

Chronic Thromboembolic Pulmonary Hypertension

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장 항 제

● 2020년 폐고혈압 진료지침

Korean guideline for diagnosis and treatment of pulmonary hypertension

대한심장학회
대한결핵 및 호흡기학회

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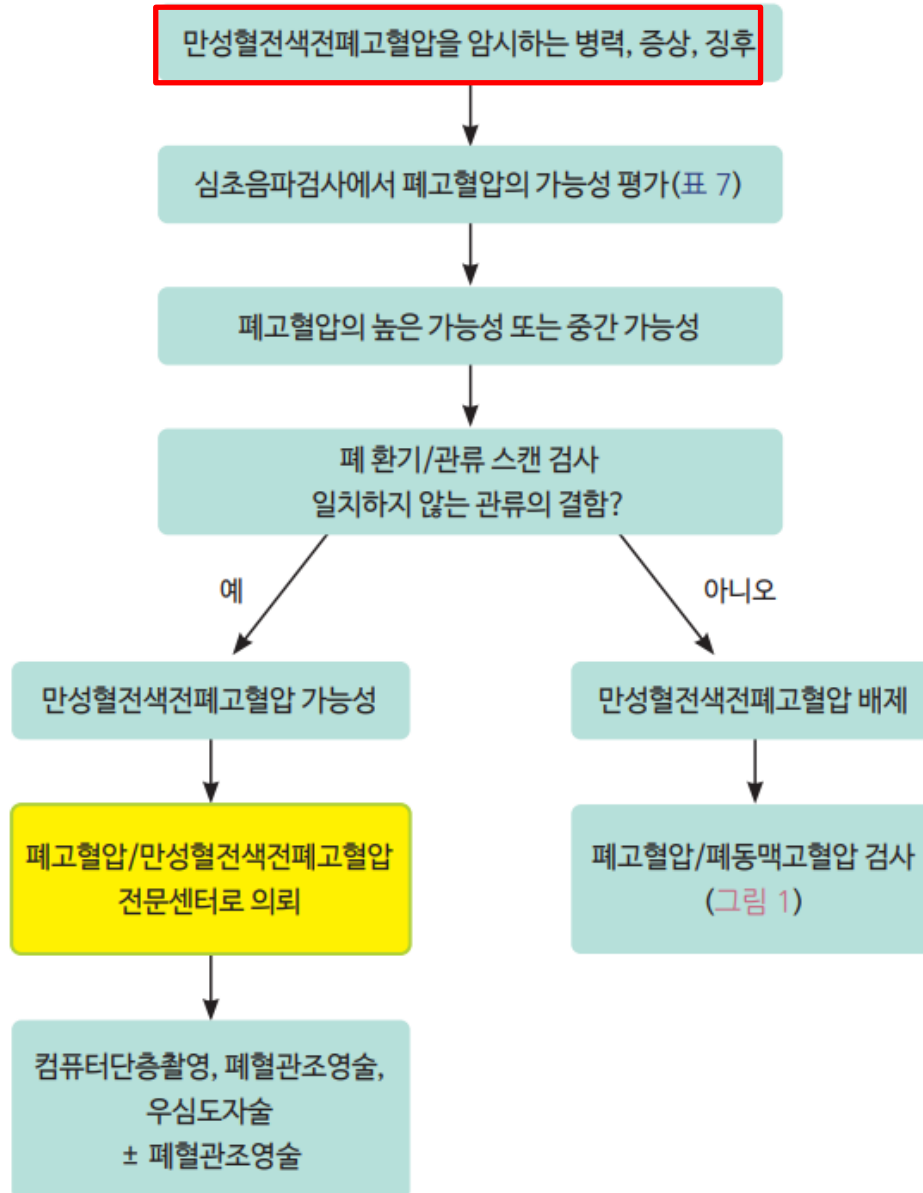
PART 10 불분명한 기전 및/또는 다인성 기전에 의한 폐고혈압(폐고혈압 5군) 177

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9. 만성혈전색전폐고혈압 (폐고혈압 4군)

만성혈전색전폐고혈압(Chronic thromboembolic pulmonary hypertension; CTEPH)은 급성폐색전증(acute pulmonary embolism) 발생 이후 0.1~9.1%의 빈도로 드물게 발생하는 합병증으로 혈전의 기질화(organized thrombus)와 혈관 재형성(vascular remodeling)으로 인한 폐혈관 저항 증가로 폐고혈압이 발생한다. 만성혈전색전폐고혈압의 정확한 유병률과 연간 발생률은 알려지지 않았지만, 일부 데이터에 따르면 연간 100만 인구당 약 5명 정도로 추정해 볼 수 있다.⁴¹⁹ 만성혈전색전폐고혈압과 감별이 필요한 질환으로는 폐동맥 육종 및 기타 혈관 내 종양, 동맥염, 기생충(hydatid cyst), 이물질 색전

만성혈전색전폐고혈압 진단 알고리즘



● 2020년 폐고혈압 진료지침

Korean guideline for diagnosis and treatment of
pulmonary hypertension

대한심장학회
대한결핵 및 호흡기학회

- 모든 급성폐색전증을 가졌던 환자에서 만성혈전색전 폐고혈압 진단을 위한 선별검사를 시행하는 것은 추천되지 않는다.
- 이는 급성폐색전증 환자에서 드물게 만성혈전색전 폐고혈압이 발생하고,
- 상당수의 만성혈전색전폐고혈압 환자가 이전에 급성 폐색전증의 병력이 없기 때문이다.

CTEPH ; symptoms & signs

Clinical presentation

- Acute VTE
 - Hx of acute PE
 - Hx of recurrent PE
- Progressive exertional dyspnea w/o PE
 - Mimic IPAH
- Signs of Rt. heart failure

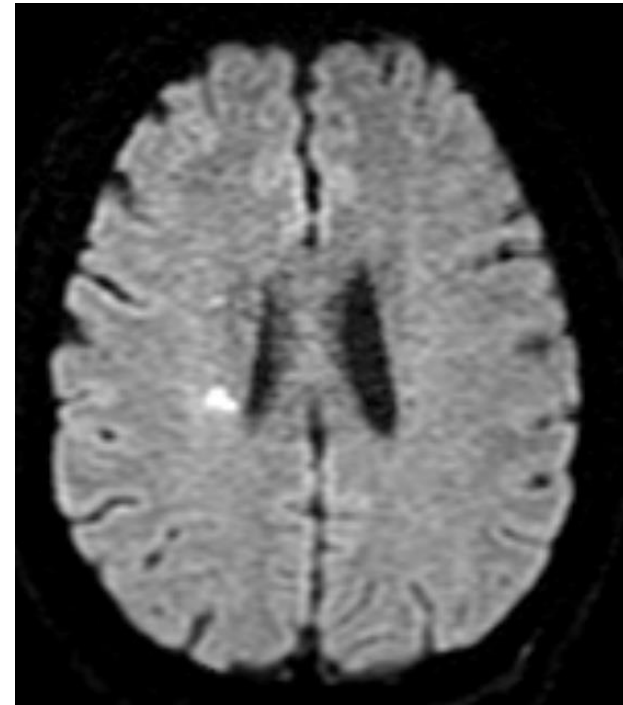
“비특이적”

→ 증상이 발생해서 진단을 받기까지 걸리는 평균 기간은
14개월

Case 68/F

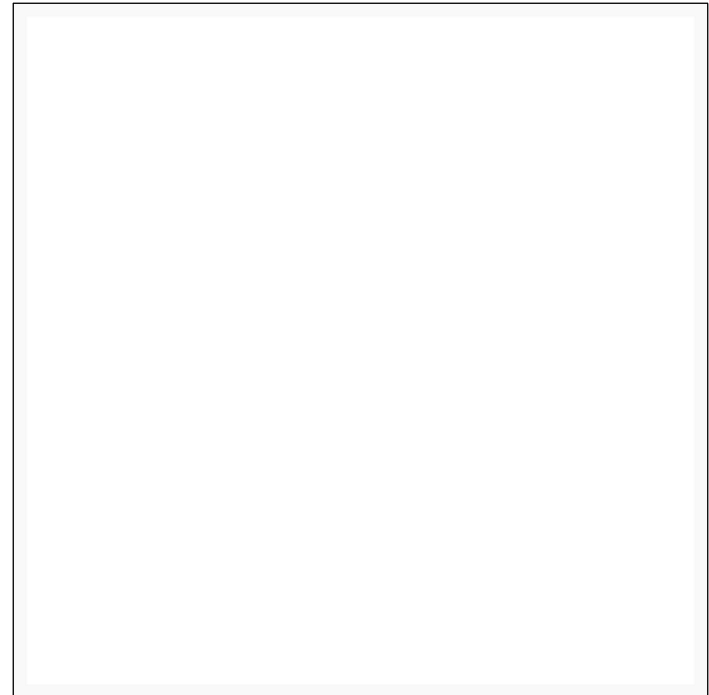
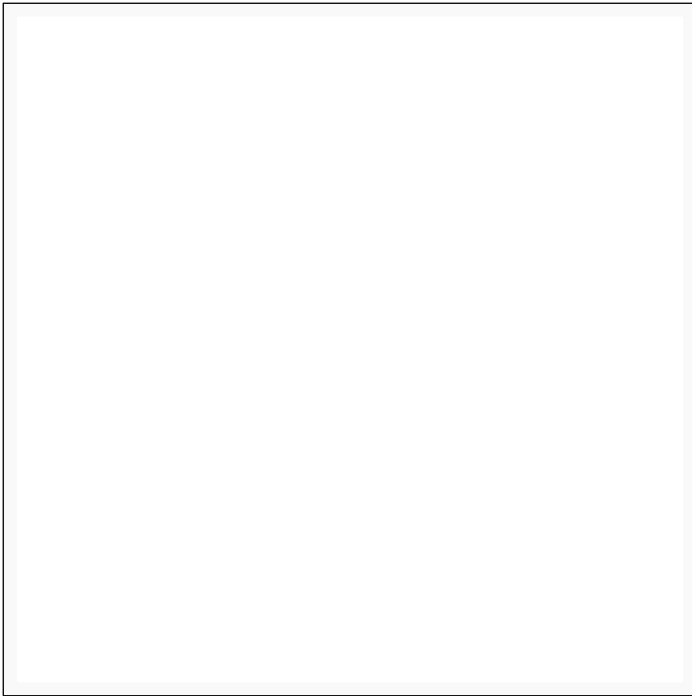
- Chief complaint: Lt hemiparesis

“화장실 가려고 일어났는데 좌측으로 힘이 빠지고 감각이 무뎠어서 내원함”

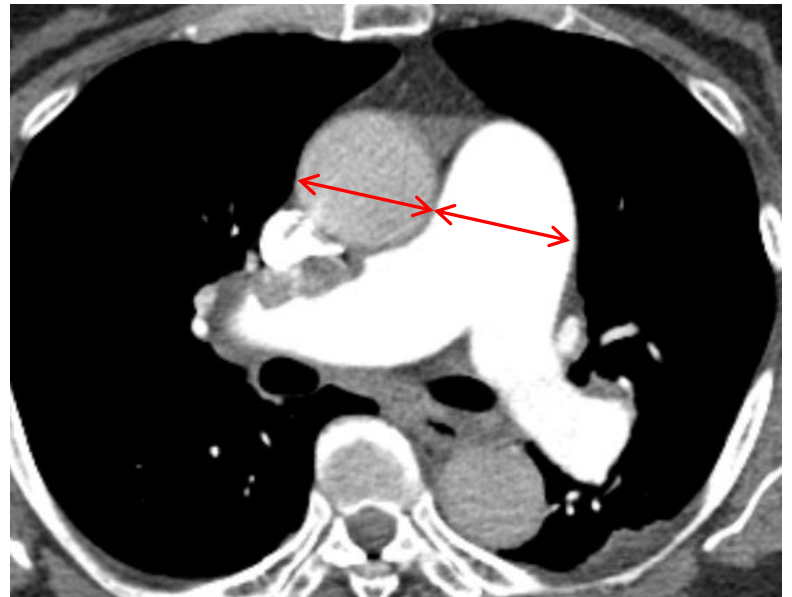
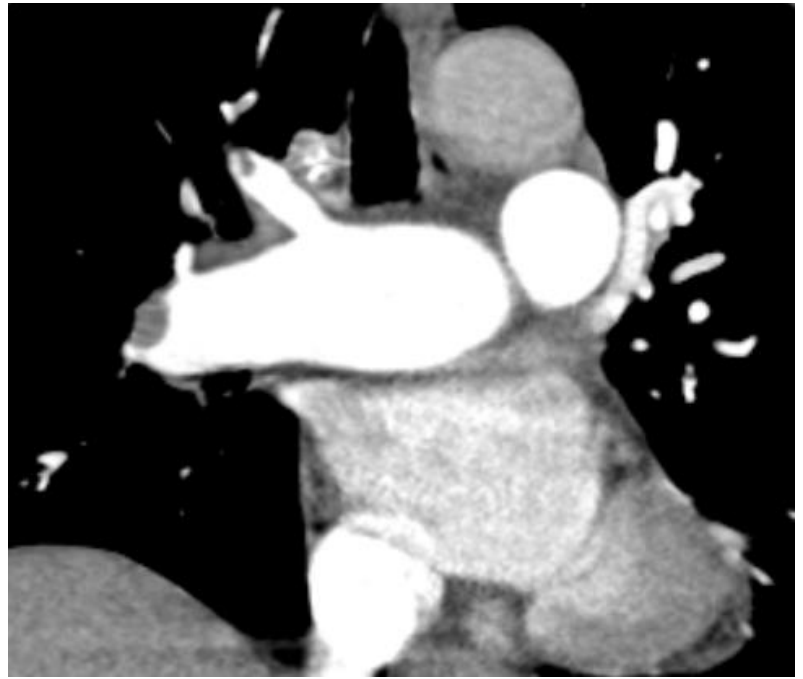
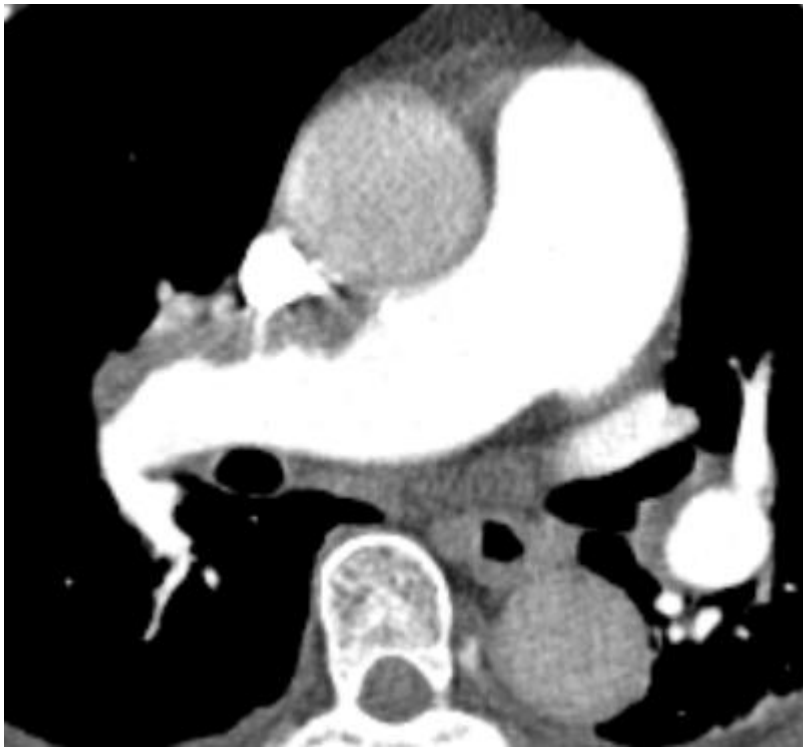


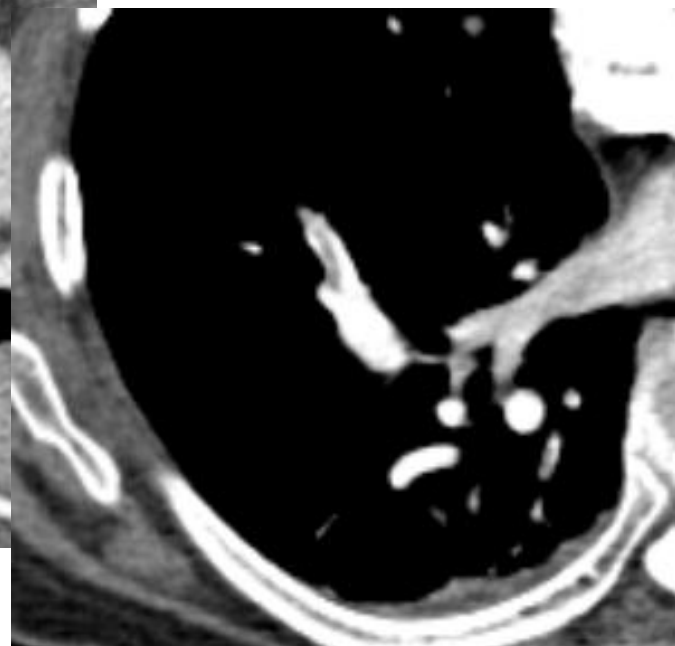
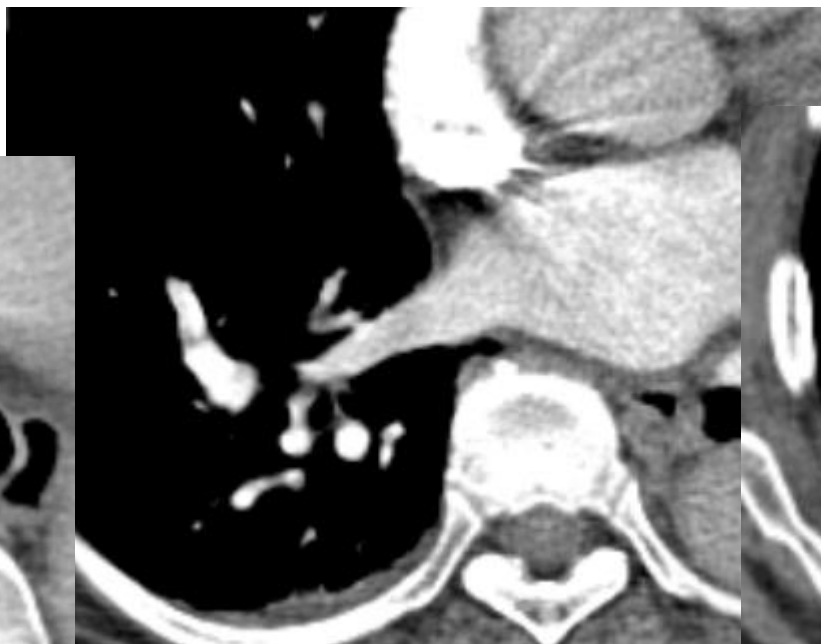
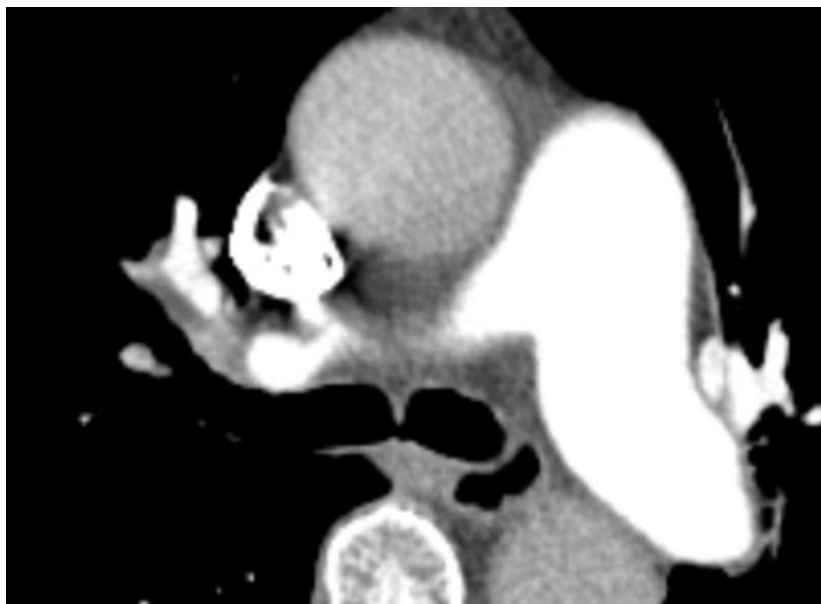
Diagnosis: Rt. cerebral infarct

- Secondary prevention 위한 evaluation
Echocardiography exam



TR Vmax = 3.71 m/s







ANT



RAO



LAO



RT LAT



POST



LPO



RPO

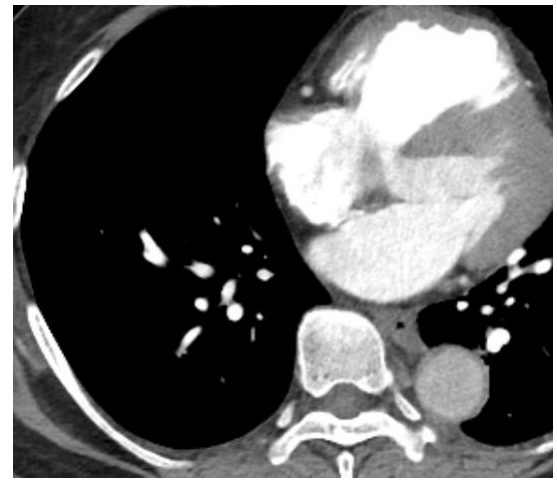
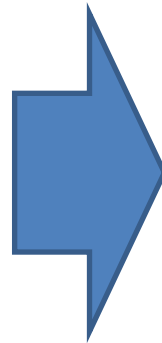


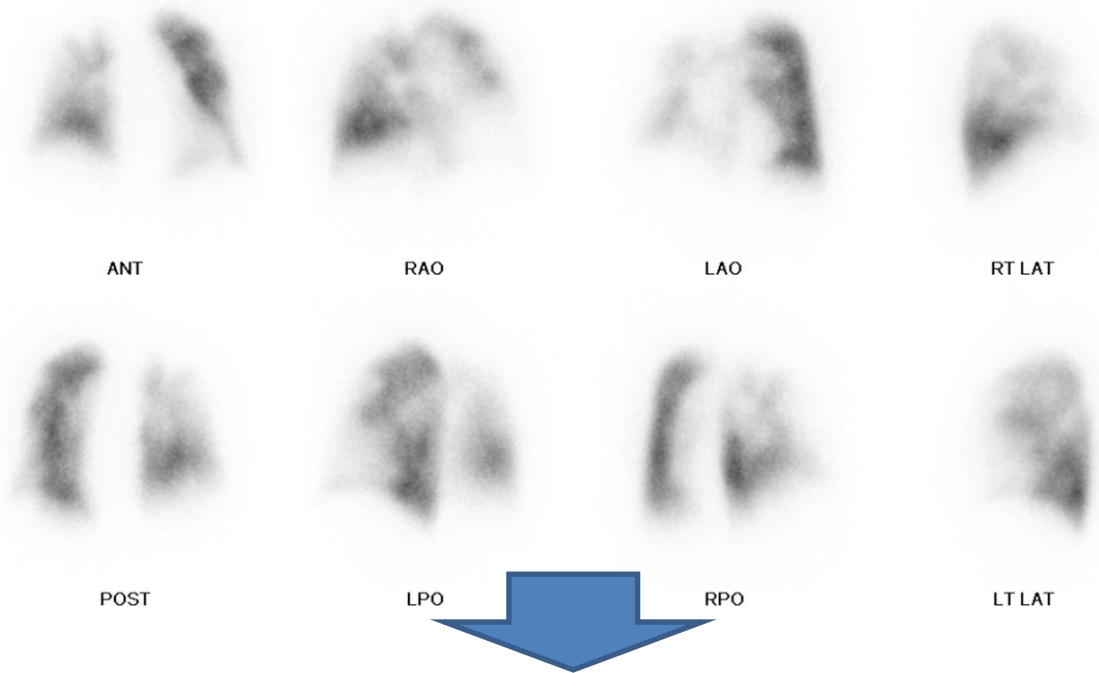
LT LAT

환자의 기억을 되살려 History taking

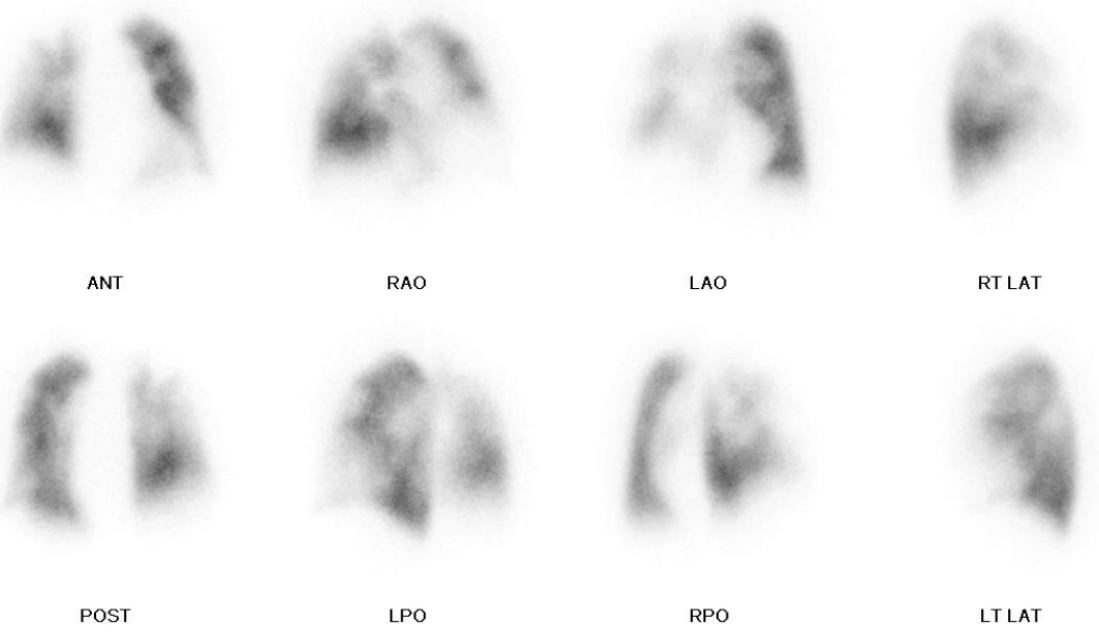
- 1년 전부터 exertional dyspnea
WHO Fc II
- 한달 전부터 progressive worsening Sx

After three months anticoagulation



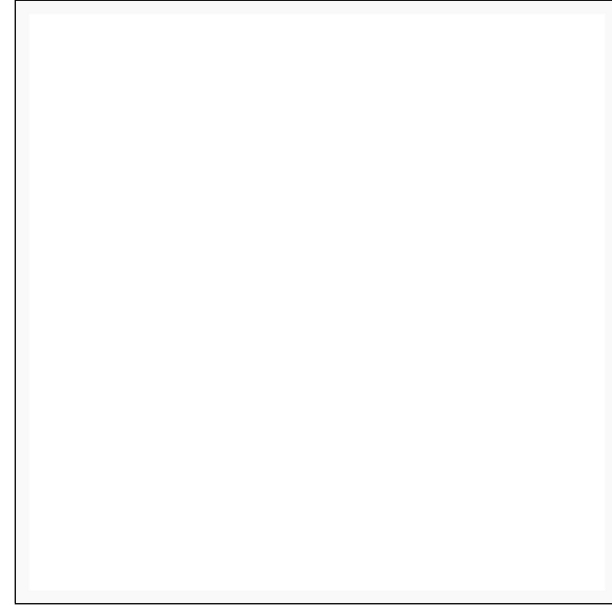
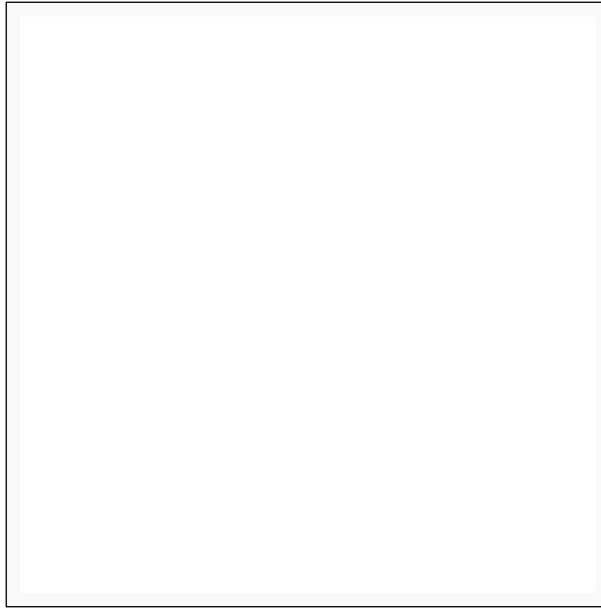
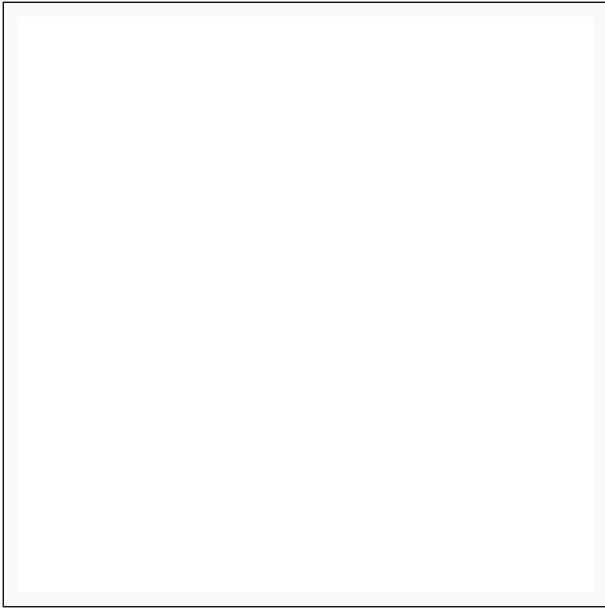


Three months follow-up after baseline lung scan



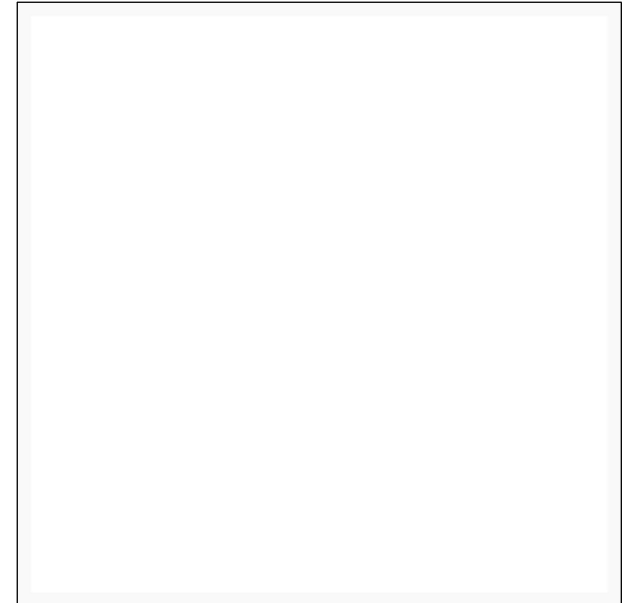
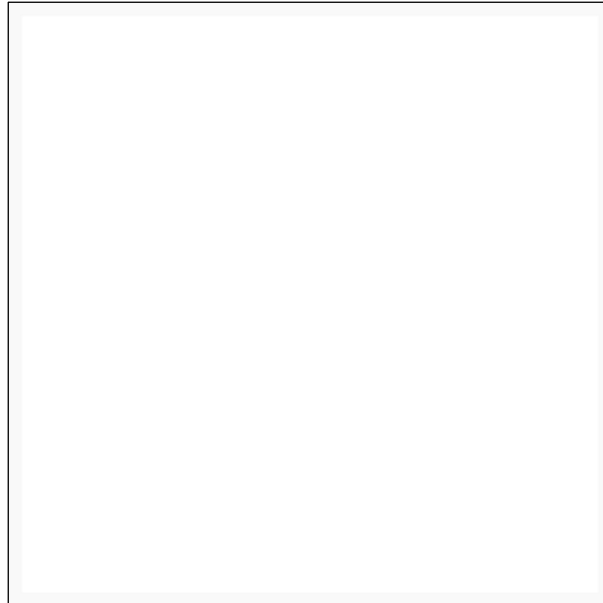
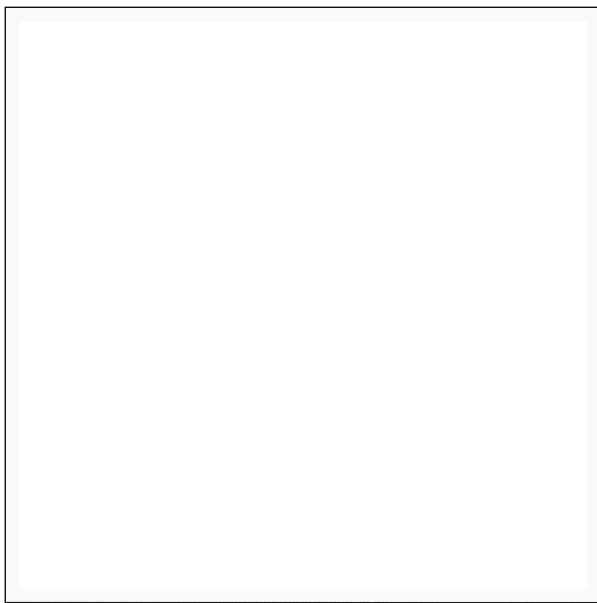
Follow-up Echo

(0 – 3 – 6 months)



Follow-up Echo

(0 – 3 – 6 months)



TR Vmax (m/s) 3.7



3.2

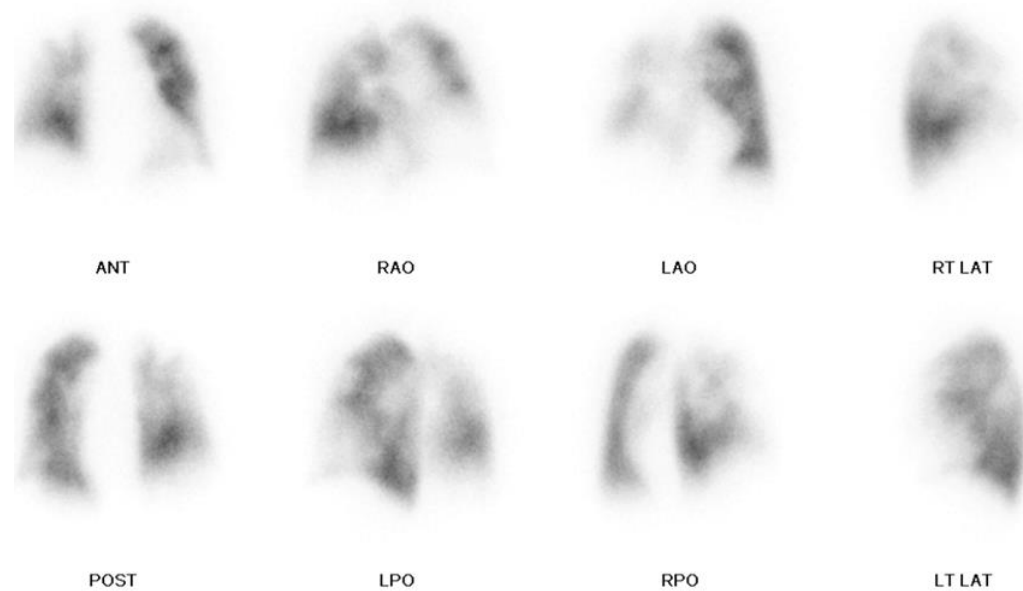
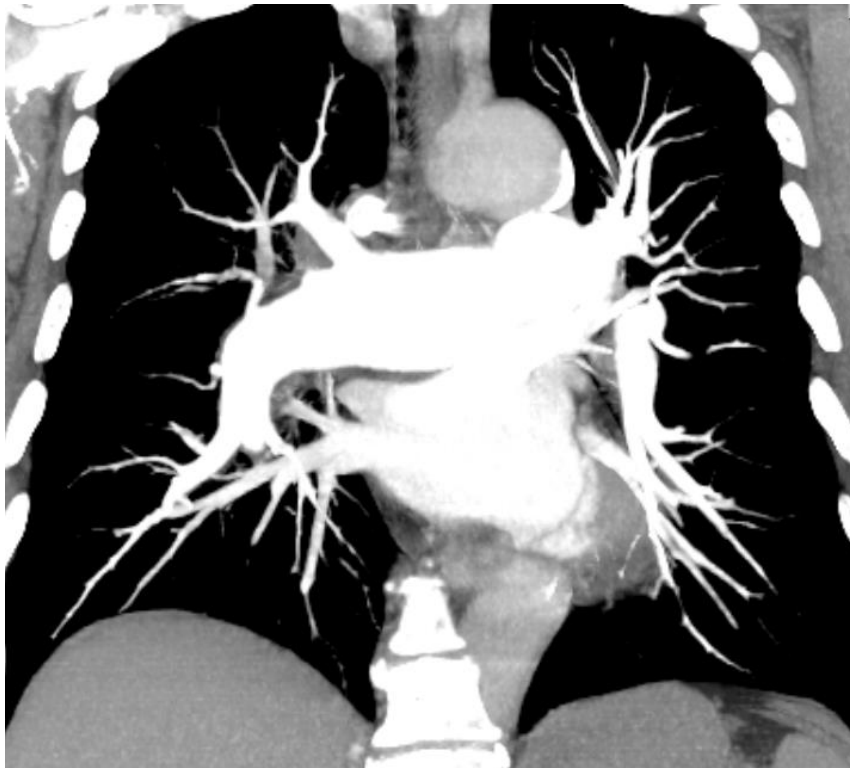


3.39

Chronic thromboembolic pulmonary hypertension (CTEPH) - definition

- pre-capillary PH as assessed by right heart catheterization (mean PAP ≥ 25 mmHg, PCWP ≤ 15 mmHg)
- presence of multiple chronic/organized occlusive thrombi/emboli in the elastic pulmonary arteries (main, lobar, segmental, subsegmental)
- **Persistent PAH despite at least 3 months effective anticoagulation
(DDX from subacute PE)**

Lung perfusion scan 의 중요성!



V/Q scan in CTEPH

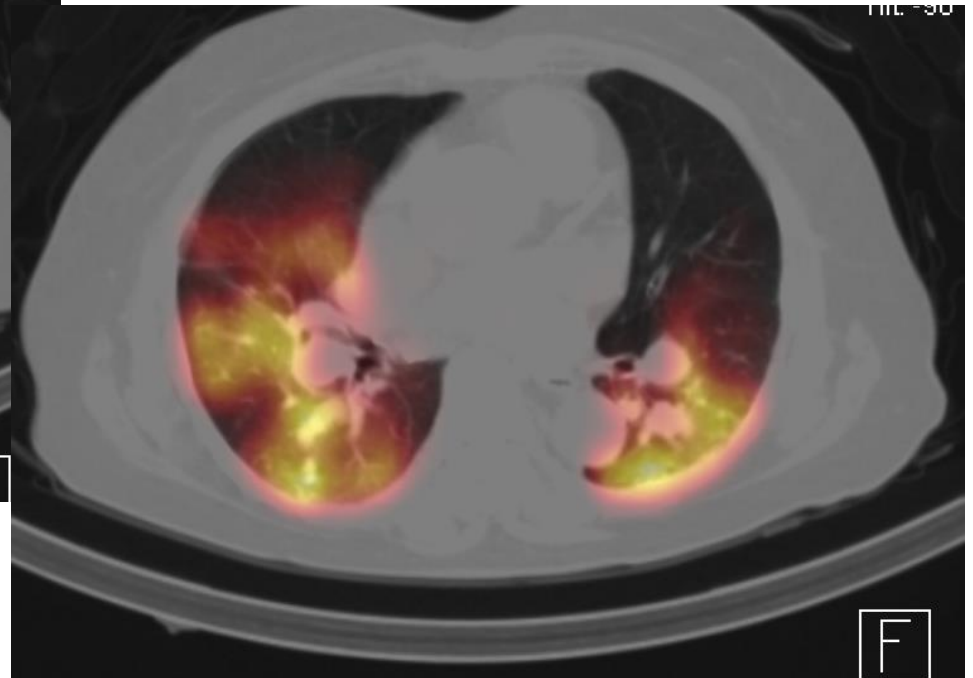
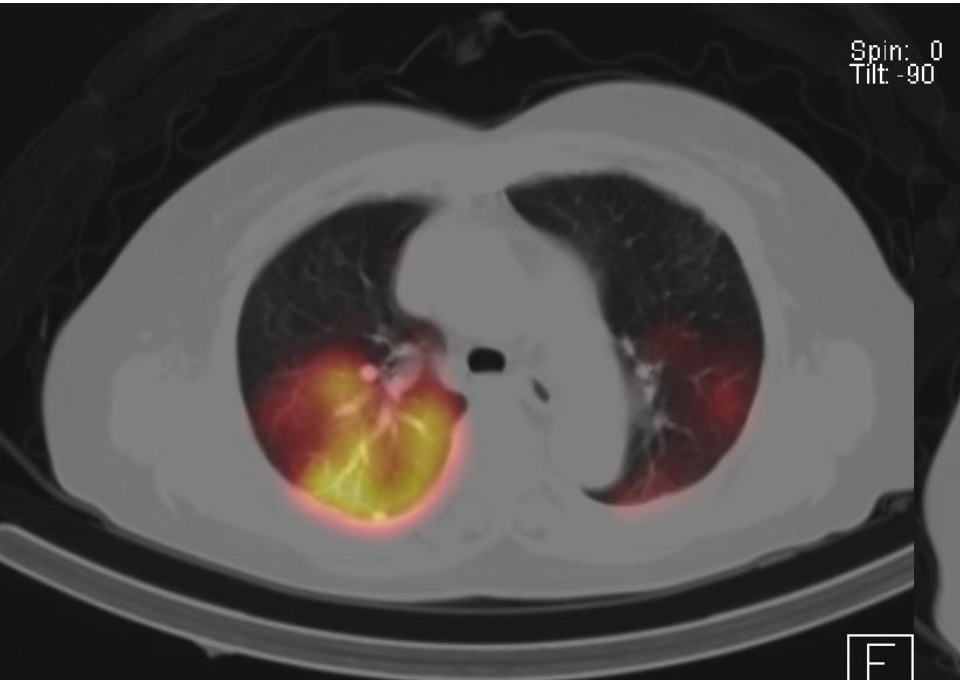
Must do! in newly diagnosed PH
Suspected CTEPH

- Normal V/Q scan excludes CTEPH

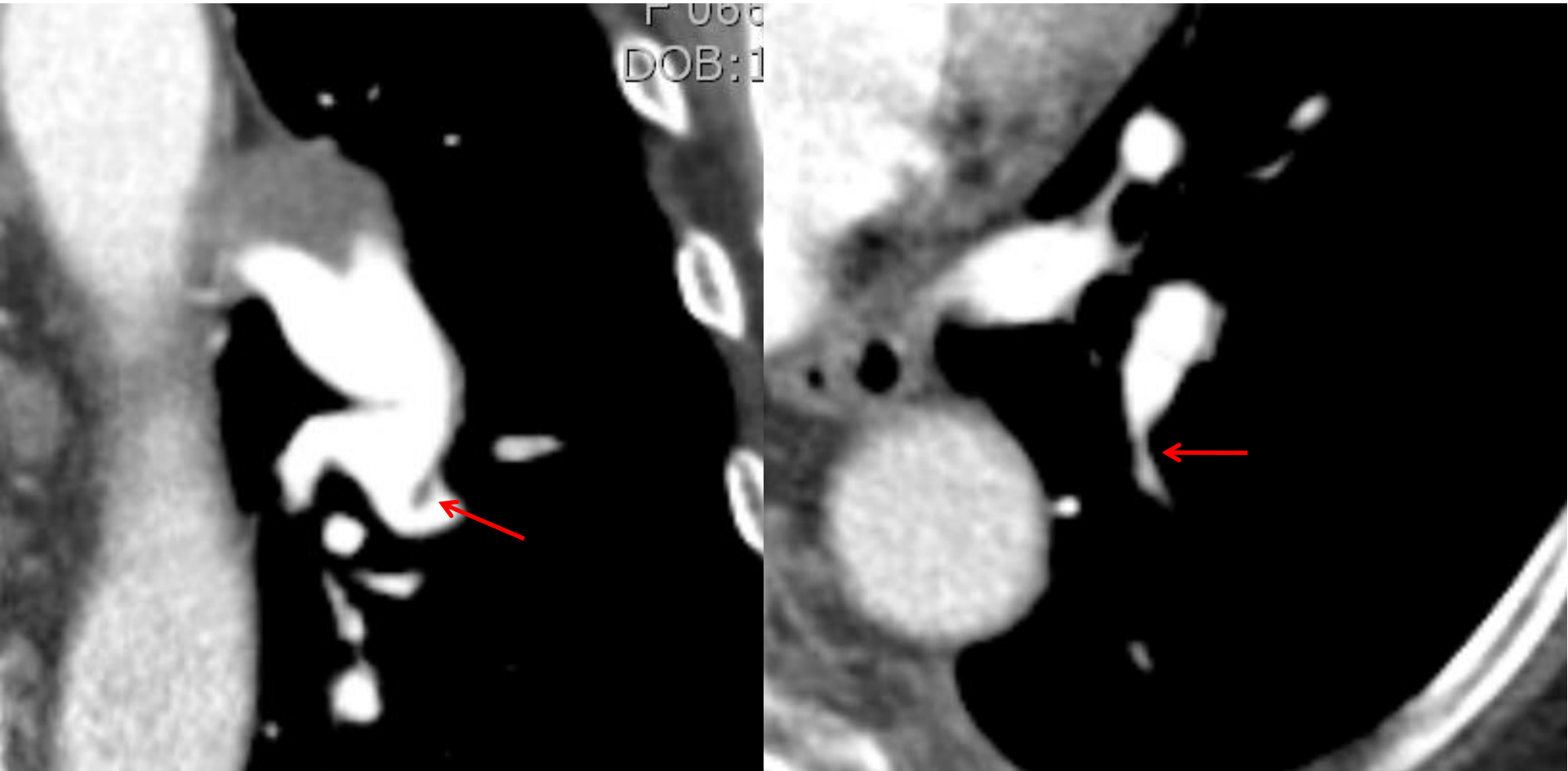
sensitivity of 96 - 97%

specificity of 90 – 95%

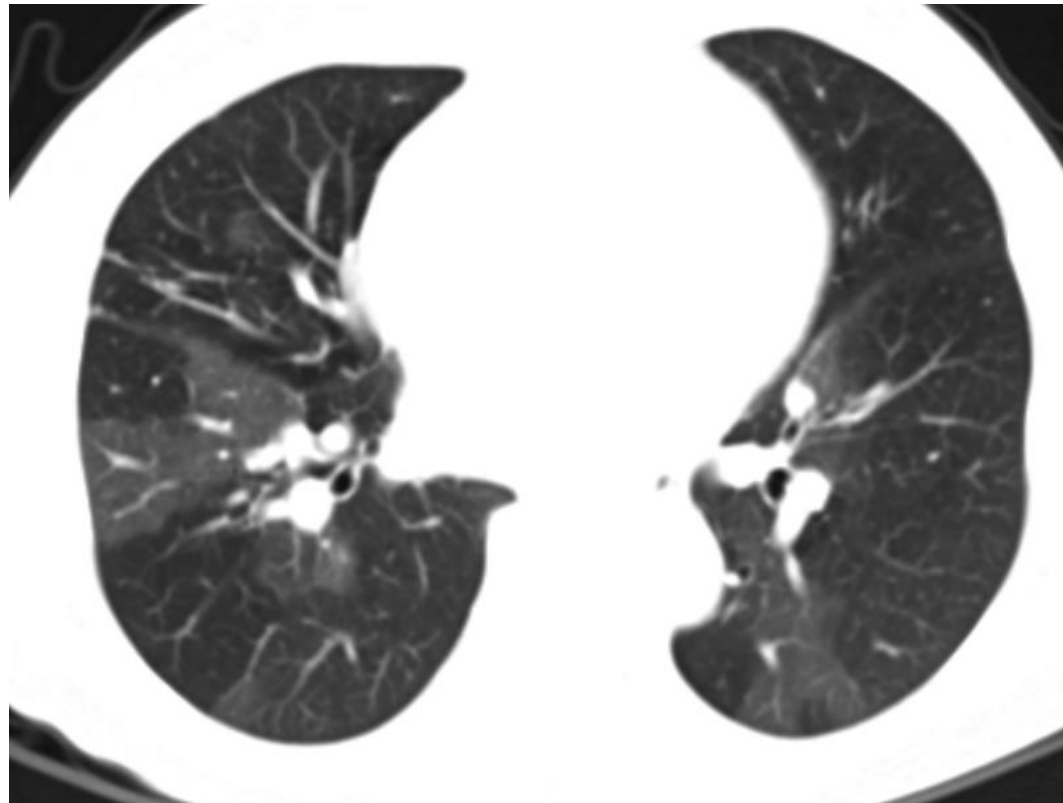
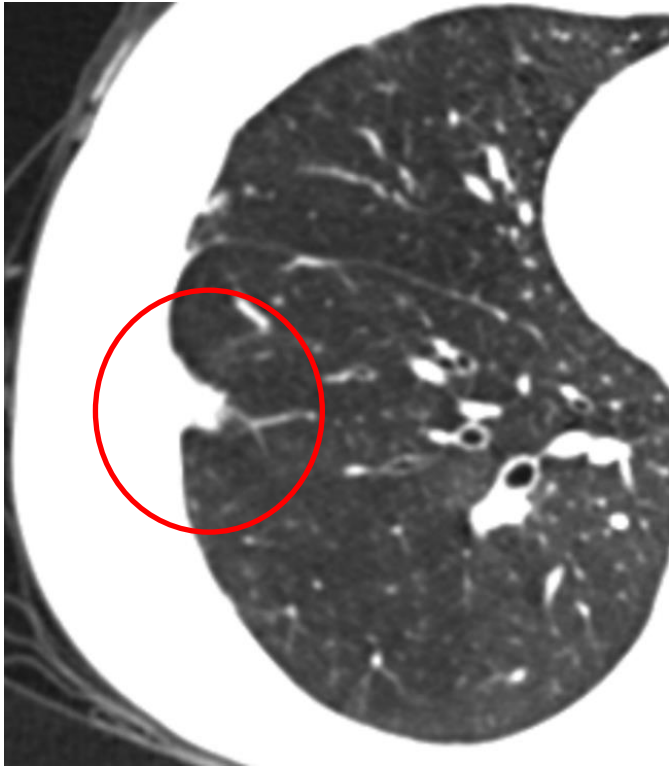
Lung perfusion scan SPECT/CT



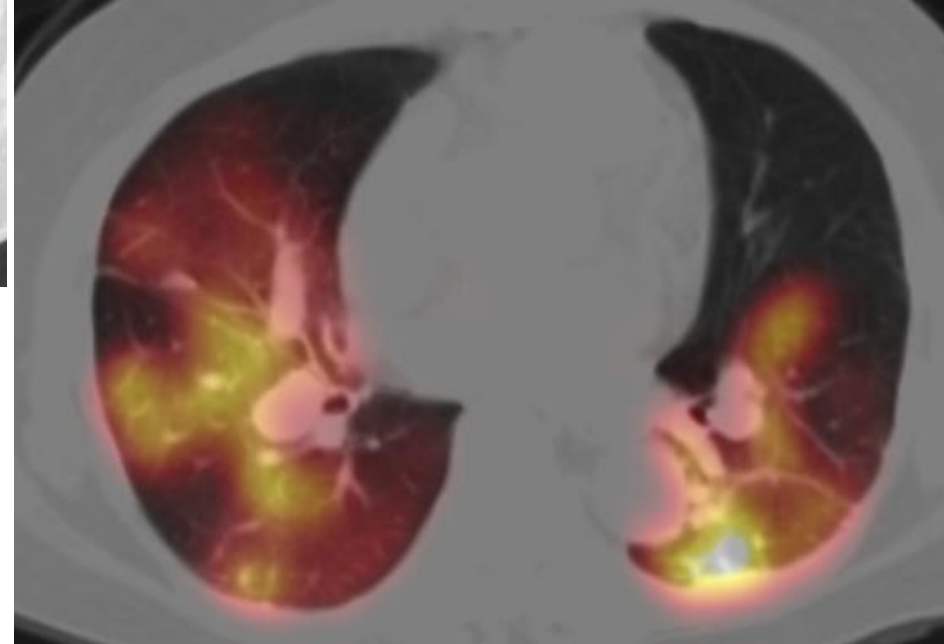
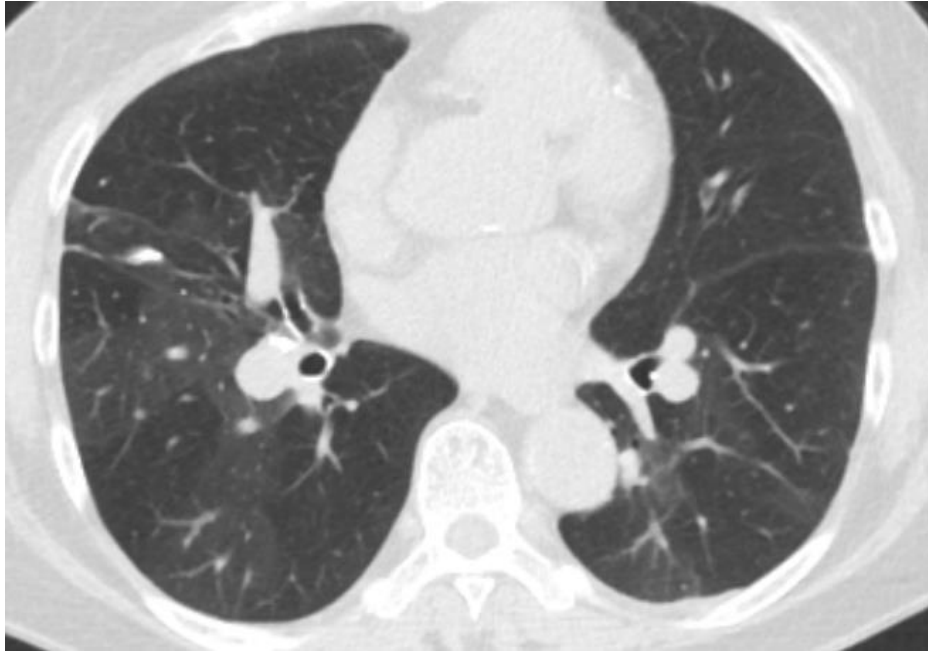
Role of CT



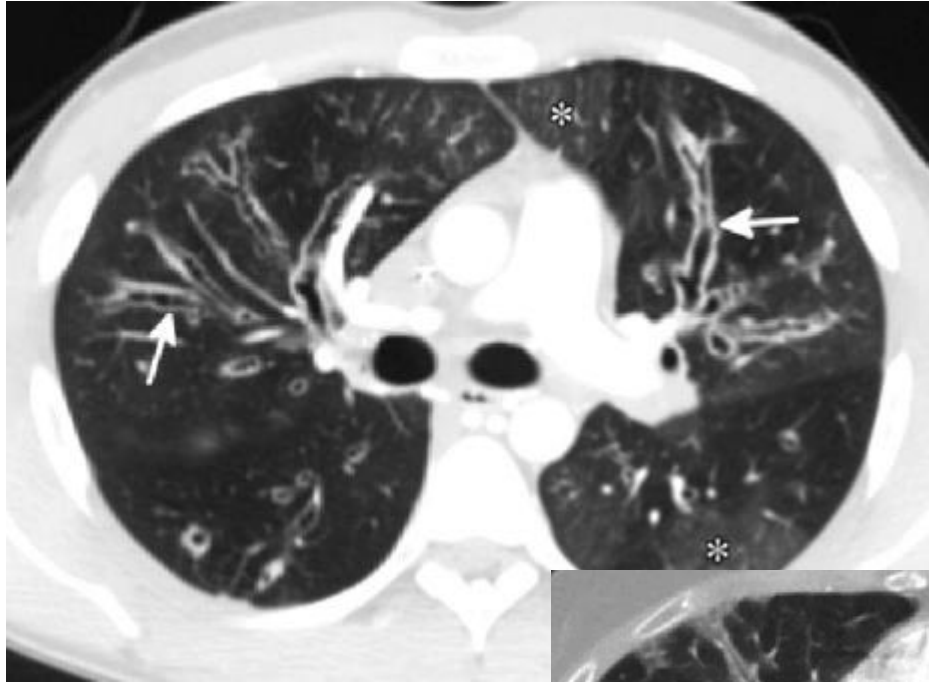
Lung parenchyma



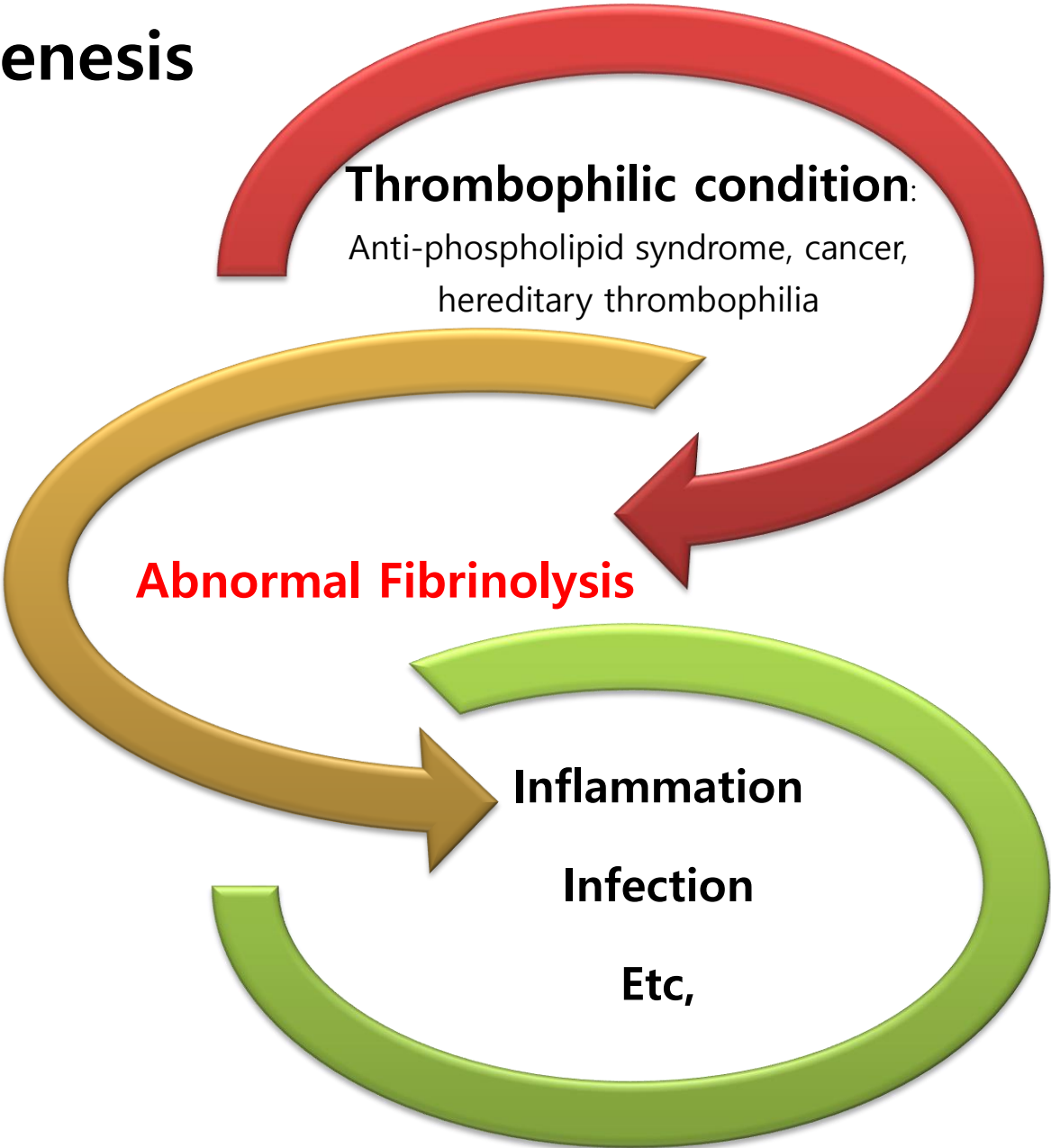
Mosaic attenuation pattern in non-contrast CT



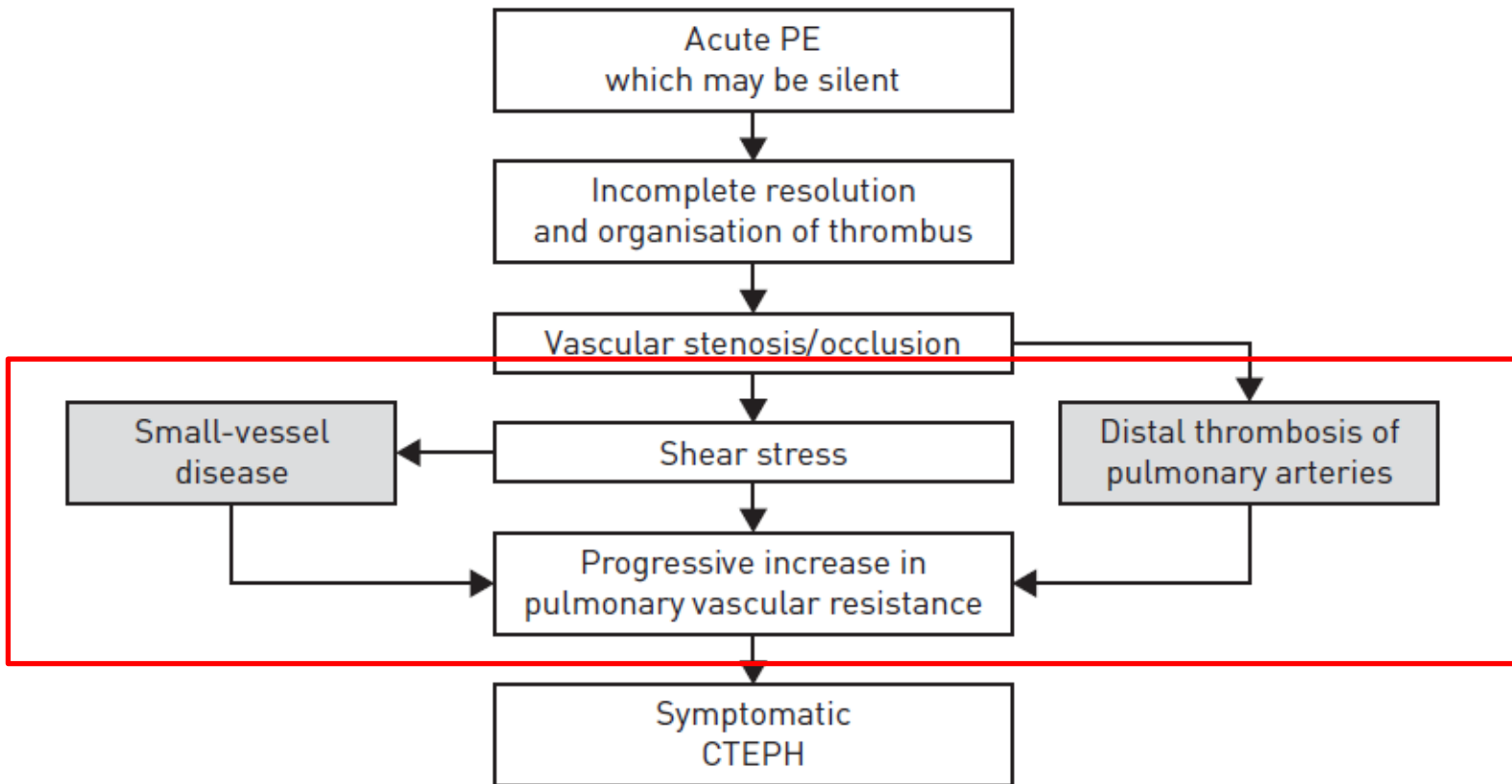
Mosaic attenuation pattern in other diseases



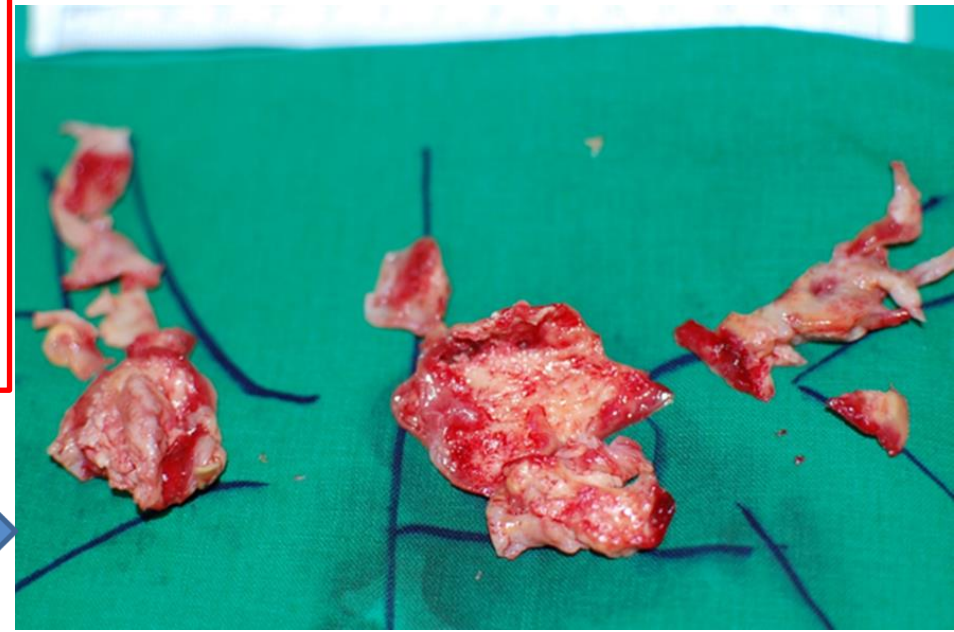
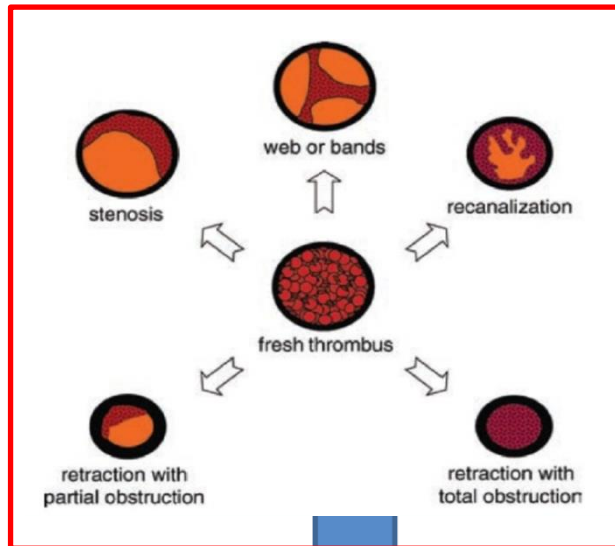
Pathogenesis



Natural history of CTEPH

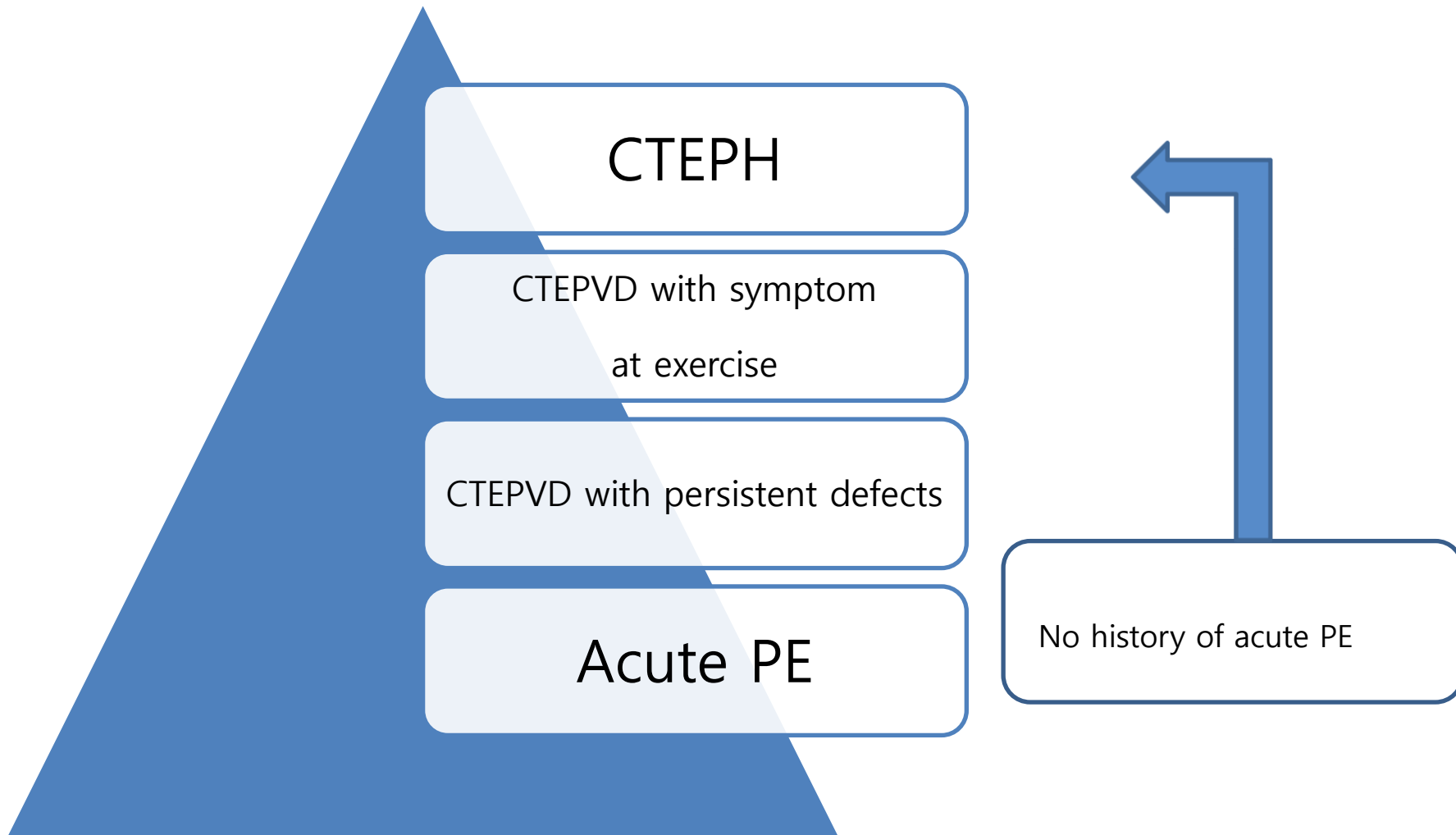


Incomplete resolution & organization

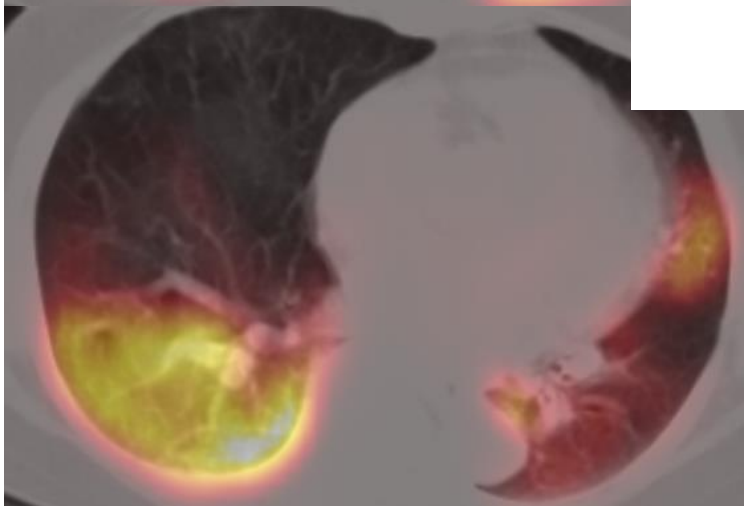
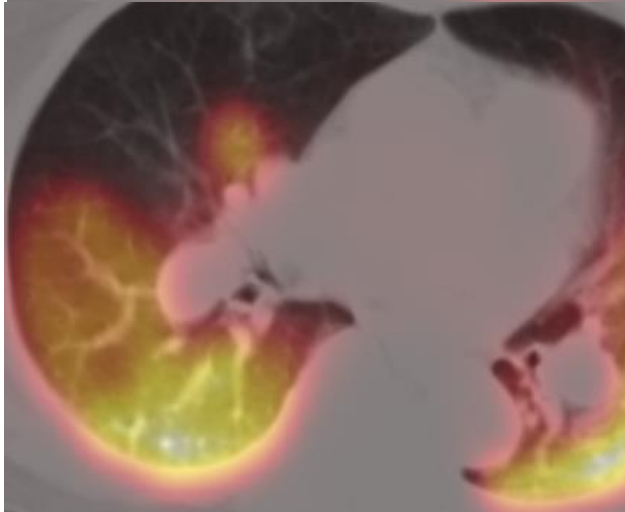
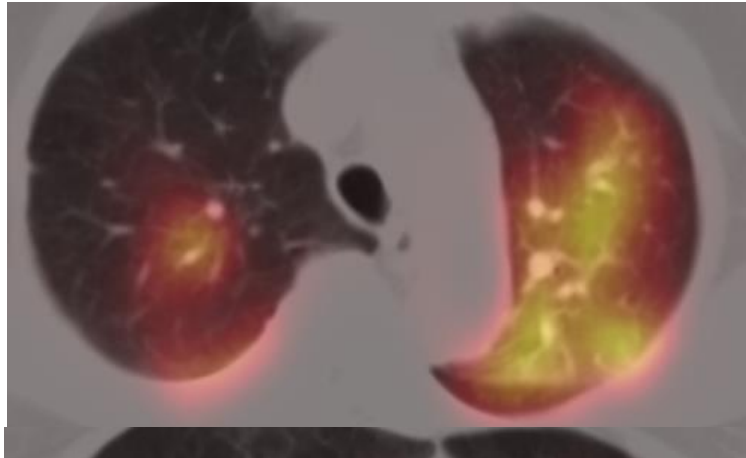


Early reperfusion therapy doesn't prevent CTEPH PEITHO study

Long-term FU (median 37.8 months)	Tenecteplase (n=190)	Placebo (n=186)	<i>p</i> value
CTEPH confirmed	4 (2.1%)	6 (3.2%)	0.79



CTEPVD=chronic thromboembolic pulmonary vascular disease



ANT

Number of laps 7 (X 60 meters) + Final partial lap 4.5
= Total distance walked in 6 minutes 424.5 (meters)

Comment	Time	SPO2	HR
	30"	92	76
	1'	90	95
	1' 30"	85	102
	2'	85	109
	2' 30"	83	110
	3'	82	117
	3' 30"	80	120
	4'	81	120
	4' 30"	81	122
	5'	80	124
	5' 30"	81	128
	6'	81	129

CTEPH - natural course

In the era of no treatment

5 yr survival

30% in mPAP > 40 mmHg

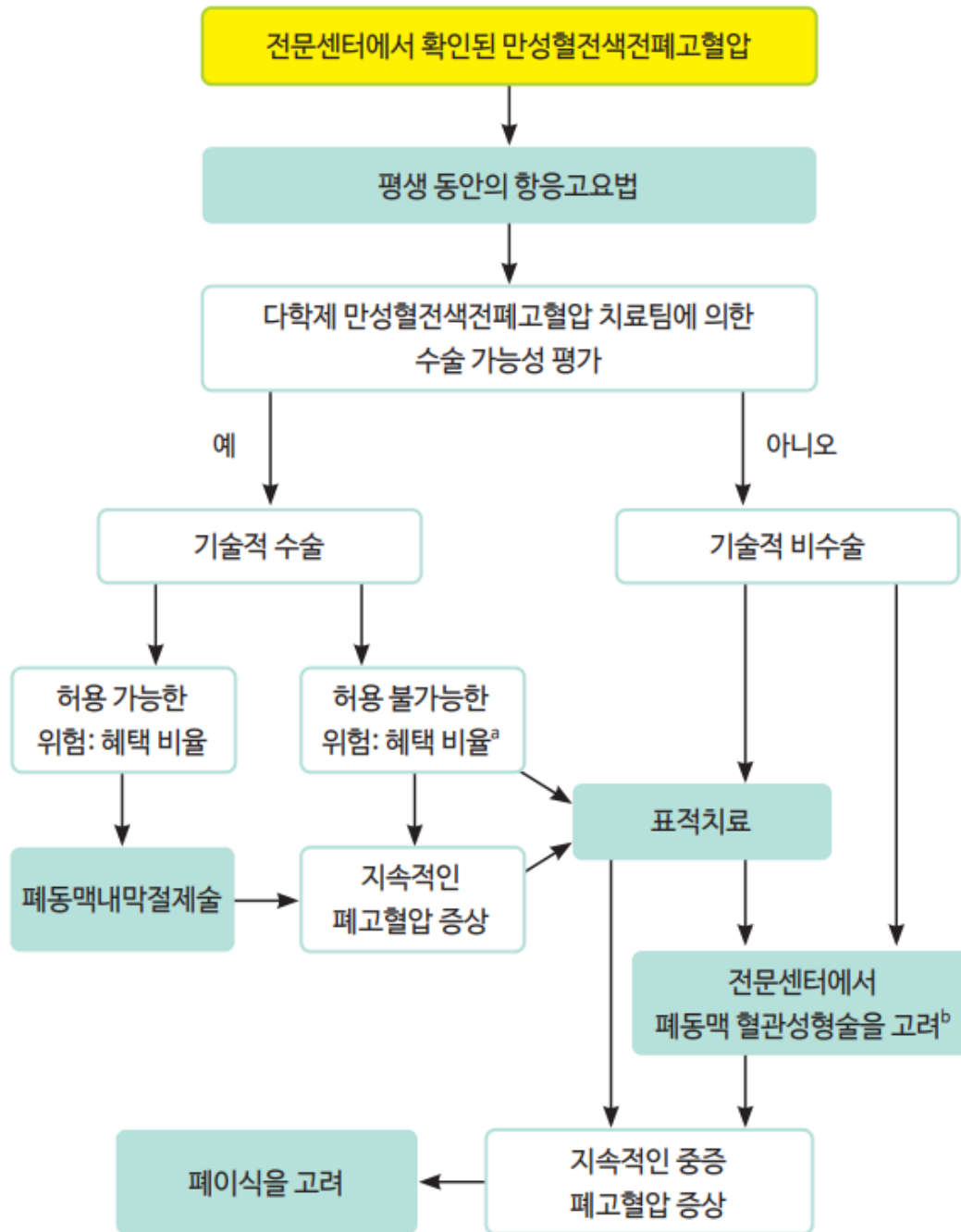
10% in mPAP > 50 mmHg

3-year survival

30% in mPAP > 30 mmHg

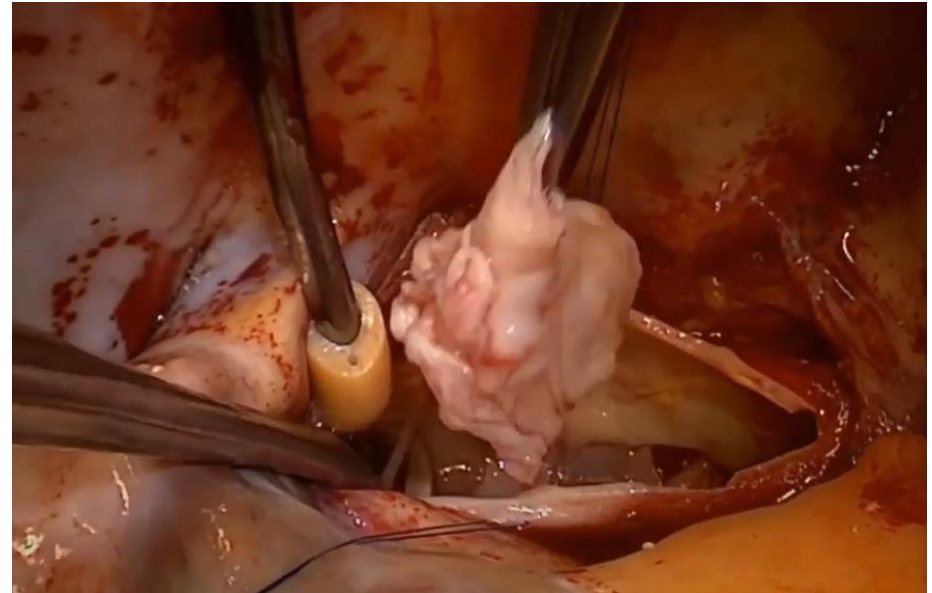
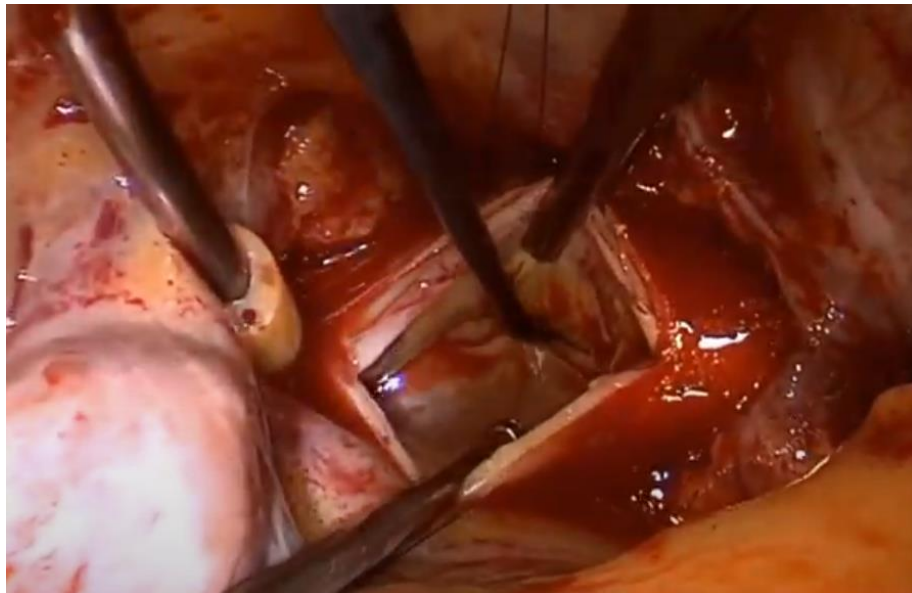
Riedel M, et al Longterm follow-up of patients with pulmonary thromboembolism: late prognosis and evolution of hemodynamic and respiratory data. Chest 1982;81:151–158.

그림 5. 만성혈전색전폐고혈압 치료 알고리즘



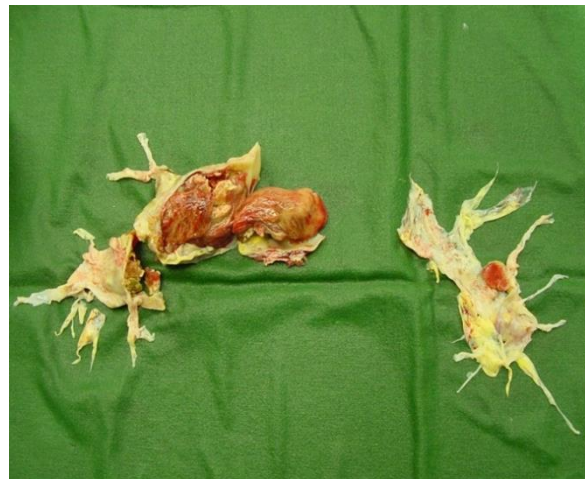
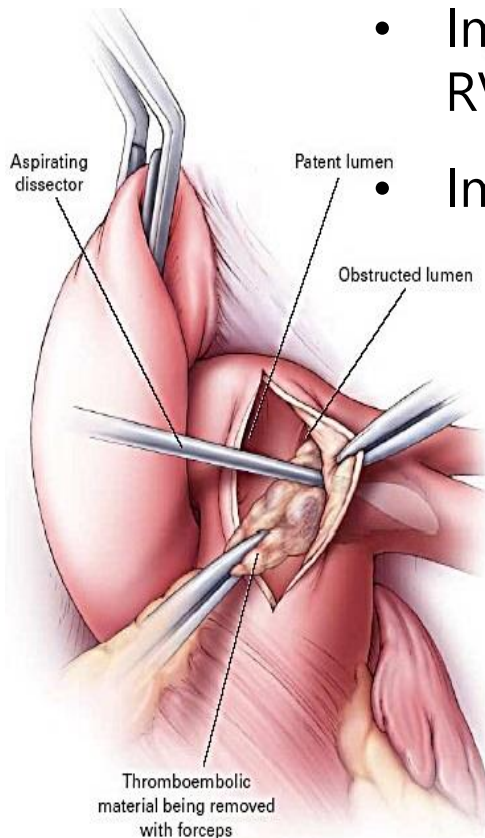
Pulmonary endarterectomy (PEA)

- Median sternotomy
- Cardiopulmonary bypass
 - gradual cooling to 20°C
- When blood obscure surgical field
 - Deep hypothermic circulatory arrest (DHCA)
- DHCA is limited to 20 min intervals



Rationale for PEA

- Complete removal and clearance of PA obstructions
- Reduces pulmonary arterial pressure
- Improve pulmonary perfusion, oxygenation, RV function and dead space ventilation
- Improve *life expectancy and quality of life*

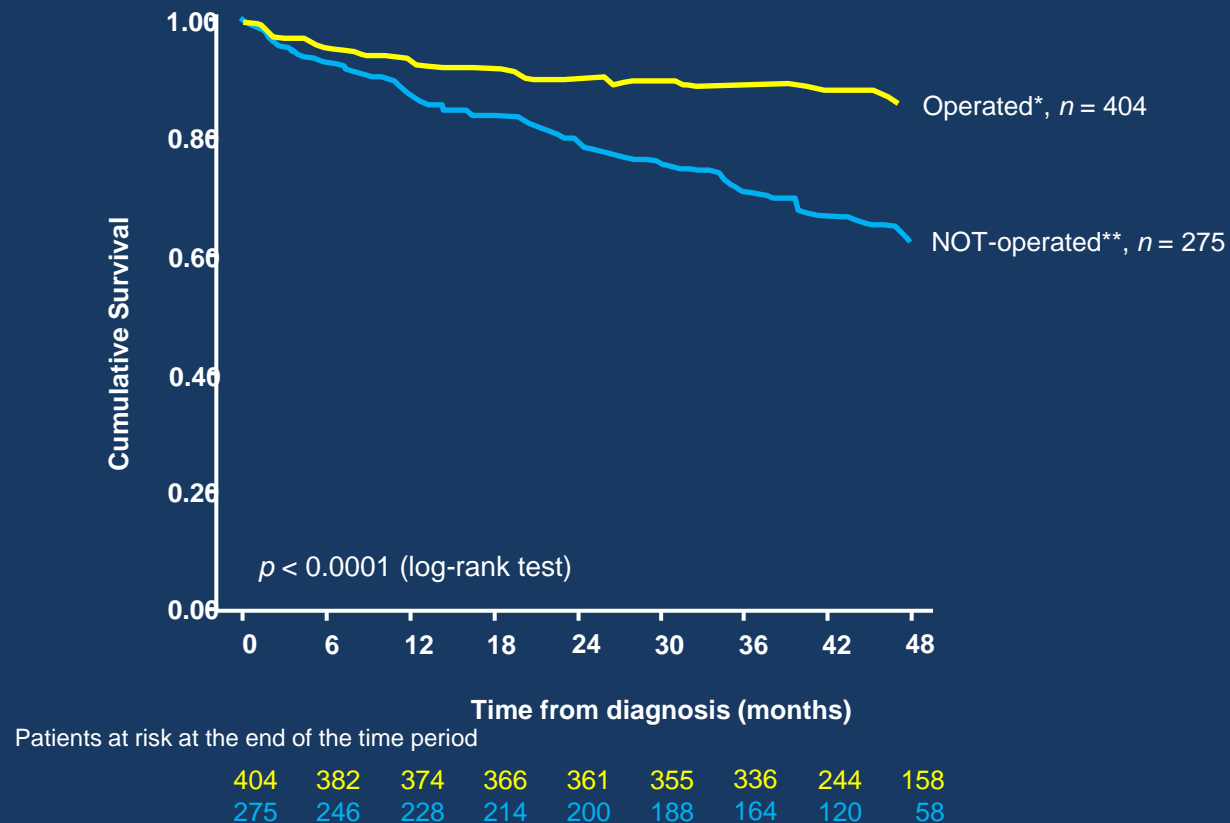


Fedullo PF, et al. *N Engl J Med* 2001; 345:1465-72;

Mayer E, et al. *Eur respir Rev* 2010; 19:64-76;

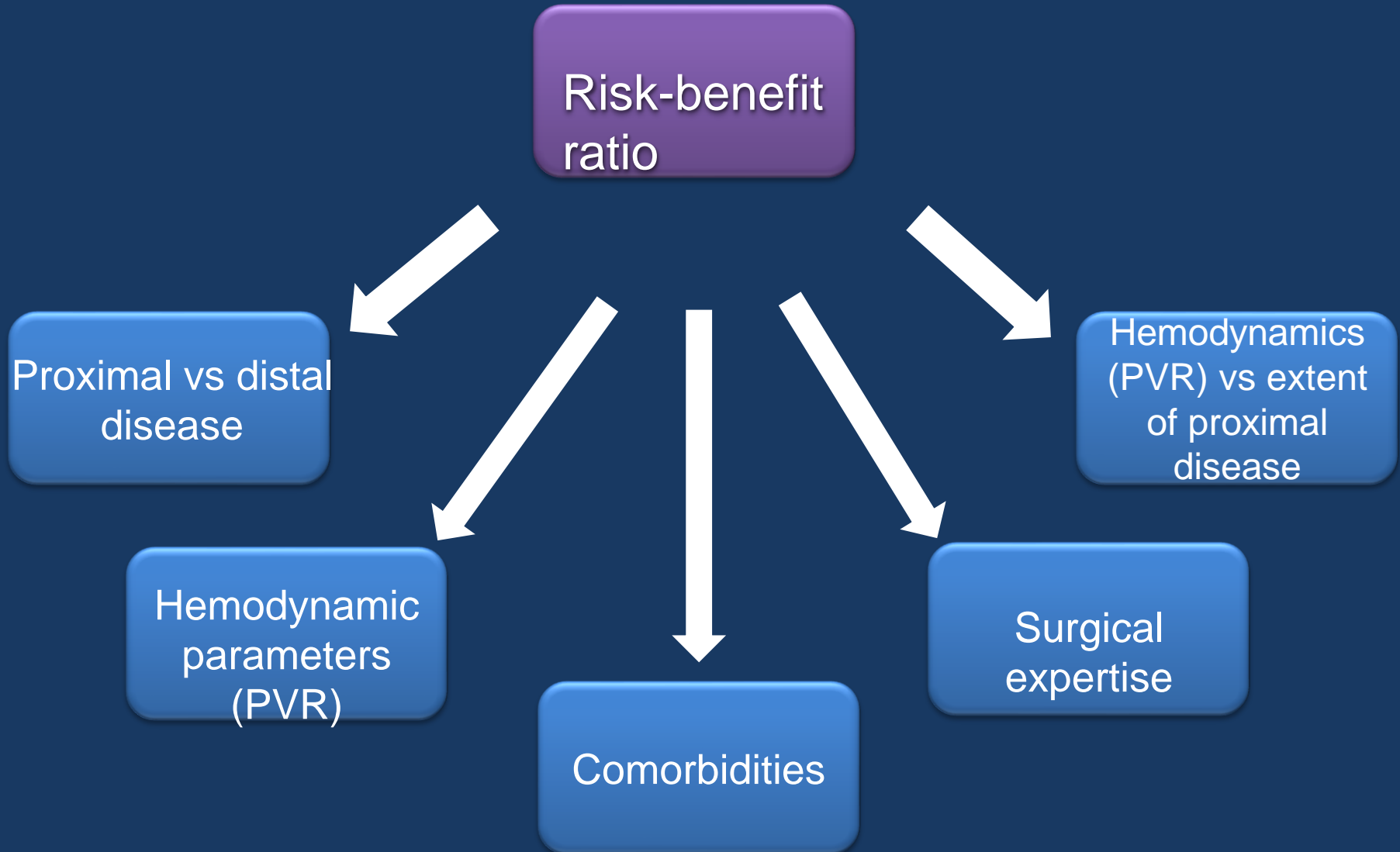
Simonneau G, et al. *Am J Respir Crit Care Med* 2013; 187:A5365

PEA significantly improves the long-term prognosis of CTEPH patients compared with non-operated patients



*Underwent pulmonary endarterectomy, **Considered inoperable for PEA for a variety of reasons including inaccessibility of lesions, indication of significant small vessel disease and co-morbidities. Delcroix M, *et al. Circulation* 2016; 133:859-71.

Assessment of operability

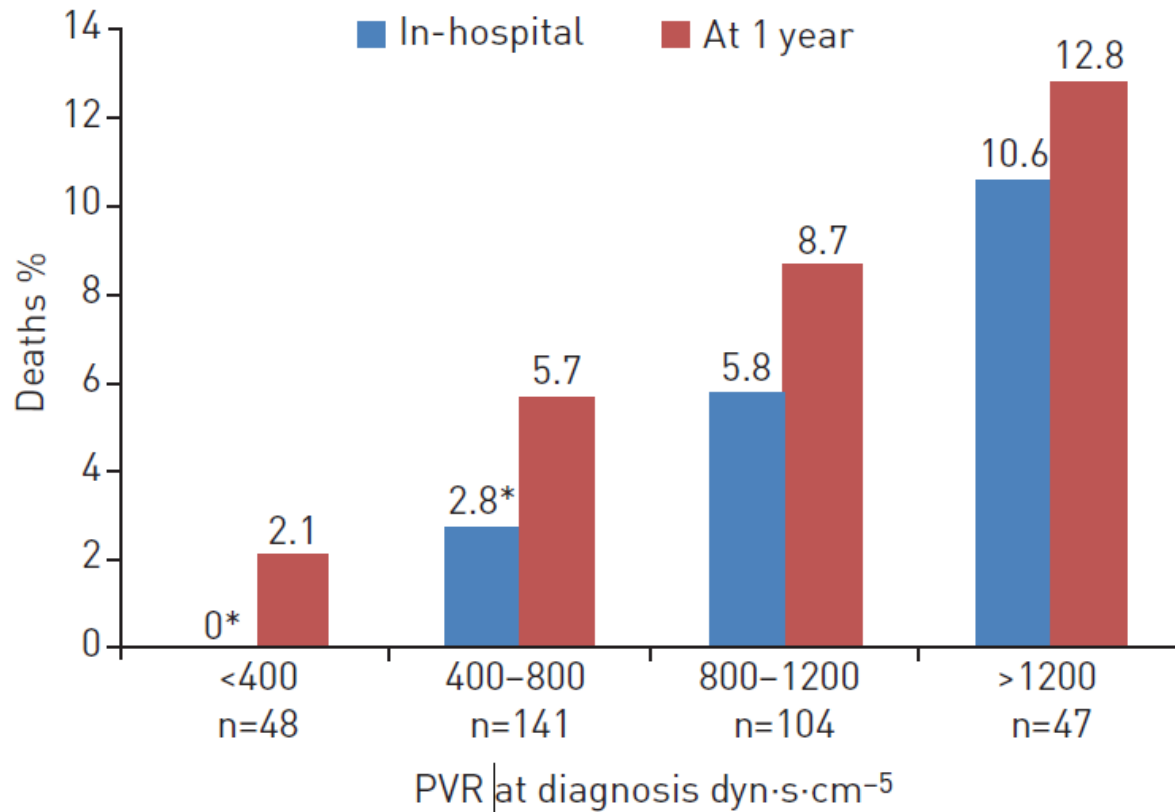


Evaluation of operability

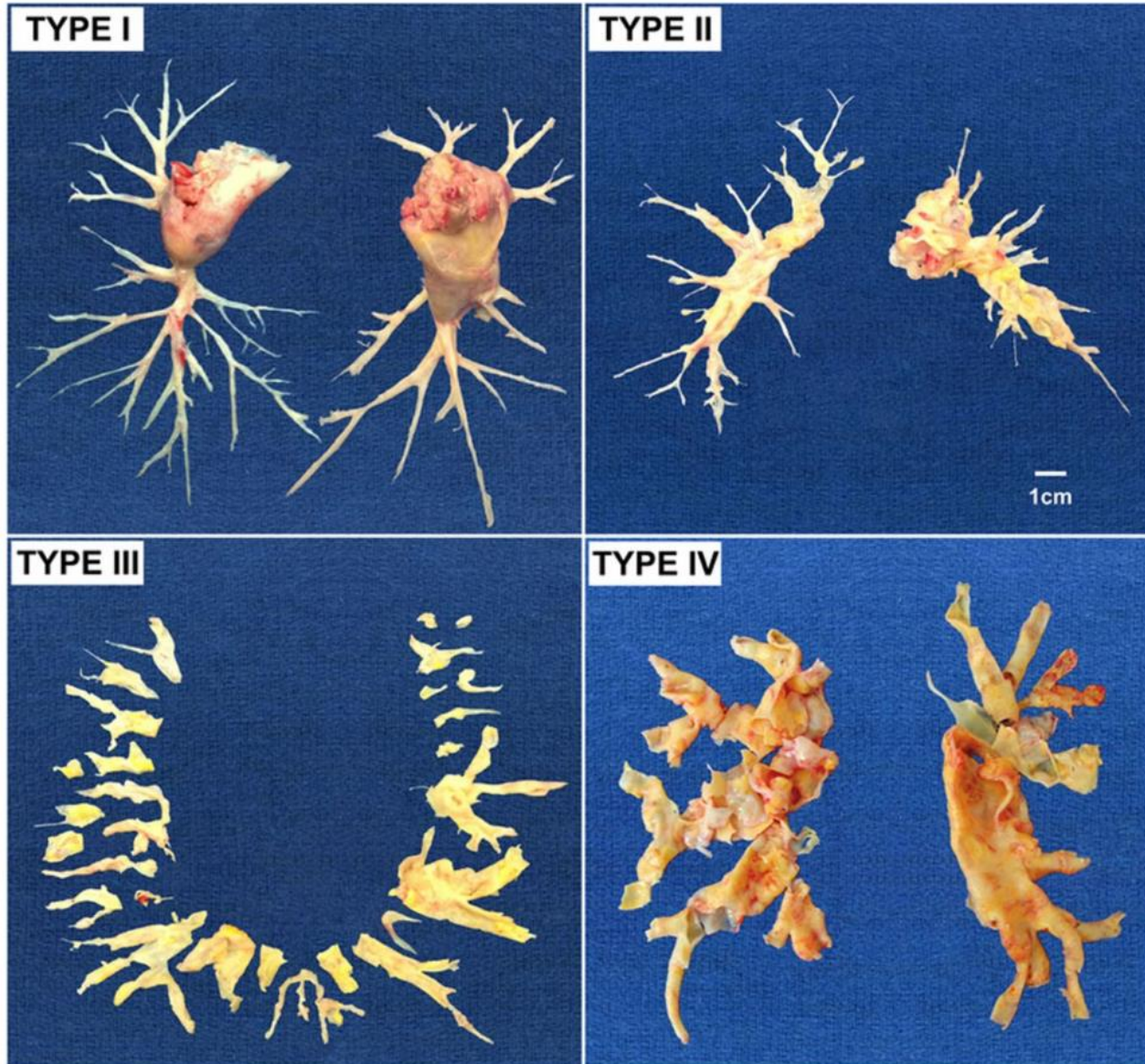
Requires consideration of:

- High quality imaging
- Interdisciplinary approach
- Surgical experience – Learning curve
- Risk factors
- Comorbidity (parenchymal lung disease, poor LV systolic function)
- Patient acceptance of risk
- Second opinion in case of inoperability

Effect of PVR at diagnosis Undergoing PEA



University of California–San Diego surgical classification (Jamieson) of pulmonary endarterectomy specimens

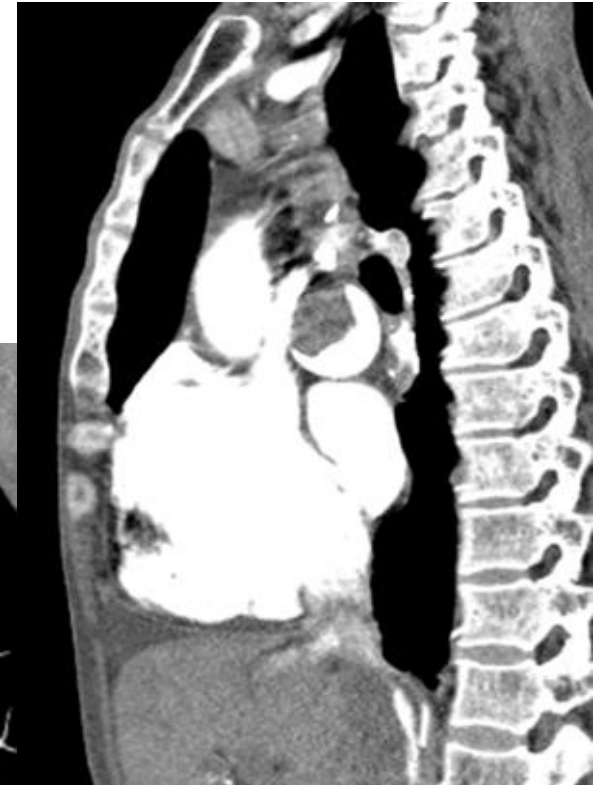


Irene Marthe Lang, Michael Madani, **Update on Chronic Thromboembolic Pulmonary Hypertension** *Circulation*. 2014;130:508-518

Type I



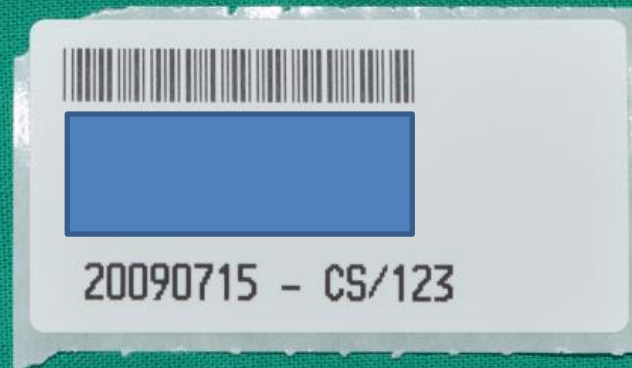
75/F
History of
Recurrent acute PE



Type I Endarterectomy specimen



Pathology: Mainly organized thrombus with some fresh thrombus



→ Normalized pulmonary artery pressure pulmonary vascular resistance after PEA

72/F recurrent PE worsening exertional dyspnea

Lung Perfusion Scan
99mTc-MAA

DOB:1943-1



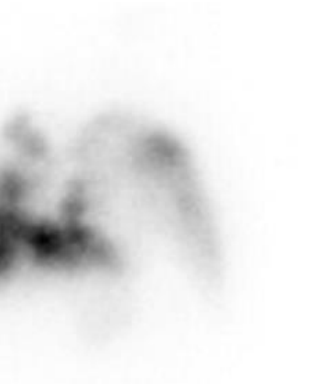
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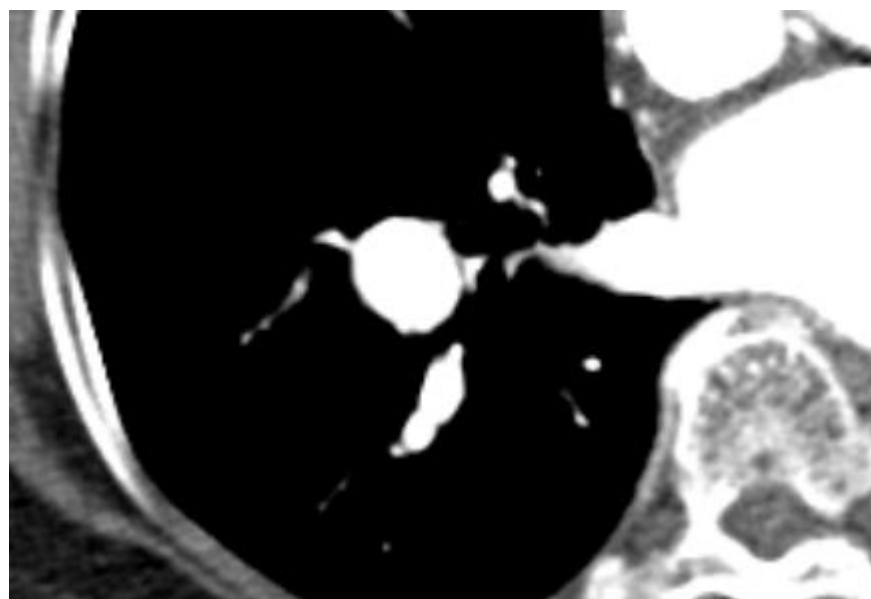
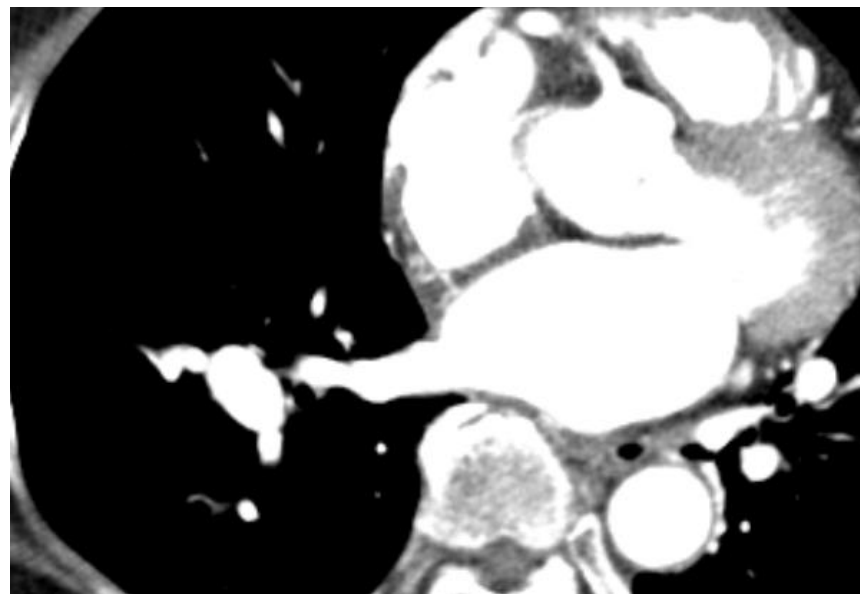


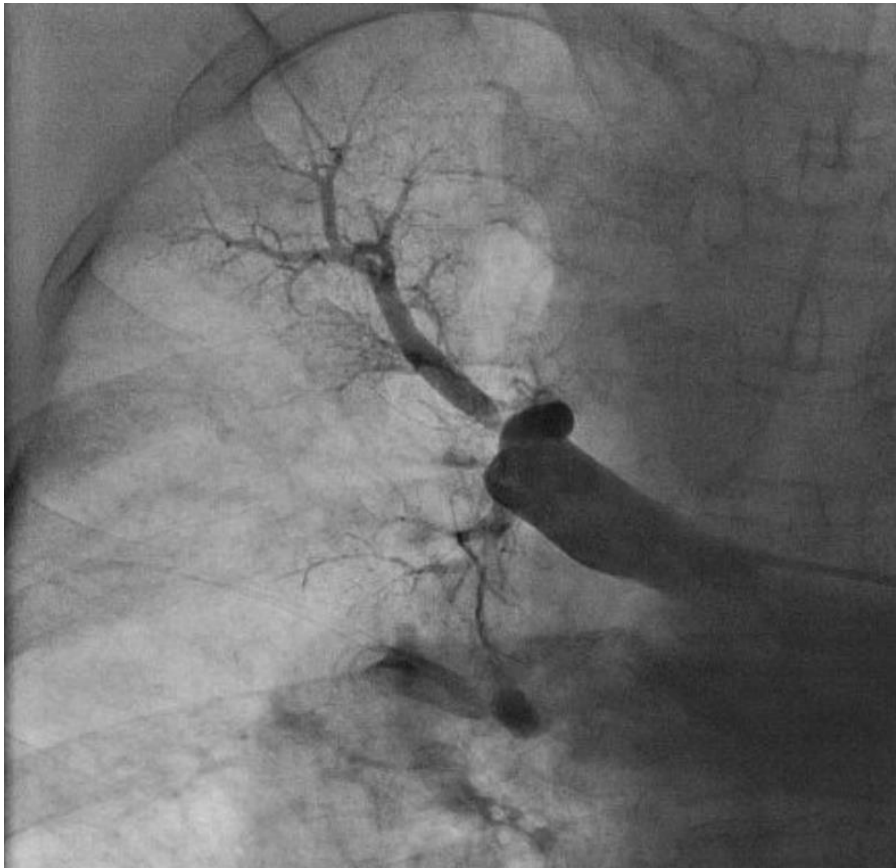
LAO



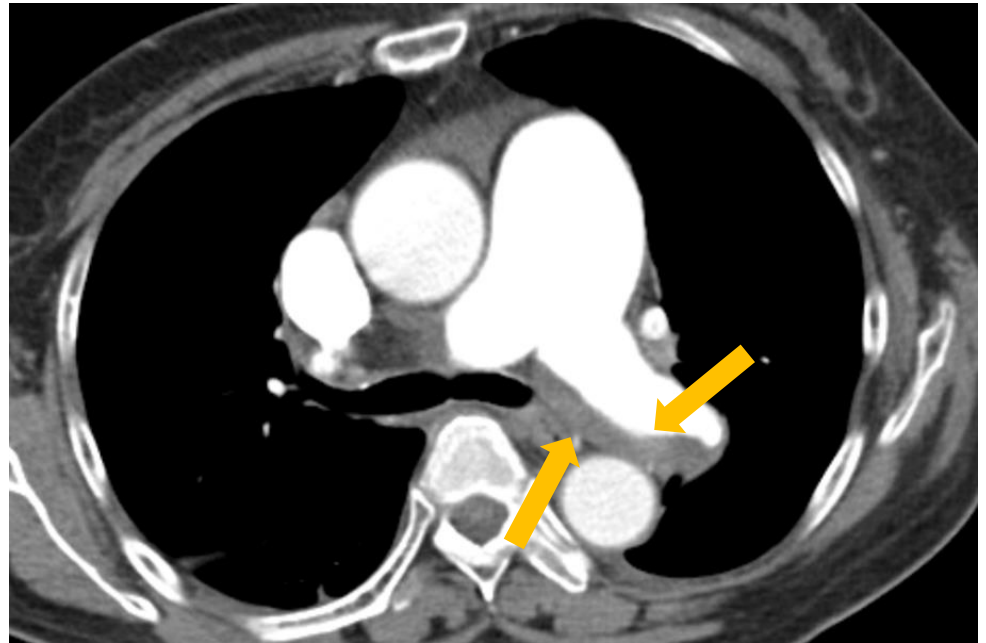
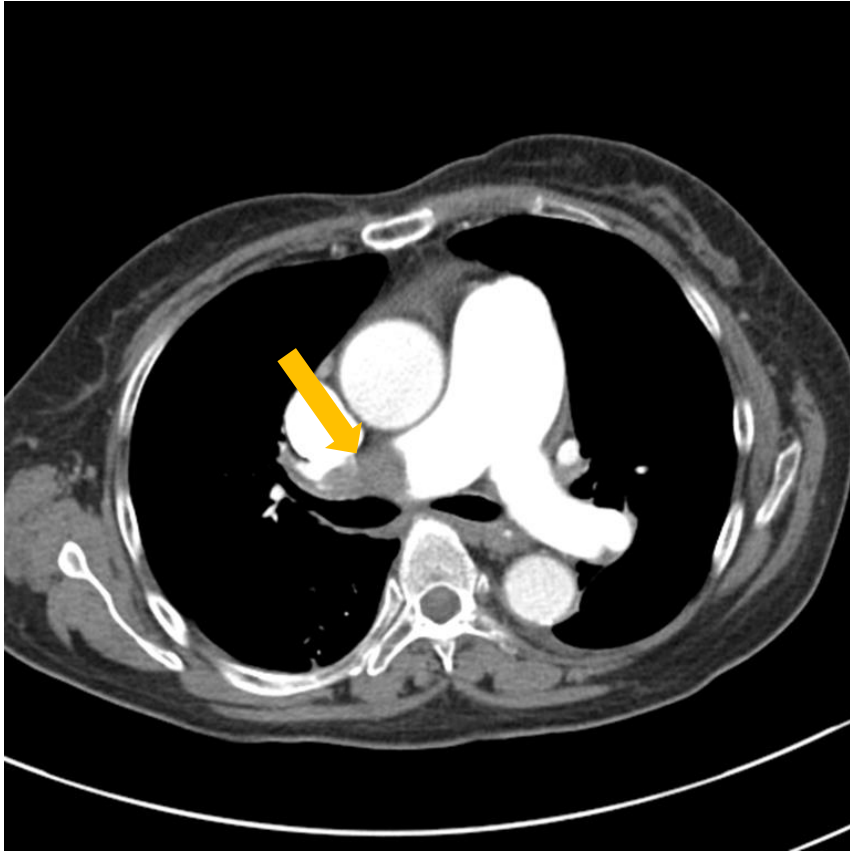
LPO



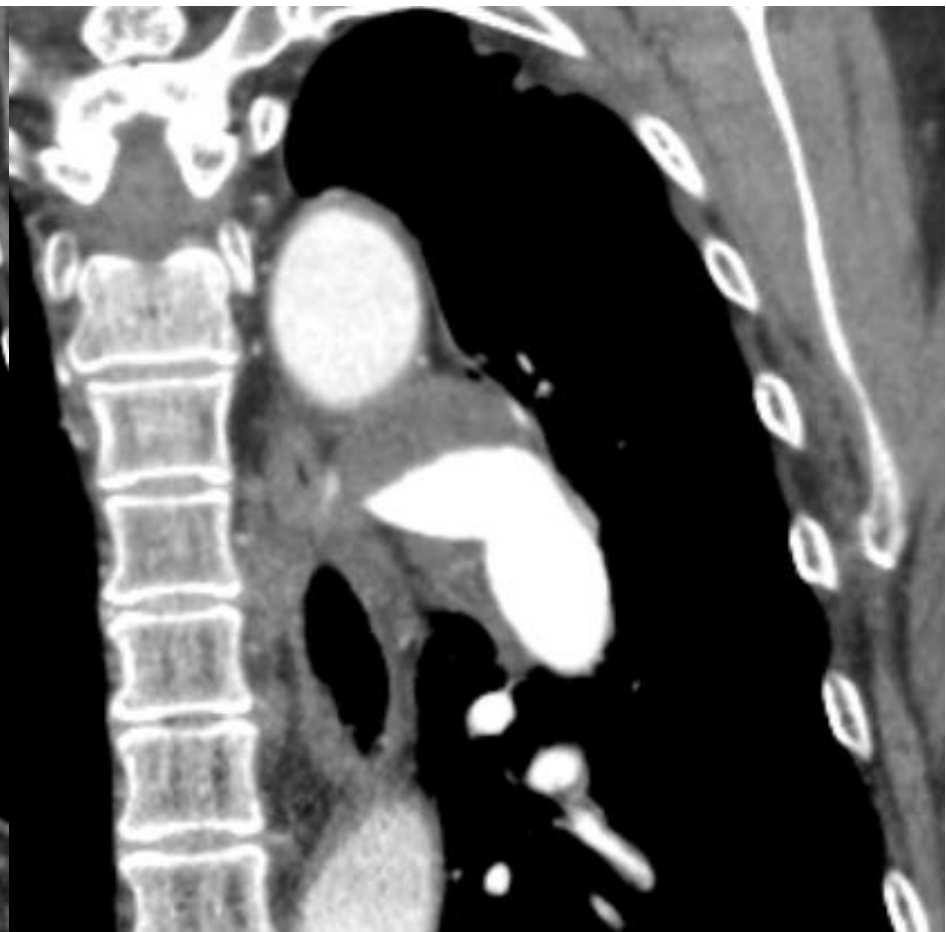




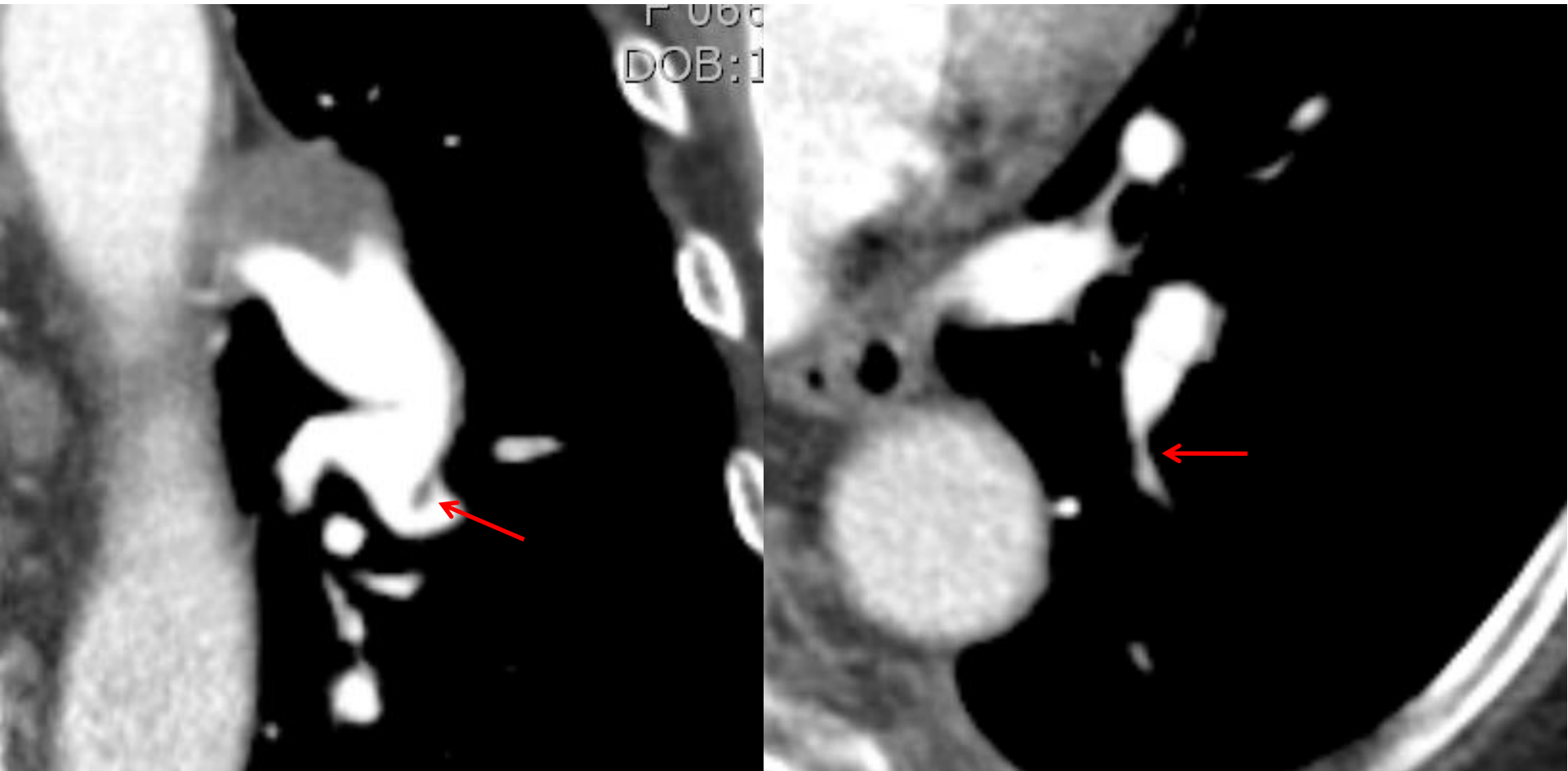
69/F exertional dyspnea



Proximal – LUL & RUL



Distal Segments



Lung Perfusion Scan



ANT



RAO



LAO



RT LAT



POST



LPO

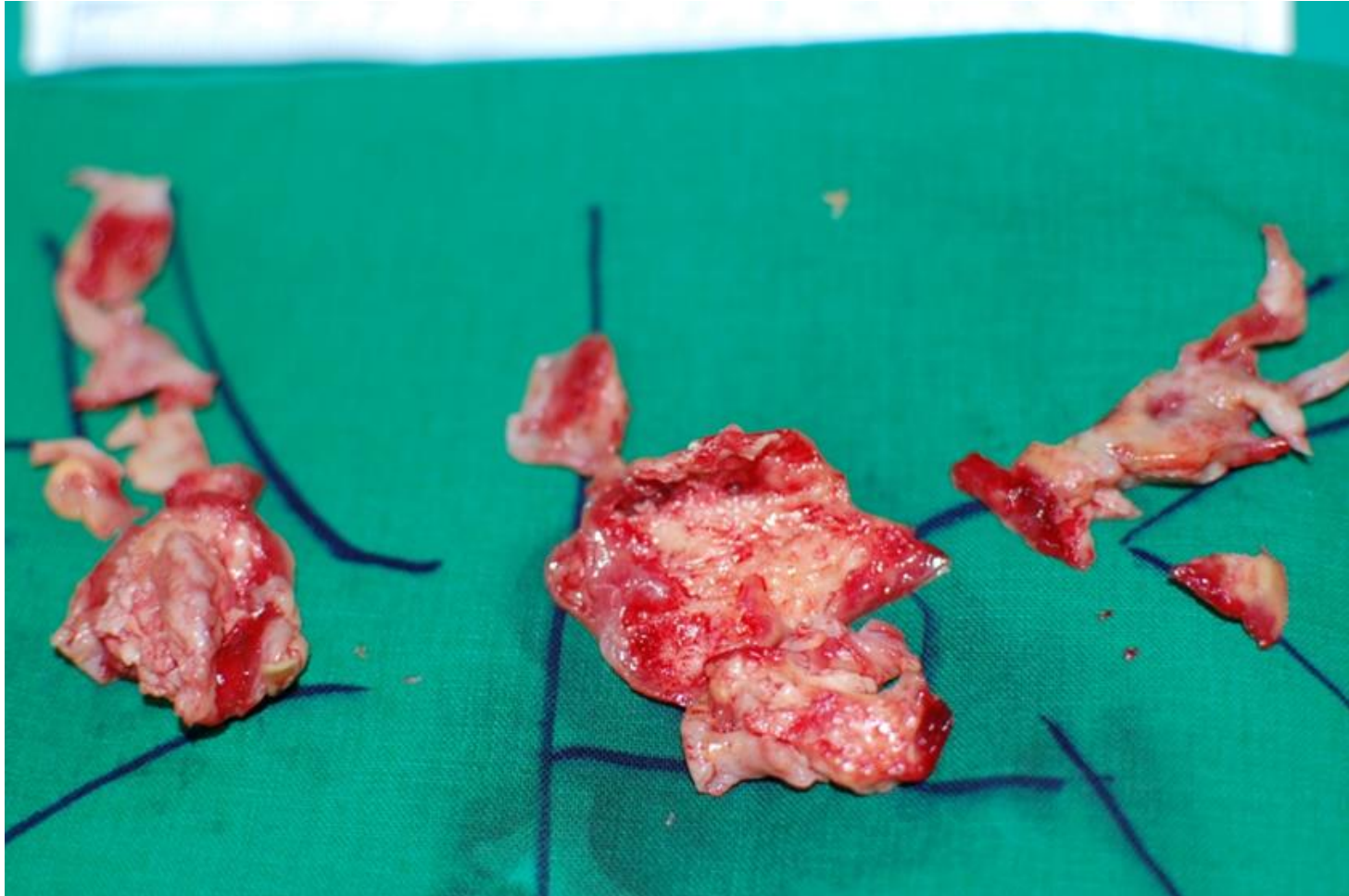


RPO

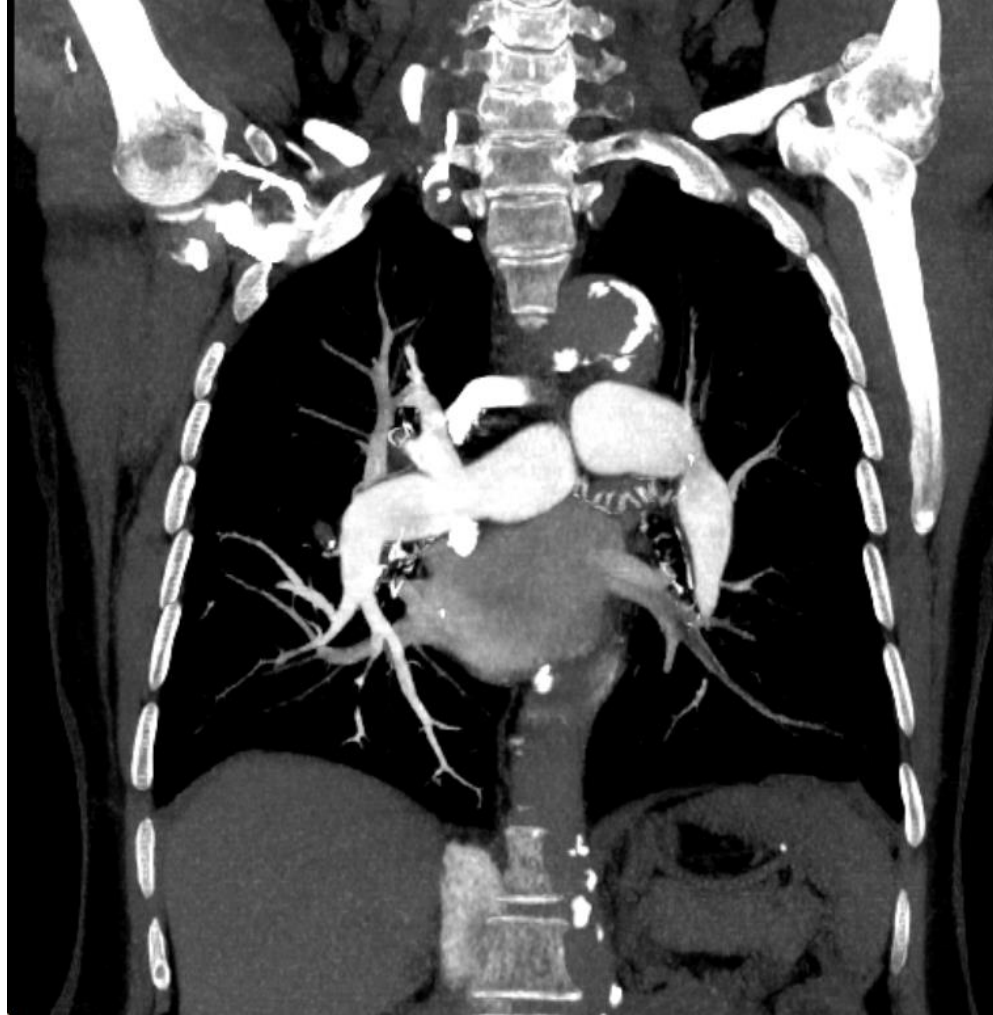


LT LAT

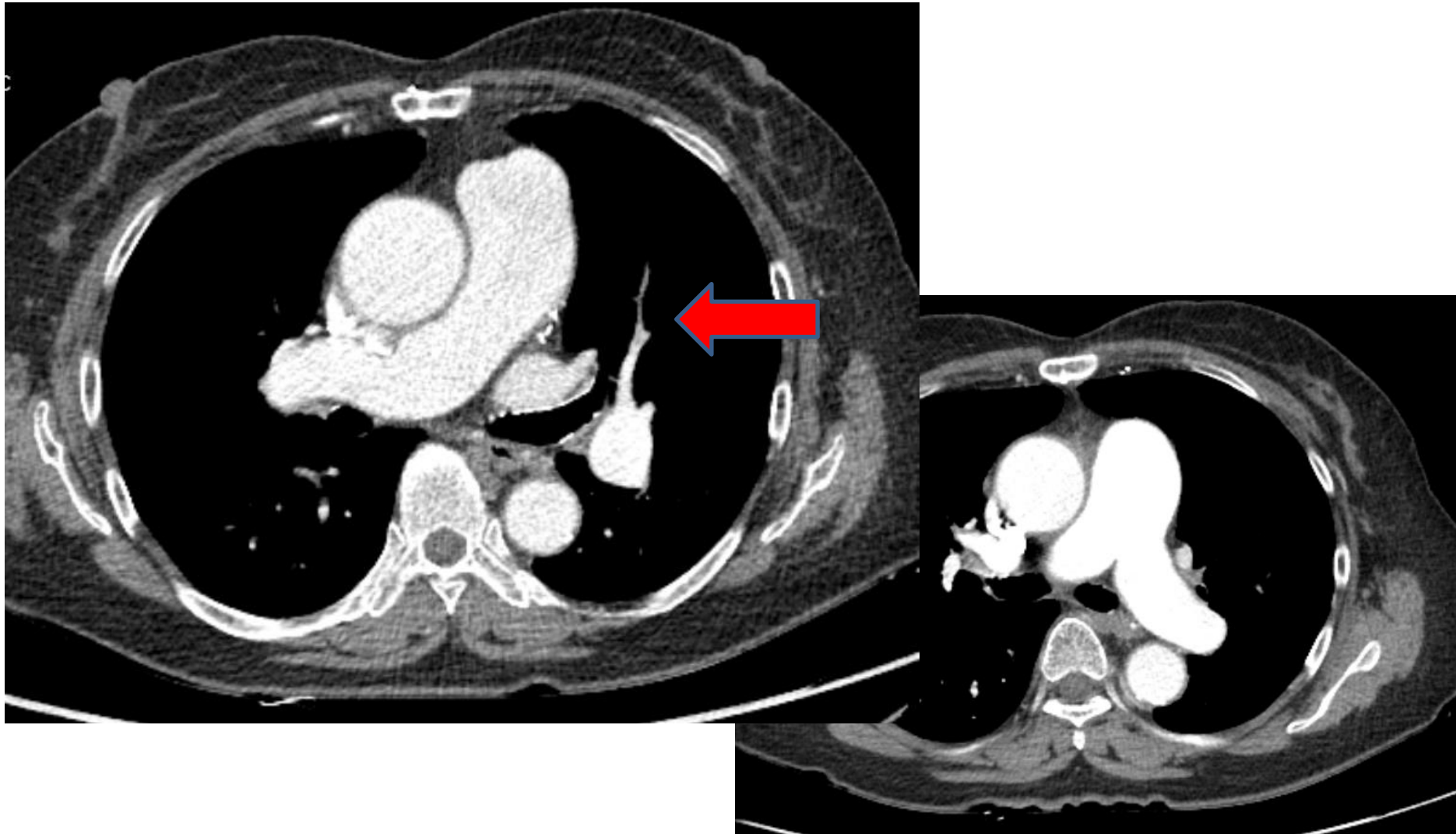
Endarterectomy specimen

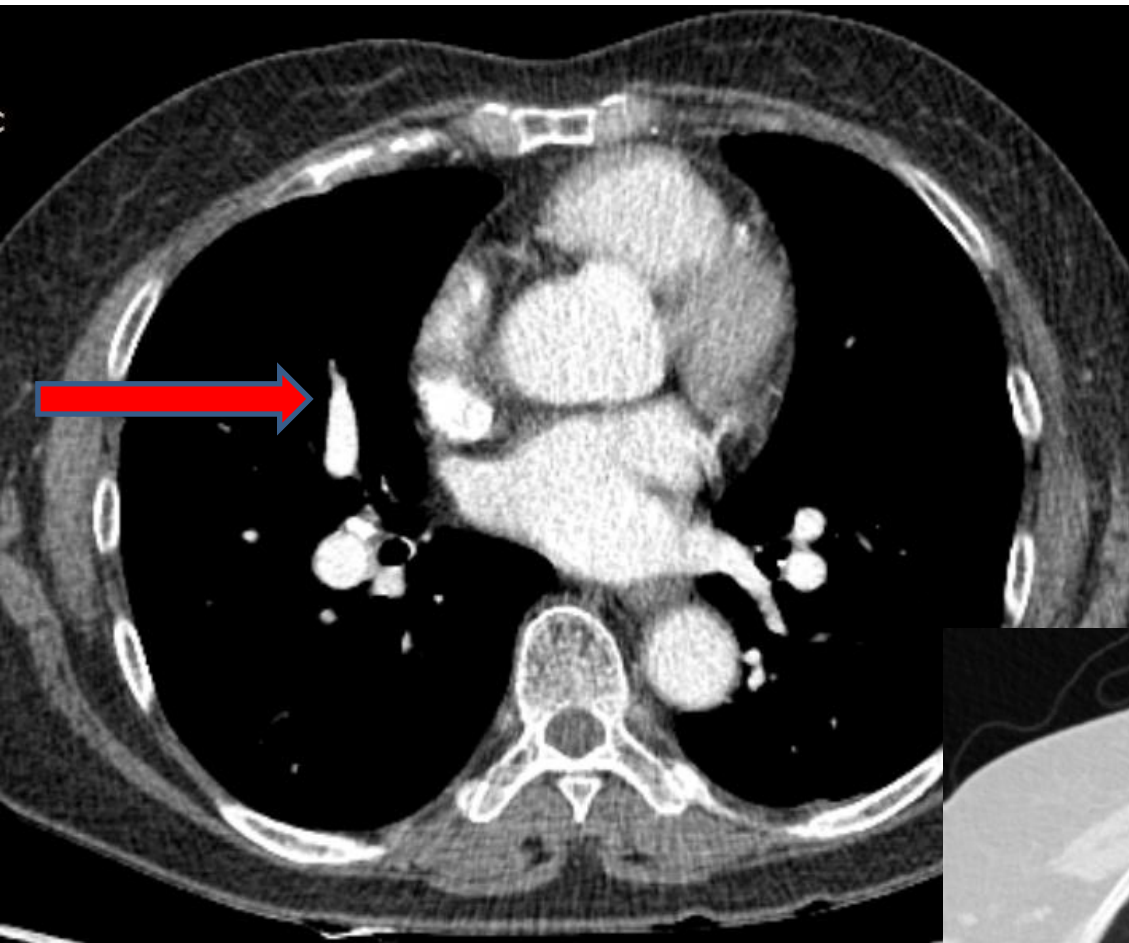


3-Yr Follow-up CT

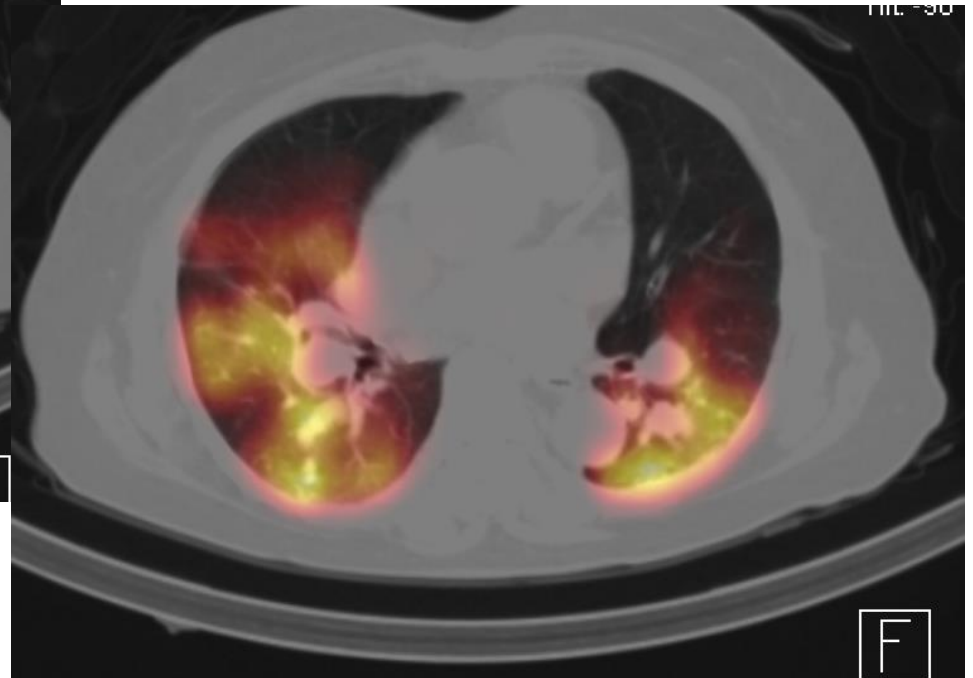
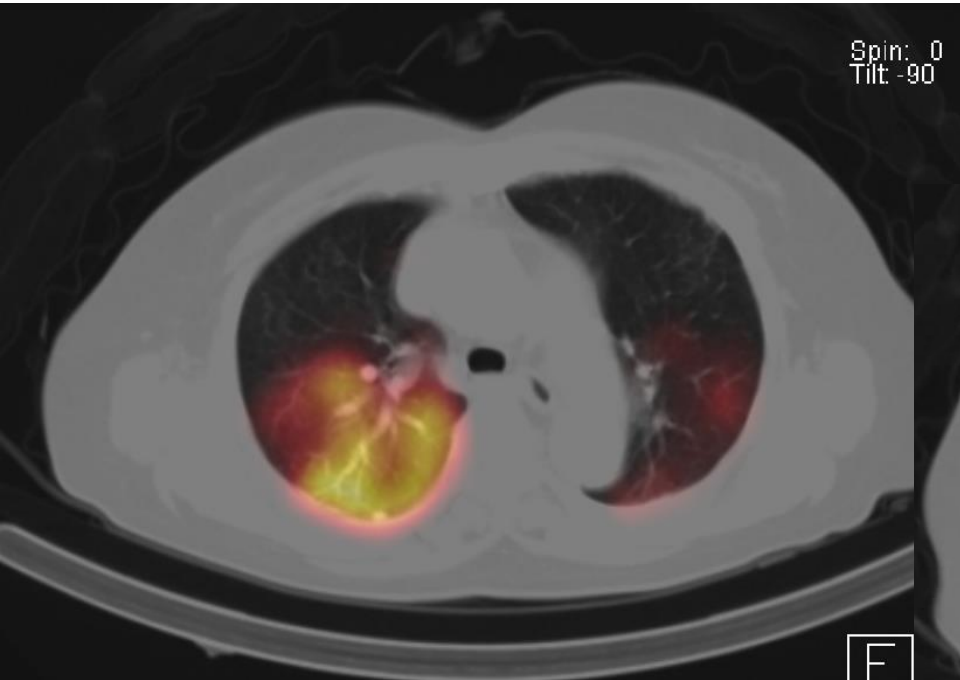


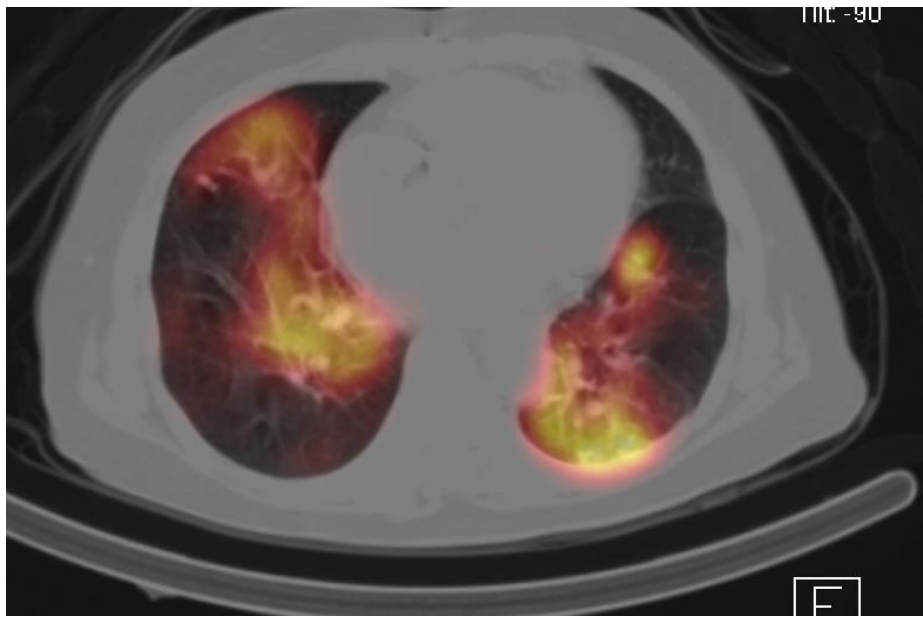
5 years follow up



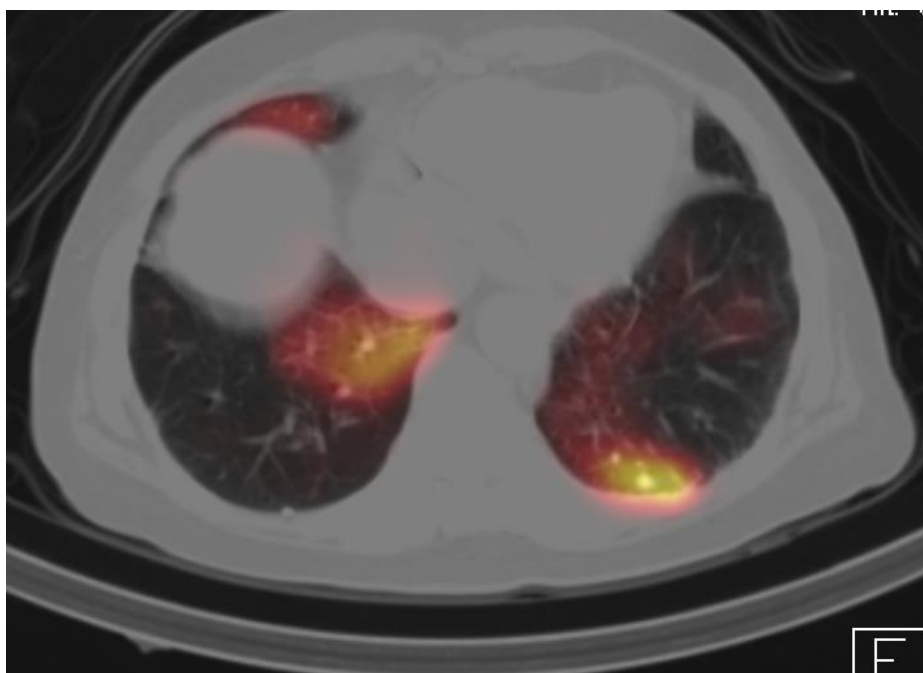


Lung perfusion scan SPECT



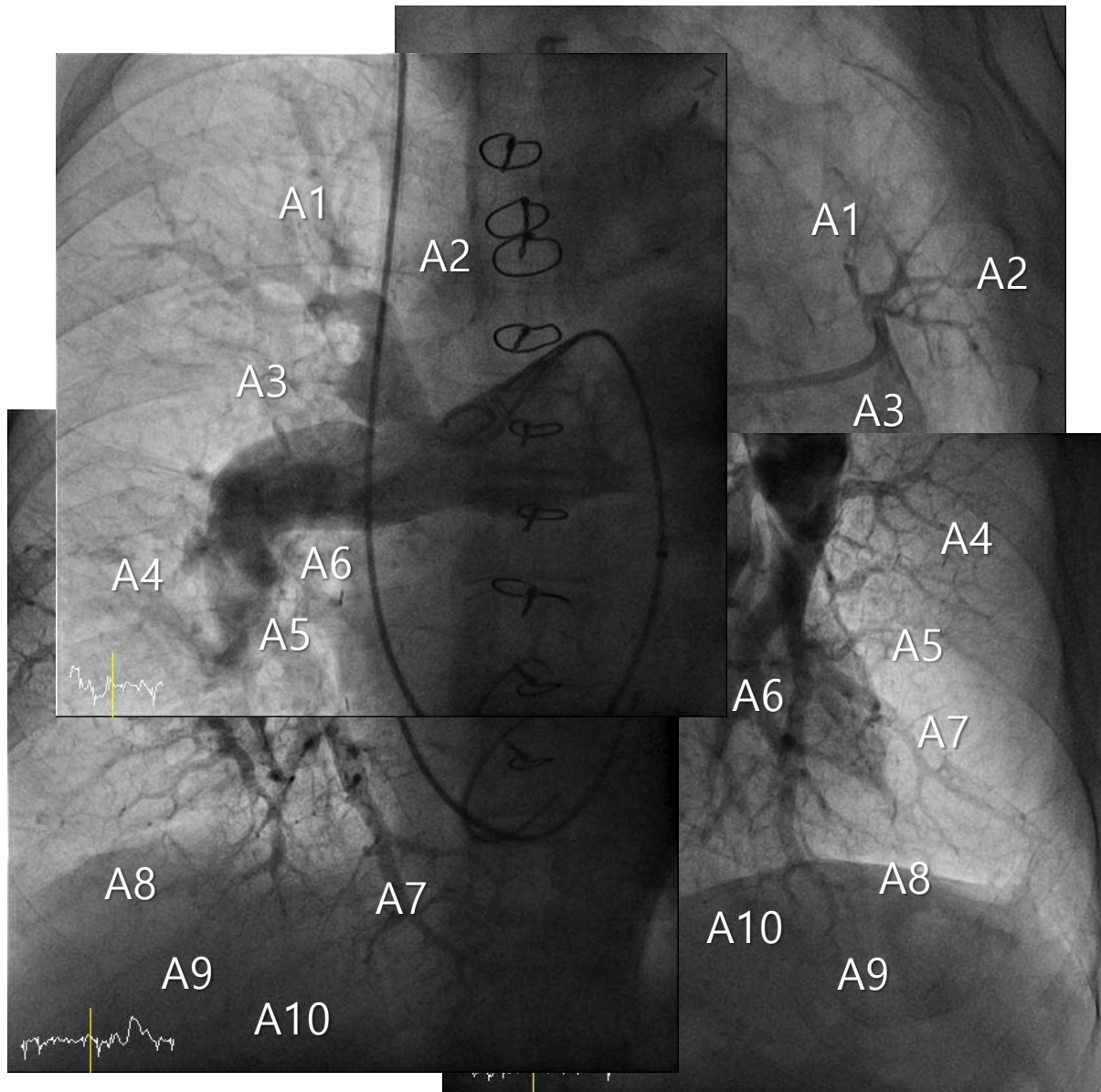


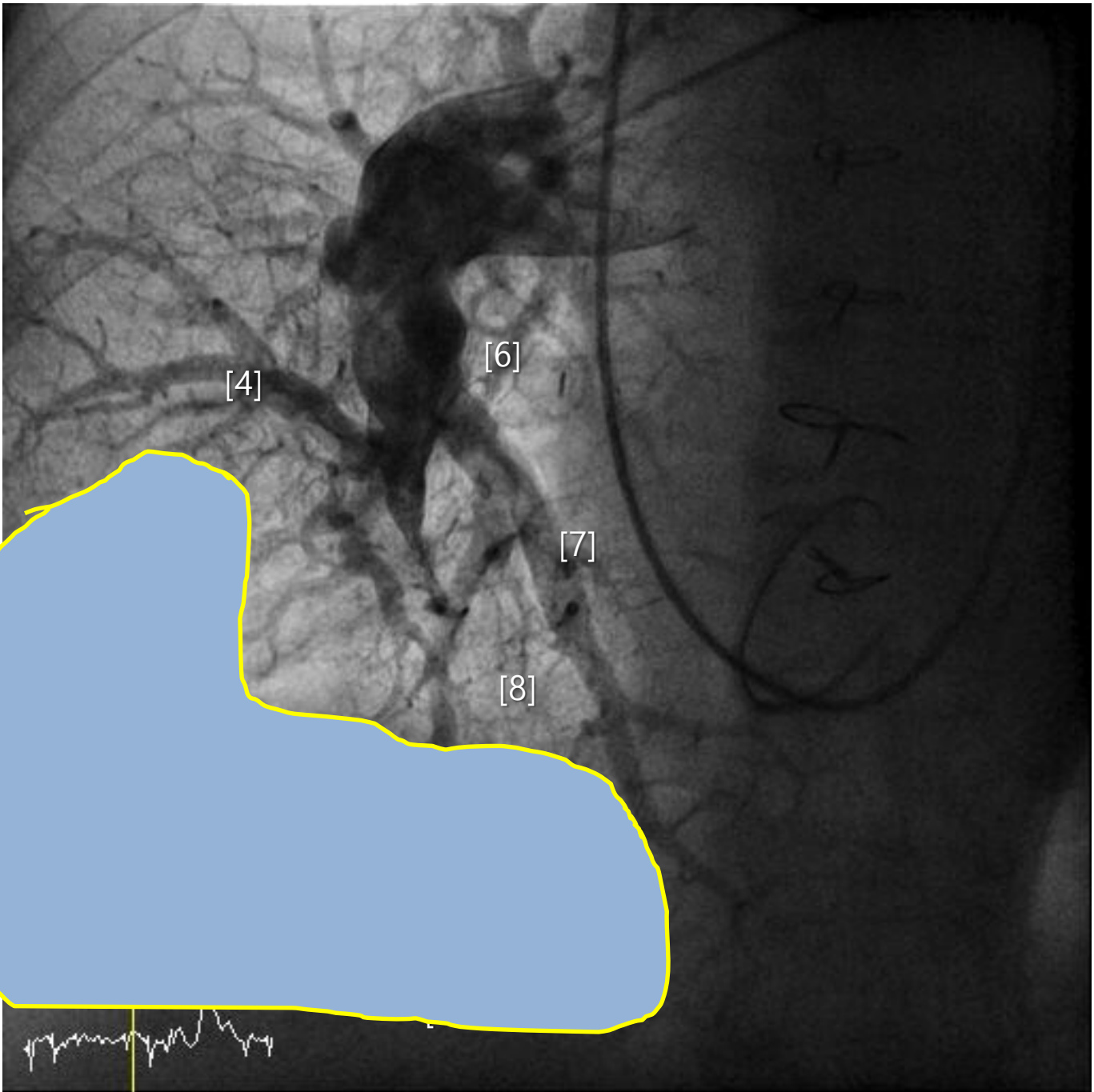
ANT



POST

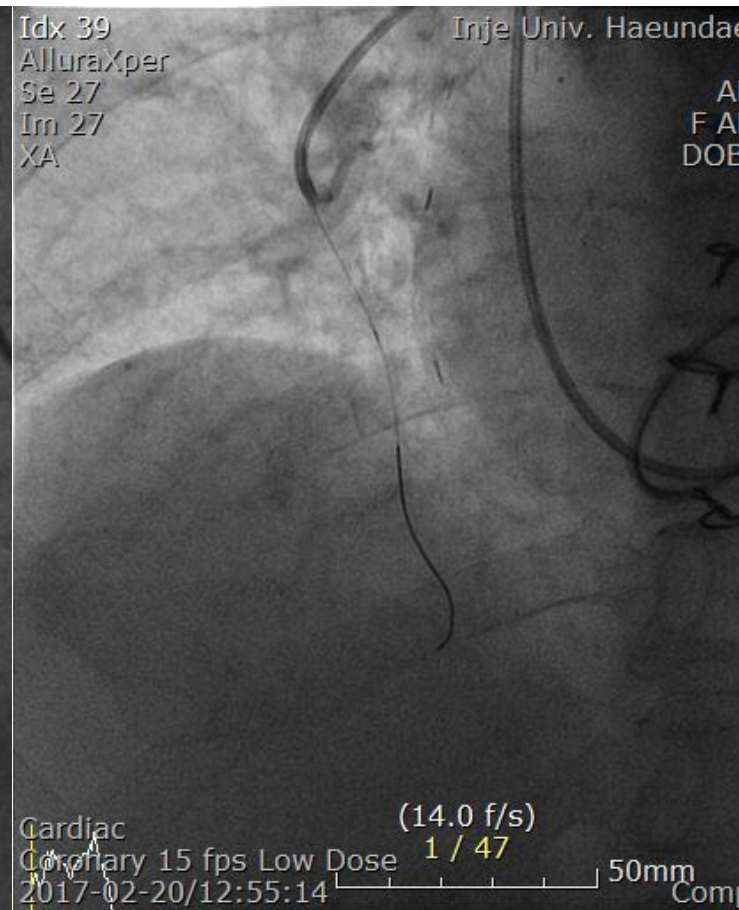
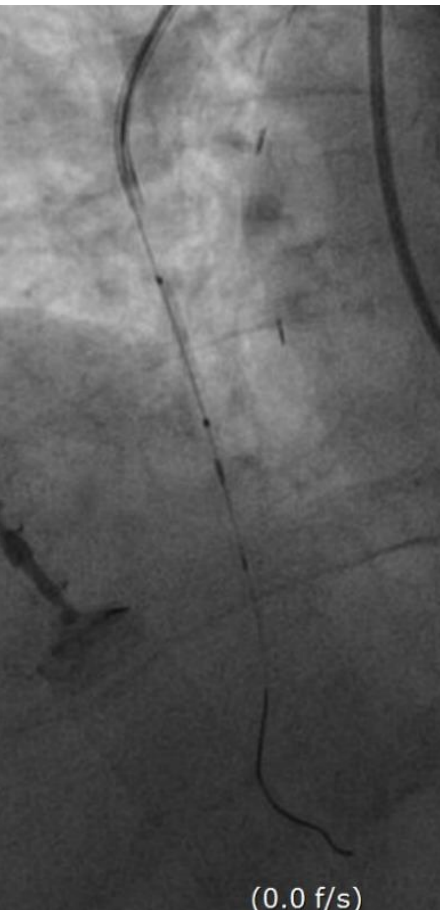
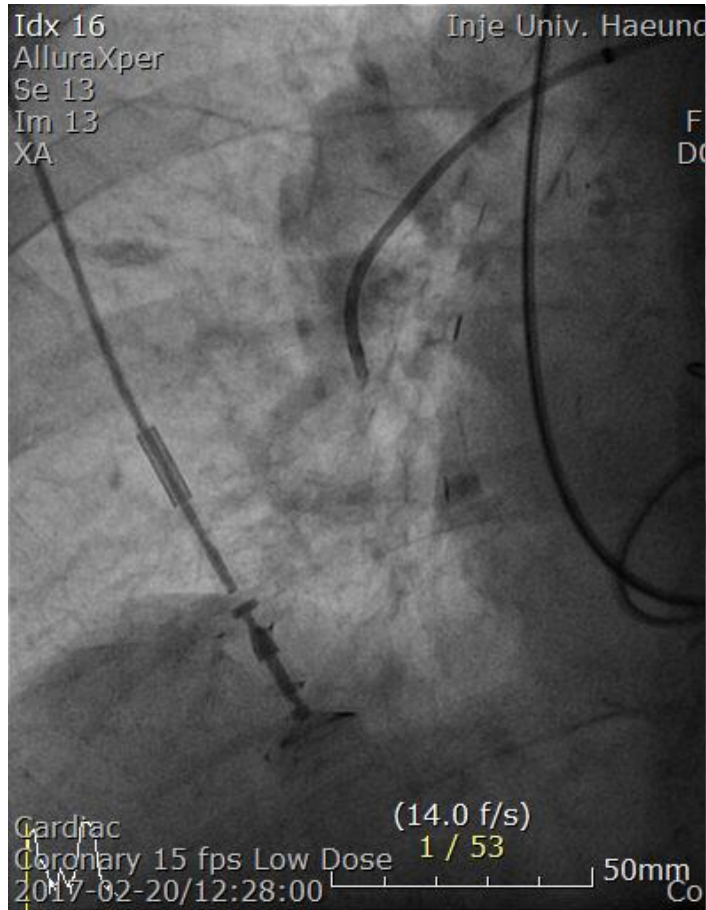
Selective pulmonary angiography



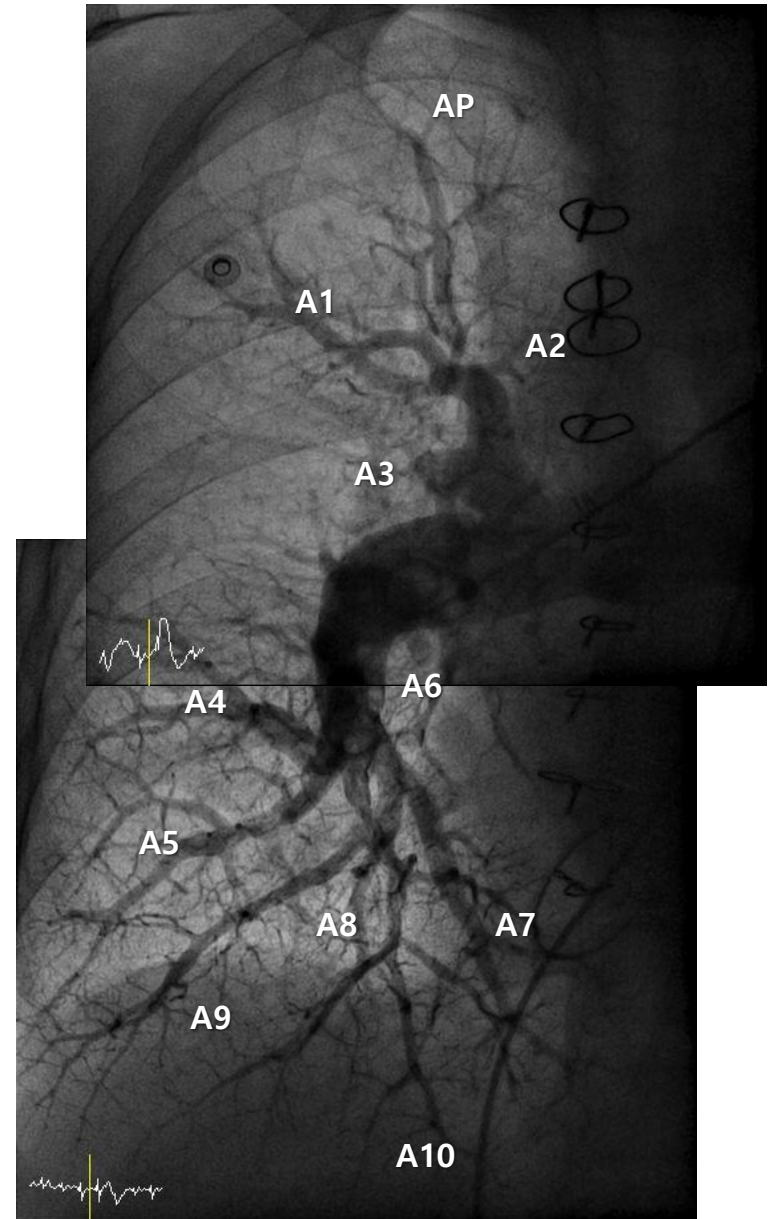


Balloon Pulmonary Angioplasty (BPA)

Rt. A10



Before and After



Clinical Improvement After 3 sessions of **Balloon pulmonary angioplasty (BPA)**

- Improvement of Resting SPO₂
 - Sitting: 94~95% (← 89~90%)
 - Supine: 91~92% (← 79~83%)
- Improvement of functional class: II (← III)

6MWT

Number of laps 4 (X 60 meters) + Final partial lap 37,8 (meters)
= Total distance walked in 6 minutes 277,8 (meters)

Comment	Time	SPO2	HR
	30"	92	87
	1'	88	90
	1' 30"	87	92
	2'	83	94
	2'30"	81	95
	3'	80	96
	3' 30"	80	97
	4'	80	97
	4' 30"	79	98
	5'	79	98
	5' 30"	79	99
	6'	79	99

Number of laps 5 (X 60 meters) + Final partial lap 53,4 (meters)
= Total distance walked in 6 minutes 353,4 (meters)

Comment	Time	SPO2	HR
	30"	96	92
	1'	96	92
	1' 30"	90	98
	2'	89	100
	2'30"	87	102
	3'	87	103
	3' 30"	87	104
	4'	87	105
	4' 30"	87	106
	5'	87	106
	5' 30"	87	107
	6'	86	108

Surgical treatment

Pulmonary endarterectomy – **curable**
proximal >> distal

Balloon pulmonary angioplasty – inoperable



Diagnosis of CTEPH

Proximal disease

Proximal vascular obstruction
No vasculopathy Vasculopathy



Cured by PEA



Residual PH
Up to 35%^{1,2}

Distal disease

Small vessel arteriopathy
Inaccessible to surgery



Inoperable

At least 40% of patients may be inoperable^{3,4}

1. Kim NH, Mayer E, Eur Respir Rev 2015; 24:173-7;
2. Freed D, et al. J Thorac Cardiovasc Surg 2011;141:383-7;
3. Delcroix M, et al. Circulation 2016; 133 (9):859-71;
4. Condliffe R, et al. Am J Resp Crit Care Med 2008; 177(10):1122-7

Improving results with BPA

Study	Year	Study location	Patients	Mean age (years)	Study duration (months)	Medical therapy before BPA	Effect in PVR	Lung injury	In-hospital mortality	Long-term outcomes
Feinstein et al.	2001	USA	18	51.8	36	0%	-23% TPR	61%	5.6%	89% at 34.2 months
Mizoguchi et al.	2012	Japan	68	62.2	26	100%	-65%	60%	1.5%	97% at 2.2 yrs
Kataoaka et al.	2012	Japan	29	62.3	6	100%	NR	53%	3.4%	NR
Andreasson et al.	2013	Norway	20	60	51	10%	-33%	35%	10%	85% at 51 months
Fukui et al.	2014	Japan	20	67	12	75%	-45%	0%	0%	NR
Roik et al.	2016	Poland	11	76	NR	54%	-48%	18%	0%	NR
Ogo et al.	2017	Japan	80	68	12	61%	-57%	17%	0%	NR
Ogawa et al.	2017	Japan	249	61.5	14	72%	-66%	35%	3%	94.5% at 2 years
Aoki et al.	2017	Japan	77	65	60	96%	-64%	23%	0%	98.4% at 5 years
Olsson et al.	2017	Germany	56	65	14	59% PDE5 inhibitor	-26%	9%	0%	NR
Average			628 (total)	63.3	25.7	72.5	-55%	29%	1.8%	

약물치료. 그나마 써 볼만한 약은?

Sildenafil

Riociguat

- The soluble guanylate cyclase stimulator
- Action in Nitric Oxide pathways

Macitentan

- Potent Endothelin receptor antagonist

하지만 급여가 문제
산정특례가 적용이 필요



감사합니다!

