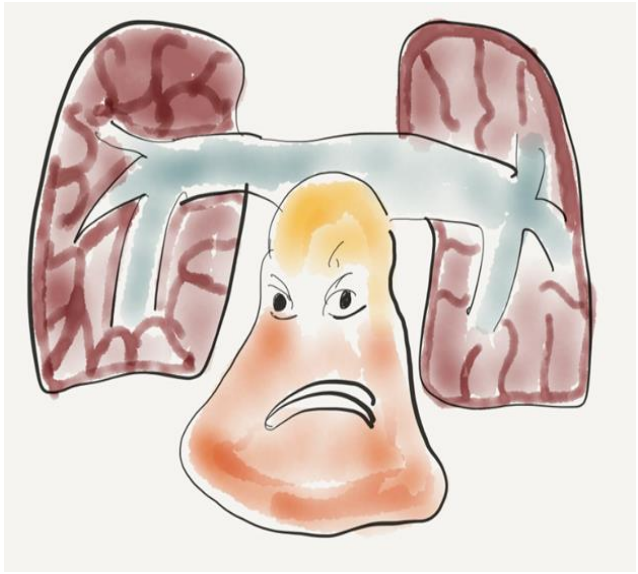
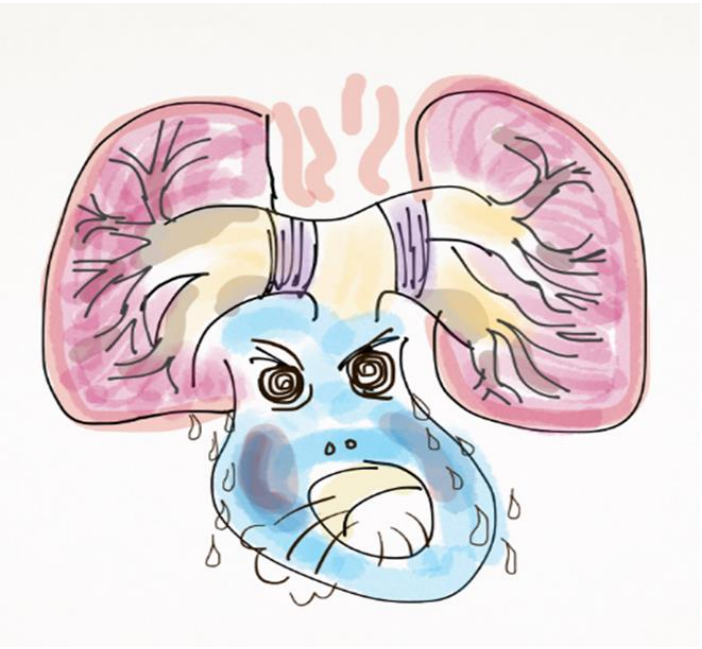
# 호흡기 영역에서 알아두면 도움되는

# 폐고혈압



인제의대 해운대백병원
장항제



# Definition of Pulmonary Hypertension (PH)

Too high blood pressure **in 'Lung'**
**in Rt. Side of heart**

**mean PA pressure at rest > 25 mmHg →** **≥20 mmHg**

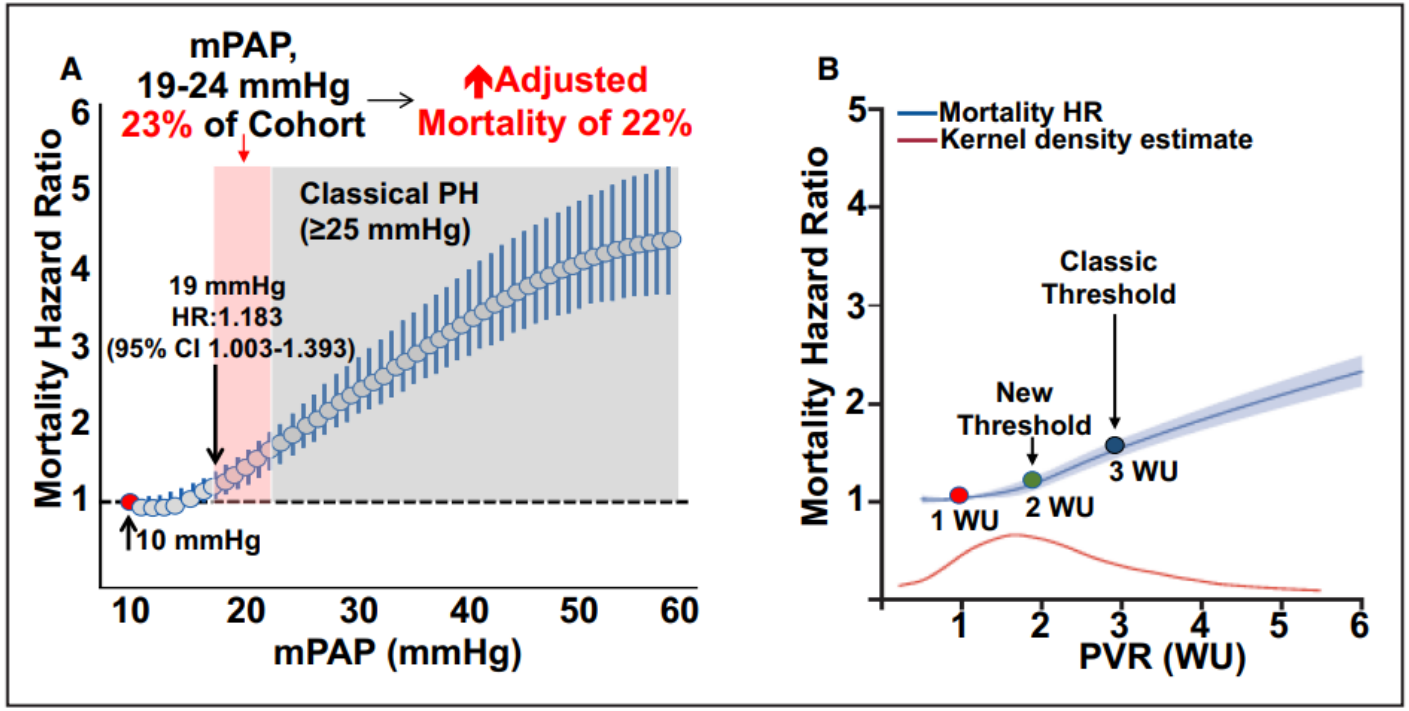
from 2018 the 6th World Symposium on Pulmonary Hypertension

**진단의 기준**
**치료의 기준?**

**Normal mean PAP = 14±3 mmHg**, Upper limit of mean PAP = 20 mmHg

Relationship between

# PH hemodynamic parameters and all-cause mortality




Bradley A. Maron J Am Heart Assoc. 2023;12:e029024

**GROUP 3** PH associated with lung diseases and/or hypoxia

- 3.1 Obstructive lung disease or emphysema
- 3.2 Restrictive lung disease
- 3.3 Lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoventilation syndromes
- 3.5 Hypoxia without lung disease (e.g. high altitude)
- 3.6 Developmental lung disorders

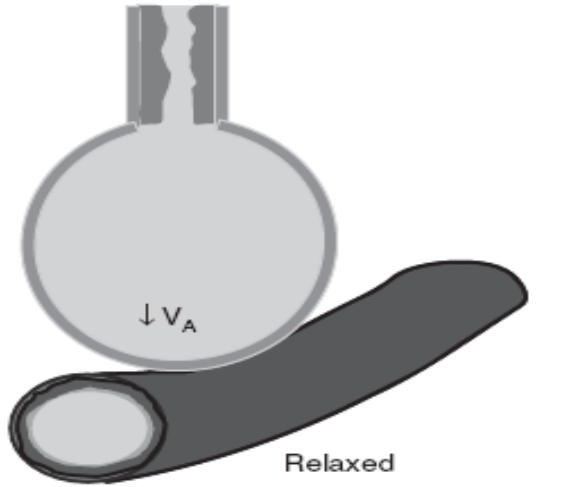
2022 ESC/ERS Guidelines

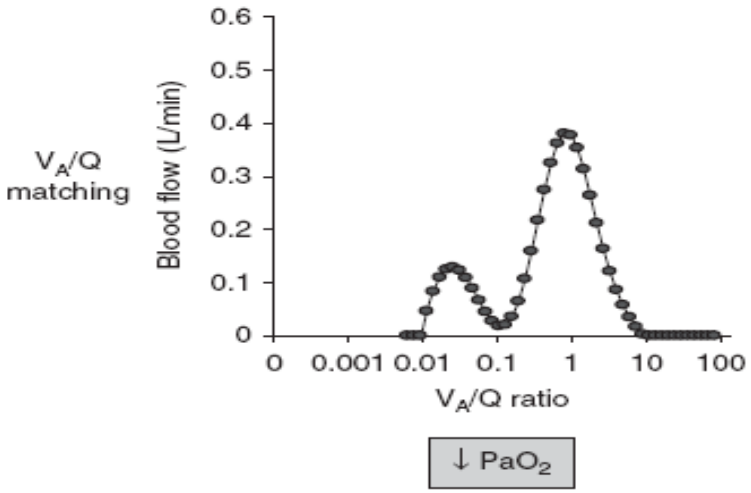
**3. PH associated with lung diseases and/or hypoxia**

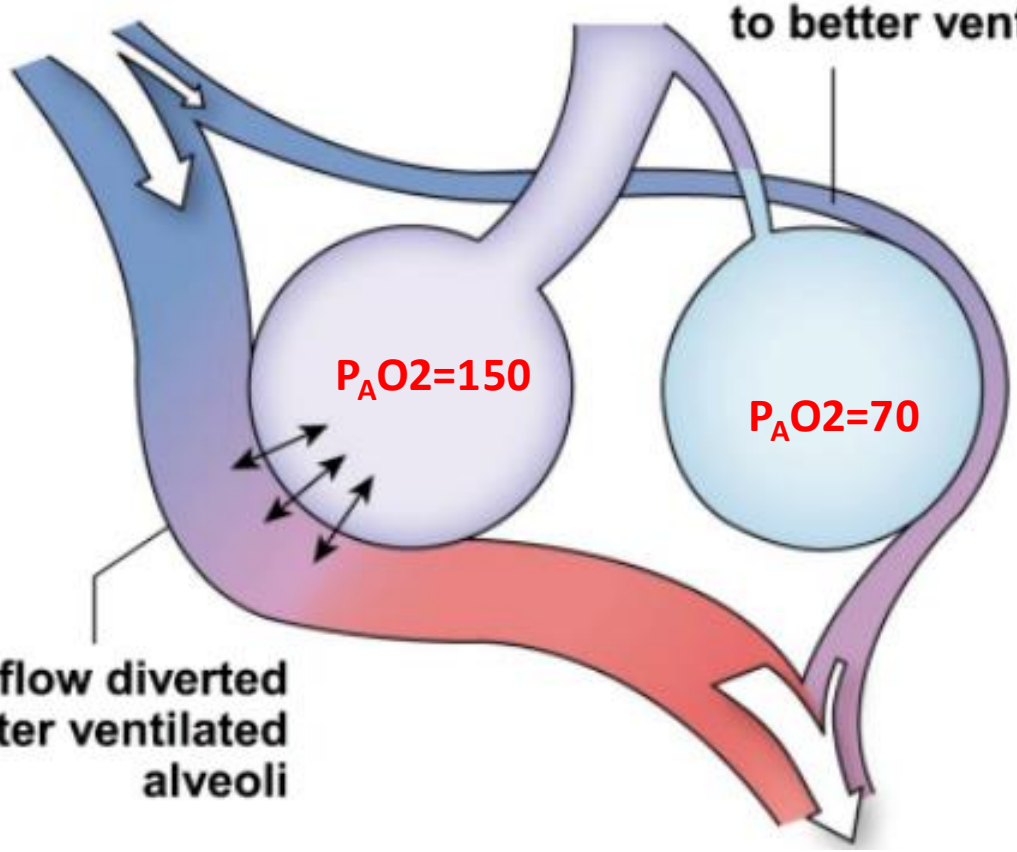
- 3.1 Chronic obstructive pulmonary disease and/or emphysema
- 3.2 Interstitial lung disease
- 3.3 Combined pulmonary fibrosis and emphysema
- 3.4 Other parenchymal lung diseases [b]
- 3.5 Non-parenchymal restrictive diseases
  - 3.5.1 Hypoventilation syndromes
  - 3.5.2 Pneumonectomy
  - 3.5.3 Musculoskeletal disorders
- 3.6 Hypoxia without lung disease (e.g. high altitude)
- 3.7 Developmental parenchymal disorders

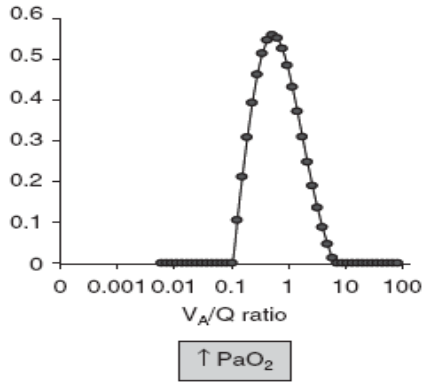
WSPH Taskforce 5, Barcelona, 2024

# **H**ypoxic **P**ulmonary **V**asoconstriction ( **HPV** )



# Pathophysiology of **PH-lung diseases**

- Acute

**Hypoxic pulmonary vasoconstriction**

Acute PTE
Air/Fat/amniotic embolism
ARDS
Severe pneumonia
Aspiration

- Sub-acute

PA pressure ↑ → **vascular remodeling**

→ **RV dilatation**

- **Chronic**

**→RV Hypertrophy**

**RV contractility ↓ → RV failure**

Chronic lung disease
: ILD
COPD
TBDL

# 폐고혈압을 유발하는 폐질환은? **급성 acute**

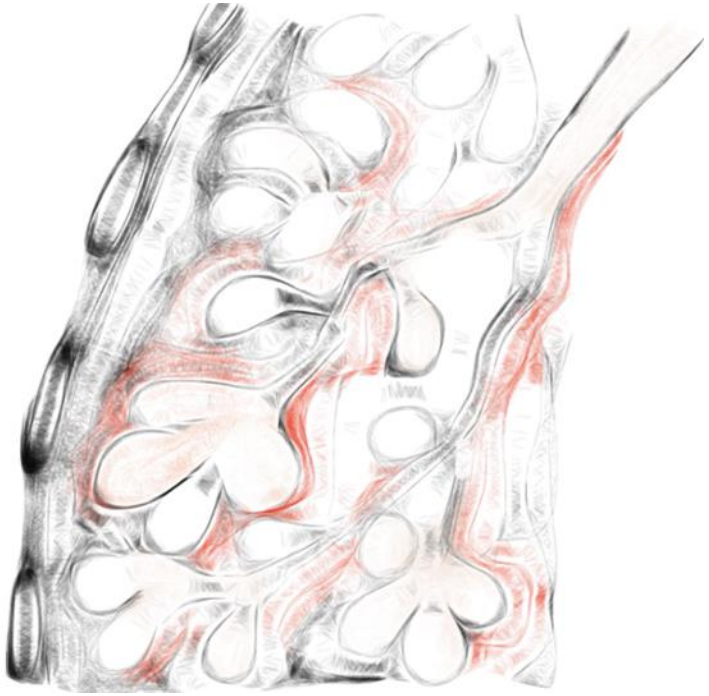
**Hypoxia**

- 고 위도 High alttitude : 고산 등정

- Acute respiratory distress syndrome (ARDS)
- pCO2 ↑, 인공환기압력 → 폐고혈압 악화요인

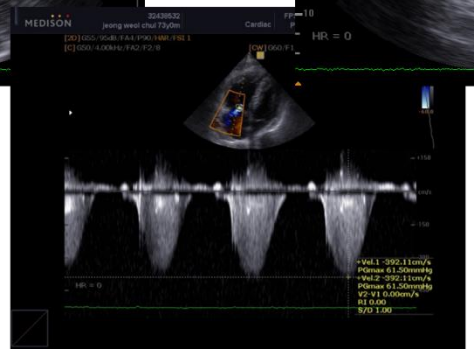
- Pulmonary embolism

Thrombus, amniotic, fat



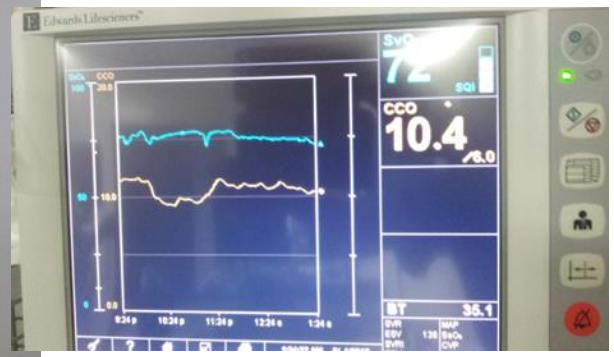
# Severe pneumonia ARDS with septic shock

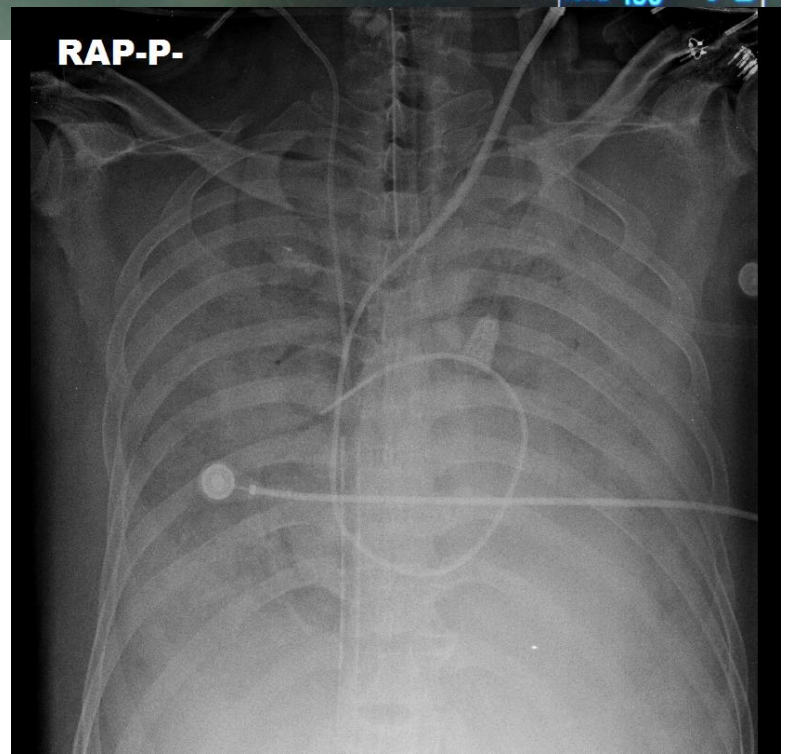
**Hypoxic pulmonary vasoconstriction**
**→ RV pressure overload**

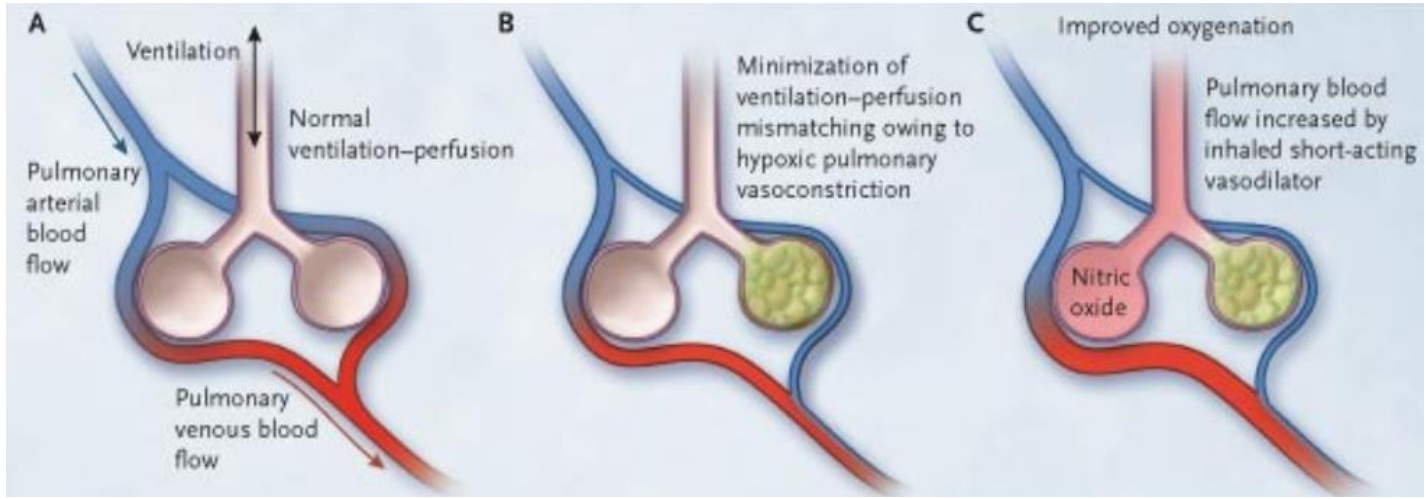


# Pulmonary hypertension – Nitric oxide gas, prostacycline inhalation



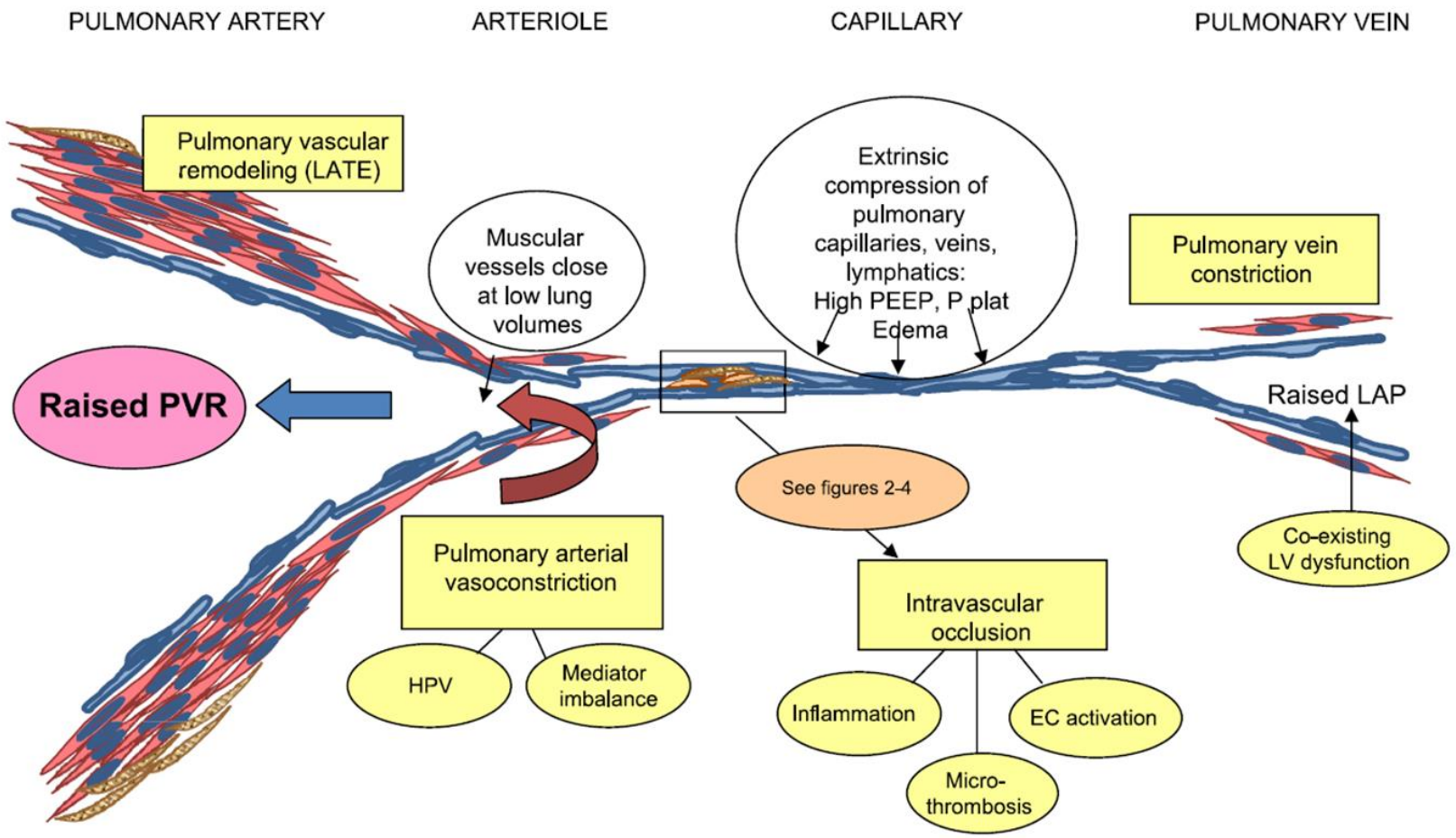



Mark J D Griffiths Timothy W Evans
N Engl J Med. 2005 Dec 22;353(25):2683-95

# Pathophysiology of PH in acute lung injury




Laura C. et al, Am J Physiol Lung Cell Mol Physiol 302: L803–L815, 2012.

# Pulmonary Hypertension in **acute pulmonary embolism**

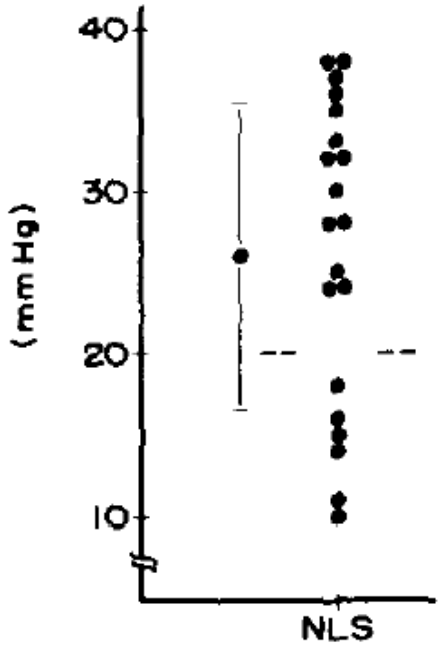

- Angiographic obstruction of PA **>50%** → PAP ↑

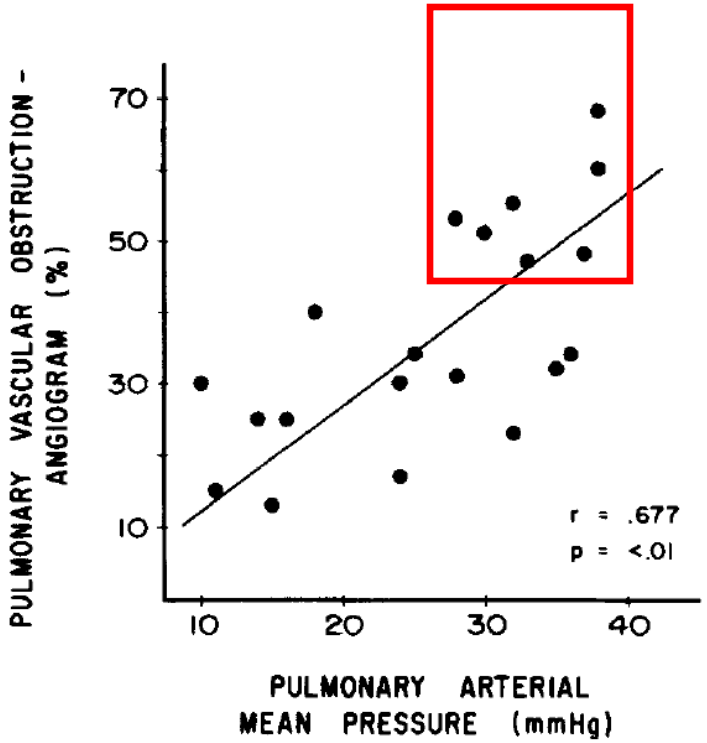
- **"Acute PE never resulted in mean PAP > 40 mm Hg in previously healthy patients"**

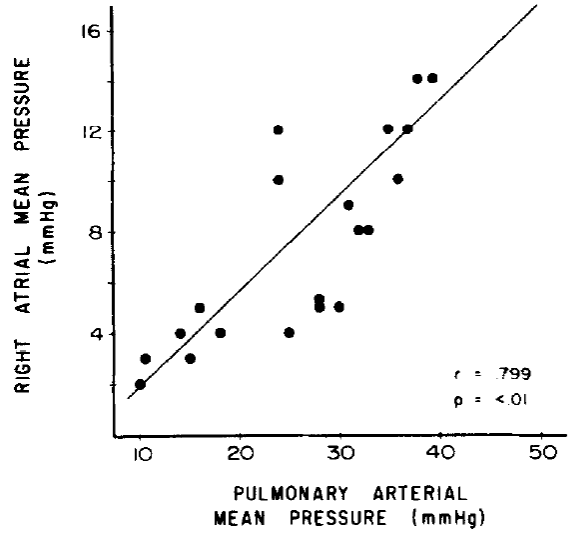
- maximum upper limit that a non-adapted right ventricle can generate when exposed to an acutely increased afterload.

# Hemodynamic response to pulmonary embolism

- Included 20 patients previously healthy



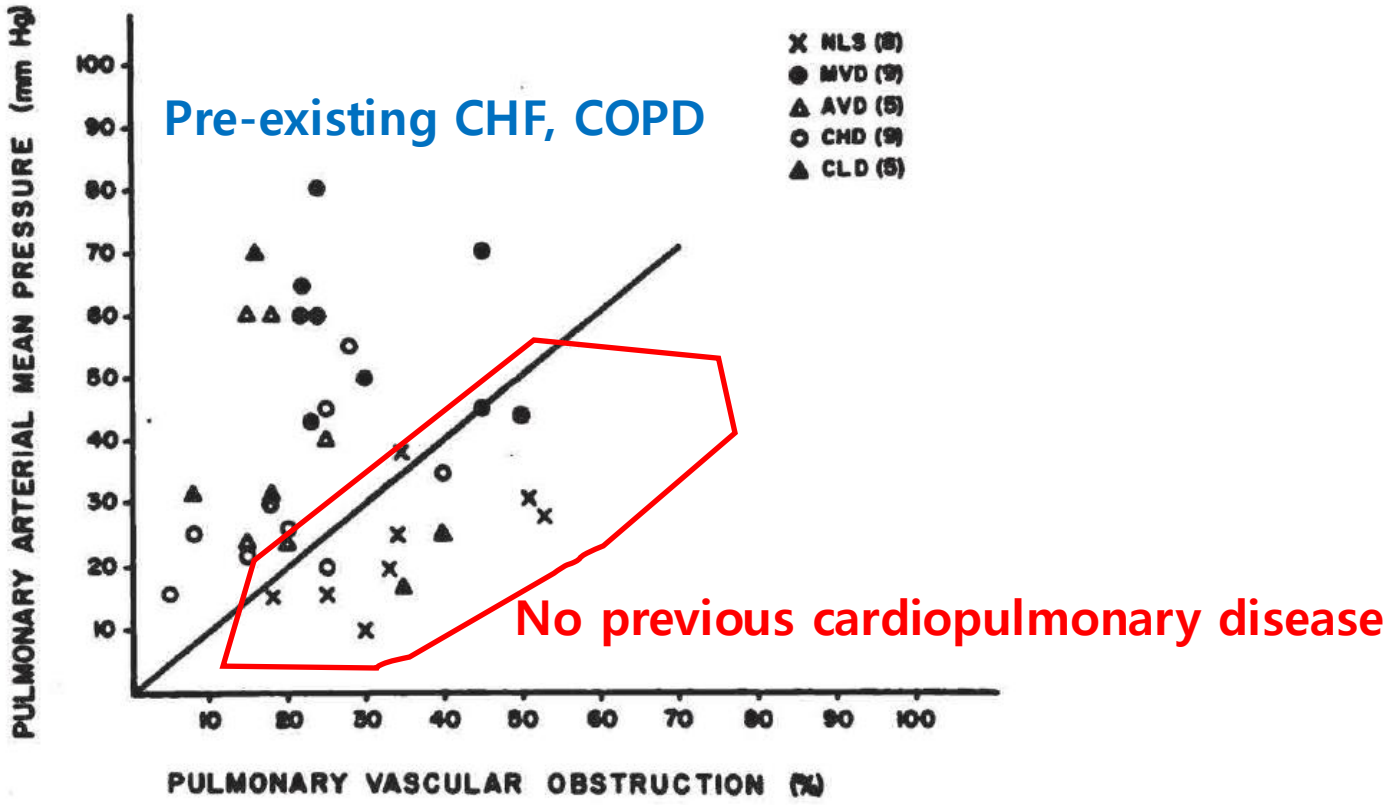




McIntyre KM. et al The hemodynamic response to pulmonary embolism in patients without prior cardiopulmonary disease. Am J Cardiol 1971;28:288–294

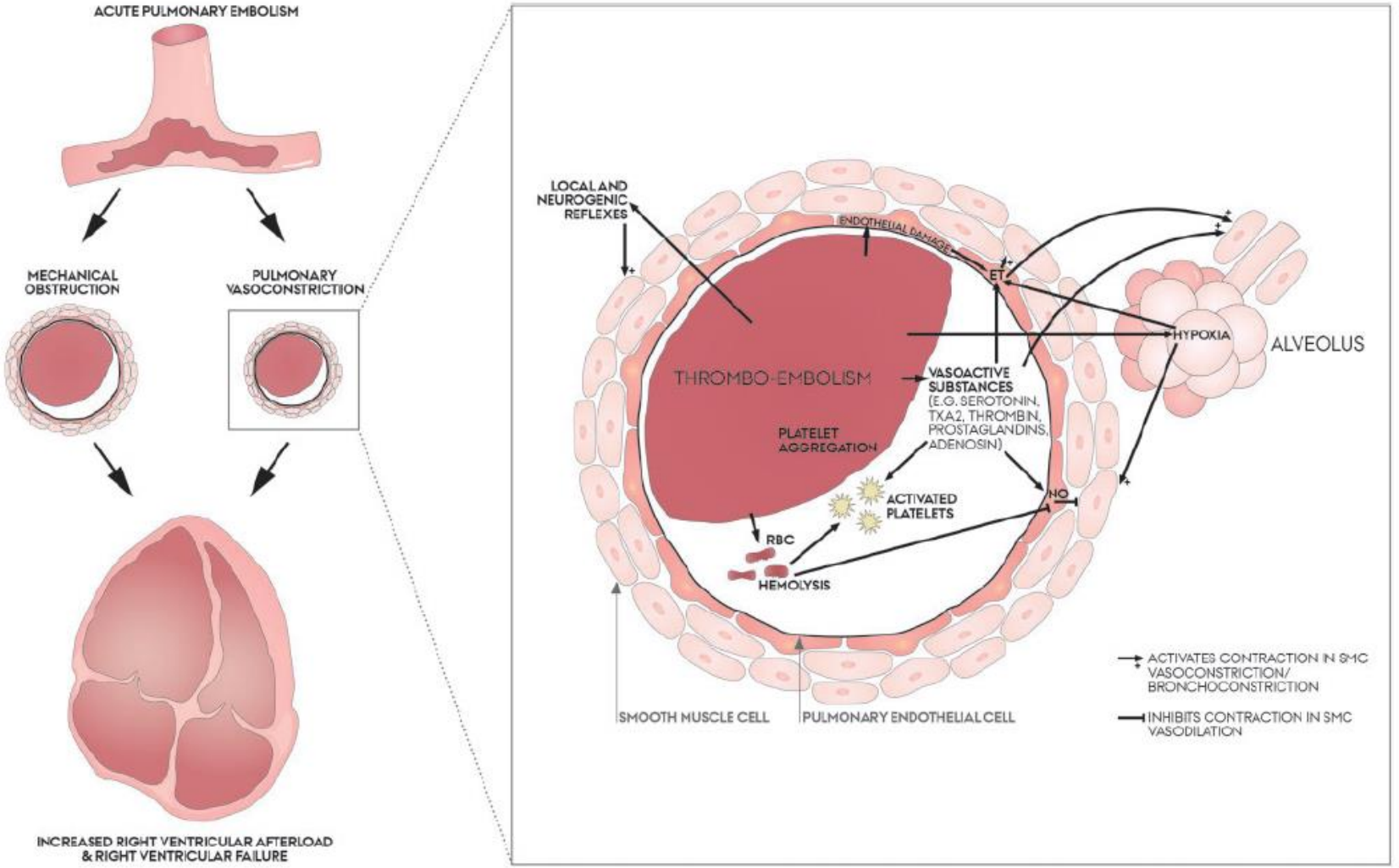
## The ratio of PAP to pulmonary vascular obstruction

: With or without previous cardio-pulmonary diseases




McINTYRE, SASAHARA, CHEST, 71: 6, JUNE, 1977

# Pulmonary Hypertension in **acute pulmonary embolism**




Lyhne et al, Pulmonary vasodilation in acute pulmonary embolismPulm Circ. 2020 Mar 4;10(1)

# **Pulmonary vasodilation** in acute pulmonary embolism systemic review

- **Inhaled Nitric oxide** → may improve the hemodynamic status

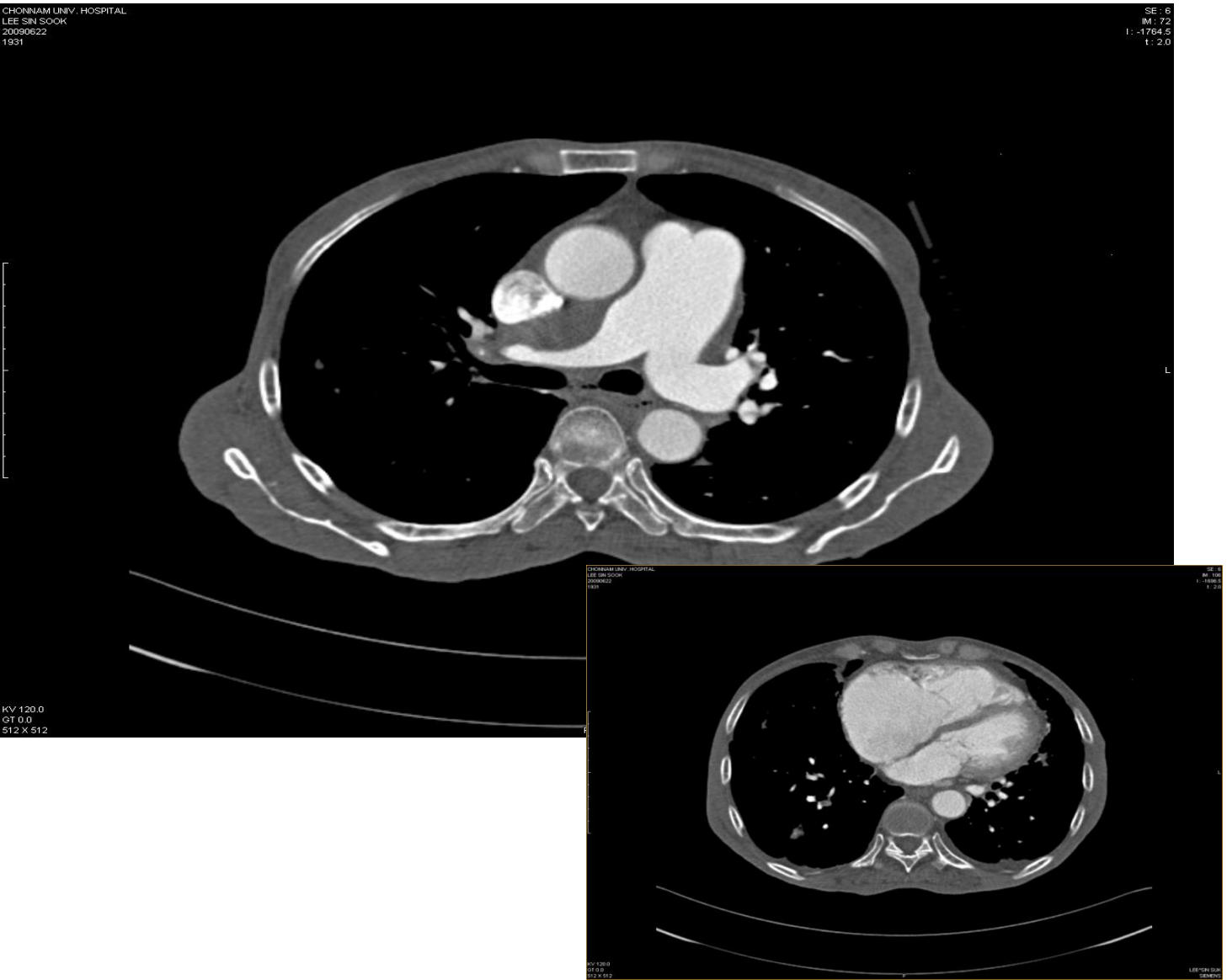
| Summary of Outcomes From Analyzed Patients | | | |
|---|---|---|---|
| **Improvement in MAP/CO** | **Improvement in PAP/PVR** | **Improvement in $PaO^2$/ $SpO^2$** | **Survival From ICU** |
| 14/14 who reported (100%) | 6/7 who reported (86%) | 16/18 who reported (89%) | 14/18 (78%) |

CO, cardiac output; ICU, intensive care unit; MAP, mean arterial pressure; $PaO^2$: partial pressure of oxygen; PAP, pulmonary arterial pressure; PVR, pulmonary vascular resistance; $SpO^2$: percutaneous oxygen saturation.

- PDE-5 inhibitors
- sCG stimulators/activators
- Prostacycline
- ERA

**No recommendation**

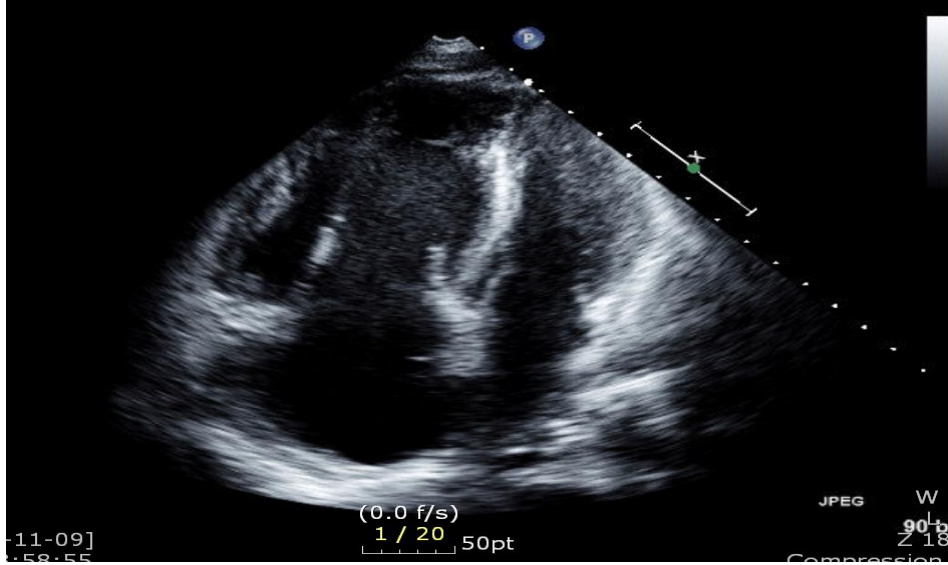
# ER resident asked about thrombolysis!




70/F
C.C : progressive exertional dyspnea
NYHA Fc III → IV
Chronic ill looking!
Worsening recently three months ago
Leg pitting edema ++
Distended Abdomen

V/S stable BP 125/80 HR 98/min

# Echocardiography




- D-shaped LV with normal LV systolic function
- Dilated RV dimension with RV dysfunction
- Thickened RV free wall
- Minimal pericardial effusion
- **Peak TR velocity 6.0 m/s**
- Pressure gradient  Sys(RV-RA)=**144 mmHg**

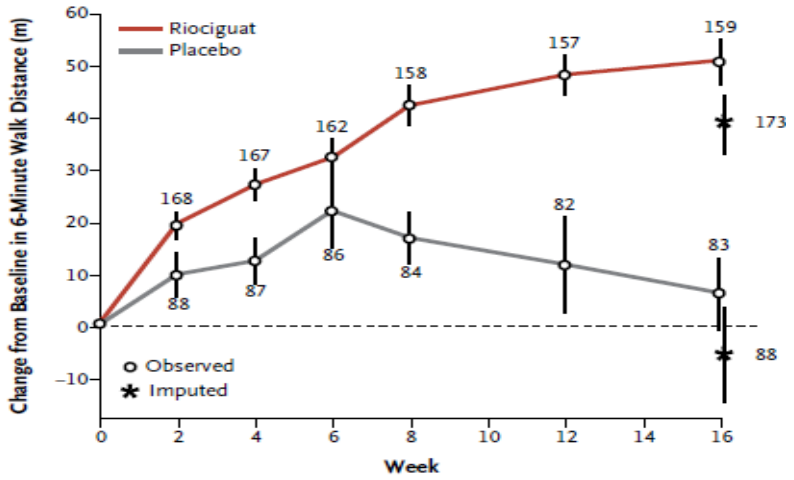
# Acute PE on chronic thromboembolic pulmonary hypertension (CTEPH)

# CTEPH Medical therapy – Riociguat

soluble guanylate cyclase stimulator로 세포 내 NO-cGMP 경로를 직접적으로 활성화시켜 작용함
Riociguat은 현재 가이드라인에서 CTEPH 환자에 Class I으로 권고되고 있는 유일한 약제

① 수술이 불가능하거나 수술 후 지속 또는 재발하는 만성 혈전색전성 폐고혈압 (CTEPH, WHO Group 4) 성인 환자에서 운동능력의 개선

② WHO 기능분류 II~III 단계에 해당하는 폐동맥고혈압(WHO Group Ⅰ) 성인 환자에서 운동능력의 개선.

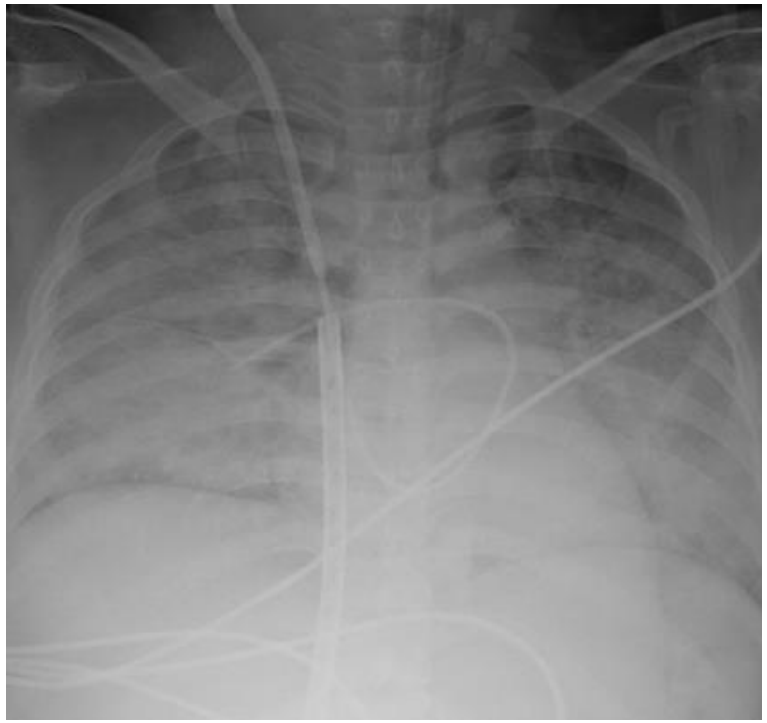


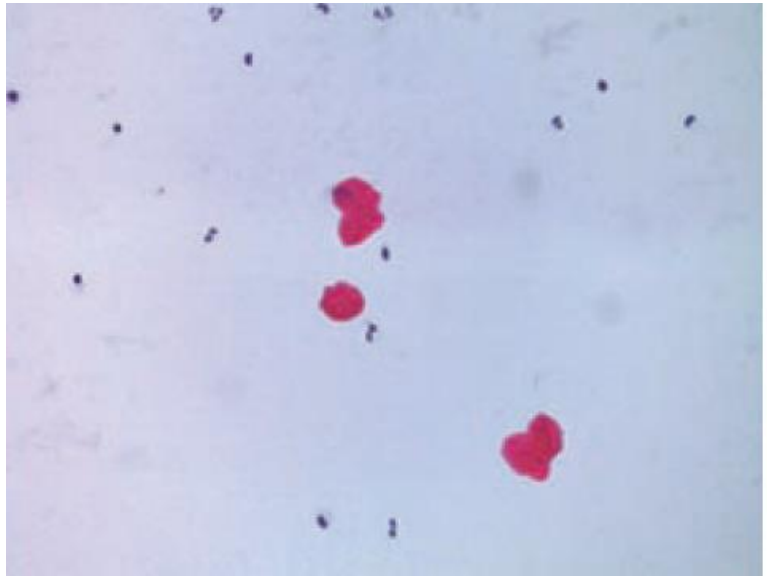

| Secondary endpoints | | |
|---|---|---|
| PVR(dyne.sec/cm⁵) | −246 (−303 to −190) | <0.001 |
| NT-proBNP(pg/ml) | −444 (−843 to −45) | <0.001 |
| Pulmonary-artery pressure (mm Hg) | −5 (−7 to −3) | <0.001 |

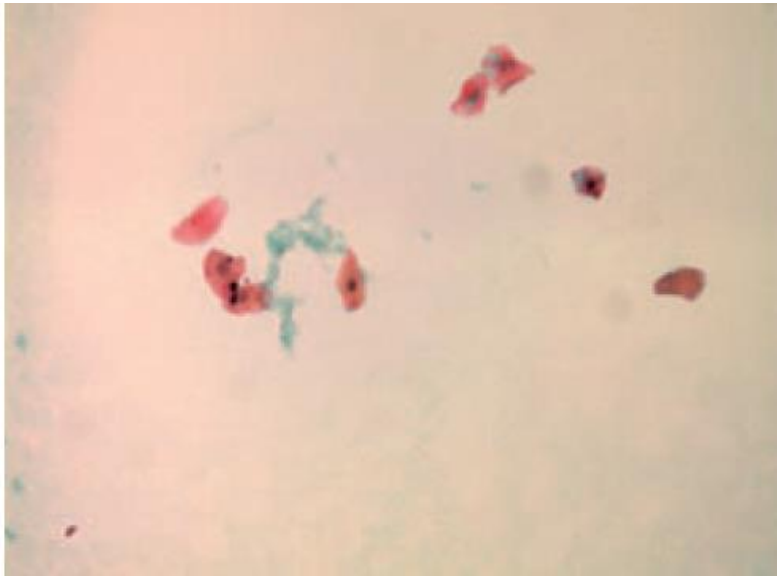
N Engl J Med, 2013

# Suspected **amniotic fluid embolism**

- Sudden cardiac arrest after delivery
  on V-A ECMO
  following ARDS
  stress induced cardiomyopathy
  DIC

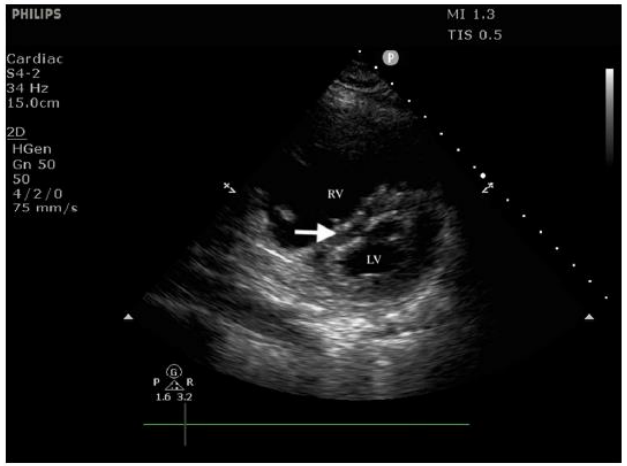


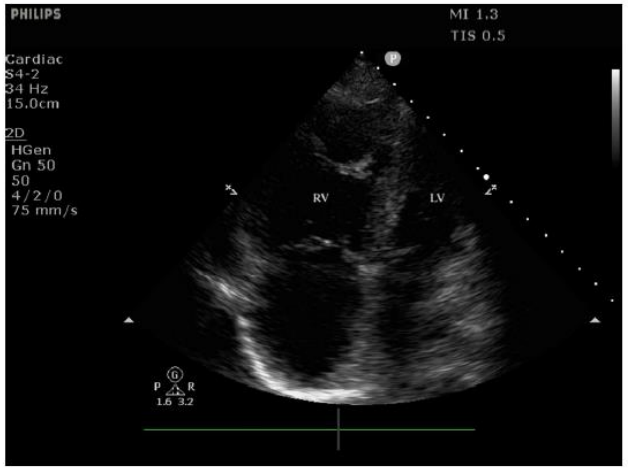




# Hemodynamic response - **amniotic fluid embolism**

- Biphasic,
- initial severe pulmonary hypertension and right ventricular failure,
- → followed by LV failure

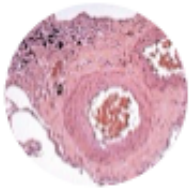
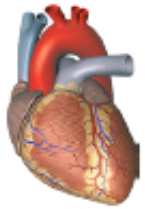


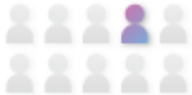
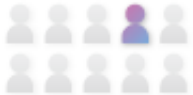
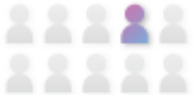
# Acute → Chronic

Pulmonary Hypertension

## Clinical Classification

| Pulmonary arterial hypertension (PAH) | PH associated with left heart disease | PH associated with lung disease | PH associated with pulmonary artery obstructions | PH with unclear and/or multifactorial mechanisms |
|---|---|---|---|---|
|  |  |  |  |  |
| • Idiopathic/heritable<br>• Associated conditions | • IpcPH<br>• CpcPH | • Non-severe PH<br>• Severe PH | • CTEPH<br>• Other pulmonary obstructions | • Haematologic disorders<br>• Systemic disorders |

## Prevalence

| Rare | Very common | Common | Rare | Rare |
|---|---|---|---|---|
|  |  |  |  |  |

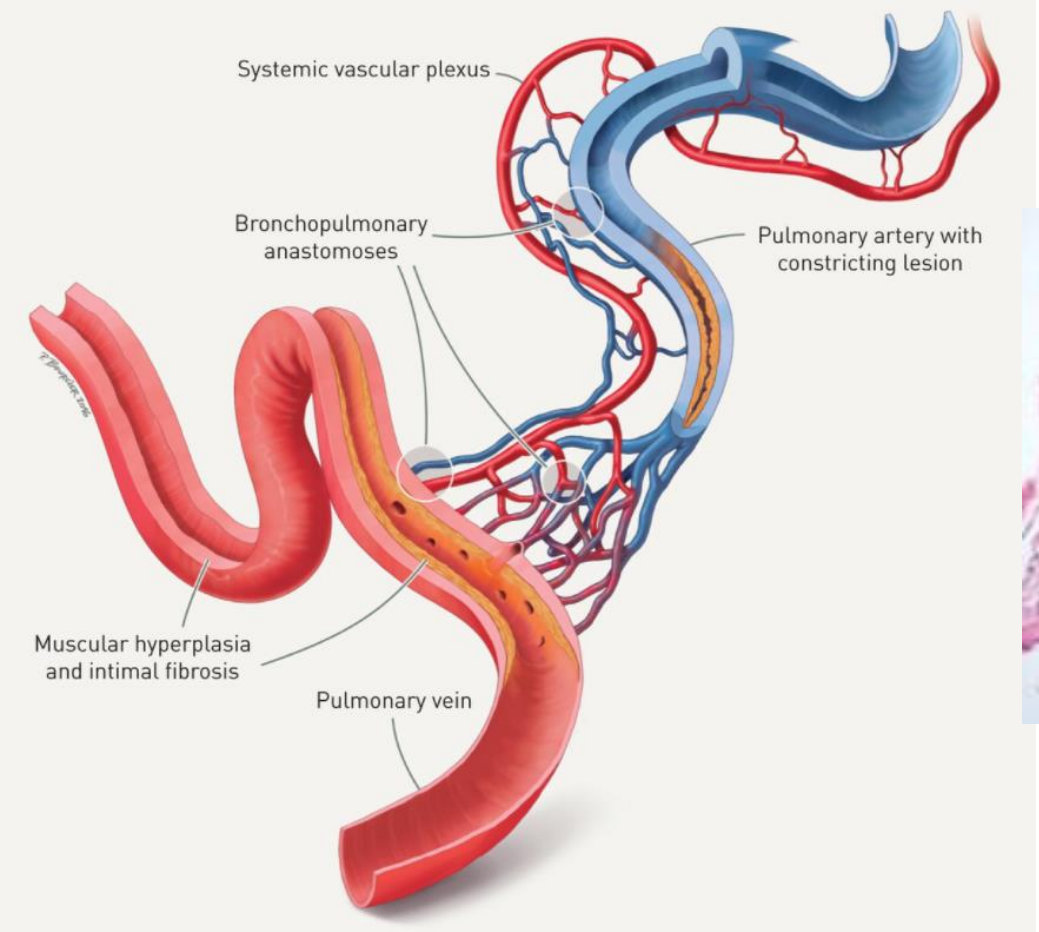
## Therapeutic Strategies

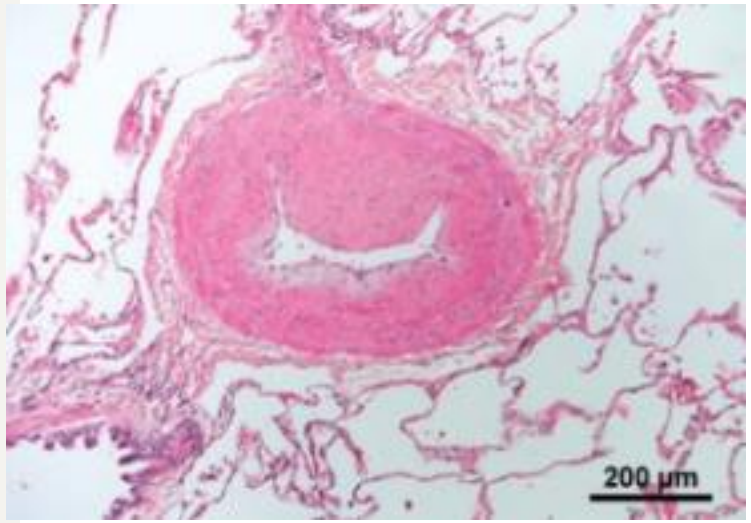
| | | | | |
|---|---|---|---|---|
| **Medical therapy**<br>• PAH drugs<br>• CCB in responders<br>**Lung transplantation** | **IpcPH:**<br>• Treatment of LHD[a]<br>**CpcPH:**<br>• Treatment of LHD[a]<br>• Potentially: PAH drugs (trials) | **PH-lung disease:**<br>• Optimized care of underlying lung disease<br>**Severe PH:**<br>• Potentially: PAH drugs (trials) | **Surgical therapy:**<br>• PEA<br>**Interventional:**<br>• BPA<br>**Medical therapy:**<br>• PH drugs | **Optimized treatment of underlying disease**<br>• Potentially: PAH drugs (trials) |

ESC ERS

# Pulmonary arterial hypertension (PAH)

: pure vascular lesion 에 의한 PH ?



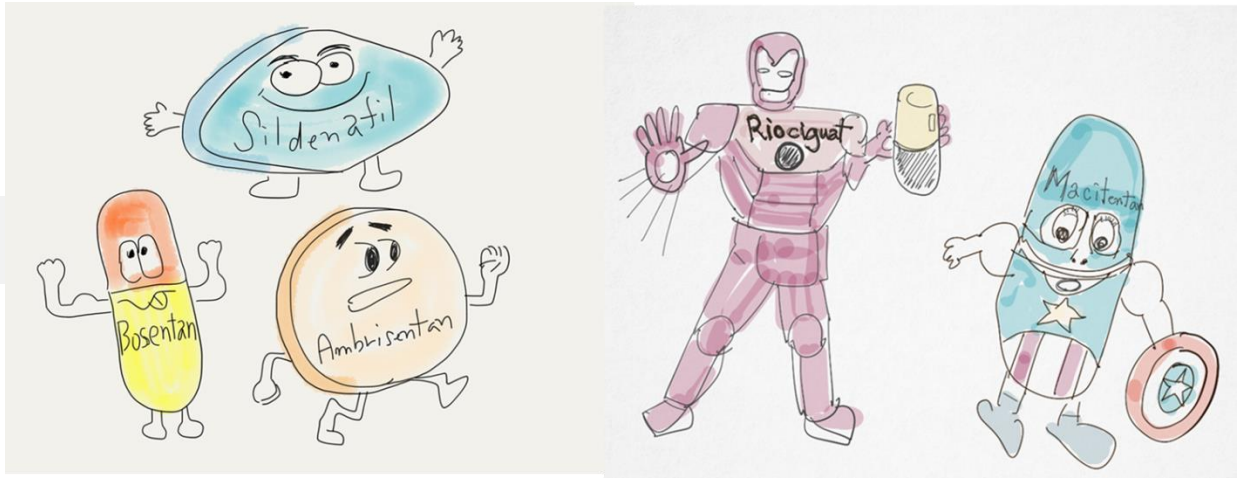

Pathology and pathobiology of pulmonary hypertension: state of the art and research perspectives
Marc Humbert et al, European Respiratory Journal 2019 53

# Pulmonary **Arterial** Hypertension

"**폐 동맥**이 직접 이환되어 좁아지는 질환"
"**PAH specific drugs** 치료 대상"

**Group 1 >**

1 PAH
1.1 Idiopathic PAH
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH (table 3)
1.4 PAH associated with:
  1.4.1 Connective tissue disease
  1.4.2 HIV infection
  1.4.3 Portal hypertension
  1.4.4 Congenital heart disease
  1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome



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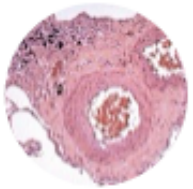
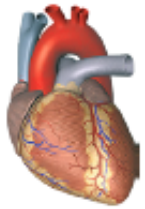
|  |  |  |  |  |
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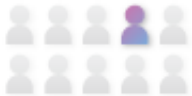
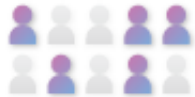
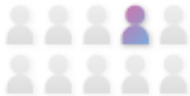
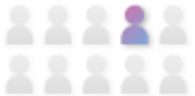
| Rare | Very common | Common | Rare | Rare |
|---|---|---|---|---|
|  |  |  |  |  |

## Therapeutic Strategies

| | | | | |
|---|---|---|---|---|
| **Medical therapy**<br>• PAH drugs<br>• CCB in responders<br>**Lung transplantation** | **IpcPH:**<br>• Treatment of LHD[a]<br>**CpcPH:**<br>• Treatment of LHD[a]<br>• Potentially: PAH drugs (trials) | **PH-lung disease:**<br>• Optimized care of underlying lung disease<br>**Severe PH:**<br>• Potentially: PAH drugs (trials) | **Surgical therapy:**<br>• PEA<br>**Interventional:**<br>• BPA<br>**Medical therapy:**<br>• PH drugs | **Optimized treatment of underlying disease**<br>• Potentially: PAH drugs (trials) |

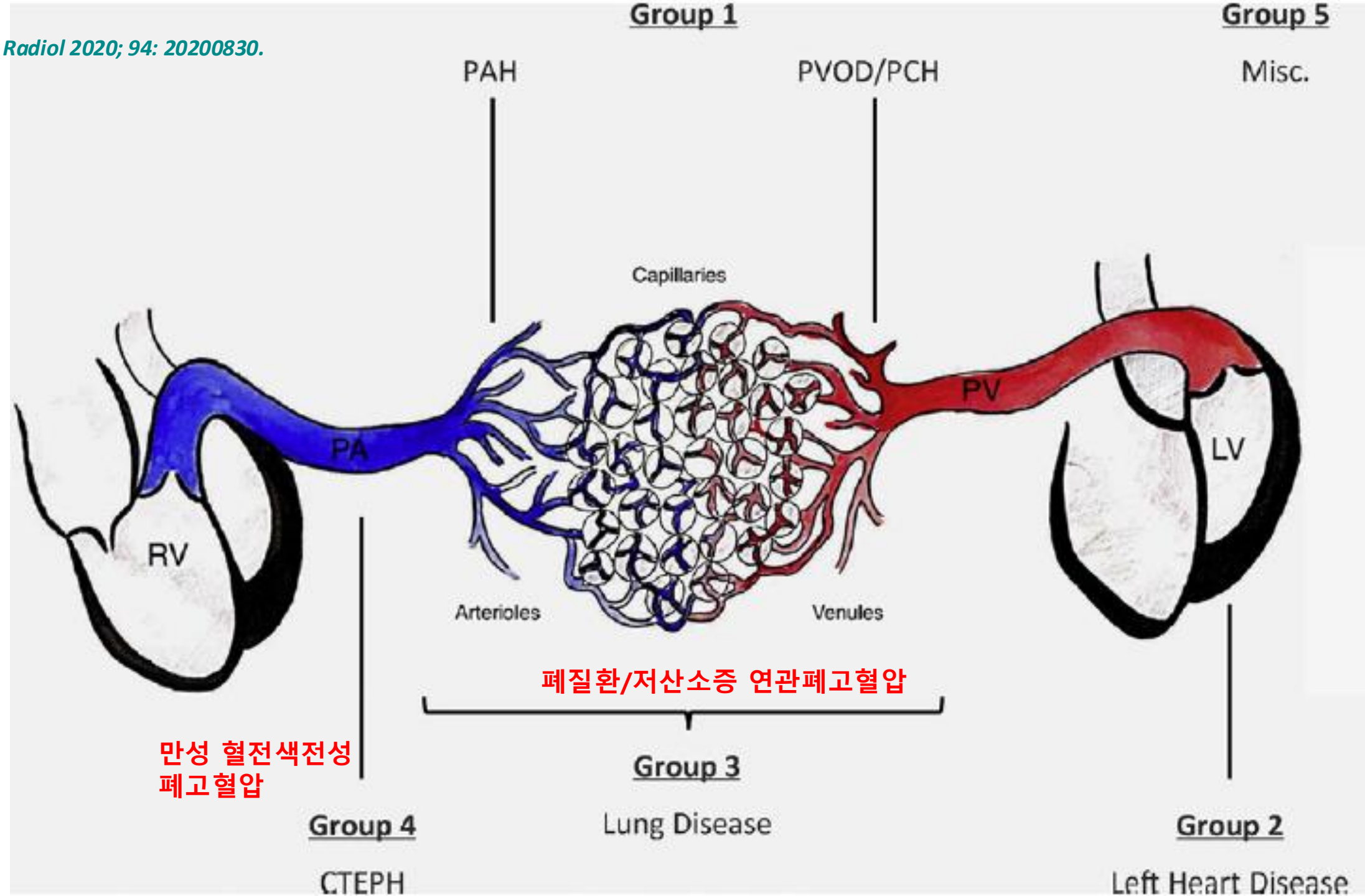
ESC ERS

# 2022 ESC/ERS recommendations for PH-LD

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| In patients with lung disease and suspected PH, it is recommended to optimize treatment of the underlying lung disease and, where indicated, hypoxaemia, sleep-disordered breathing, and/or alveolar hypoventilation | I | C |
| Inhaled treprostinil may be considered in patients with PH associated with ILD [734] | IIb | B |
| The use of ambrisentan is not recommended in patients with PH associated with IPF [740] | III | B |
| The use of riociguat is not recommended in patients with PH associated with IIP [181] | III | B |
| The use of PAH medication is not recommended in patients with lung disease and non-severe PH[e] | III | C |

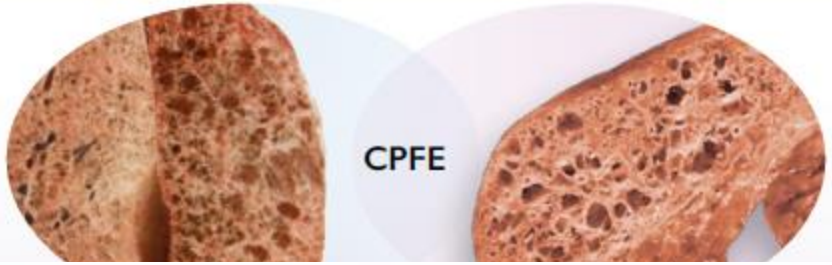
| Recommendations | GRADE | | Class[a] | Level[b] |
|---|---|---|---|---|
| | Quality of evidence | Strength of recommendation | | |
| PDE5is may be considered in patients with severe PH associated with ILD (individual decision-making in PH centres) | Very low | Conditional | IIb | C |
| The use of PDE5is in patients with ILD and non-severe PH is not recommended | Very low | Conditional | III | C |

*Br J Radiol 2020; 94: 20200830.*



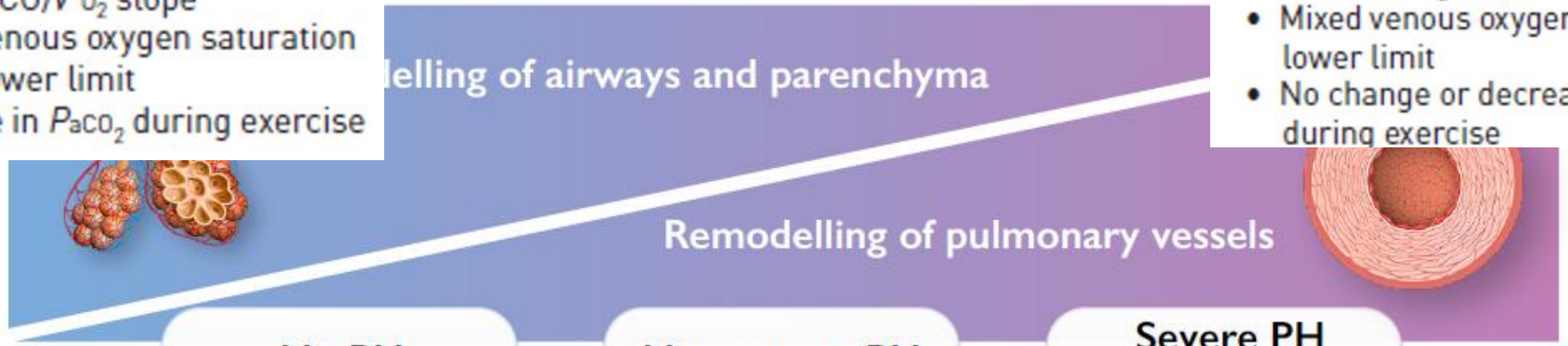
Features of exhausted ventilatory reserve:

- Reduced breathing reserve
- Normal oxygen pulse
- Normal $CO/\dot{V}O_2$ slope
- Mixed venous oxygen saturation above lower limit
- Increase in $P_{aCO_2}$ during exercise




Features of exhausted circulatory reserve:

- Preserved breathing reserve
- Reduced oxygen pulse
- Low $CO/\dot{V}O_2$ slope
- Mixed venous oxygen saturation at lower limit
- No change or decrease in $P_{aCO_2}$ during exercise




| | No PH | Non-severe PH | Severe PH (PVR >5 WU) |
|---|---|---|---|
| Prevalence | ~70% | ~20% | ~5–10% |

Mostly ventilatory exercise limitation

Mostly circulatory exercise limitation

Hypoxaemia at rest and/or during exercise

exercise limitation
exercise limitation
Hypoxaemia at rest and/or during exercise

ESC ERS

# Adjustments in cardiorespiratory function
# After **pneumonectomy**

- 88 patients had measurable TR by echocardiography,
  Mean systolicPAP = 36.9±9mmHg ( RA pressure=5mmHg 로 가정)
- PH was present in 32/88 patients (36%)

25 patients → Mild : systolic PAP 36-50mmHg

7 patients → Moderate : systolic PAP 50–60mmHg

Jean Deslauriers et al, J Thorac Cardiovasc Surg. 2011 Jan;141(1):7-15

# Pulmonary hypertension after **pneumonectomy** for lung cancer

- One year postoperatively,

The calculated mean systolic PAP
at 1, 6, and 12 months postoperatively
was 21.9±6.6, 27.3±9.3, and 34.1±14mmHg

**37.9% → mild to moderate PH**
**3.4% → severe pulmonary hypertension.**

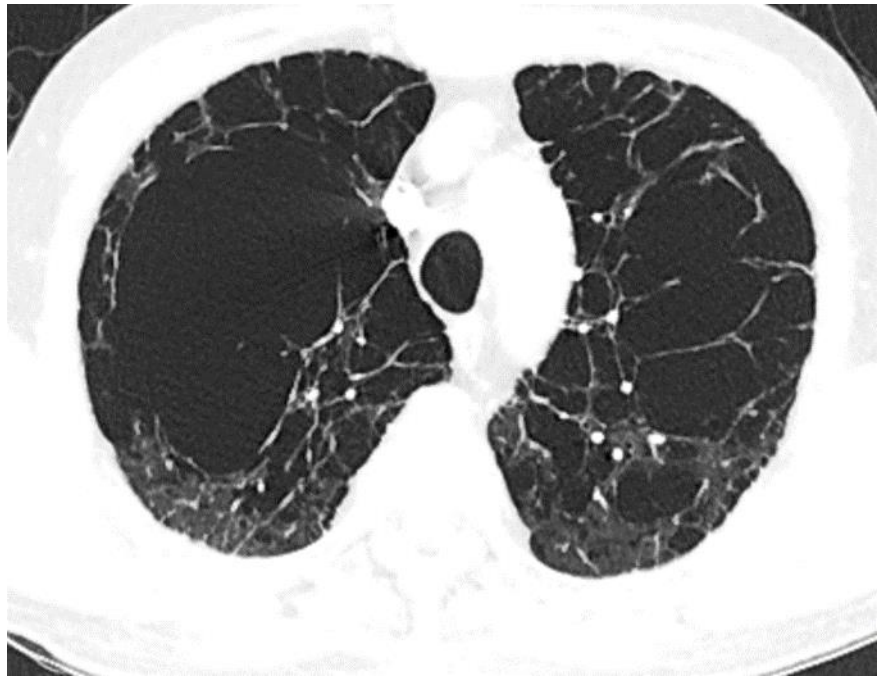
Konstantinos P. et al, Asian Cardiovasc Thorac Ann. 2014 Nov;22(9):1072-9.

# 폐고혈압을 유발하는 폐질환은?
# 만성 chronic

## 만성폐쇄성폐질환 COPD

**Slow progression**

**Prevalence > 50%  (severe 1-5%)**



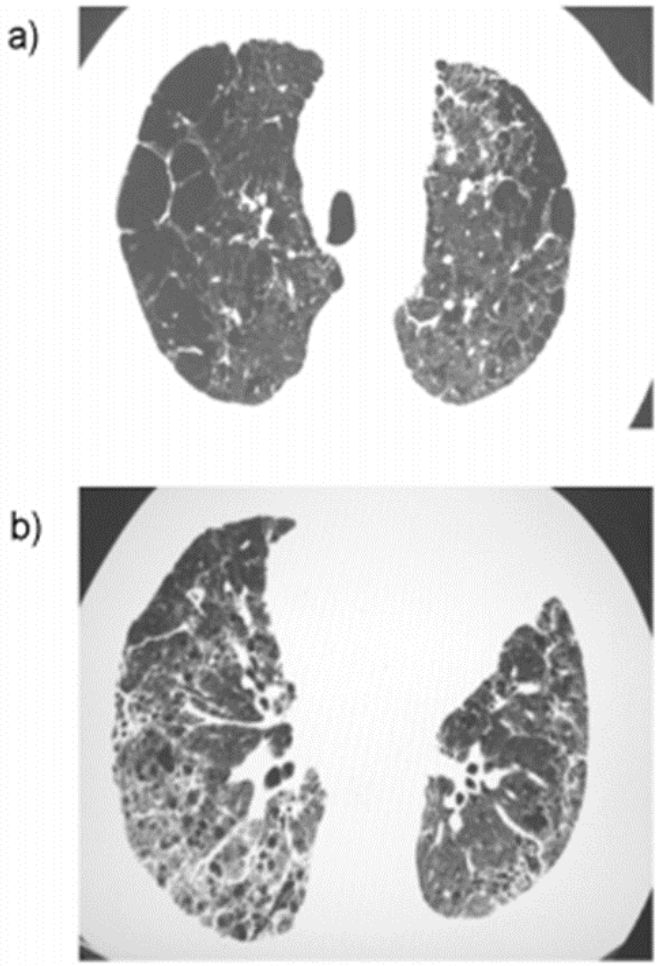
## 간질성폐질환 ILD

**Rapid progression**

**Prevalence 8-40% (severe < 10% )**

폐고혈압을 유발하는 폐질환은?
만성 chronic

- **Combined pulmonary fibrosis and emphysema (CPFE)**




| 40 patients with CPFE and PH<br>27 patients (68%) had severe PH | |
|---|---|
| **Parameters** | **Mean±SD** |
| Age | 68±2 |
| **FEV1 % predicted** | **78±18** |
| **FVC % predicted** | **86±19** |
| FEV1/FVC | 75±18 |
| **DLco % predicted** | **24±14** |
| 6MWD (m) | 244±126 |
| **SpO2 decrease test** | **-15±8** |
| **Mean PAP (mmHg)** | **40±9** |
| CO $L \cdot m^{-1}$ | 4.7±1.3 |
| PVR $dyn \cdot s \cdot cm^{-5}$ | 521±205 |

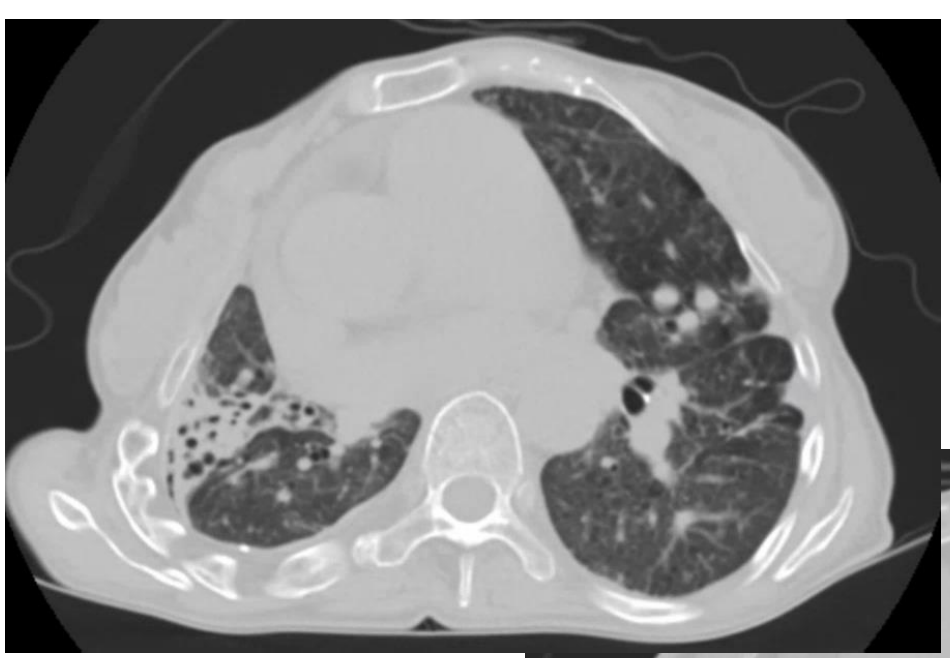
**Rapid progression**

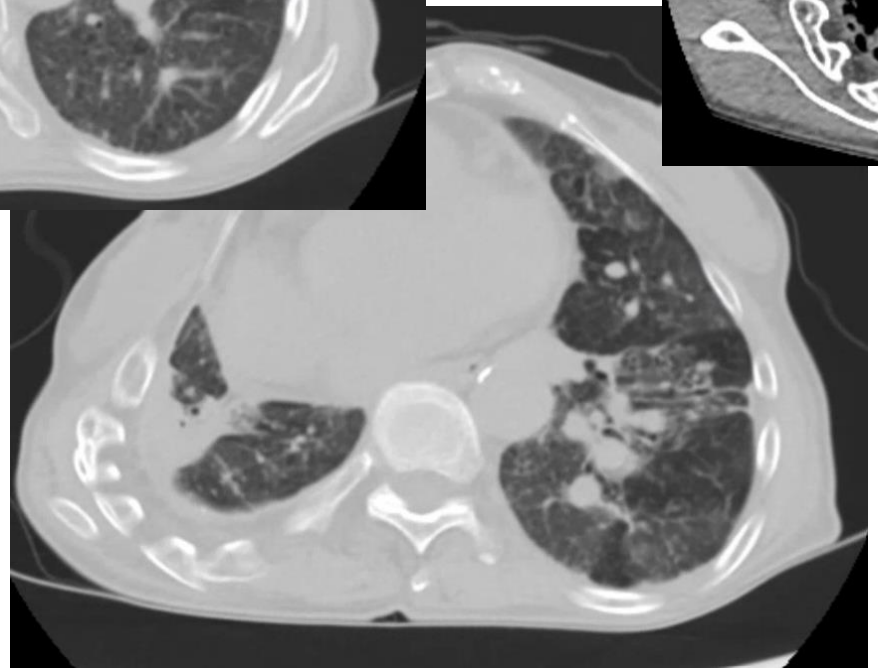
**Prevalence ~50%**

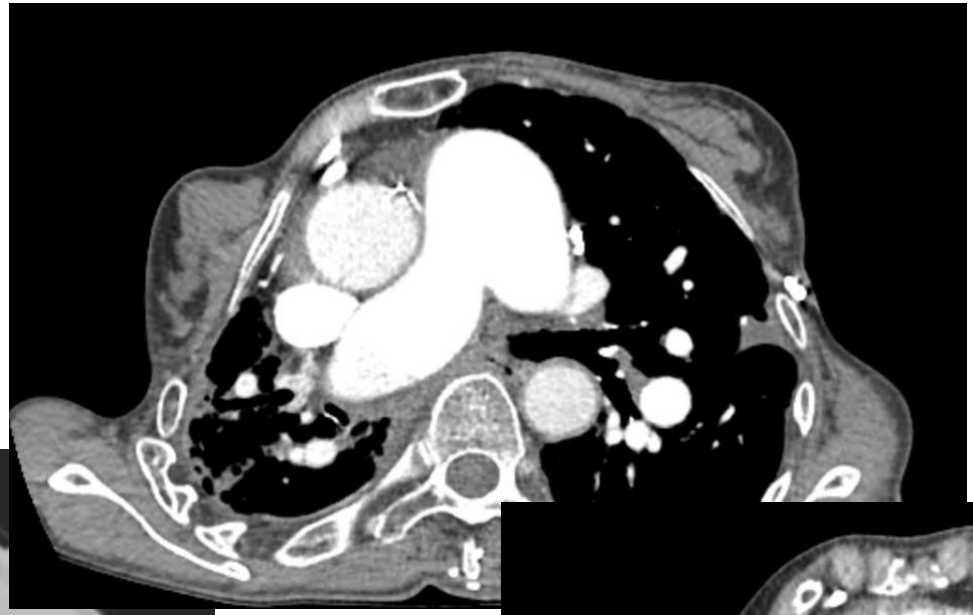
**Severe PH ~ 70%**

Cottin et al. Eur Respir J 2010; 35: 105–111

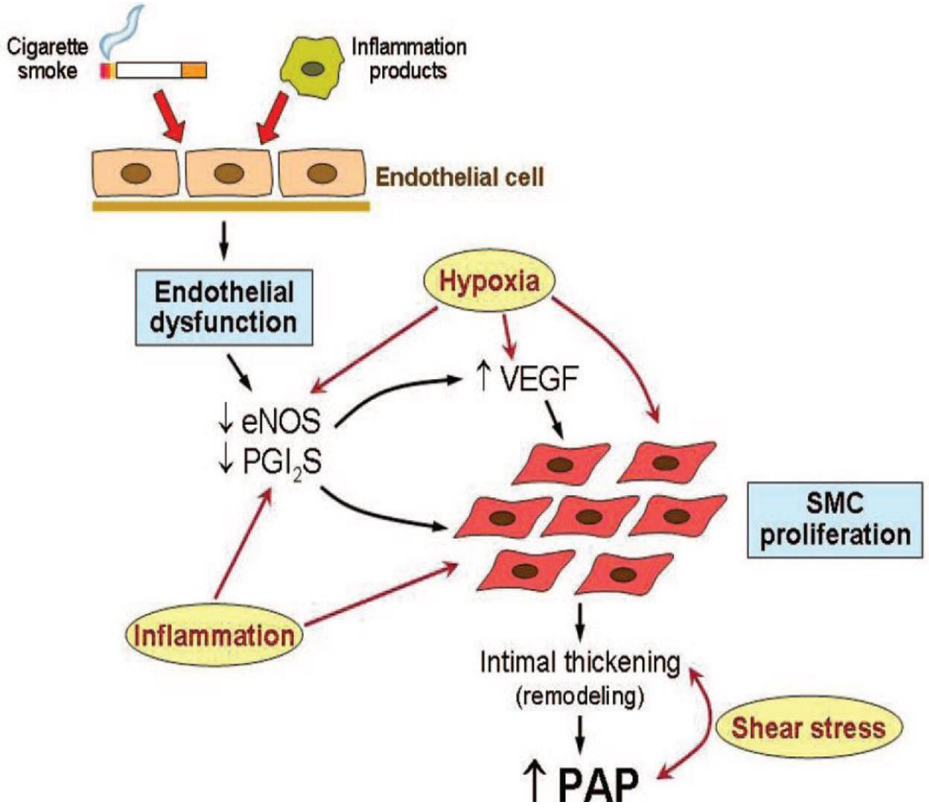
# TB destroyed lung



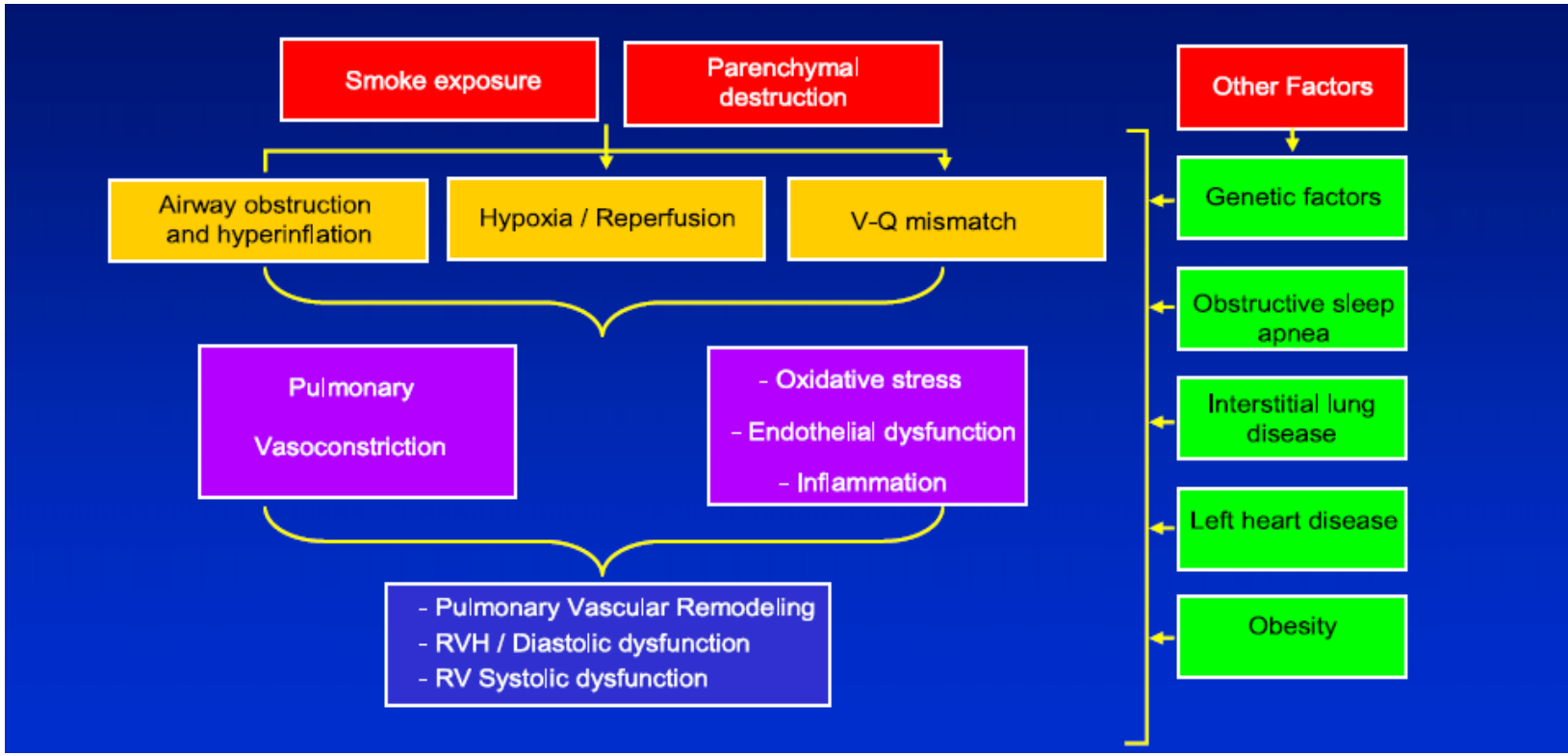




# Pathogenesis of PH in COPD
# Endothelial dysfunction
# + multi-factorial process



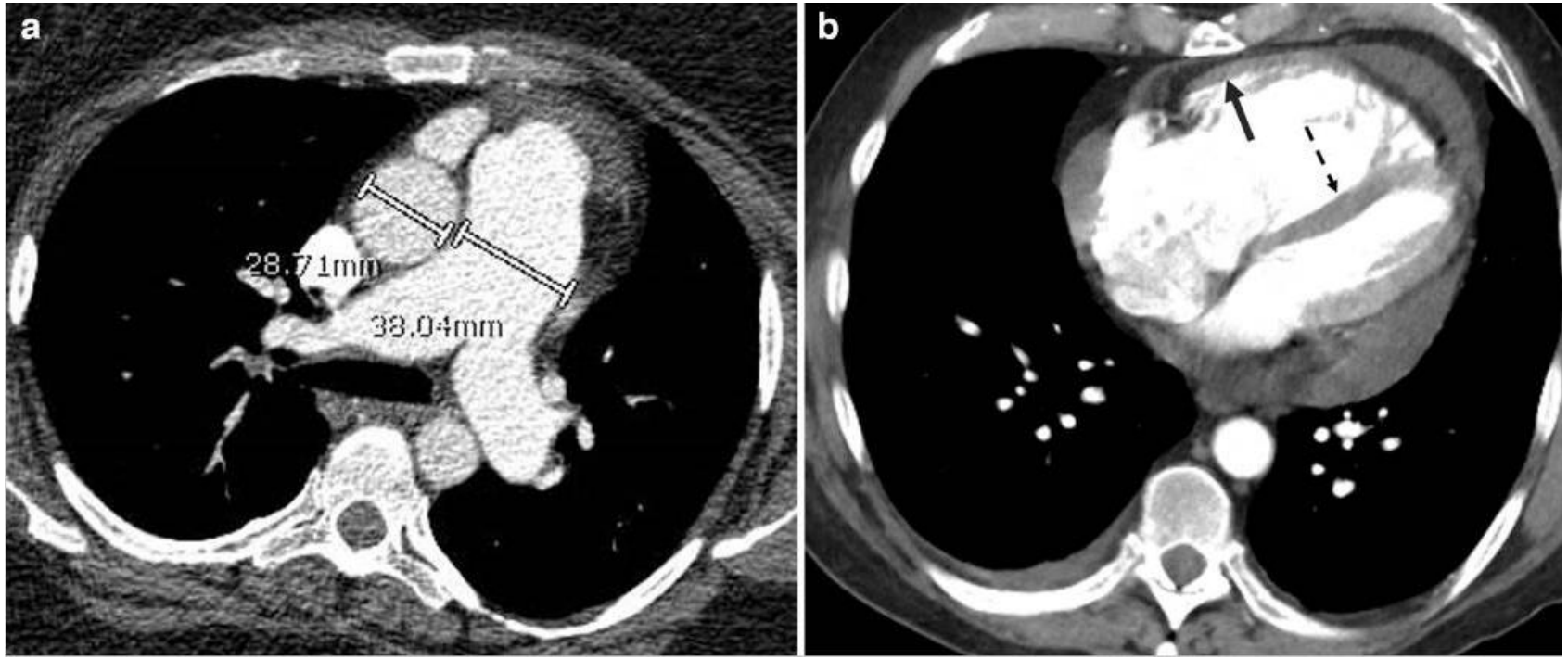

Peinado et al. CHEST 2008; 134:808–814




Minai et al. CHEST 2010; 137(6)(Suppl):39S–51S

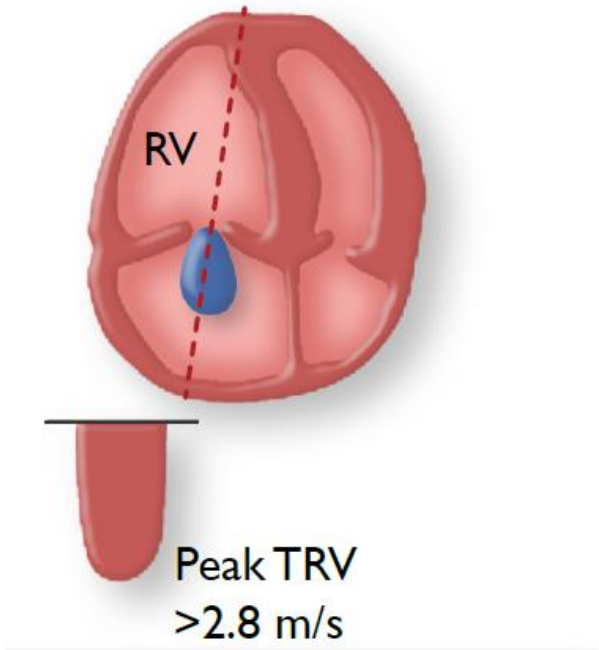
# PH in CT

- Main pulmonary artery: aortic ratio >1.1
- RV:LV ratio of >1.0




*Br J Radiol 2020; 94: 20200830.*

# Estimation of systolic pulmonary artery pressure (sPAP)



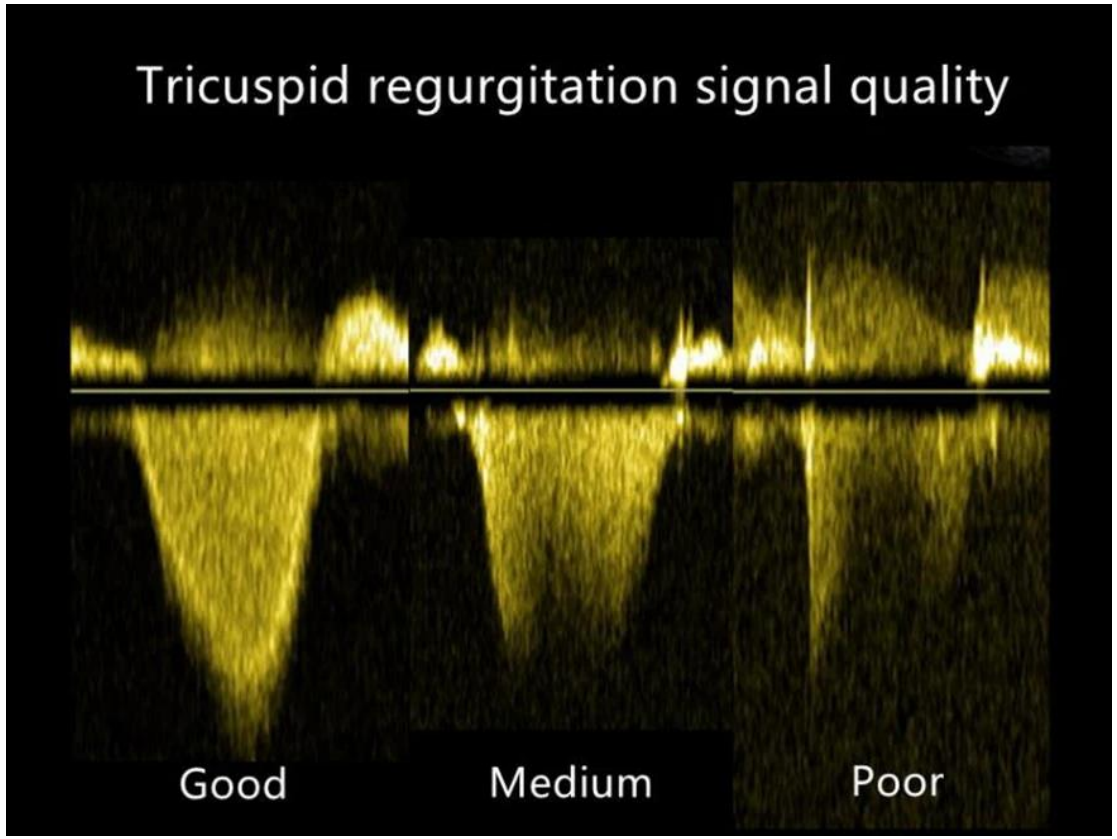

- sPAP = $4[\text{TR Vmax}]^2$ + estimated RAP

| IVC | Collapse[a] | eRAP |
|---|---|---|
| <2.1 cm | >50% | 3 (0-5) |
| >2.1 cm | >50% | 8 (5-10) |
| >2.1 cm | <50% | 15 (10-20) |

- Commonly poor sonic window!
- Commonly unmeasurable TR Vmax
- Tendency to overestimate PAP
- Accuracy of echo in patients with advanced respiratory diseases is low

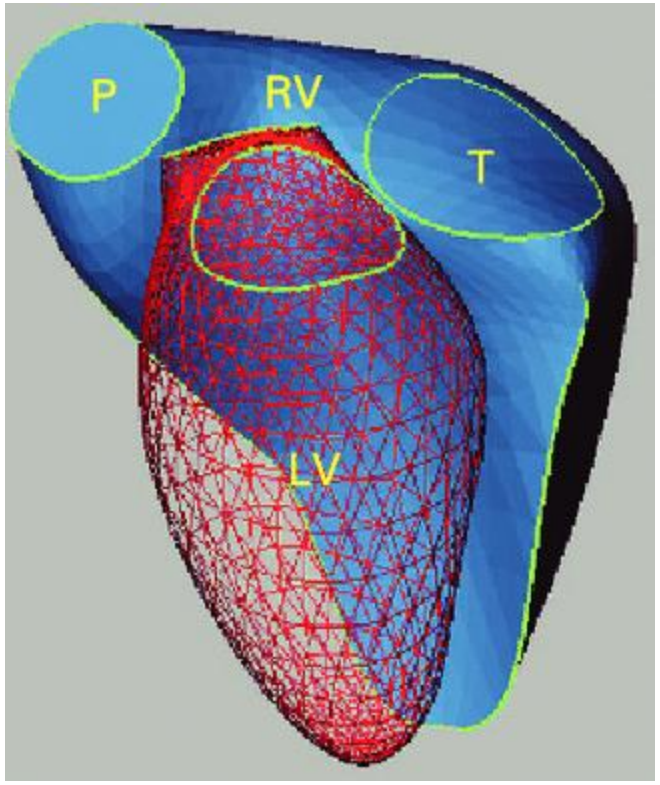
**→ Severe PH 추정 위해서는 other echo signs of PH 중요**

# The accuracy of Doppler echocardiography

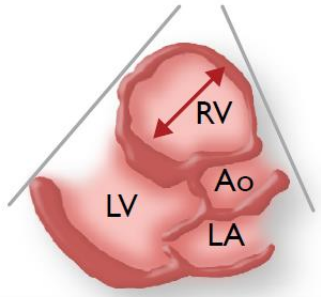



Lv et al. BMC Medical Imaging (2022) 22:91

# **Right heart function** - evaluation by echo

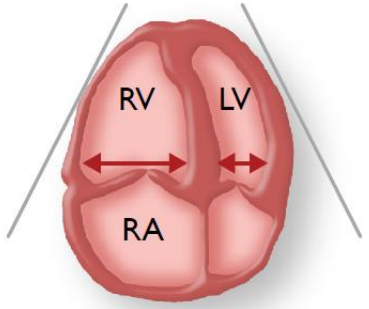



A



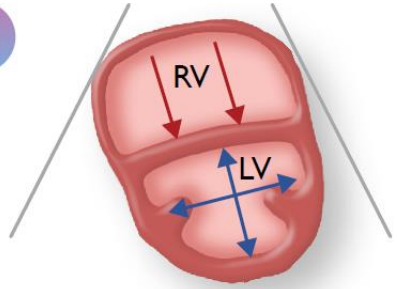

Enlarged right ventricle;
parasternal long-axis view

B




Dilated RV with basal RV/LV ratio >1.0;
four-chamber view

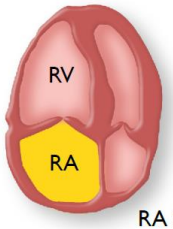
C




Flattened interventricular septum (arrows) leading to 'D-shaped' LV; decreased LV eccentricity index; parasternal short-axis view

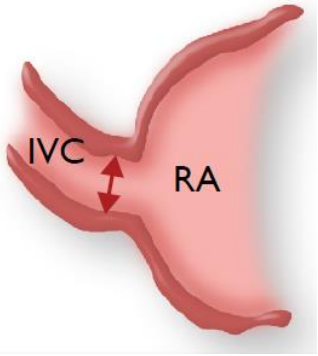
I

End-systolic

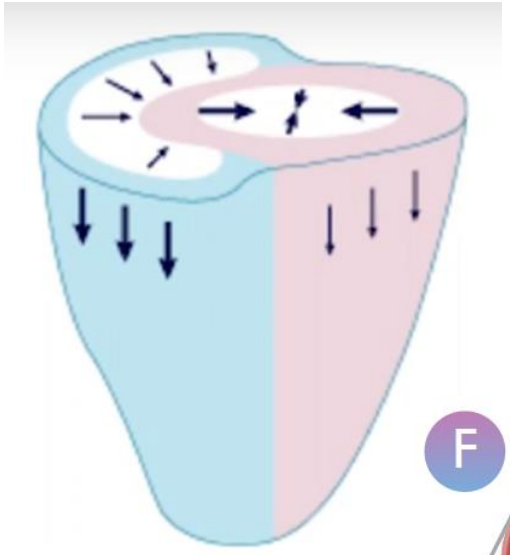


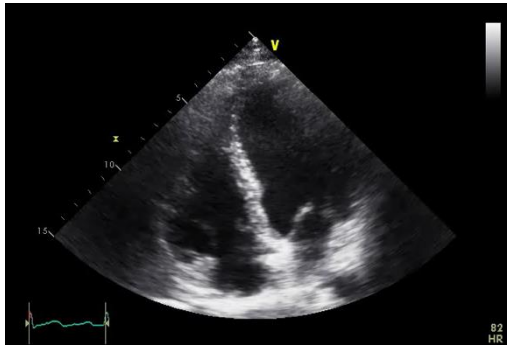

RA >18 $cm^2$

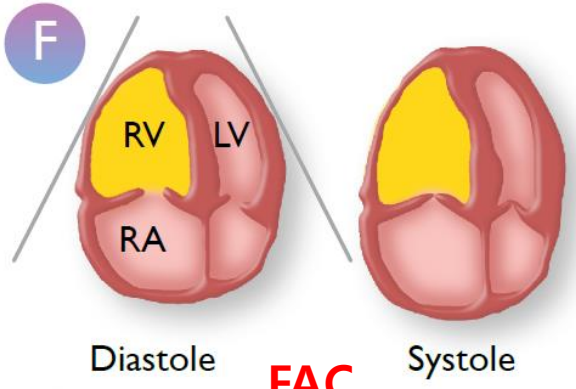
Enlarged right atrial area (>18 $cm^2$);
four-chamber view



# **Right heart function** - evaluation by echo

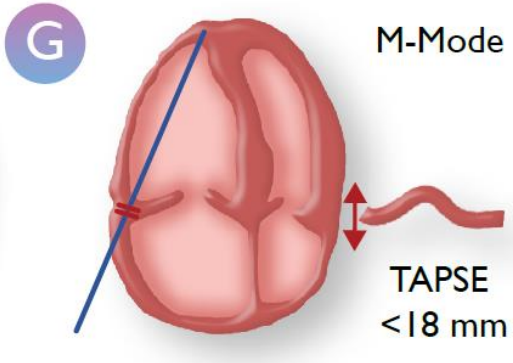




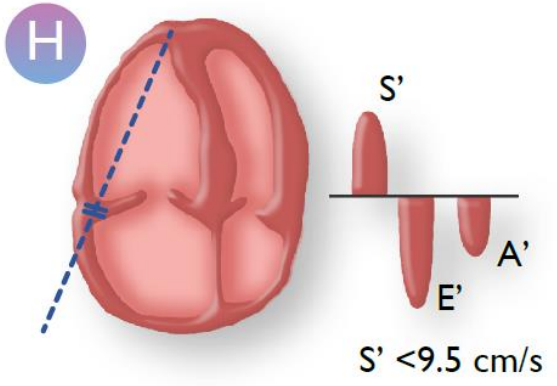



**FAC**

Reduced right ventricular fractional area change (<35%); four-chamber view



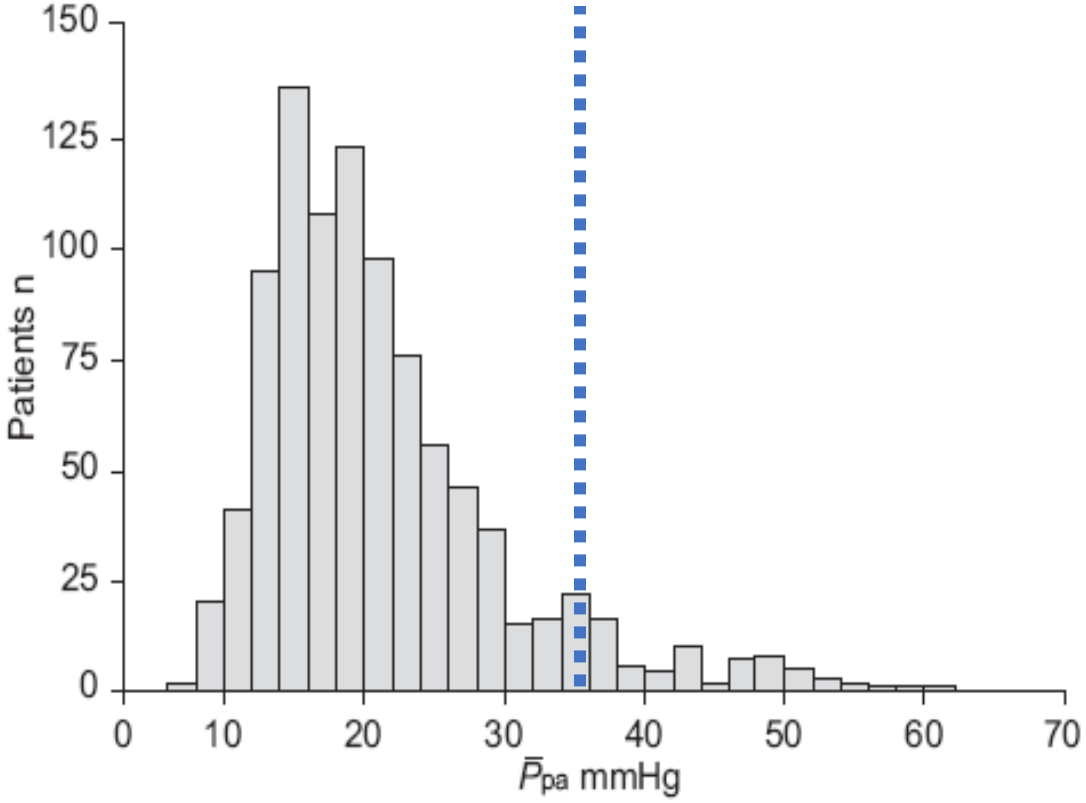

Decreased tricuspid annular plane systolic excursion (TAPSE) measured with M-Mode (<18 mm)



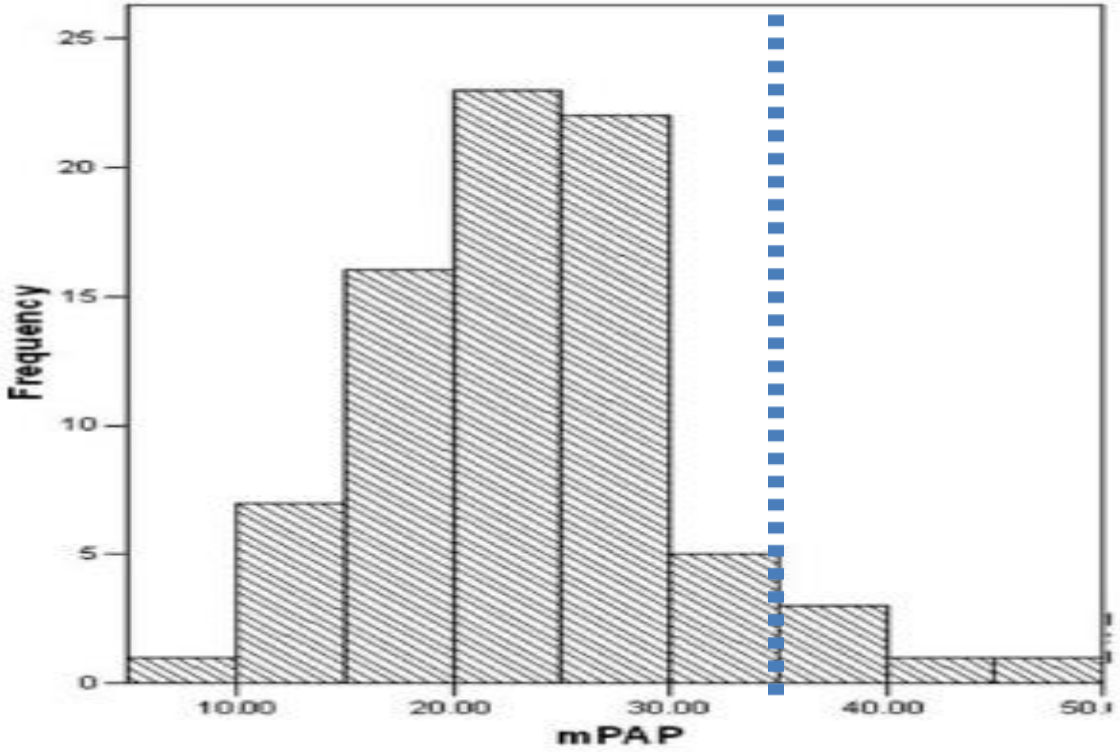

Decreased peak systolic (S') velocity of tricuspid annulus (<9.5 cm/s) measured with tissue Doppler

# Mean PAP in patients with COPD and IPF

## COPD




## IPF




Chaouat et al. Am J Respir Crit Care Med 2005;172: 189–194

Lettieri CJ, et al. CHEST 2006; 129:746 –752

# Pulmonary vascular resistance **PVR ( Wood units )**

- Quantitative value for **right ventricular afterload**.

**Ohm's law** V=IR

Pressure gradient=Flow x Resistance

혈관저항= 압력차이/심박출량

- 저항 (R) = $\dfrac{\text{압력차이 Pressure gradient}}{\text{유량 Flow}}$

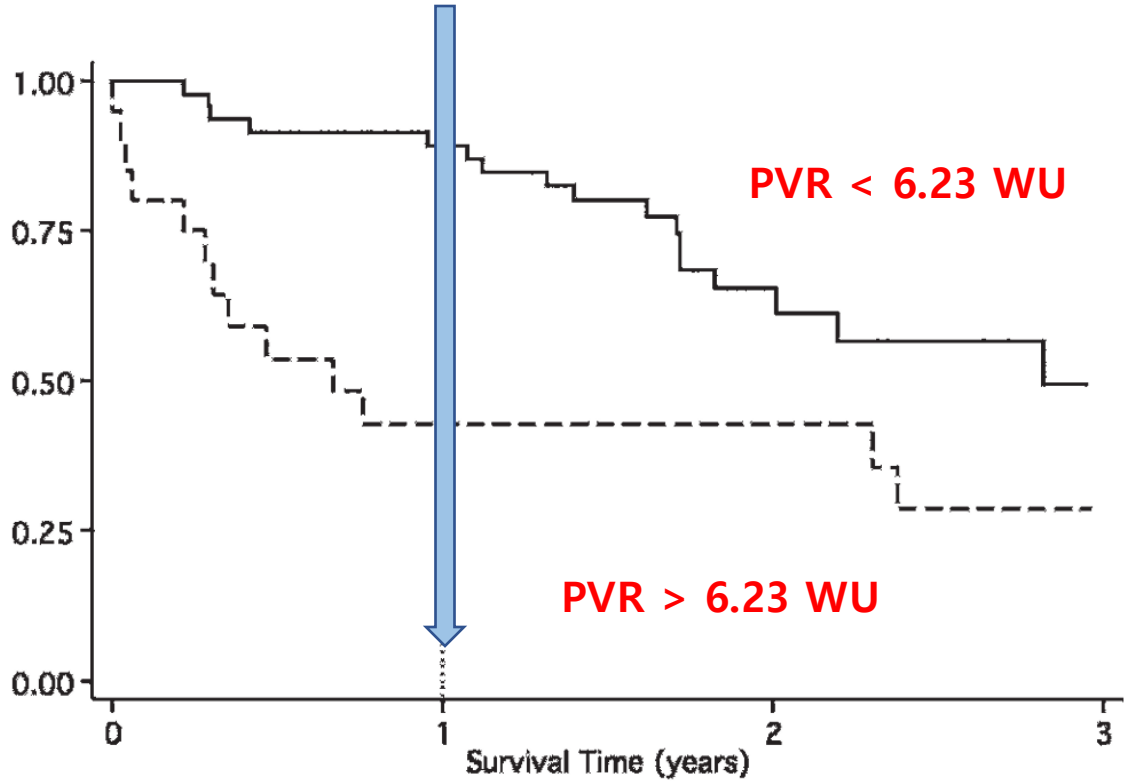
$$\frac{\text{(input pressure – output pressure )}}{\text{blood flow}}$$

$$\frac{\textbf{Mean PA pressure - left atrial pressure (PCWP)}}{\textbf{Cardiac output}}$$

**ex)** $\dfrac{\textbf{15 – 10}}{\textbf{5}}$ **= 1 WU**

# **PVR predicts early mortality**
in patients with diffuse fibrotic lung disease and suspected PH

Hospital records of consecutive patients with difuse lung diseases undergoing right heart catheterization (RHC) were reviewed (n=66)

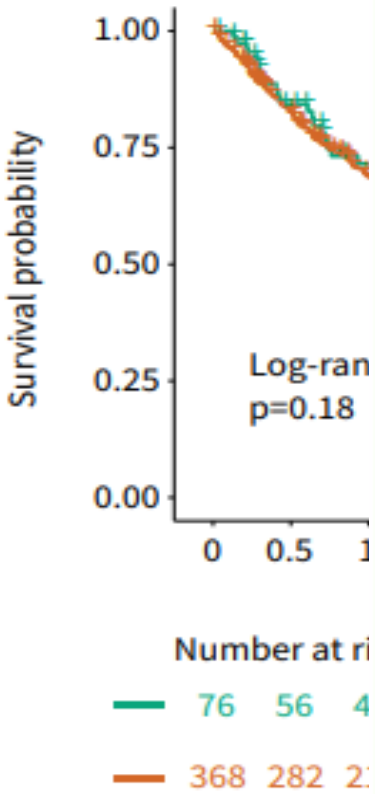


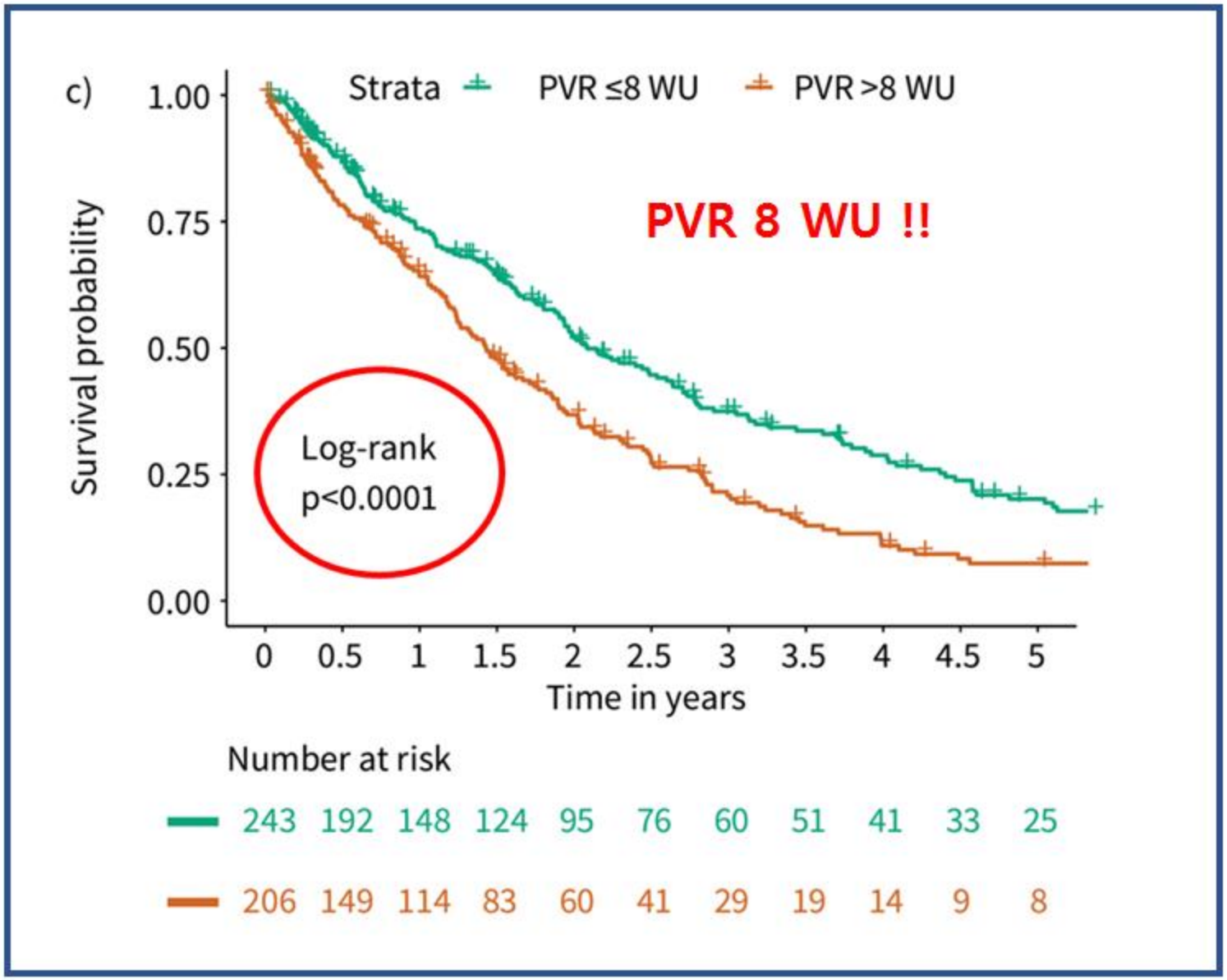

TJ Corte et al, Thorax 2009;64:883–888.

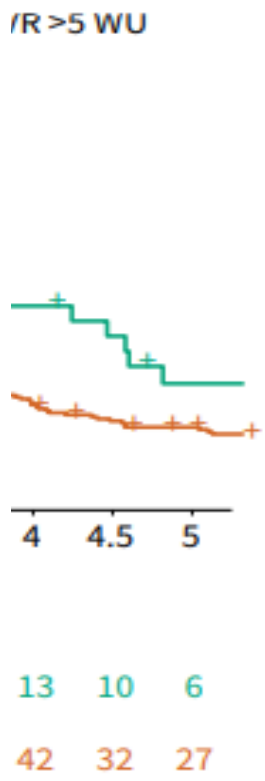
**PVR** provic
with PH-ILI

in patients

- **449 patient**




Olsson KM, et l. Eur Respir J 2021; 58: 2101483

Pulmonary vascular resistance (PVR)

$$PVR = \frac{mPAP - PCWP}{CO}$$

$$PVR = \frac{15 - 10}{5} = 1.0 \text{ Wood units}$$

$$PVR = \frac{35 - 10}{5} = 5.0 \text{ Wood units}$$

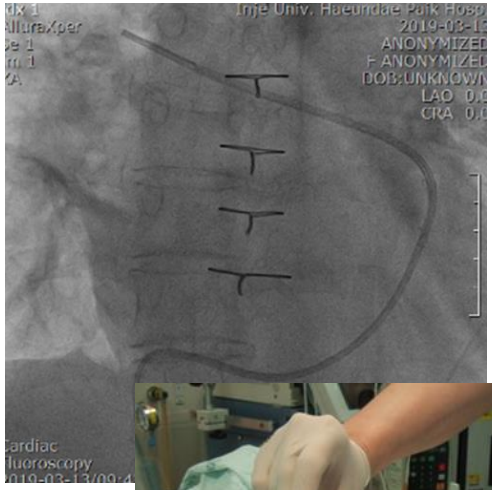
Pulmonary vascular resistance (PVR)

$$PVR = \frac{mPAP - PCWP}{CO}$$

$$PVR = \frac{35 - 10}{5} = 5.0 \text{ Wood units}$$

$$PVR = \frac{25 - 10}{3} = 5.0 \text{ Wood units}$$

# Rt. Heart catheterization (RHC) 반드시 해야 하나?



- **Golden standard** to confirm pulmonary hypertension
- DDx> Group 2 PH associated with Lt heart disease

  Cardiac output
  PCWP, direct mearsure of LVEDP

- Group 2 이외 다른 그룹간에 hemodynamic 구별 안됨

- inconclusive echocardiographic findings in cases with a high level of suspicion and potential therapeutic implications

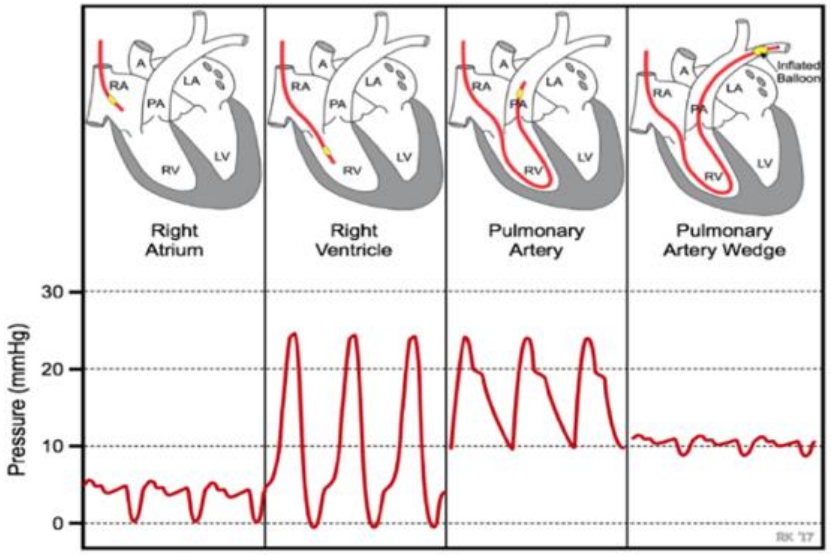
- Candidate for lung transplantation

| | | |
|---|---|---|
| In patients with lung disease and suspected PH, RHC is recommended if the results are expected to aid management decisions | I | C |

2022 ESC/ERS guidelines for PH

# Right heart catheterization (RHC)

- The risk of major complications is usually < 1%,
- the risk of mortality of 0.05%




# **Rare complications** may include:

Ventricular tachycardia

Cardiac tamponade

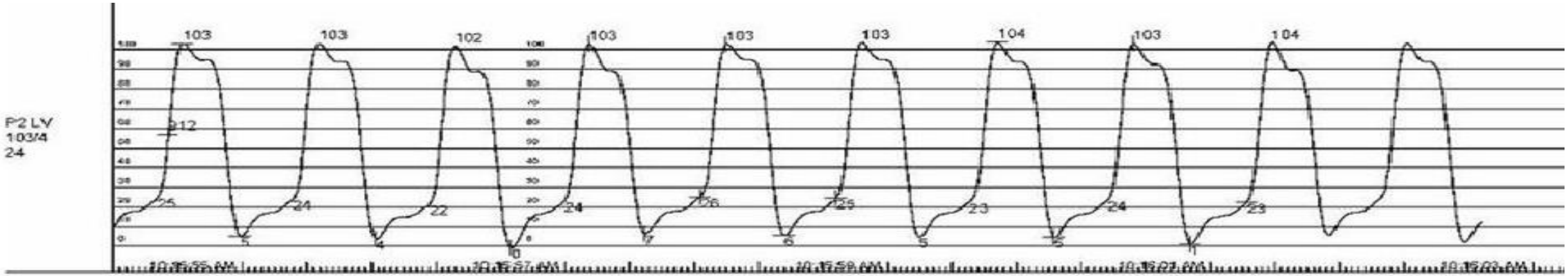
Infection

Air embolism

Pulmonary artery rupture

# Direct measurement of LVEDP in case of in-conclusive PCWP

**LVEDP=24 mmHg**




$$PVR = \frac{mPAP - PCWP}{CO}$$

$$PVR = \frac{34 - 24}{5} = 2.0 \text{ Wood units}$$

# 증례 #1　PH associated with lung disease

# 증례#1

- **67/남자**
- C.C : 내원 10
- Present illnes
  한달 전 피로
  7-8년 전부터
  느꼈다고 함.
- 가족력 : 어머
- 과거력
  - **40갑년 현**

측 하지 부종

## 진 료 의 뢰 서

차트번호 : 6954
연 번 호 : 7-2020-216

| 보험자기관기호 | | 보험자기관명칭 | | 증번호 | 81015196694 |
|---|---|---|---|---|---|
| 피보험자 성명 | | | | | |
| 수진자 성명 | | | | | |
| 수진자 주소 | ( | | | | |
| 상병명 | 호흡곤란. 다리부종<br>우심실부전 의증<br>급성 신부전 의증 | | | 한국질병 분류기호 | |
| 진료기간 | 2020년 9월 18일 부터<br>2020년 9월 18일 까지 ( 일간) | | | 진료구분 | 외래 |
| 환자상태 및 진료소견 | 상기환자 최근에 과로한 이후로, pitting edema 심해지며 호흡곤란까지 동반되었습니다. 소변량도 감소하여 정밀검사 및 치료위해 진료의뢰드립니다. 감사합니다.<br>+)<br>간이 심초음파에서 우심실이 확장되어 D-shape 이 의심됩니다. | | | | |

본인은 병원에서 진료받은 진료정보가 의뢰의사에게 제공되는 것에 동의합니다.
본인 : 서명

# 증례#1

체계별 문진 (review of system)

**전반적 위약 (+)**

**기침/가래 (+/+)**

**호흡곤란 (+, 움직이면)**

**chest discomfort/palpitaion (+/-)**

**소변 양 감소, 색 진해짐**

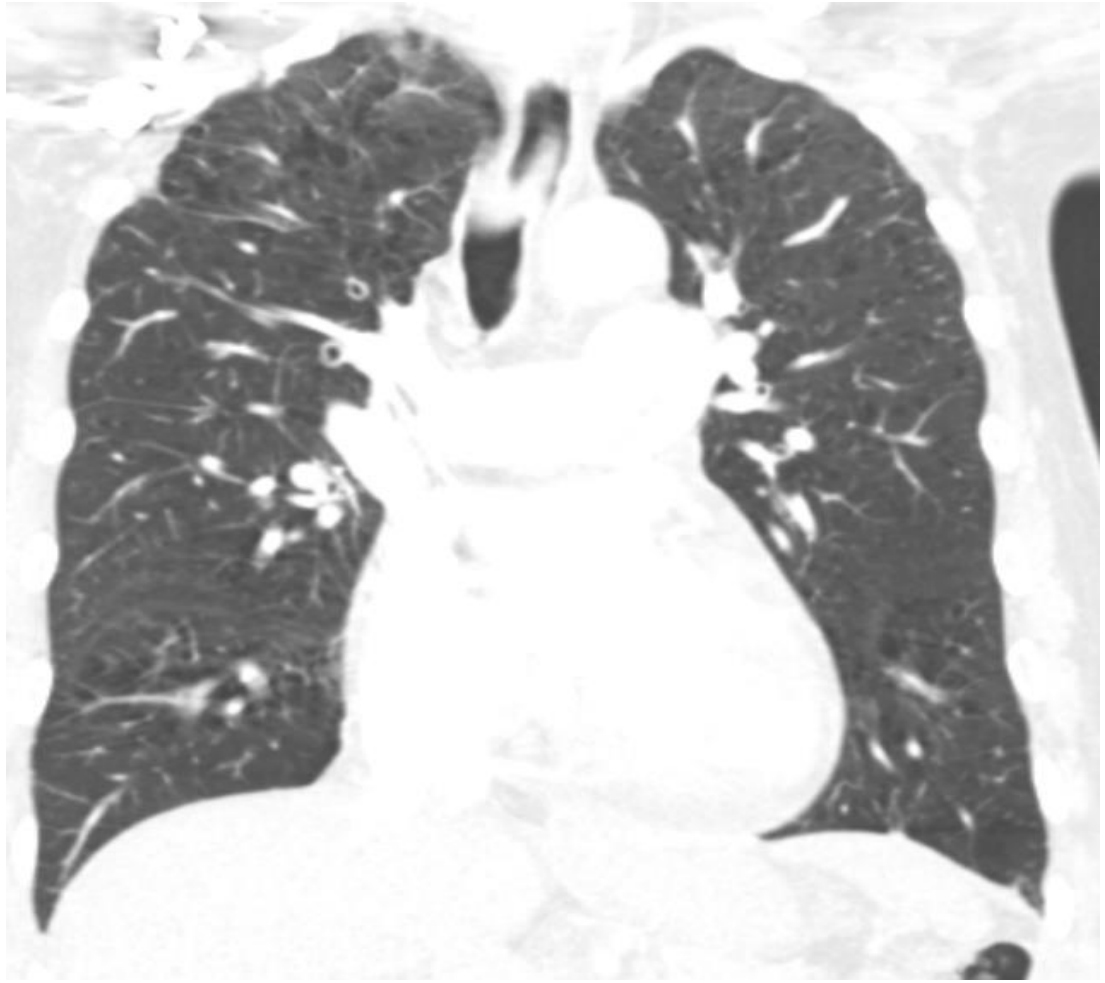
신체검진 (P/Ex)

혈압 : 143/82mmHg, 체온 : 36.8℃, 맥박수 : 107회/분, 호흡수 : 20회/분)

의식 명료 천명음 (-) 수포음 (-) 심잡음 (-)

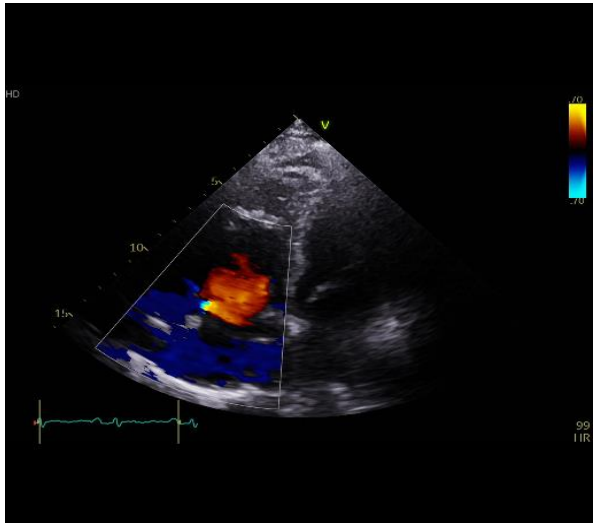
**양측 하지 부종 (++/++) pitting**

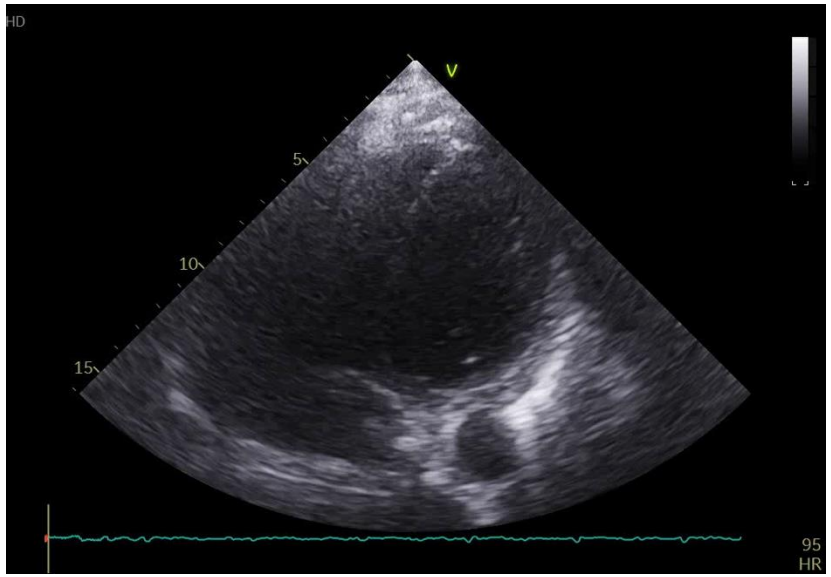
# Chest embolism CT

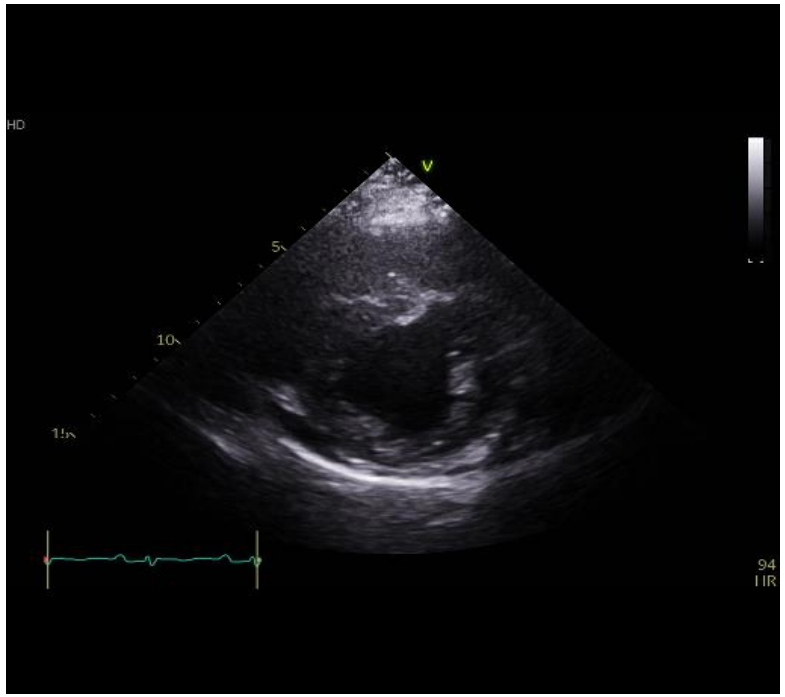


# ICU admission #3 Echocardiography

- Enlarged RA & RV dimension
- No RWMA with normal global LV systolic function.
- Decreased RV contractility(FAC = 16%).
- **TR Vmax 3.29 m/s** (RVSP =48.3 mmHg )







# 일반병실 입원 HD#2 ,,,,

응급실 내원 직후 spO2 60% 저하 보여 nasal prong O2 투여하며 조절

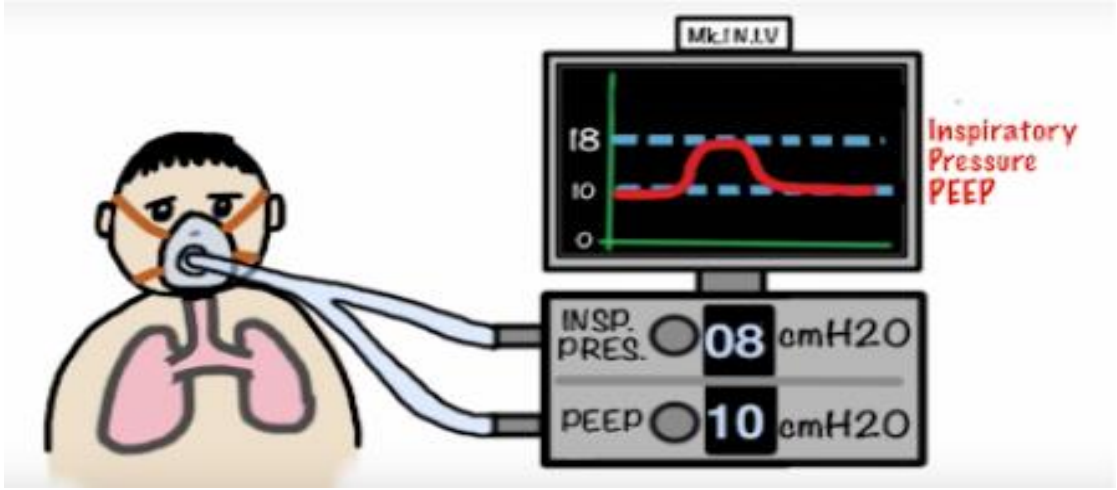
| A2009194261<br>2020-09-19 13:21 | C2009185991<br>2020-09-18 20:33 |
|---|---|
| 7.16 | 7.49 |
| 144 | 42 |
| 116 | 182 |
| 1.10 | 0.83 |
| 22.6 | 8.7 |
| 11.9 | 7.5 |
| 34.2 | 30.9 |
| 51.3 | 32.0 |
| 55.7 | 33.3 |
| 97 | 100 |

Decreased mentality → intubated

# ICU admission #3

- 2일 후 weaning, extubation 성공!

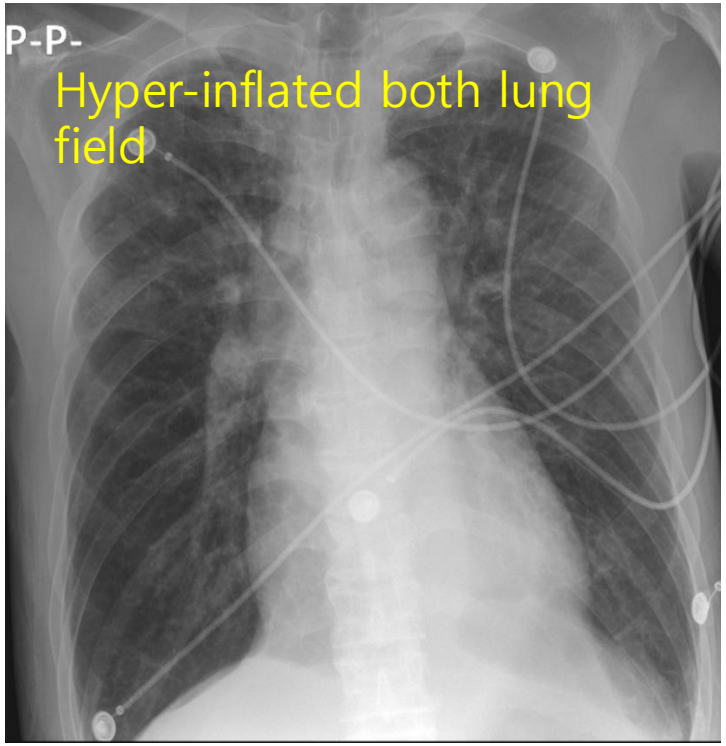
- Intermittent Non-invasive positive pressure ventilation (NIPPV)



# ICU admission #6  일반병실 전동 대기 중,,,,,,

- Room air 로 spO2 96%  → spO2 70%
- Wheezing ++  in thorax  ABGA : pH 7.15 **pCO2 109**

- → Re-intubation → ventilator care, steroid Tx
  4일 후 다시 extubation

# Home ventilator 로 NIPPV 적용하며 일반병동 전동대기 중,,,

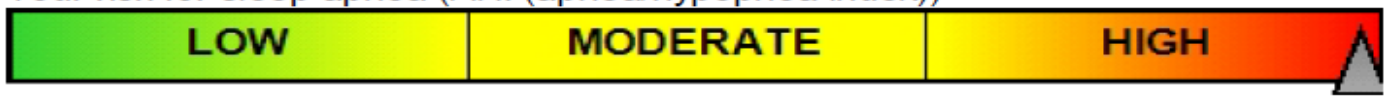
- Room air 상태로 intermittent NIPPV 적용 중
- **NIPPV 적용 안하는 수면 중에 desaturation down to spO2 ~80%** 자주 목격됨

-→ portable somnography (간이 수면 검진기) 시행하기로 함

# 간이수면검진기 결과 = Severe OSA

## Risk summary

Your risk for sleep apnea (AHI (apnea/hypopnea index))




Risk for fragmented sleep (AAI)


## Respiration

| | | | |
|---|---|---|---|
| AHI (apnea/hypopnea index) | 27.0 / h (< 5 / h) | oAHI (obstructive AHI) | **25.4 / h** |
| AI (apnea index) | **24.5 / h** | cAHI (central AHI) | **1.4 / h** |
| HI (hypopnea index) | **2.6 / h** | snoring | **0 %** |
| longest apnea | **59 s** | flattening | **1 %** |
| mean apnea duration | **19 s** | | |

## Oxygen

| | | | |
|---|---|---|---|
| Oxygen desaturation index | **23.7 / h** | Time below 95 % | **06:12:44 [100 %]** |
| lowest saturation | 65 % (90–96 %) | Time below 90 % | **02:02:31 [33 %]** |
| mean saturation | 89 % (94–98 %) | Time below 85 % | **00:31:12 [08 %]** |
| | | Total hypoxemia duration (SpO2 <90% for >5 min.) | **00:39:49 [11 %]** |

## Heart rate

| | | | |
|---|---|---|---|
| mean pulse rate | **86 / min** | highest pulse rate | 98 / min (60–90 / min) |
| | | lowest pulse rate | 38 / min (50–70 / min) |

# Diagnosis

#1 Pulmonary hypertension with Rt. heart failure
#2 COPD with asthma = probable ACOS
#3 recurrent hypercapnic respiratory failure
**#4 obstructive sleep apnea**

Impression >>
PH due to COPD or OSA
vs.
**lung disease (COPD, OSA) + Combined idiopathic PAH ?**

# Bedside Rt. Heart catheterization in ICU

- **PAP 36/21  mean PAP 27  mmHg**
- PCWP 10 mmHg
- Cardiac output ( thermodilution ) 3 회 평균  10.1 L/min
- PVR  1.683  WU/㎡
- SvO2  76%


# **Discharge and follow up**
optimizied care of underlying lung disease

- Home NIV – BiPAP  titration

  Day – evening – night

  → **Only at Nighttime**

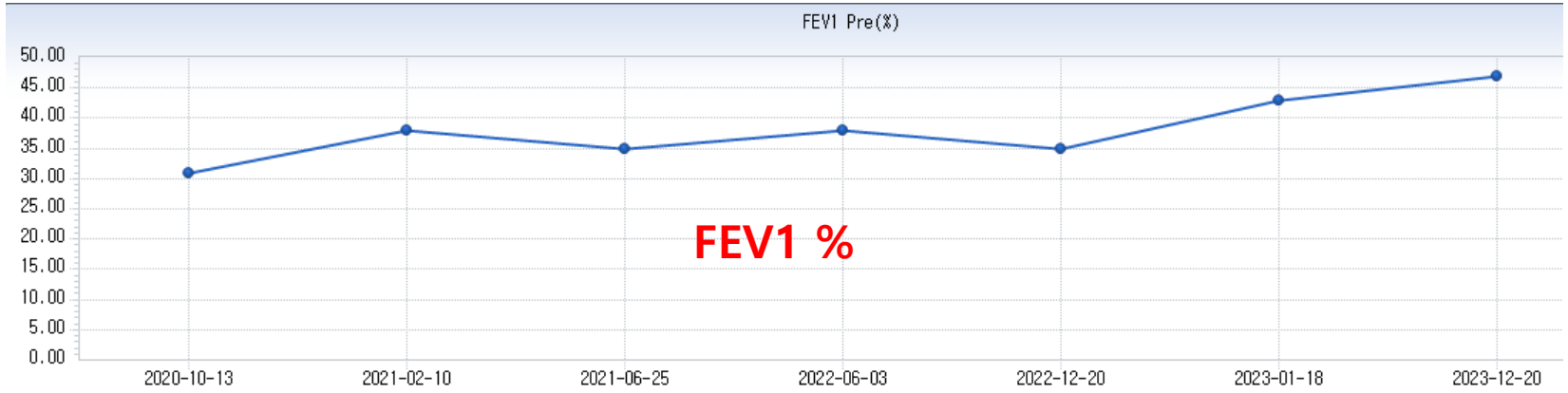
- Maintaining normocapnia

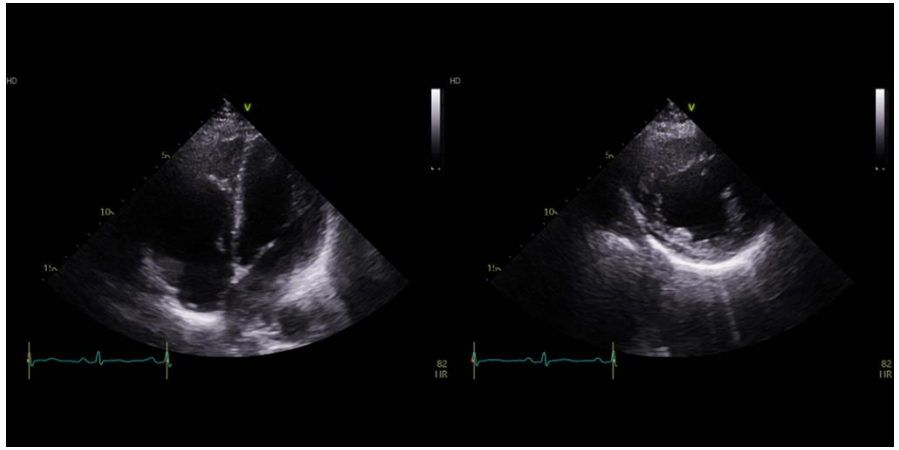
| | | | |
|---|---|---|---|
| PH | 7.35 ~ 7.45 | | 7.444 |
| $PCO_2$ | 35.0 ~ 45.0 | mmHg | 42.7 |
| $PO_2$ | 75.0 ~ 100.0 | mmHg | 80.6 |

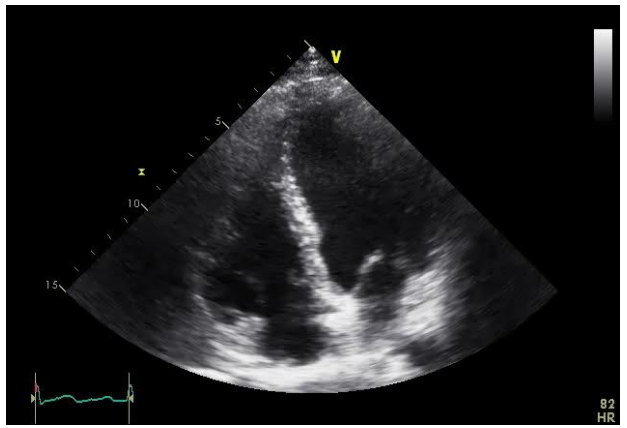
# **Discharge and follow up**
optimized care of underlying lung disease

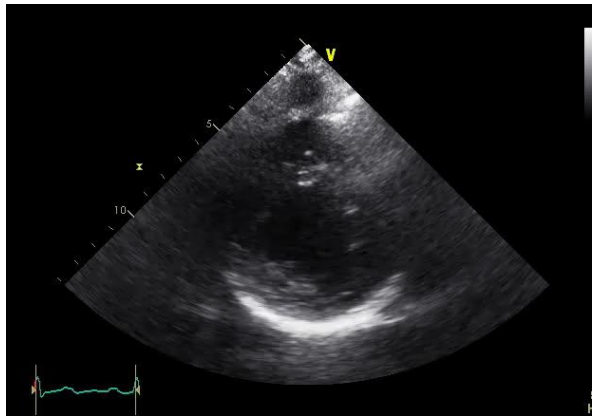
Spirometry

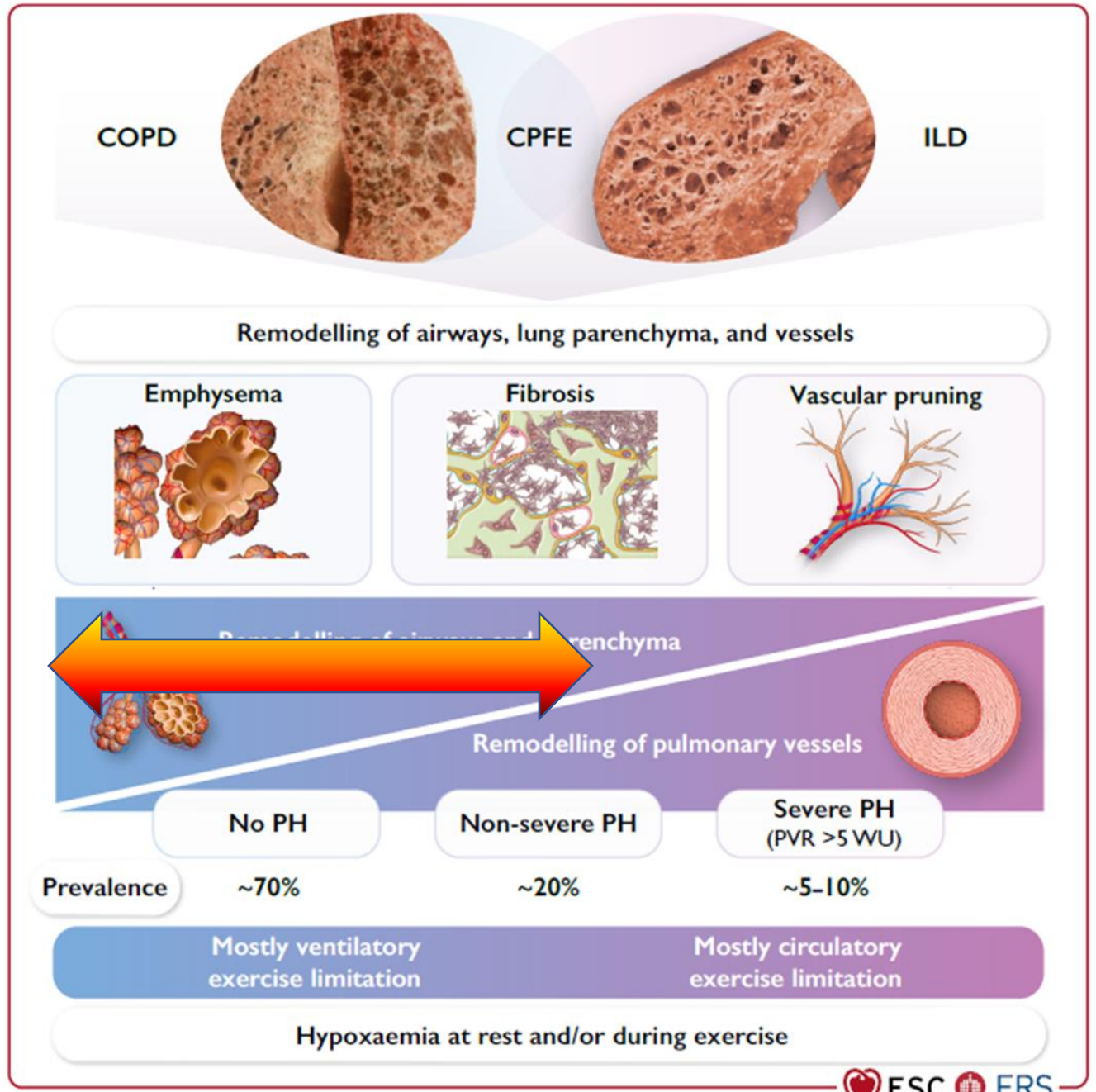
| | | | | |
|---|---|---|---|---|
| FVC | Liters | 4.77 | 3.45 | 72 |
| FEV1 | Liters | 3.57 | 1.12 | 31 |





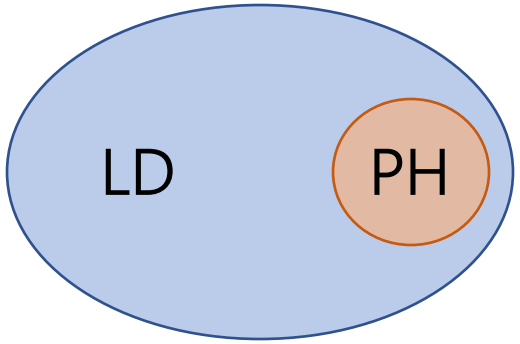


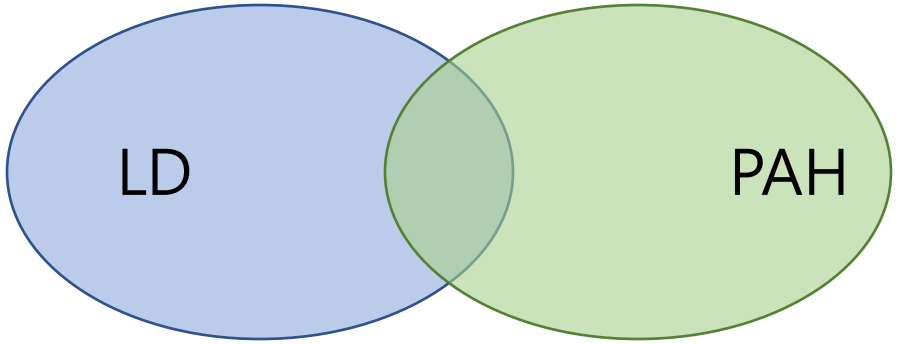

COPD
CPFE
ILD
Remodelling of airways, lung parenchyma, and vessels
Emphysema
Fibrosis
Vascular pruning
Remodelling of pulmonary vessels
No PH
Non-severe PH
Severe PH
(PVR >5 WU)
Prevalence
~70%
~20%
~5–10%
Mostly ventilatory exercise limitation
Mostly circulatory exercise limitation
Hypoxaemia at rest and/or during exercise
ESC ERS

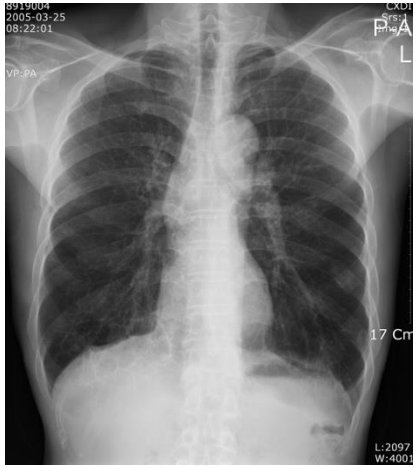
# General treatment for group 3 PH

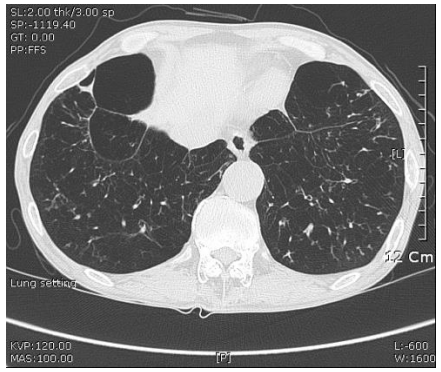
- 기저 폐질환 약물 치료 최적화
- Home O2 , portable O2 on ambulation
- Hypercapnia → home NIPPV (NIV)
- Sleep disordered breathing
- Rehabilitation
- Vaccination

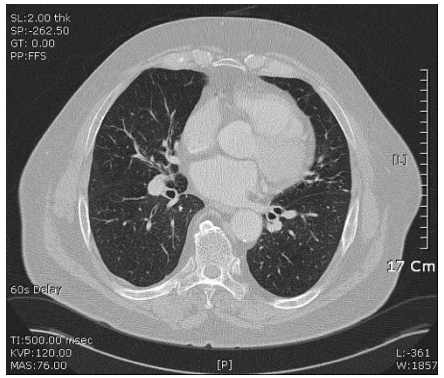
# PH-Lung Disease (LD) or PAH with LD ? Vascular phenotype ?

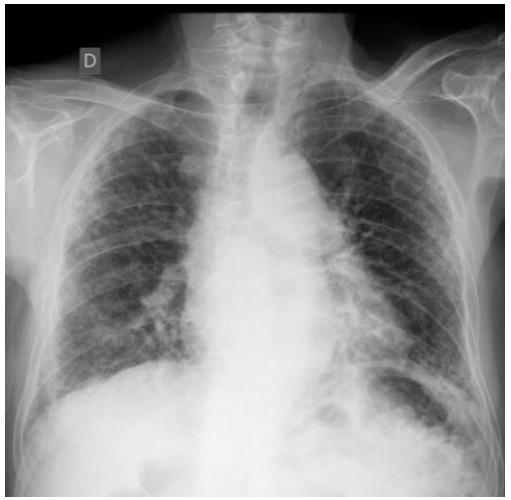


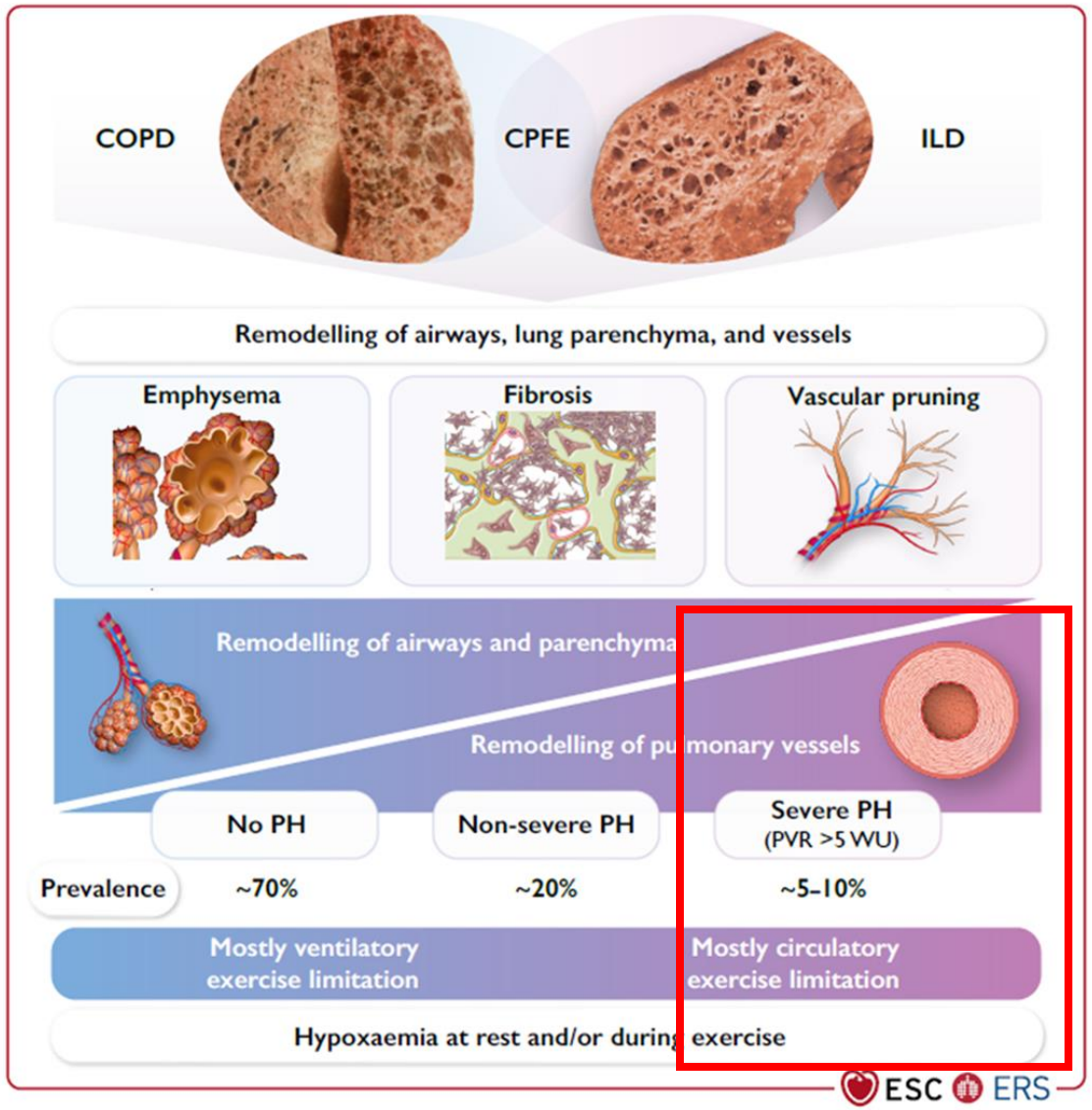





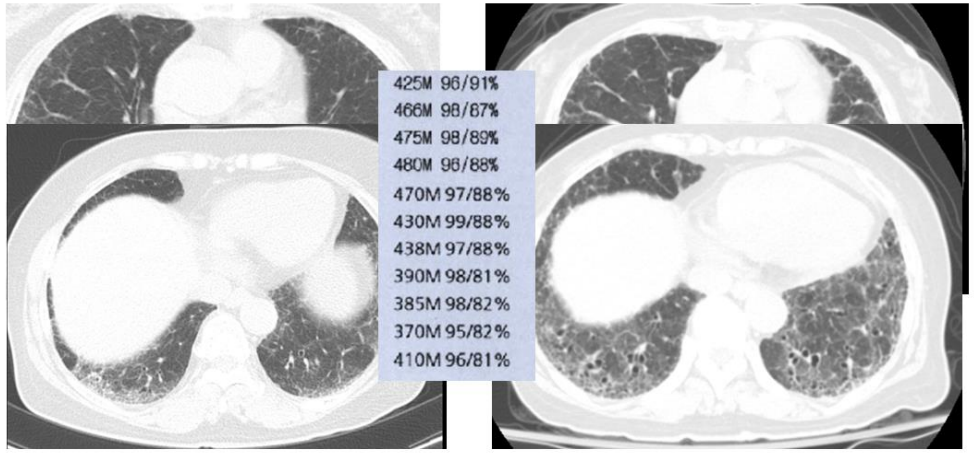



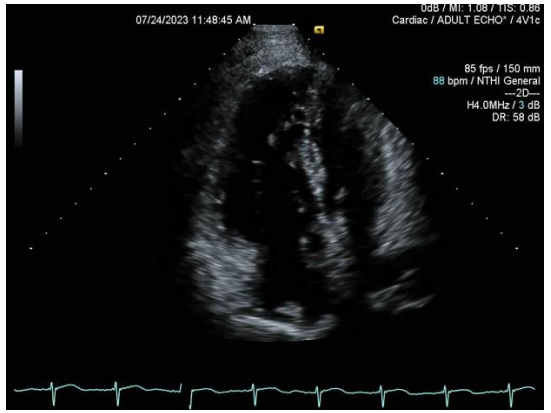
# 적극적으로 PAH target drug 치료를 고려해 볼만한 환자군은?




2018 at diagnosis → 5years→ 2023




**Biopsy proven UIP → IPF**
**Slow decline of FVC**
Episodes of Rt. heart failure




| RHC | 2023.3.16 |
|---|---|
| mean PAP, mmHg | 43 |
| PCWP, mmHg | 8 |
| RAP, mmHg | 11 |
| CO, L/min | 2.12 |
| PVR | 17 |
| Svo2 % | 45 |

# Inhaled Treprostinil in PH due to Interstitial Lung Disease

## INCREASE trial

*N Engl J Med* 2021; 384:325-334

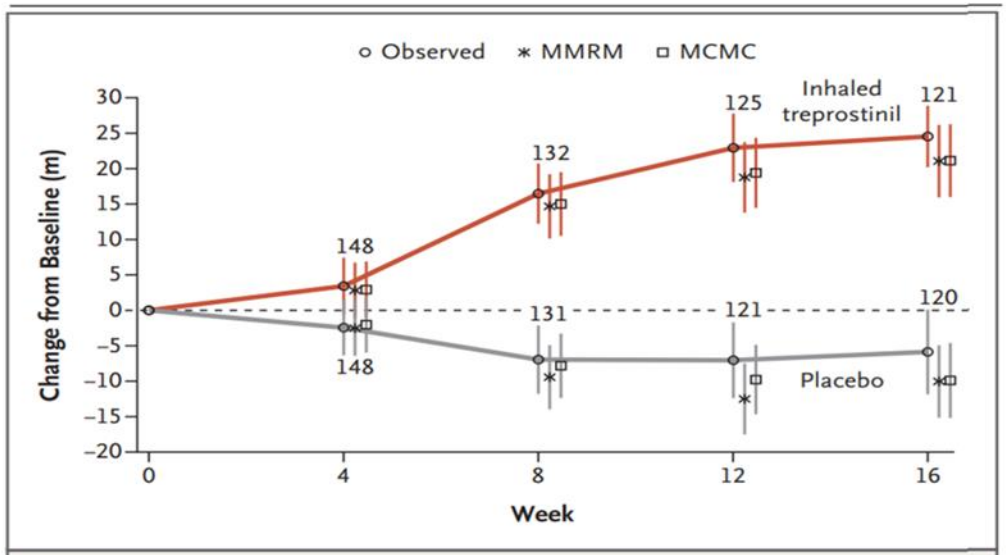
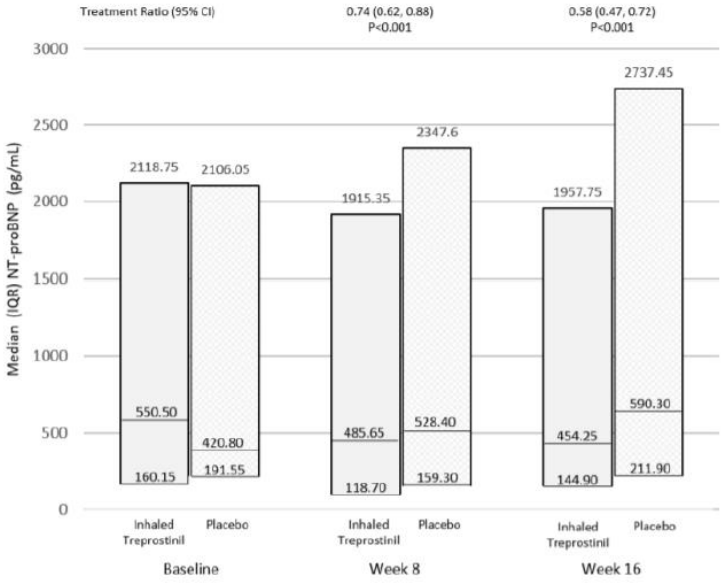
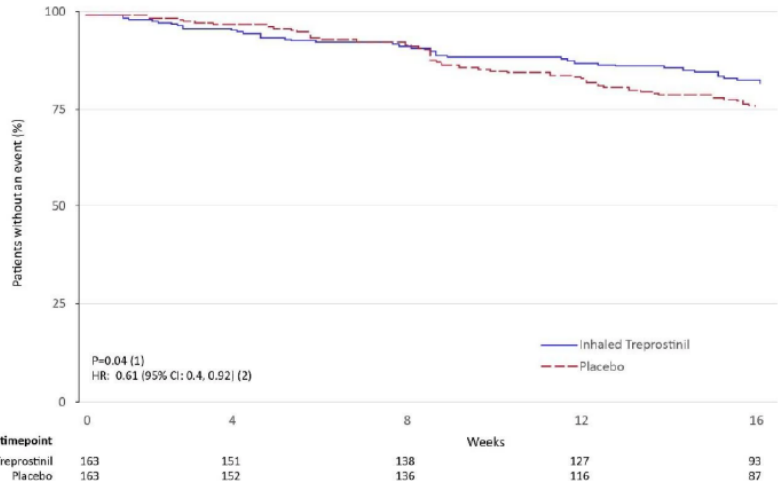



**Figure 2.** Mean Change from Baseline in Peak 6-Minute Walk Distance through Week 16.




**6MWT – exercise capacity ↑**
**NT-proBNP ↓**
**Risk of clinical worsening ↓**



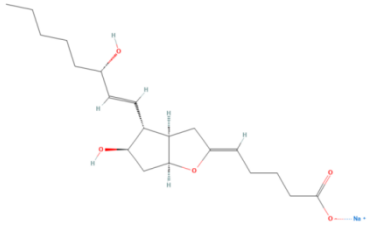
# **INCREASE trial**

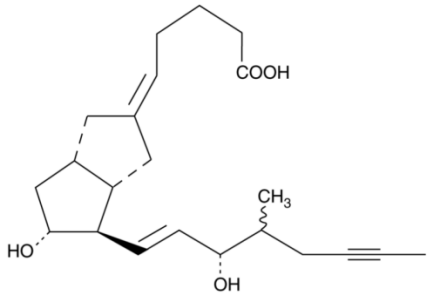
Greater treatment effect in higher **PVR** & **NT-proBNP**

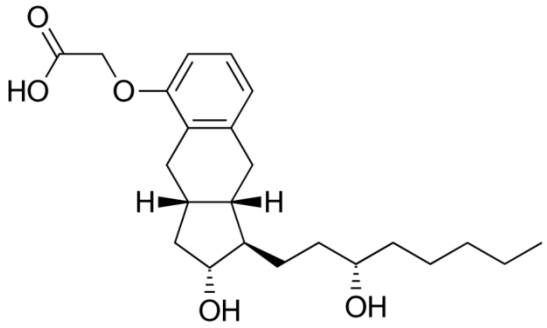
| | Inhaled treprostinil (n) | Placebo (n) | Placebo-corrected difference in week-16 FVC, mL | p value |
|---|---|---|---|---|
| **Pulmonary vascular resistance, Wood units** | | | | |
| <5·275 | 64 | 75 | −1·6 (47·9; −95·9 to 92·8) | 0·97 |
| ≥5·275 | 65 | 49 | 112·5 (52·6; 9·0 to 215·9) | 0·033 |
| **NT-proBNP, pg/mL** | | | | |
| <503·85 | 62 | 75 | 19·9 (53·7; −86·3 to 126·1) | 0·71 |
| ≥503·85 | 63 | 47 | 94·4 (47·4; 0·7 to 188·2) | 0·048 |

Placebo-corrected difference in week-16 FVC stratified by median baseline clinical characteristics

# Prostanoids – for **inhalation**




2024.7.5 국내 품목허가 취득
진료상 필수약제로 보험약가 신청

IPF 산정특례 대상으로 추진 예정

Epoprostenol Sodium

Iloprost
현재 국내사용중

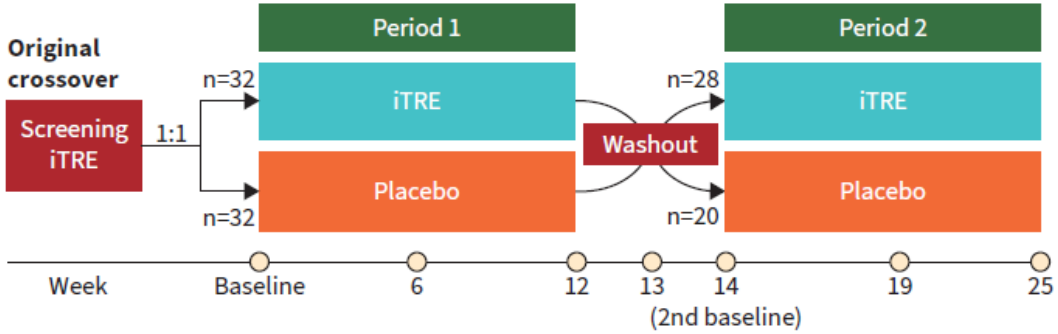
**Treprostinil**

환율계산기 (매매기준율 기준)

| 미국 달러 USD | | 대한민국 원 KRW |
|---|---|---|
| 200,000 $ | = | 275,180,000.00 ₩ |

S.D. Nathan et al,
Eur Respir J. 2024 Jun 6;63(6)

# Inhaled treprostinil in pulmonary hypertension associated with COPD: PERFECT study results




76 patients ( FVC 74.8±17.6, FEV1 42.6±18.4 Dlco 30.4±12.5 )
moderate to severe PH
based on RHC : mPAP ⩾30 mmHg, PVR ⩾4 WU
Resting spO2 ⩾90%

**The study was terminated early**
increased the risk of serious adverse events
suggestive evidence of an increased risk of mortality.
The change in 6MWD was numerically worse

# Take-home message


Group 3 PH 의 기본적인 치료 전략은 기저 폐질환에 대한 최적화된 치료

Lung disease and non-severe PH 에 대해서는 일반적으로 PAH target medication 이 권장되지 않는다.

환자에 따라 선택적으로
Individual decision making
필요하다

다른 원인에 의한
PH 가능성도 고려하고
배제해야 한다

# 감사합니다!