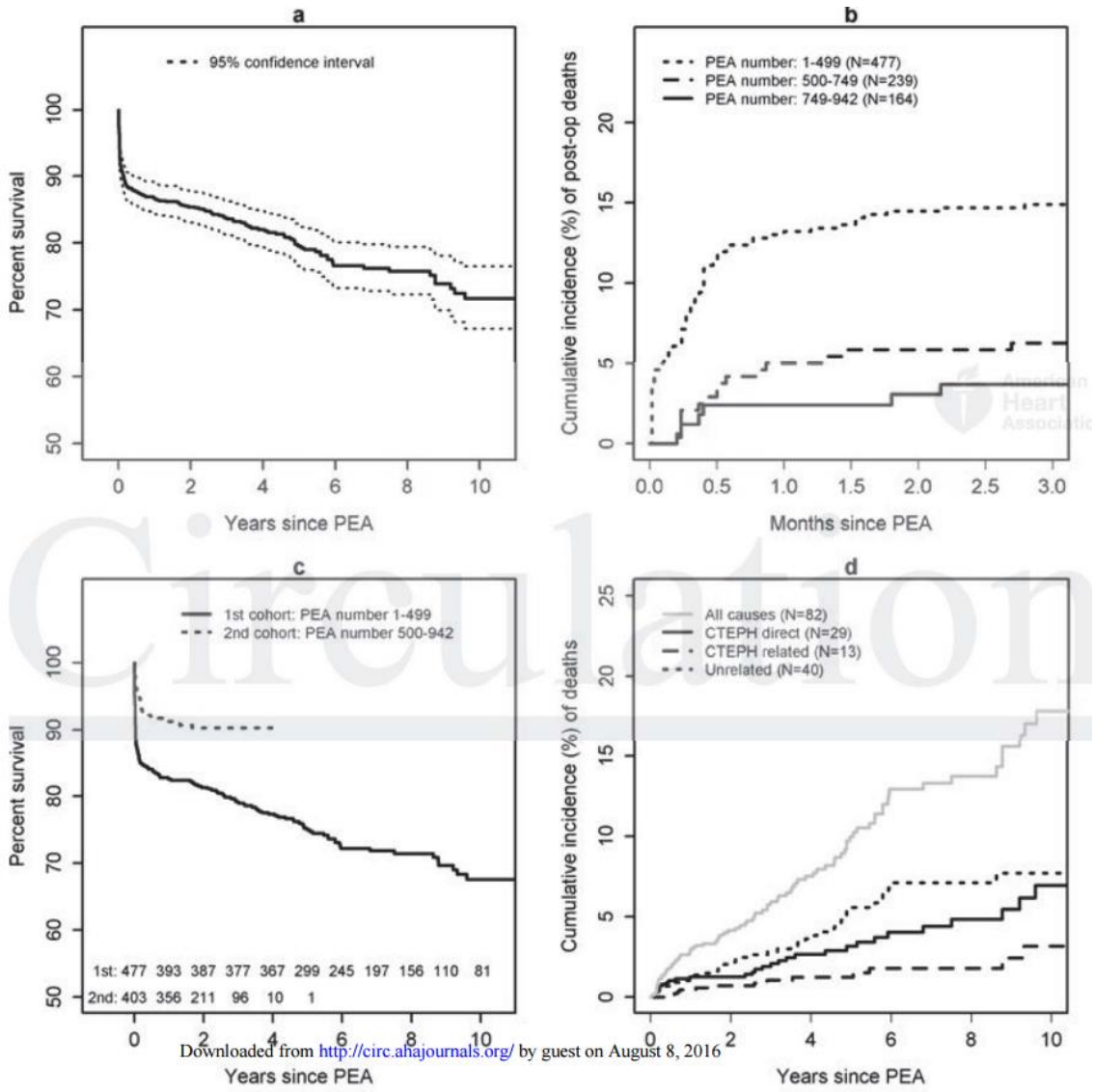
- Performed through bilateral or unilateral mini-anterior thoracotomies
- Central or peripheral cannulation
- No cross clamp or cardioplegia.
- Patients with unsuitable chest anatomy, obesity, Severe PH/RVF, and/or limited distal disease were not offered MIS PTE.
- Limited number of eligible patients

PTE: Immediate and Sustained Improvement

- Improvements of PVR from >800 dyn.sec.cm^{-5} to values below 400 dyn.sec.cm^{-5}
- Results are similarly robust for improvements in CO/CI and mPAp.
- 66 % of preoperative patients were functional class III or IV → 88 % of patients had improved to functional class I or II at 12-month follow-up
- Mean improvement in 6-min walk test following PTE of 103 ± 22.7 m was also sustained at 12-month follow-up

1. Rahnavardi M, Yan TD, Cao C, Vallely MP, Bannon PG, Wilson MK (2011) Pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension: a systematic review. Ann Thorac Cardiovasc Surg 17:435–445
2. Condliffe R, Kiely DG, Gibbs JS, Corris PA, Peacock AJ, Jenkins DP, Hodgkins D, Goldsmith K, Hughes RJ, Sheares K, Tsui SSL, Armstrong IJ, Torpy C, Crackett R, Carlin CM, Das C, Coghlan JG, Pepke-Zaba J (2008) Improved outcomes in medically and surgically treated chronic thromboembolic pulmonary hypertension. Am J Respir Crit Care Med 177:1122–1127

Survival Benefit after PTE Surgery



Downloaded from http://circ.ahajournals.org/ by guest on August 8, 2016

Cannon, John E., et al. "Dynamic Risk Stratification of Patient Long-Term Outcome After Pulmonary Endarterectomy: Results From the UK National Cohort." Circulation (2016)

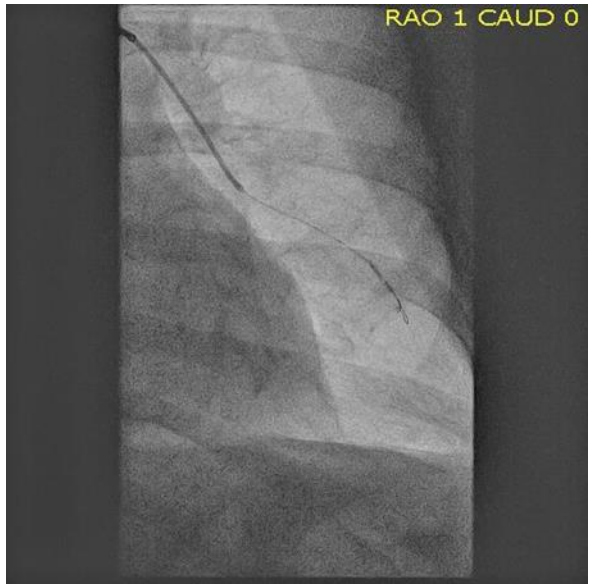
Balloon Pulmonary Angioplasty: An option for those deemed inoperable

- BPA is an interventional procedure using telescoping catheters placed in a central vein through which wires and balloons are used to mechanically disrupt chronic clot material and relieve pulmonary vascular obstruction.

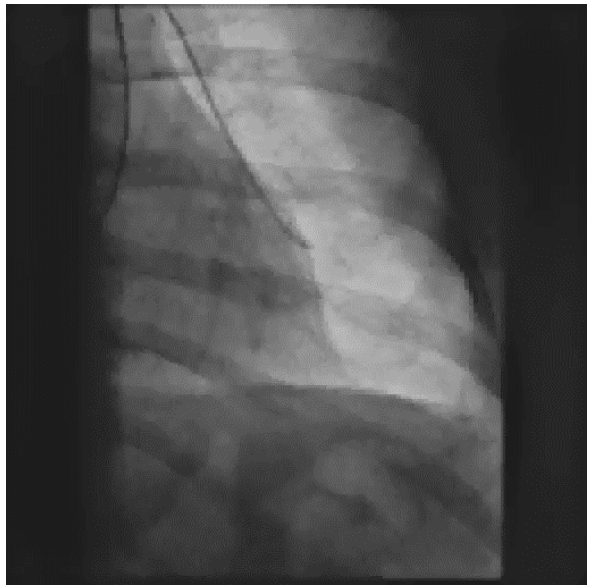
TABLE 4 Balloon pulmonary angioplasty complications

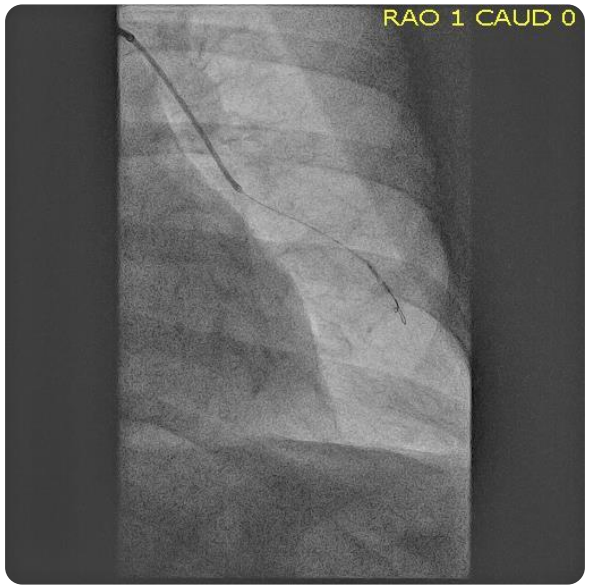
During the procedure
Vascular injury[#] with/without haemoptysis
Wire perforation
Balloon overdilatation
High-pressure contrast injection
Vascular dissection
Allergic reaction to contrast
Adverse reaction to conscious sedation/local anaesthesia
After the procedure
Lung injury[¶] (radiographic opacity with/without haemoptysis, with/without hypoxaemia)
Renal dysfunction
Access site problems

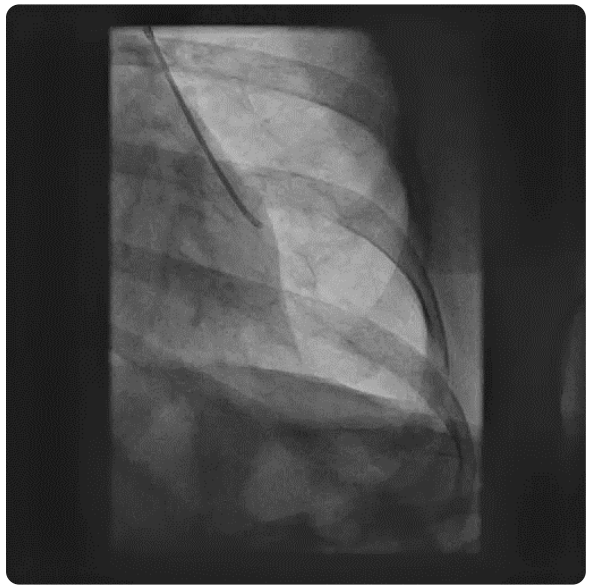
[#]: signs of vascular injury: extravasation of contrast, hypoxaemia, cough, tachycardia, increased pulmonary arterial pressure; [¶]: causes of lung injury: vascular injury much greater than reperfusion lung injury.



Balloon Angioplasty

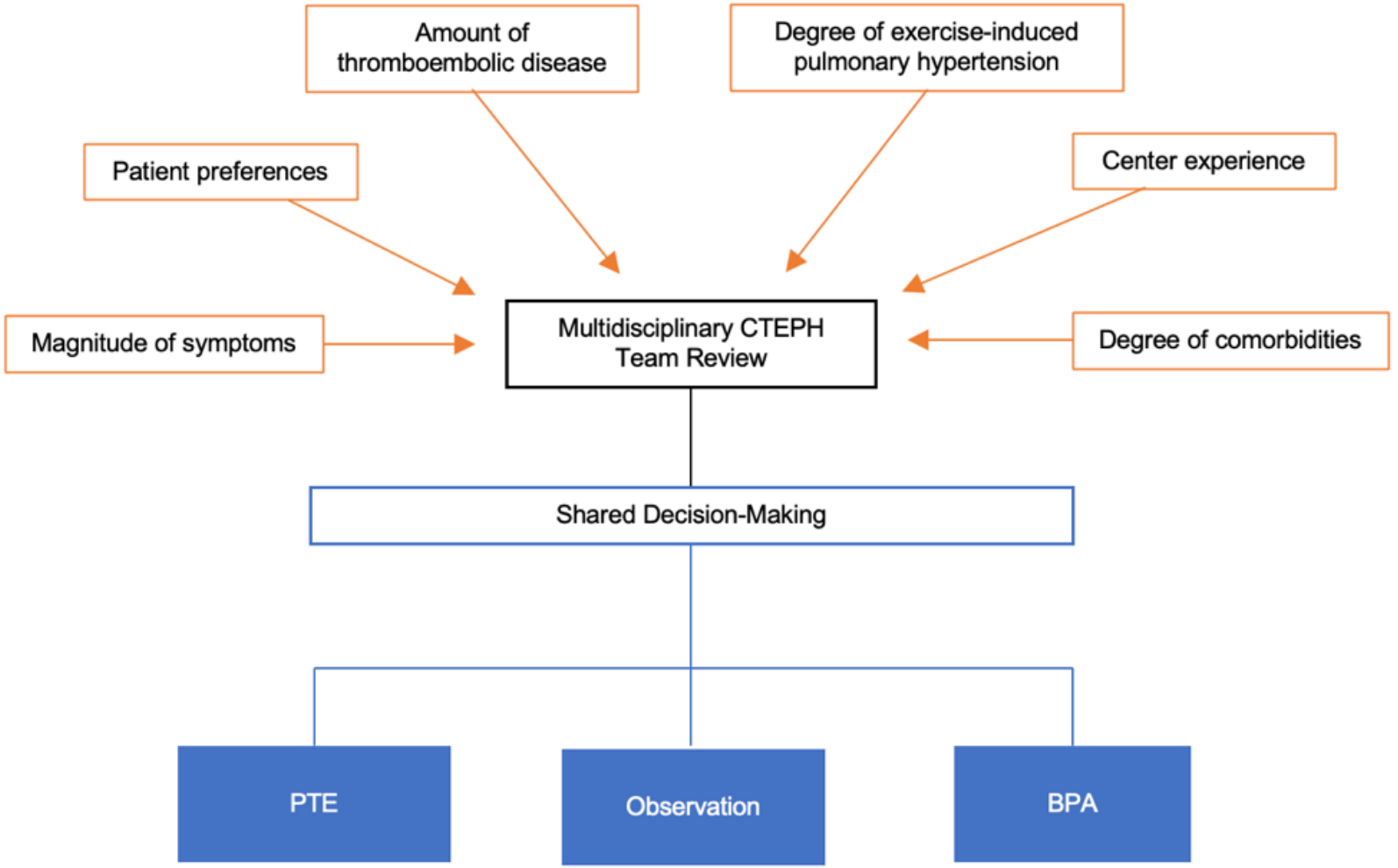






What about those with no pulmonary hypertension? CTED treatment

An Approach to the Management of CTED



- Kabadi A, Kerr K, Fernandes TM. Updates in the diagnosis and management of chronic thromboembolic disease. Curr Opin Pulm Med. 2023;29(5):340-347.

The Case for Observation

- No one died of RV failure or need PAH-targeted therapy but…

Variable	mPAP ≤ 20 (n = 28)			mPAP 21–24 (n = 35)		
	Baseline	36 months	corr. *p*	Baseline	36 months	corr. *p*
WHO FC			0.23			0.12
I	4 (14.3)	7 (25.0)		3 (8.6)	6 (17.1)	
II	16 (57.1)	14 (50.0)		17 (48.6)	22 (62.9)	
III	7 (25.0)	7 (25.0)		15 (42.9)	7 (20.0)	
IV	1 (3.6)	0		0	0	
NT pro-BNP	38 [23–87]	40 [25–92] N = 16	0.87	73 [29–179]	96 [26–145] N = 22	0.72
TTE						
RA area	15.0 (± 3.6)	16.1 (± 4.1)	0.56	16.8 (± 5.3)	18.5 (± 4.3)	0.34
RV basal diameter	3.6 (± 0.6)	3.9 (± 0.6)	0.56	4.0 (± 0.7)	4.3 (± 0.7)	0.29
RV FAC	45.1 (± 12.1)	38.6 (± 9.6)	0.77	35.5 (± 8.3)	44.0 (± 14.3)	0.69
RV TAPSE	2.2 (± 0.5)	2.3 (± 0.4)	0.91	2.1 (± 0.4)	2.4 (± 0.4)	0.29
LVEF	60.8 (± 5.0)	60.3 (± 5.7)	0.91	57.9 (± 4.3)	57.2 (± 4.1)	0.69
Estimated sPAP	29.1 (± 4.5)	28.0 (± 3.2) N = 16	0.84	36.0 (± 18.1)	38.3 (± 10.8) N = 22	0.62
6 MW distance	422.3 (± 108.1)	447.4 (± 135.4) N = 16	0.56	408.0 (± 99.2)	440.3 (± 92.7) N = 20	0.29

FAC, fractional area change; LVEF, left ventricular ejection fraction; mPAP, mean pulmonary artery pressure; 6 MW, 6 min walk; RA, right atrium; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; WHO FC, World Health Organization functional class.

Data presented as counts (%), mean ± standard deviation or median [interquartile range].

PTE surgery is safe in CTED…

	CTEPH n=923	CTED n=163	p-value
Vent Days	1 (1)	1 (0)	<0.001
ICU LOS	4 (3)	2 (2)	<0.001
Postop LOS	10 (5)	9 (4)	<0.001

	CTEPH	CTED	p-value
Death Prior to Discharge	16 (2)	0 (0)	0.09
ECMO	12 (1)	0 (0)	0.14
RTOR	26 (3)	3 (2)	0.47
Postop Bleeding	87 (9)	8 (5)	0.06
RPE	95 (10)	9 (6)	0.05
Atrial Arrth	262 (29)	36 (22)	0.09
HD Paresis	46 (5)	4 (2)	0.15
Postop Thrombosis	36 (4)	3 (2)	0.19
Pericardial Effusion	23 (3)	1 (2)	0.71
Pneumonia/Tracheobronchitis	68 (7)	5 (3)	0.04
D/C O	572 (62)	41 (25)	<0.001

- UCSD data, in press.

PTE surgery is safe in CTED…and effective

	CTEPH n=923	CTED n=163	p-value
Vent Days	1 (1)	1 (0)	<0.001
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Pneumonia/Tracheobronchitis	68 (7)	5 (3)	0.04
D/C O	572 (62)	41 (25)	<0.001

	CTED		
	Pre PTE	Post PTE	p-value
Heart rate (bpm)	73 (17)	83 (14)	<0.001
RA (mmHg)	7 (4)	--	--
Systolic PAP (mmHg)	39 (14)	27 (10)	<0.001
Diastolic PAP (mmHg)	15 ± 5	12 ± 3	<0.001
mPAP (mmHg)	23 (8)	19 (6)	<0.001
PAWP (mmHg)	11 (5.7)	--	--
CVP (mmHg)	--	8 (5)	--
PVR (dyn*s*cm^{-5})	172 ± 47	135 ± 45	<0.001
TPR (dyn*s*cm^{-5})	332 (108)	237 (110)	<0.001
CO (L/min)	5.6 (1.5)	5.9 (1.6)	0.007
CI (L/min/m^2)	2.8 (0.6)	2.8 (0.8)	0.024
C_{PA} (mL/mmHg)	3.4 (1.1)	4.7 (2.2)	<0.001
RC Time (ms)	571.4 (212.4)	606.1 (265.2)	0.025

- UCSD data, in press.

What about long term outcomes after PTE for CTED?

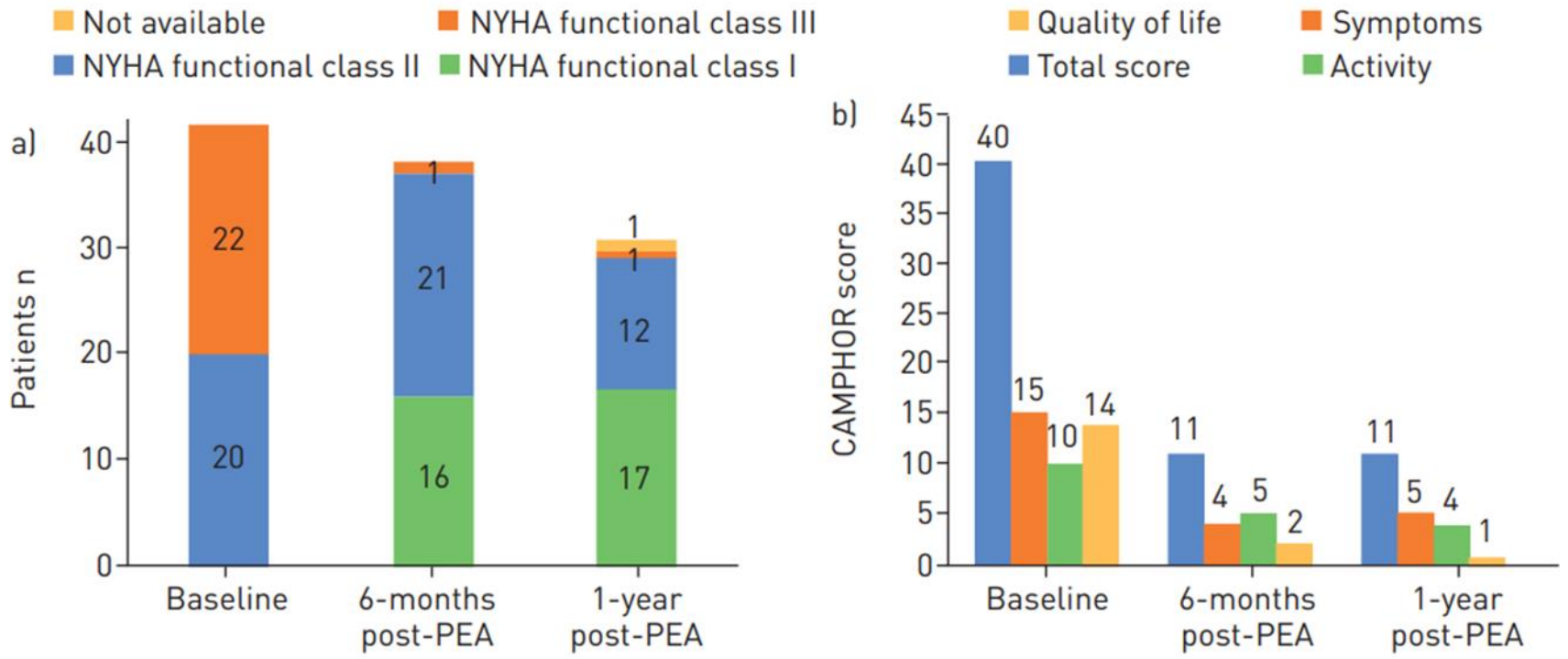
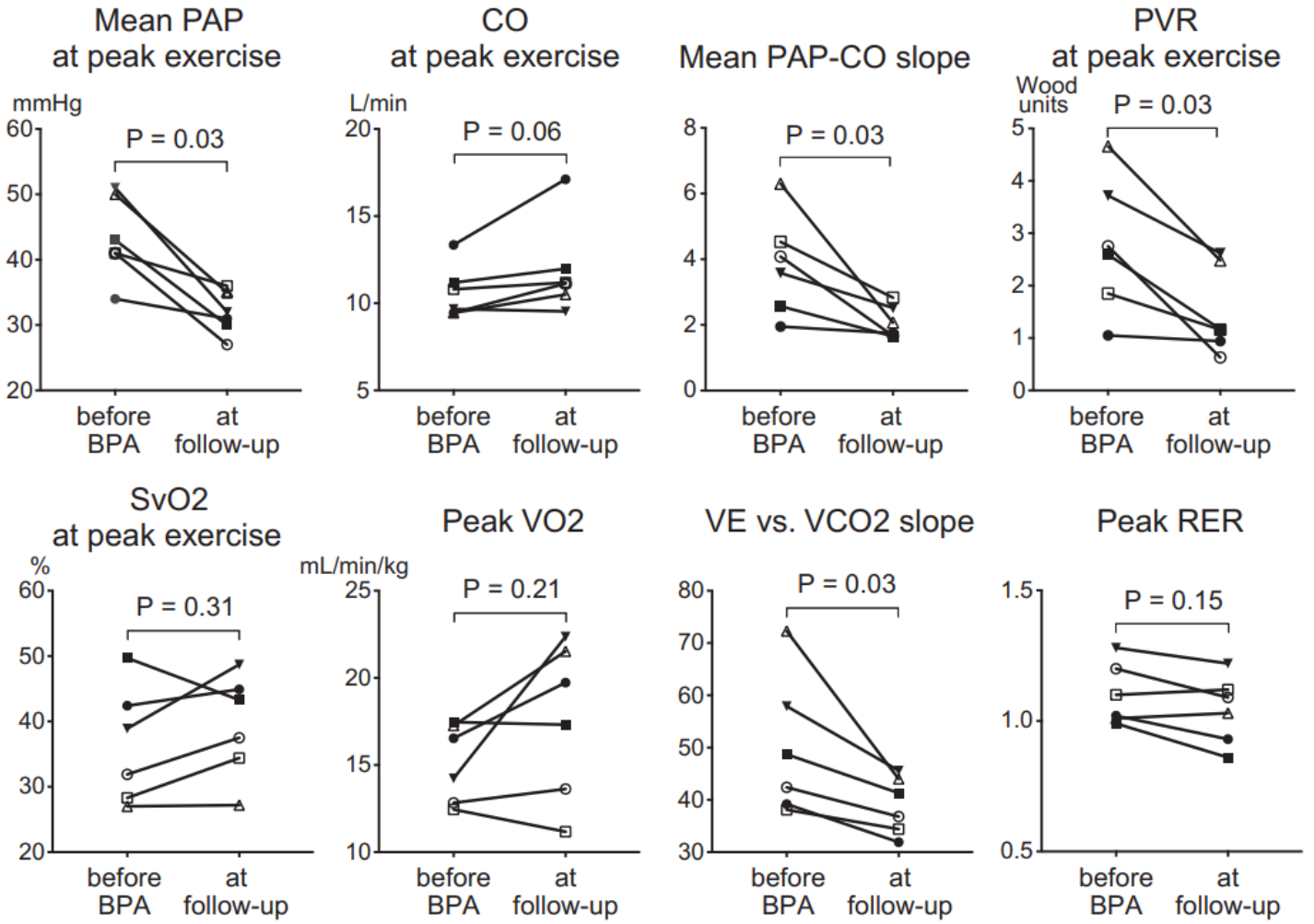


FIGURE 3 Individual changes in patient outcomes with respect to a) New York Heart Association (NYHA) functional class and b) Cambridge pulmonary hypertension outcome review (CAMPHOR) score during the study. PEA: pulmonary endarterectomy.

Taboada, D., et al. (2014). "Outcome of pulmonary endarterectomy in symptomatic chronic thromboembolic disease." European Respiratory Journal 44(6): 1635-1645.

Balloon Pulmonary Angioplasty for CTED



Inami T, Kataoka M, Kikuchi H, Goda A, Satoh T. Balloon pulmonary angioplasty for symptomatic chronic thromboembolic disease without pulmonary hypertension at rest. Int J Cardiol. 2019;289:116-118.

Post-Thrombotic Syndrome

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What is Post-Thrombotic Syndrome (PTS)?

- Definition: Chronic complication of deep vein thrombosis (DVT) characterized by symptoms like leg pain, swelling, and skin changes.
- Causes: Occurs when a DVT damages the vein valves, leading to chronic venous hypertension and pooling of blood in the affected area.
- Symptoms: Pain, heaviness, swelling, skin discoloration, and in severe cases, ulcers.



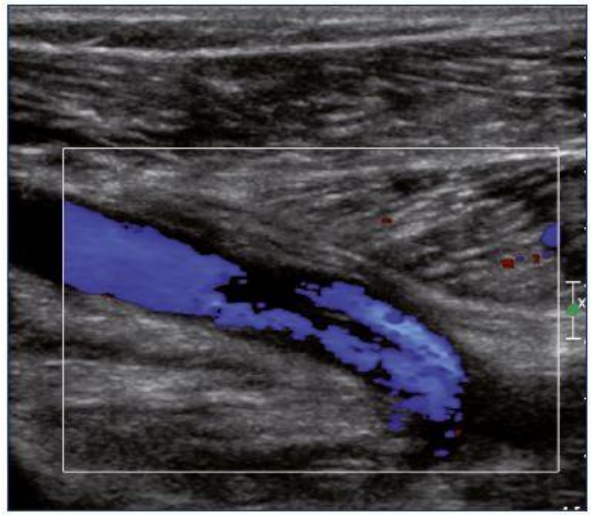
Risk Factors for PTS

- Previous DVT
- Obesity
- Inadequate anticoagulation treatment
- Recurrent DVT



Diagnosis

- Based on symptoms and physical examination
- Duplex ultrasound to assess blood flow and rule out active DVT



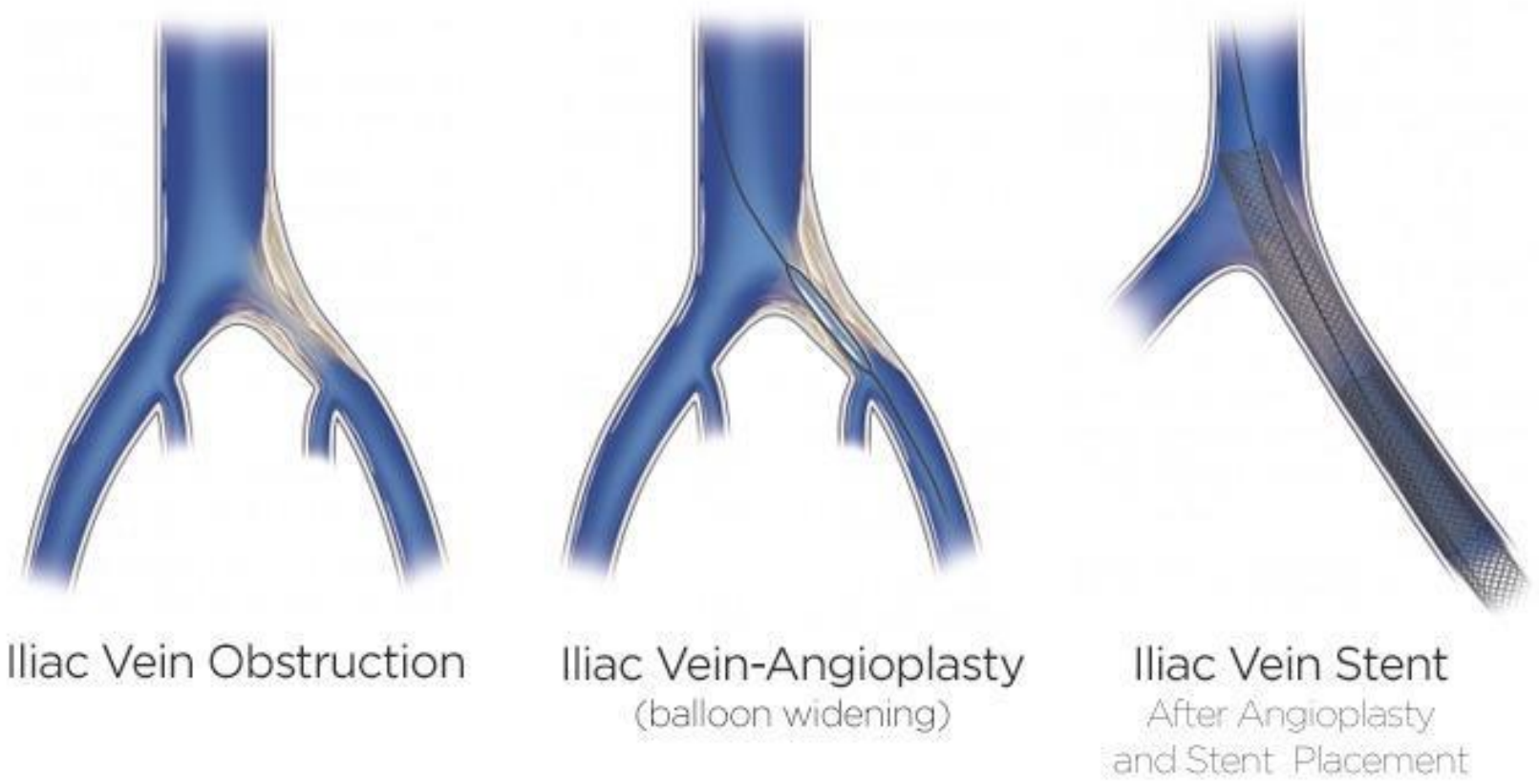
Treatment of PTS

- **Compression Therapy**: Graduated compression stockings to reduce symptoms and prevent worsening.
- **Lifestyle Modifications**: Elevate legs, weight management, and exercise to improve circulation.
- **Prevention**: Optimal DVT treatment, early mobilization post-DVT, and adherence to anticoagulation therapy.



Interventions for PTS

- Stenting or venoplasty may be options in severe cases



Thank you



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