Pathophysiology of COPD

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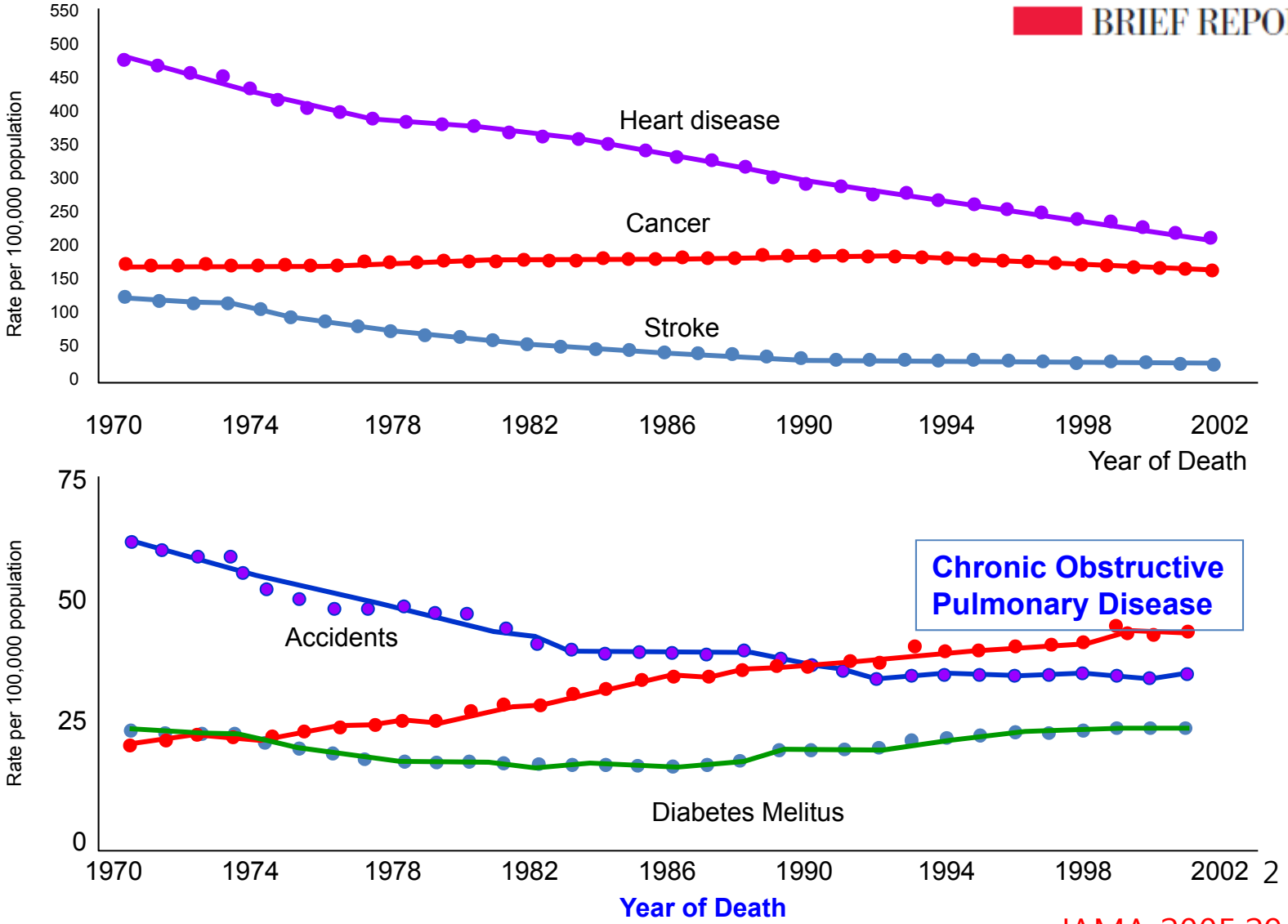
유 광하

Trends in the Leading Causes of Death in the United States, 1970-2002

BRIEF REPORT



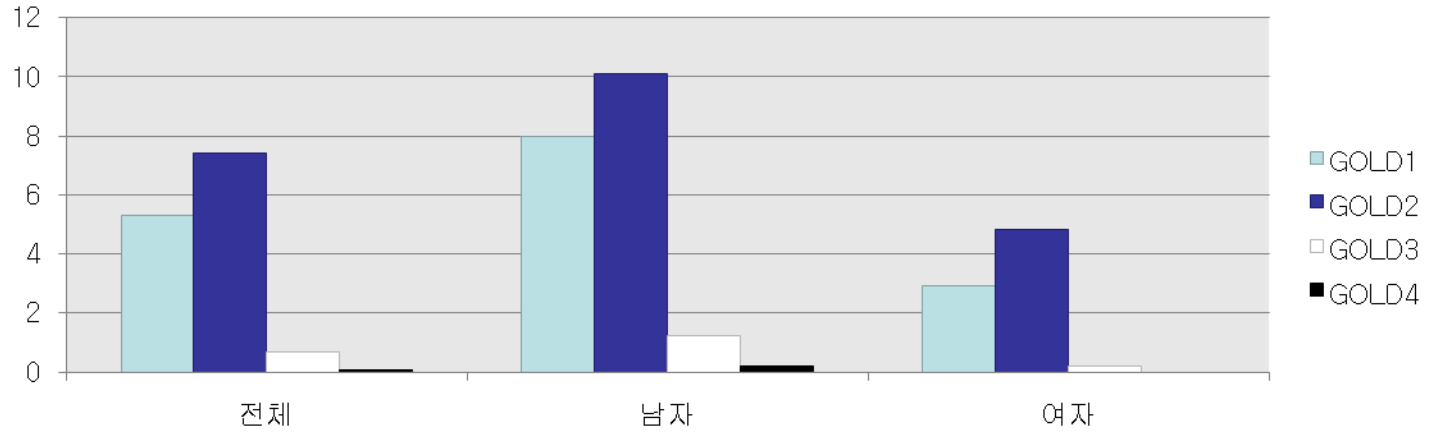
JAMA 2005;294:1255

Prevalence of chronic obstructive pulmonary disease in Korea: The fourth Korean National Health and Nutrition Examination Survey, 2008

KWANG H. YOO,[1*] YOUNG S. KIM,[2*] SEUNG S. SHEEN,[7] JOO H. PARK,[7] YONG I. HWANG,[8]

	전체(40세 이상)	남자	여자
대상자수	2501	1056	1445
정상	86.6 (0.9)	80.6 (1.5)	92.1 (1.0)
GOLD 1	5.3 (0.6)	8.0 (1.0)	2.9 (0.6)
GOLD 2	7.4 (0.6)	10.1 (1.1)	4.8 (0.8)
GOLD 3	0.7 (0.2)	1.2 (0.4)	0.2 (0.1)
GOLD 4	0.1 (0.1)	0.2 (0.1)	0.0 (-)
Total	**13.4 (0.9)**	**19.4 (1.5)**	**7.9 (1.0)**

94%

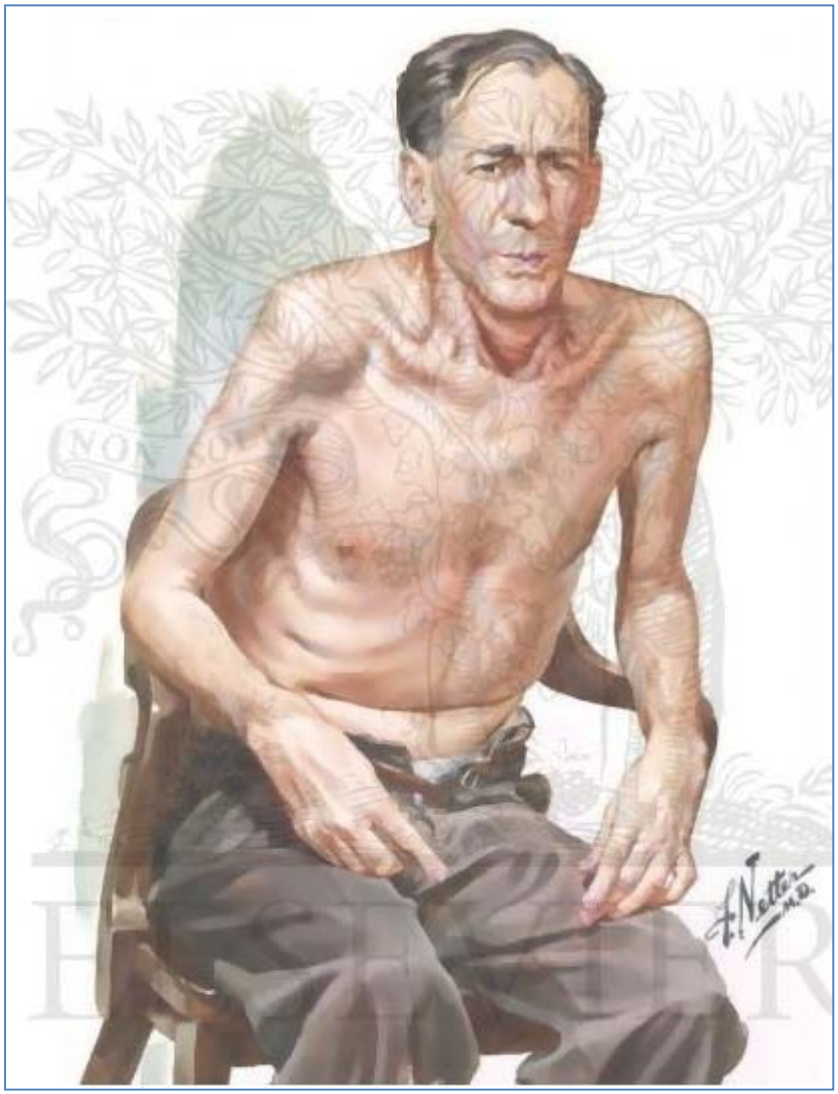


Respirology 2011;16:659

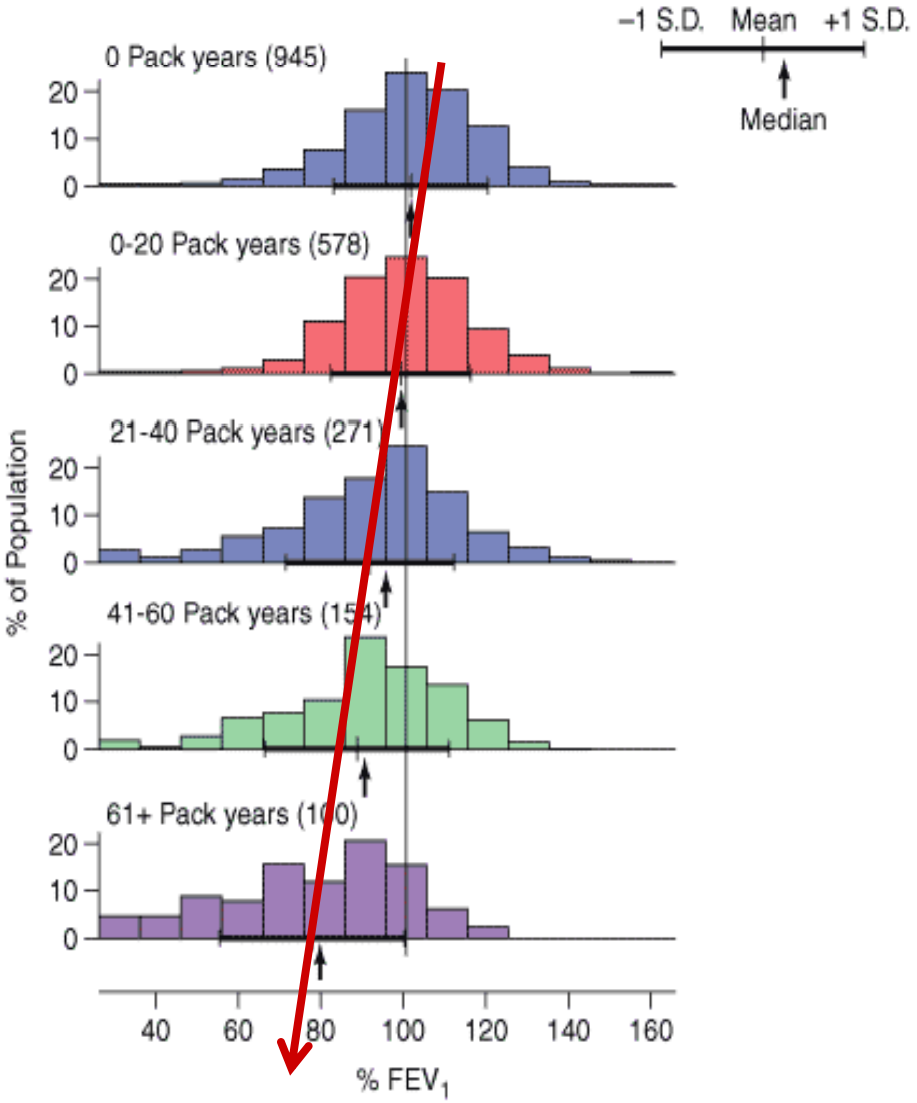
Definition of COPD

- COPD is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients.
- Its pulmonary component is characterized by airflow limitation that is not fully reversible.
- The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.

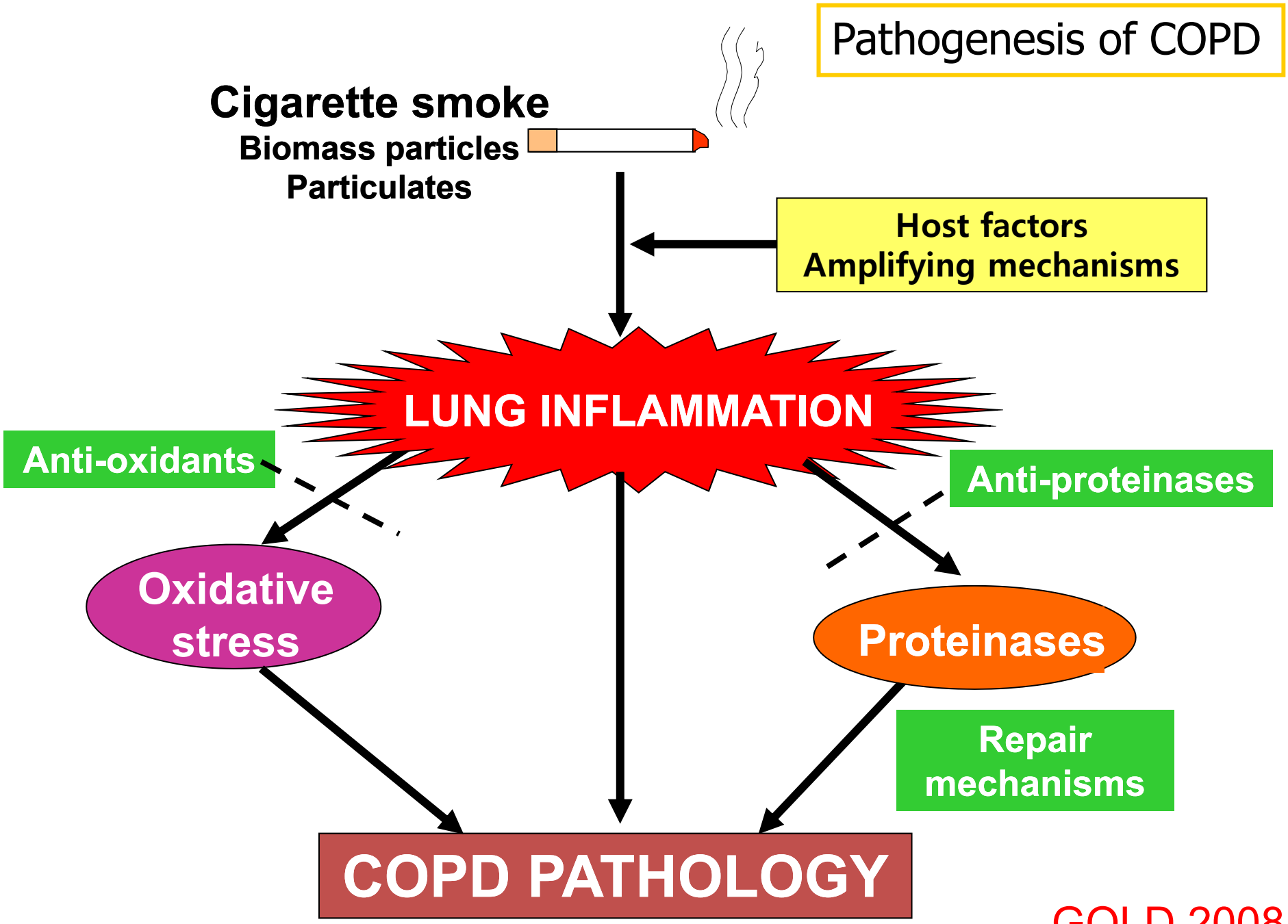
GOLD 2008



Smoking


−1 S.D.
Mean
+1 S.D.
Median
0 Pack years (945)
0-20 Pack years (578)
21-40 Pack years (271)
41-60 Pack years (154)
61+ Pack years (100)
% of Population
20
10
0
40
60
80
100
120
140
160
% FEV1

Pathogenesis of COPD



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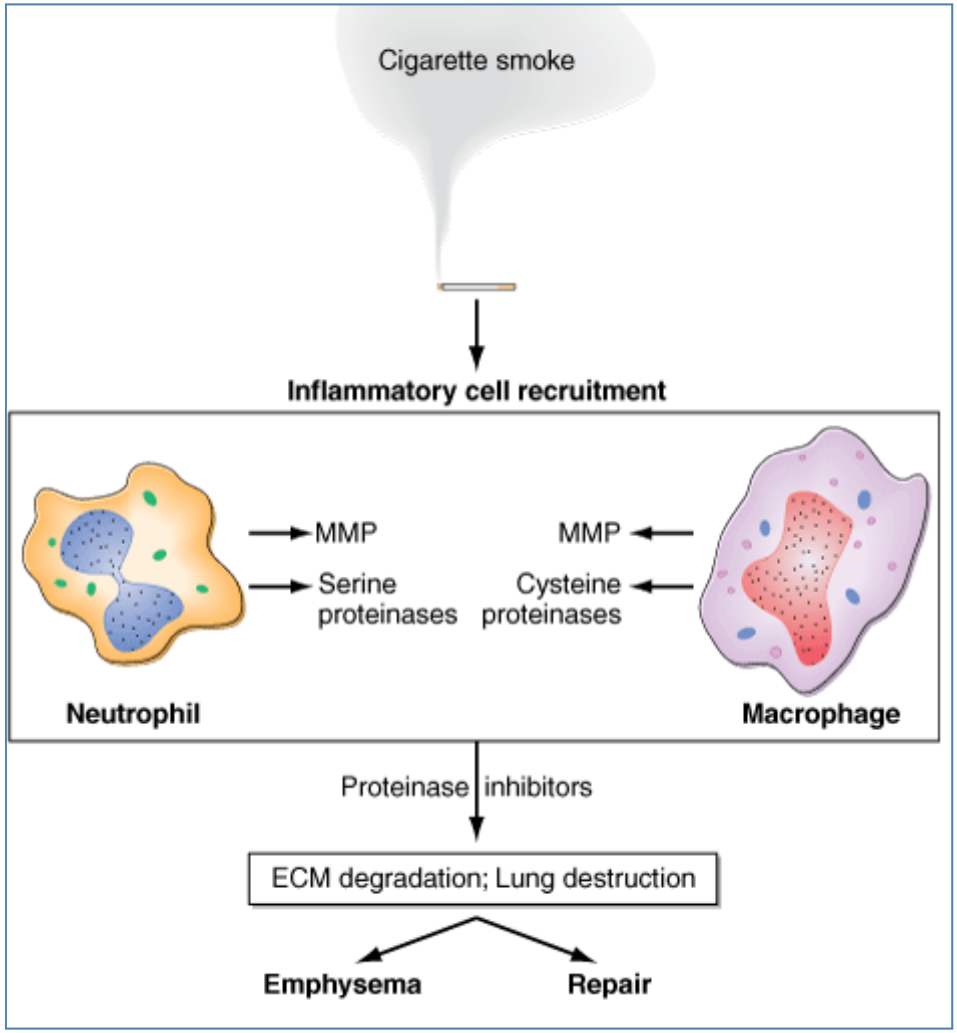
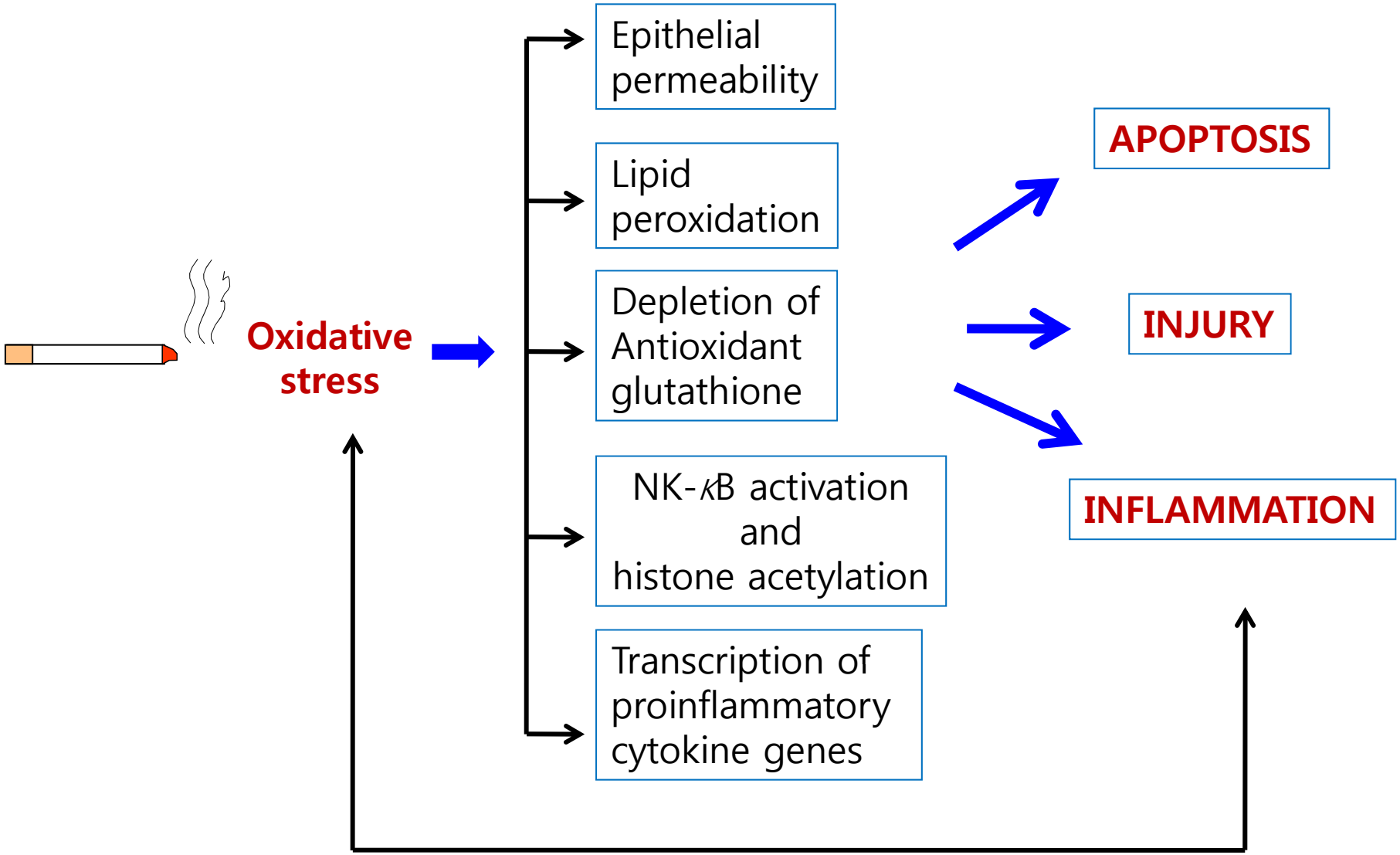
Variation of Inflammatory cells and markers in the bronchial submucosa

	Neutrophils	EOS	Mast Cells	CD68	CD8
Severe COPD	↑ 14	→ 14	→ 14	↑ 14	↓ 23
Mild/moderate COPD	→ 99, 100 ↑ 14	→ 14, 99, 100	→ 14, 99, 100	↑ 99, 100 → 14	↑ 13, 100 → 23, 99
Control smokers	→ 14, 100	→ 14, 100	→ 14, 100	→ 14, 100	↑ 13 → 23, 100
Control nonsmokers	→ 99, 100	→ 99, 100	→ 99, 100	→ 99, 100	→ 13, 99, 100

Proteases and Antiproteases involved in COPD

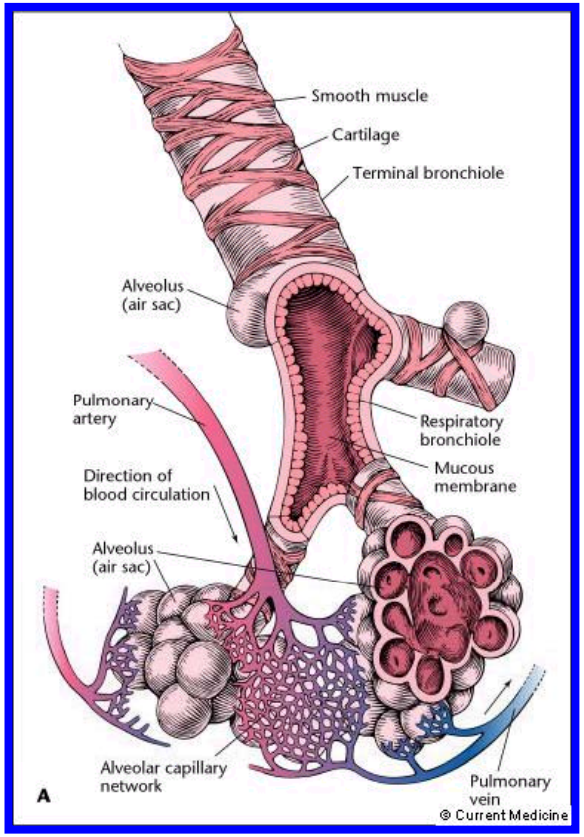


Oxidative Stress-Mediated Lung Injury in COPD

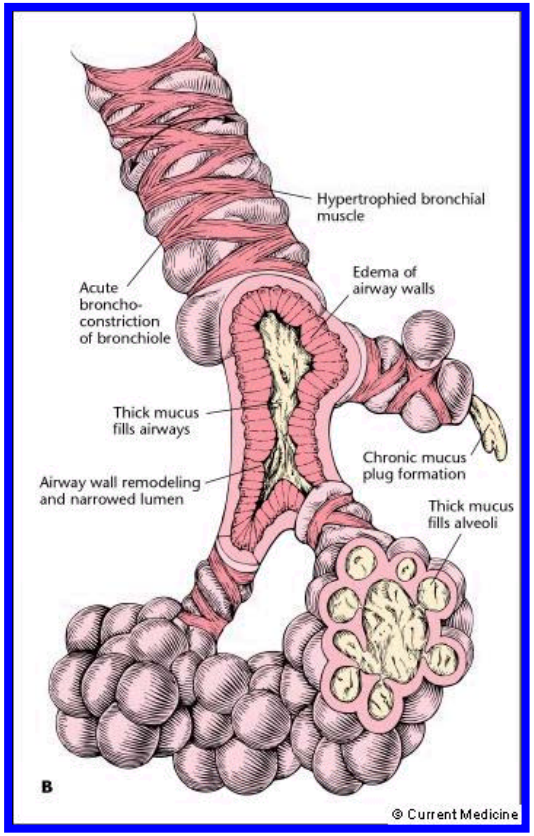


만성 기관지염 (Chronic Bronchitis)

특별한 원인 없이 1년에 기침을 유발할 정도의 과도한 객담이 일년에 3개월 이상 최소한2년 이상 지속될 때: 임상적 진단



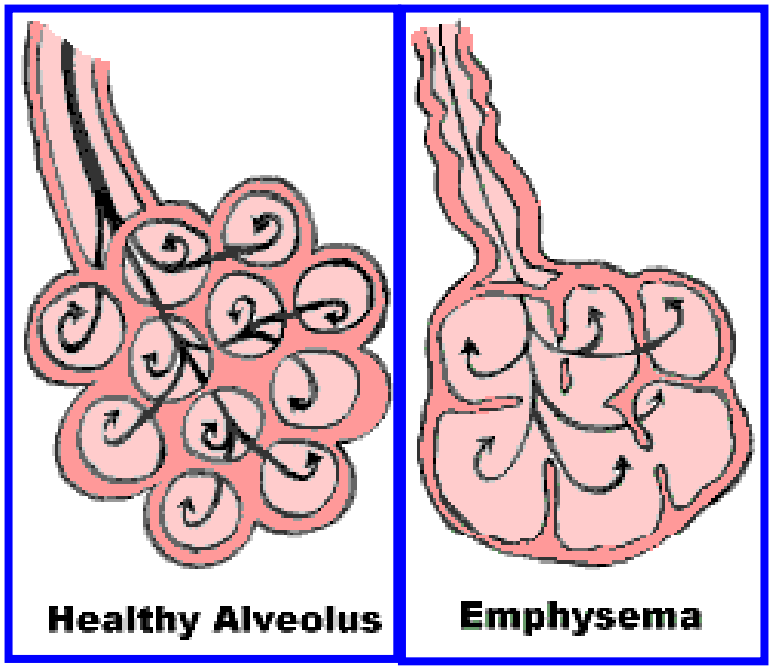
Normal

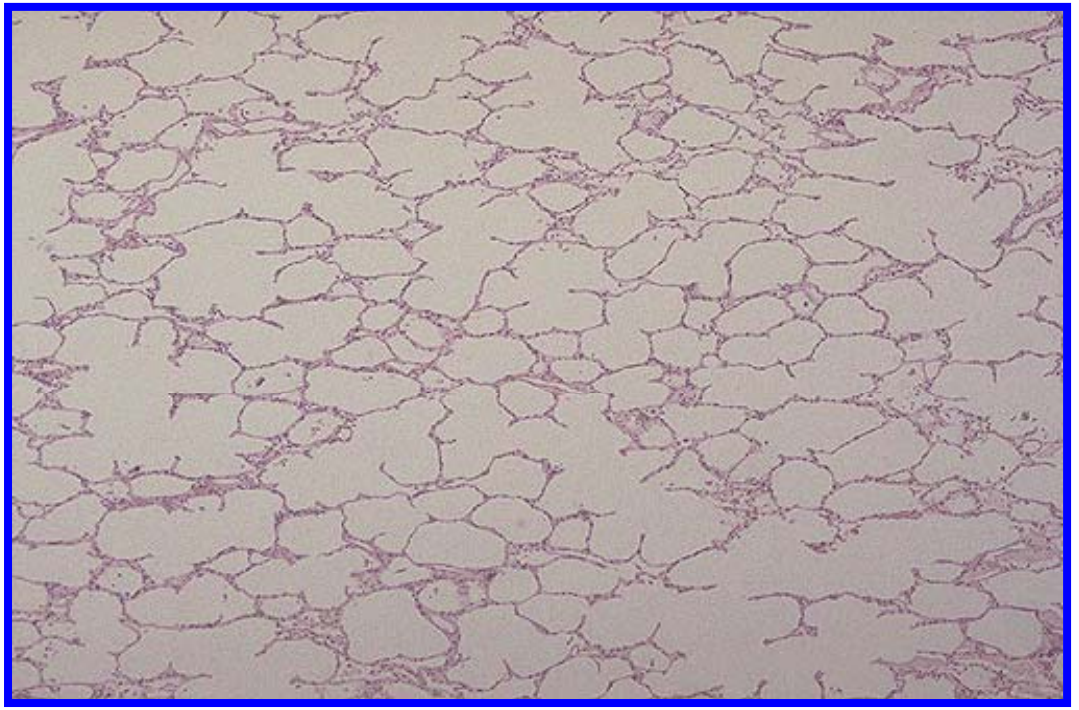


Chronic bronchitis

폐기종 (Emphysema)

종말기관지(terminal bronchiole)이하 폐포 중격 (alveolar septa)의 파괴로 인해 air space가 확장되는 것: 해부학적 진단



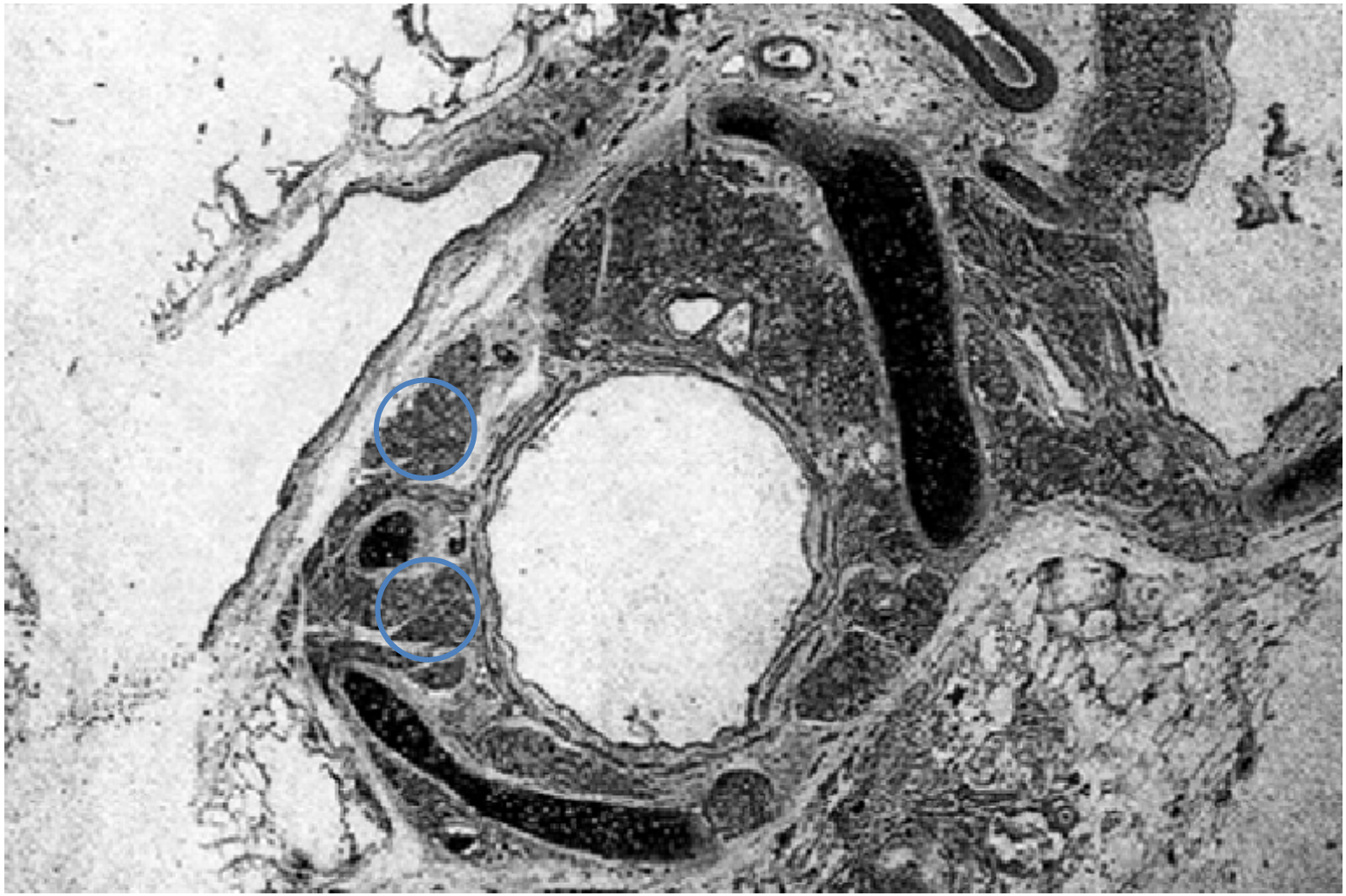


Pathophysiology of COPD

1. Mucus hypersecretion & ciliary dysfunction
2. **Airflow limitation & hyperinflation**
   - inflammation and narrowing of pph airways
3. Gas exchange abnormalities
   - parenchymal destruction of emphysema
4. Pulmonary hypertension & Cor pulmonale
5. Systemic effects

GOLD. AJRCCM 2007;176:532

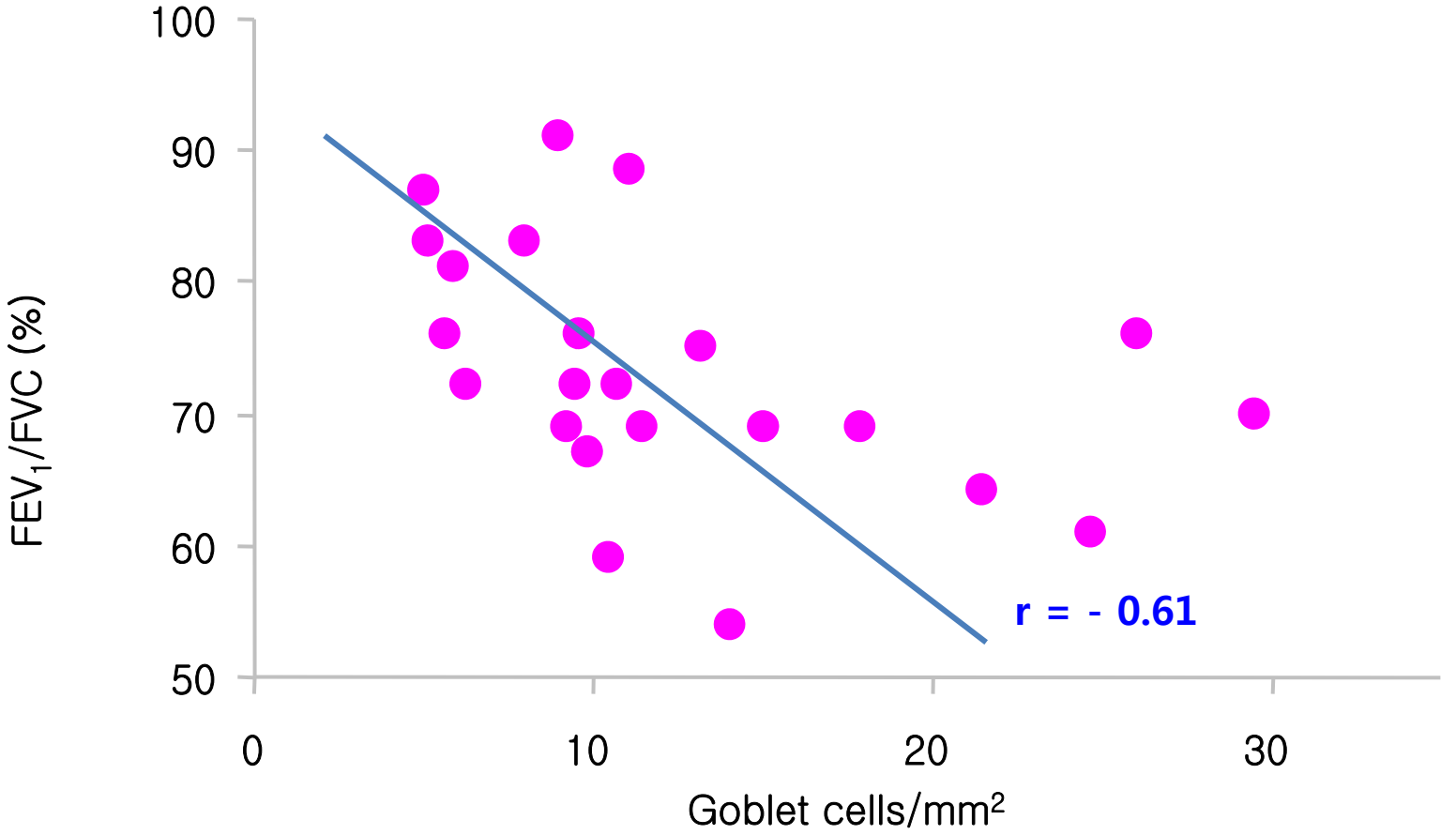
Glandular hypertrophy



Goblet Cell Hyperplasia and Epithelial Inflammation in Peripheral Airways of Smokers with Both Symptoms of Chronic Bronchitis and Chronic Airflow Limitation

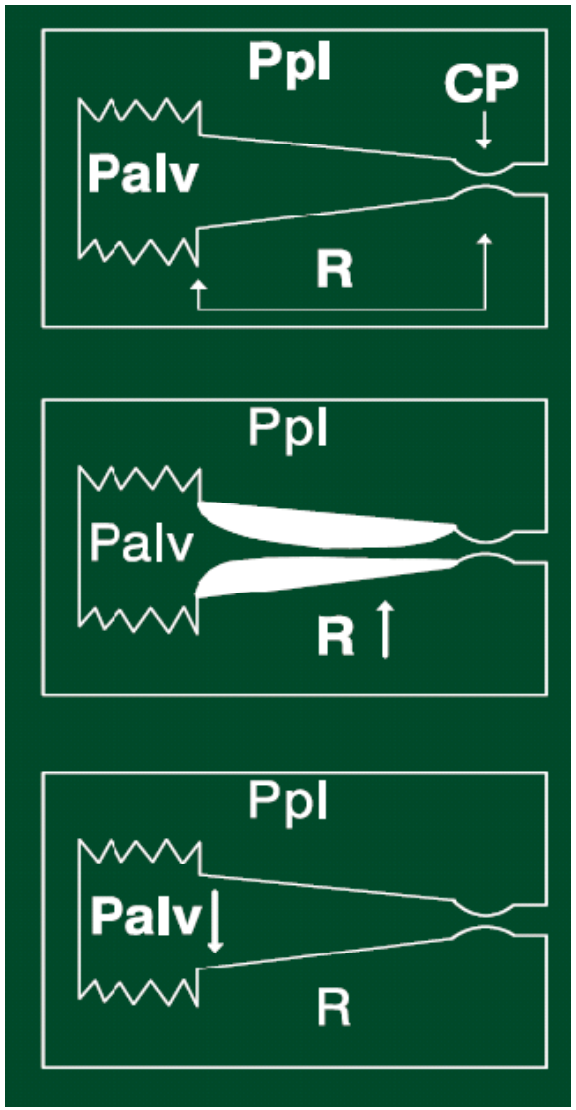
MARINA SAETTA, GRAZIELLA TURATO, SIMONETTA BARALDO, ANNALISA ZANIN,

Lung resection from 10 smoker with CB and chronic airflow limitation, 10 smoker with normal lung function, 9 non-smoker



Am J Respir Crit Care Med 2000;161:1016

Mechanisms of airflow limitation



Pel= Palv - Ppl

V′ = Pel / R

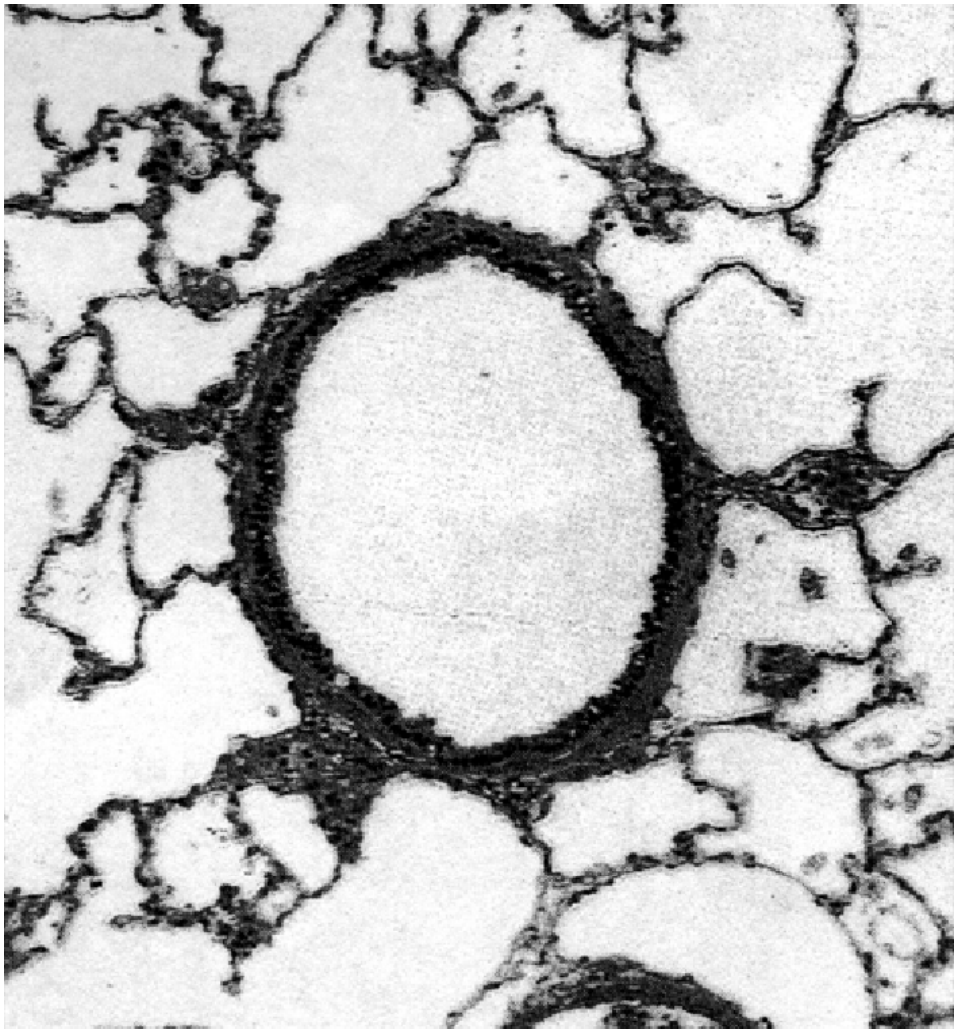
V′ ↓ = Pel / R ↑

Airway dysfunction

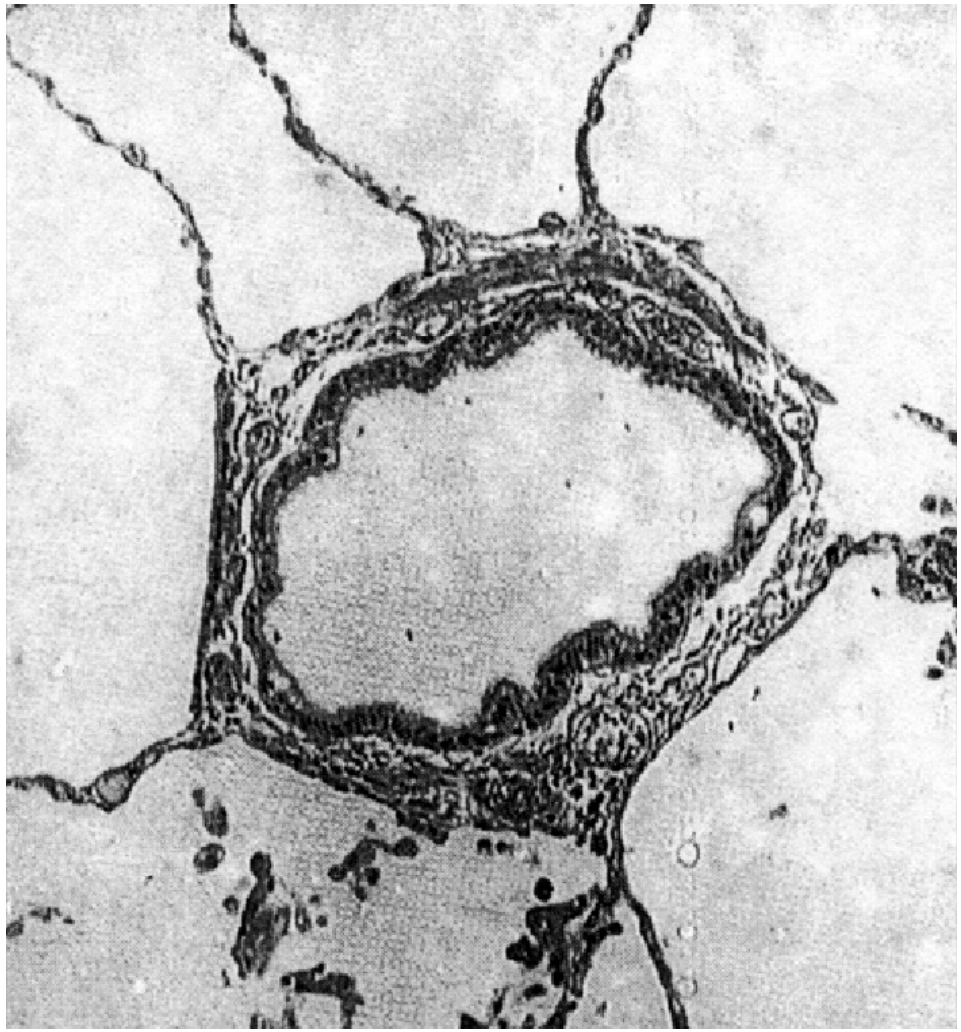
V′ ↓ = Pel ↓ /R

Loss of elastic recoil

Parenchymal tethering

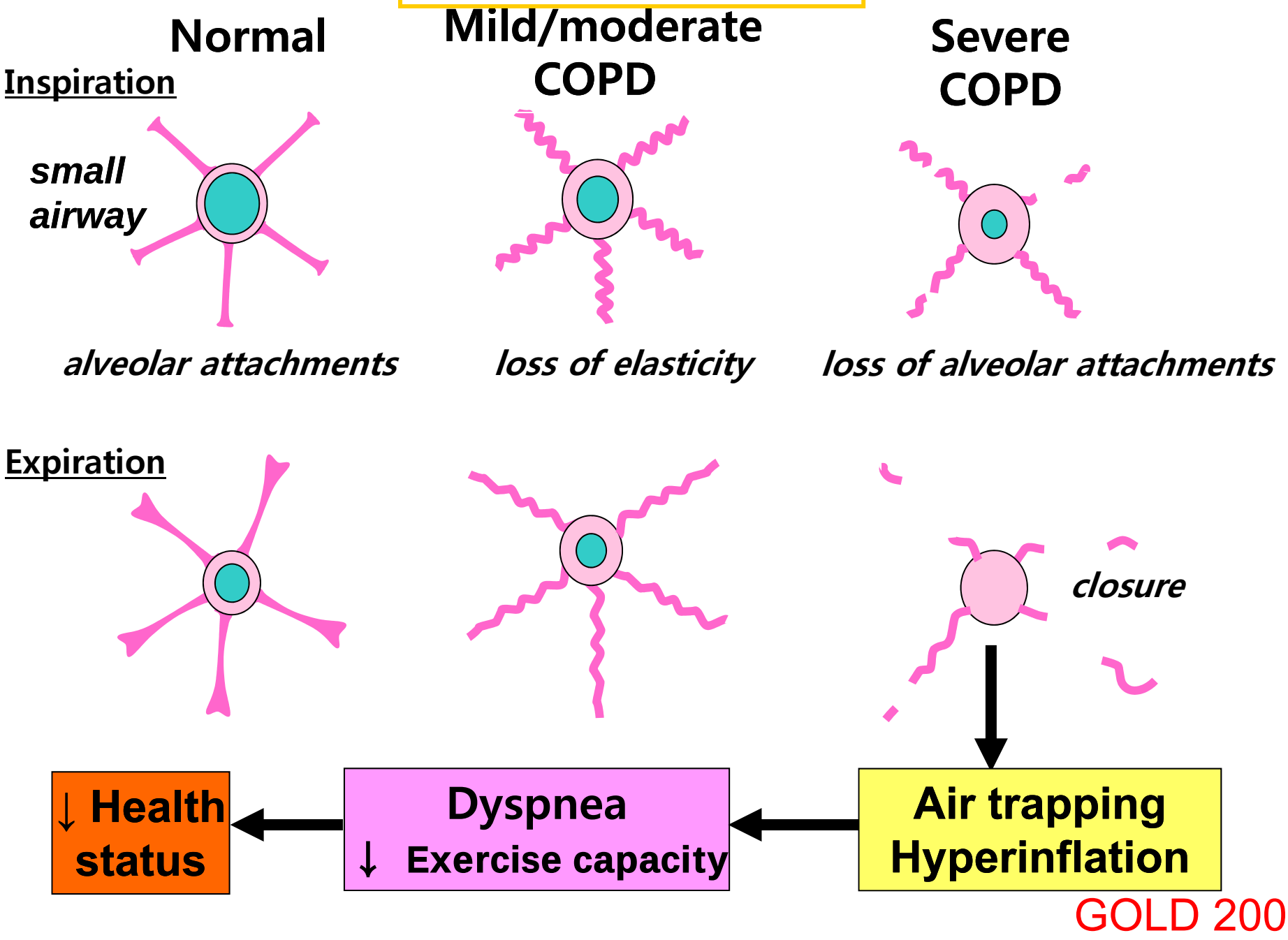


정상



COPD

Air Trapping in COPD



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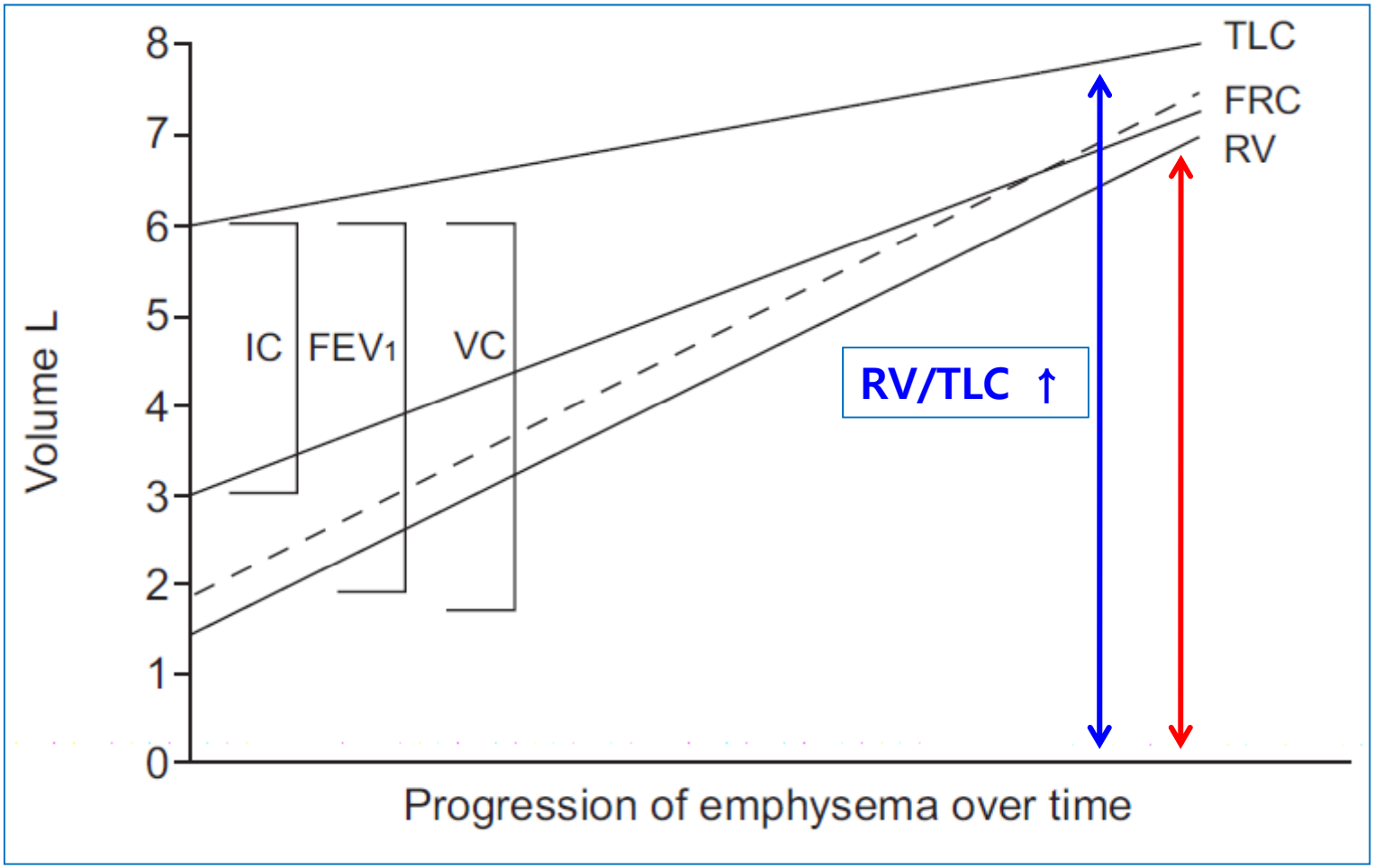
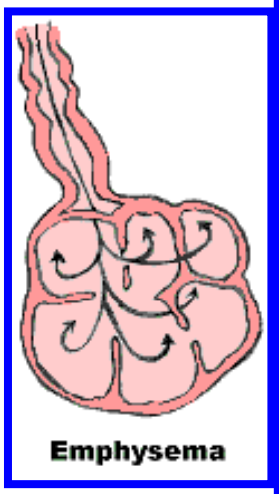
Natural History of COPD

TLC=IC+FRC=VC (IC+ERV)+RV

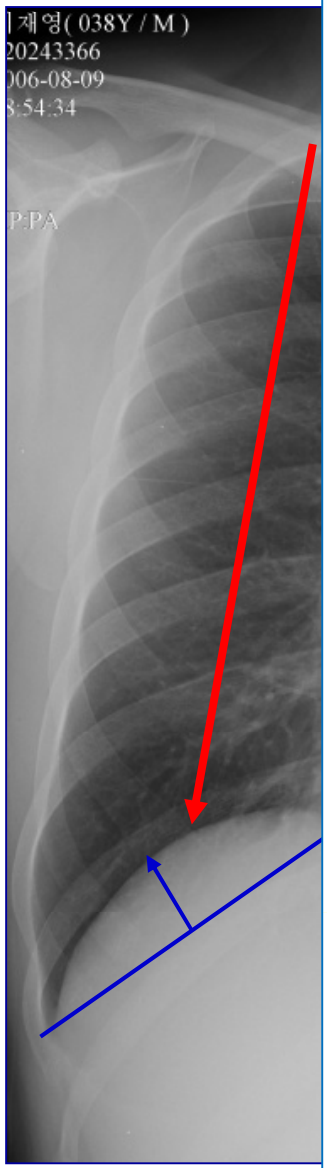


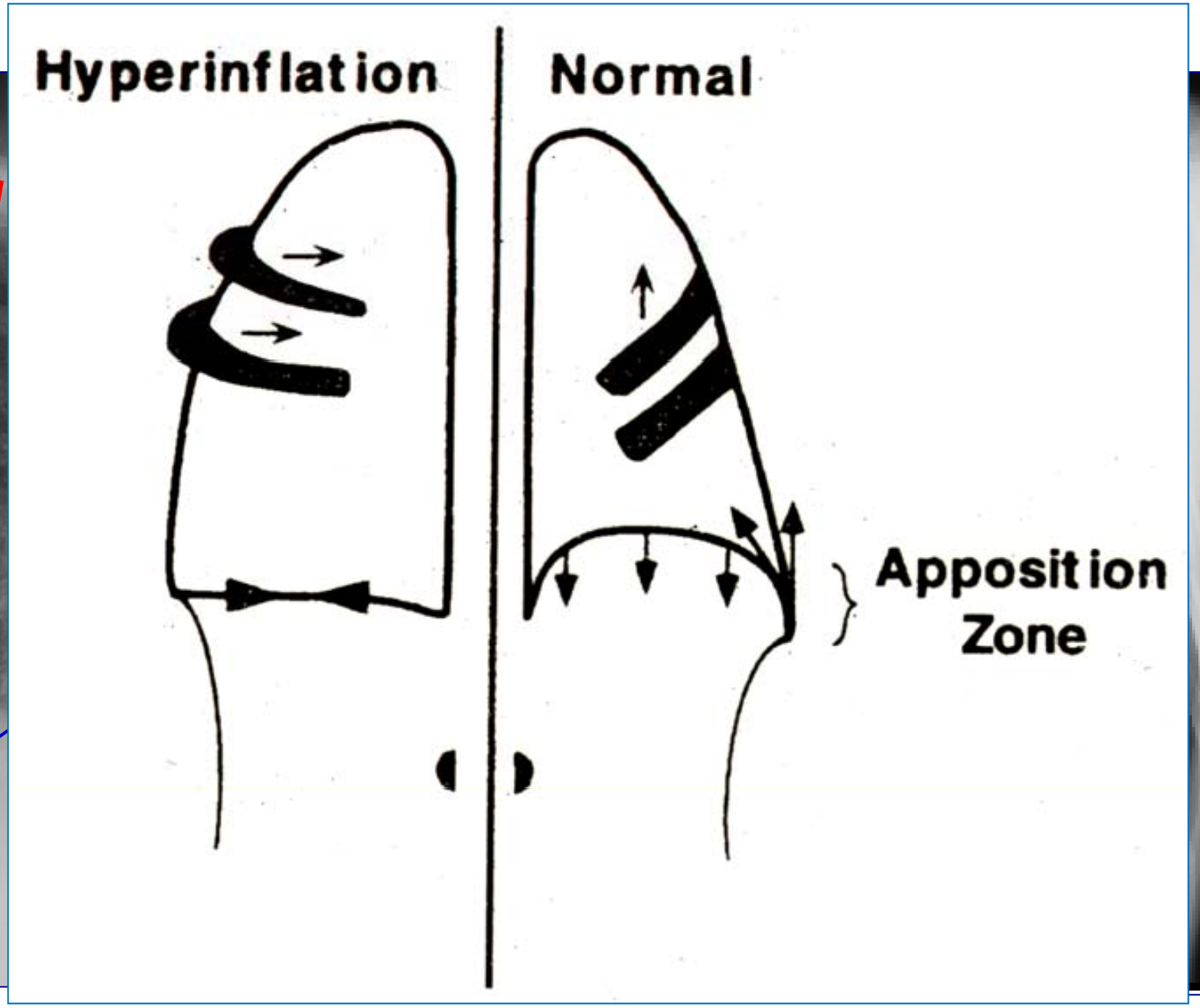
Emphysema

Normal lung

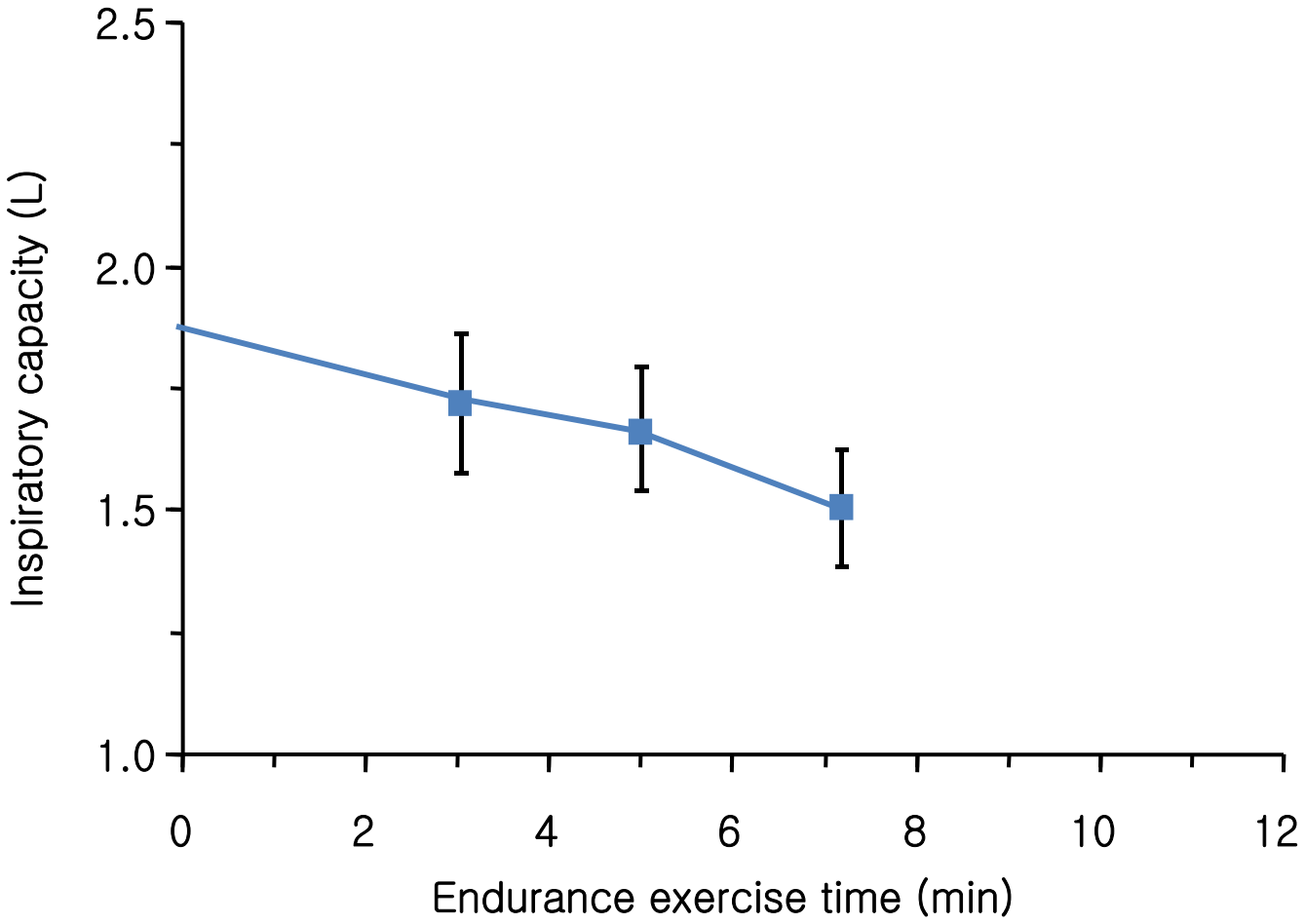


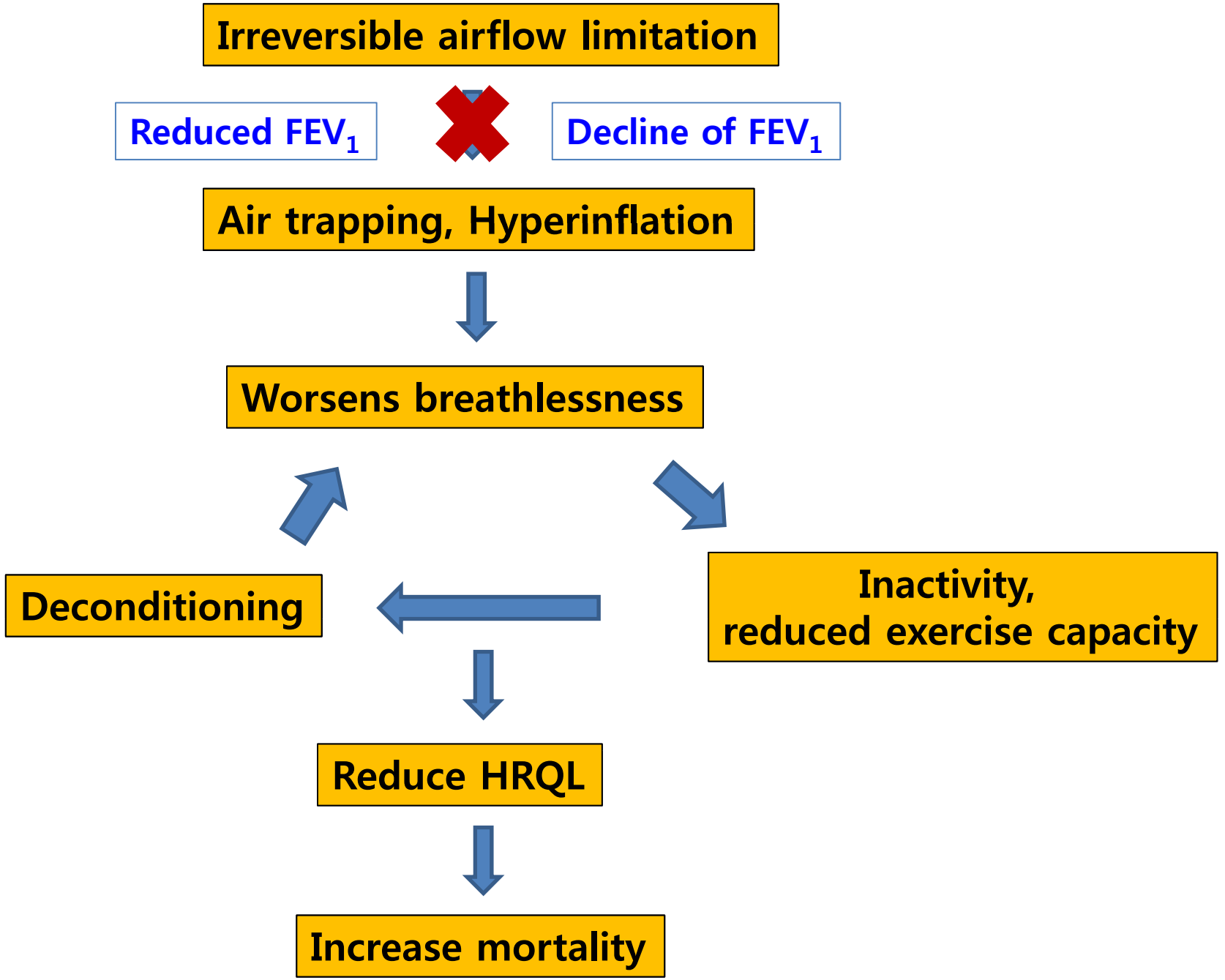
Bullous emphysema


재영(038Y / M)
20243366
006-08-09
8:54:34
P-PA

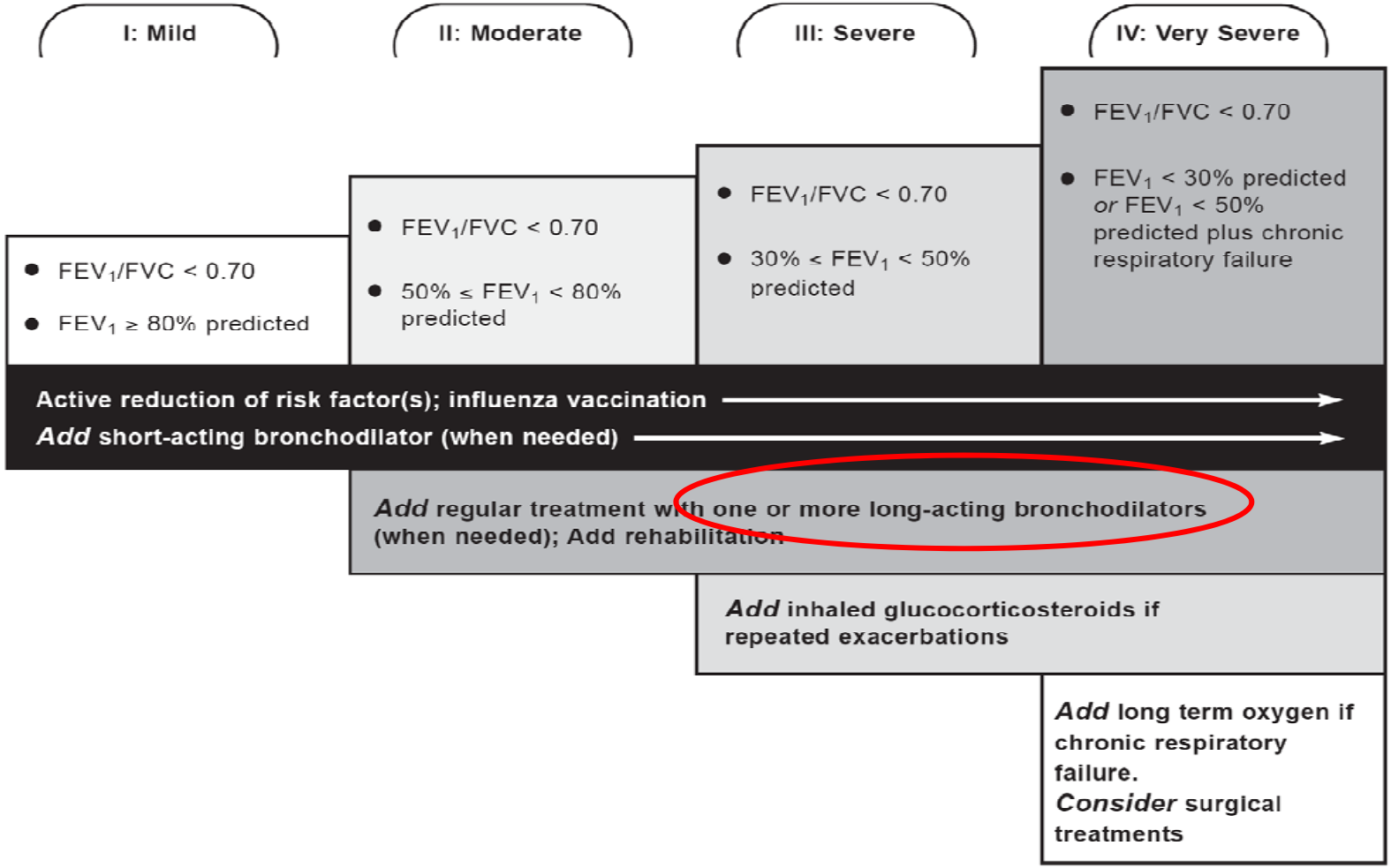

Hyperinflation
Normal
Apposition
Zone

Decrease in inspiratory capacity with exercise in COPD



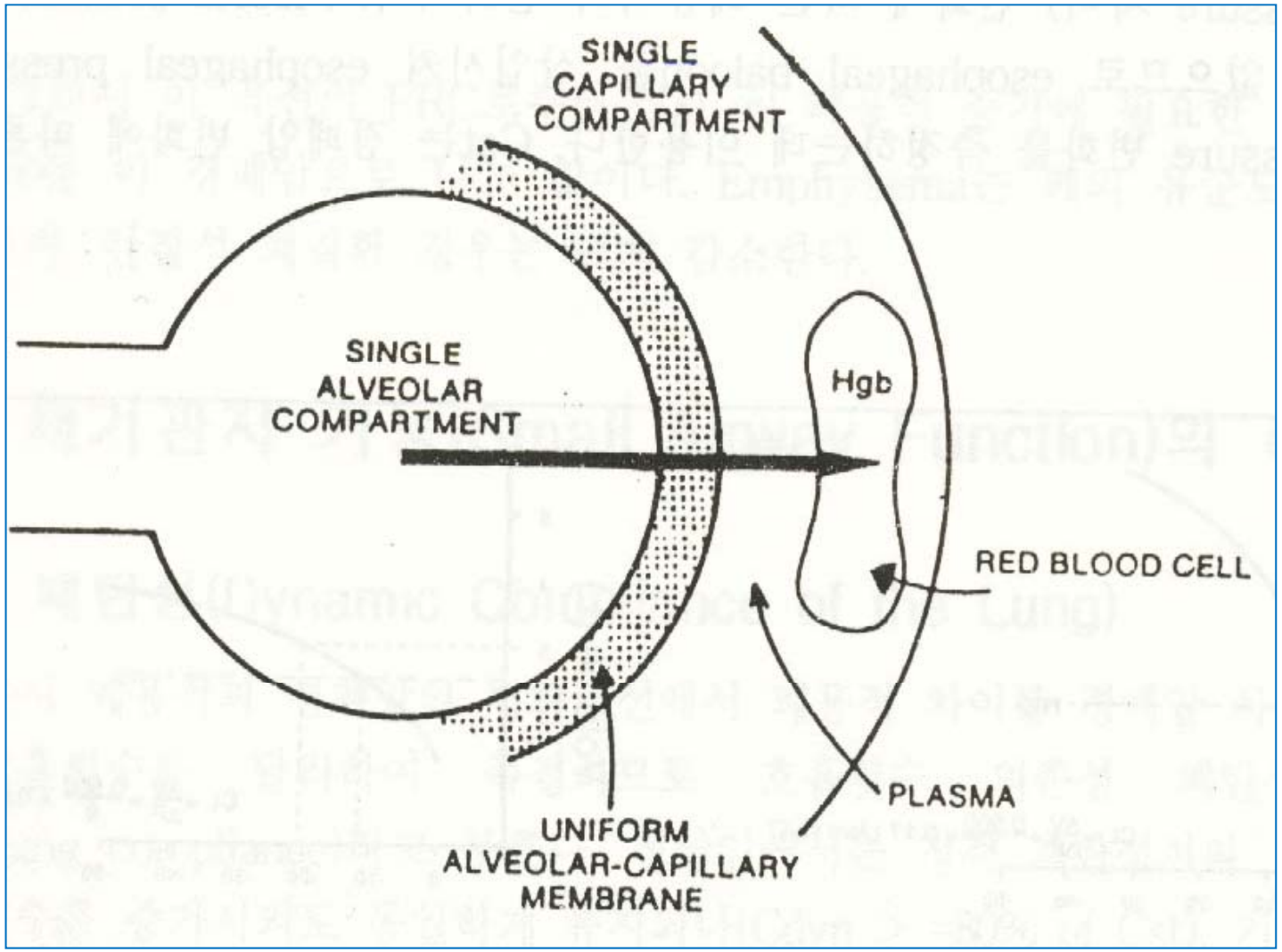

Irreversible airflow limitation
Reduced FEV_1
Decline of FEV_1
Air trapping, Hyperinflation
Worsens breathlessness
Inactivity,
reduced exercise capacity
Deconditioning
Reduce HRQL
Increase mortality

Current treatment guidelines



GOLD 2009

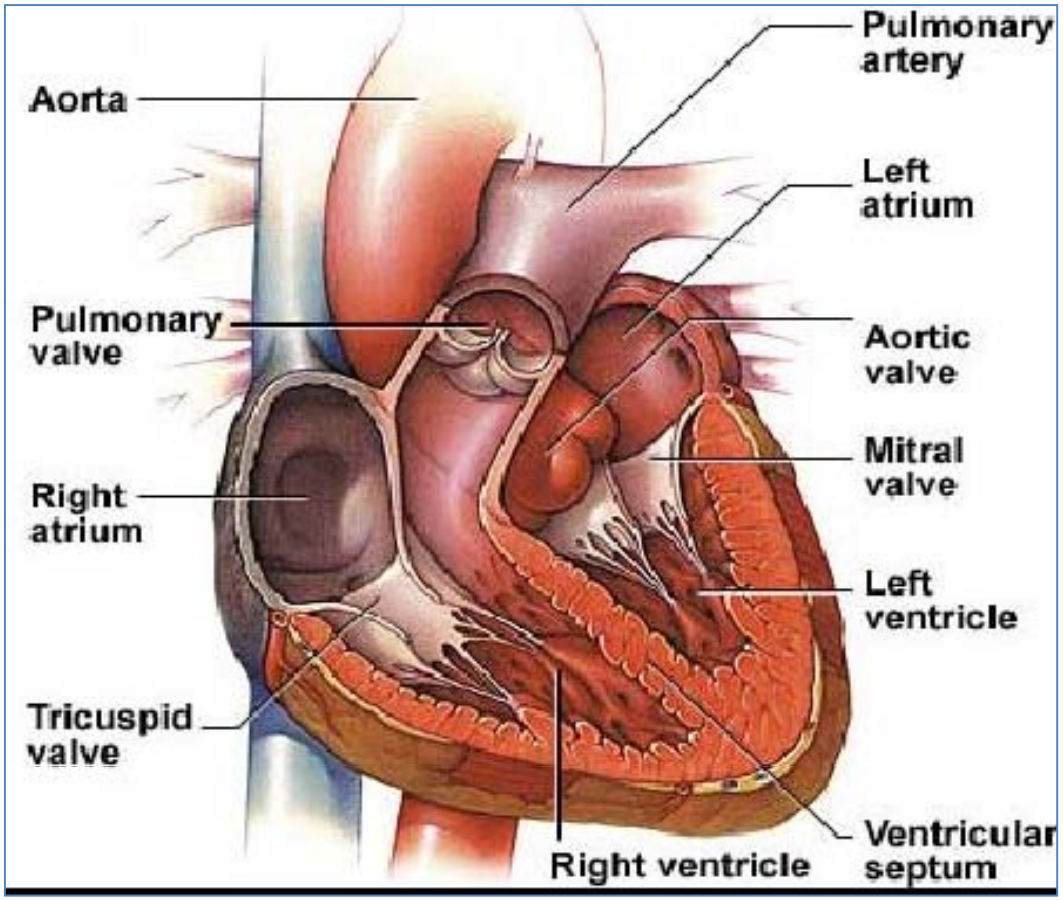
Diffusion Lung Capacity (DLco)



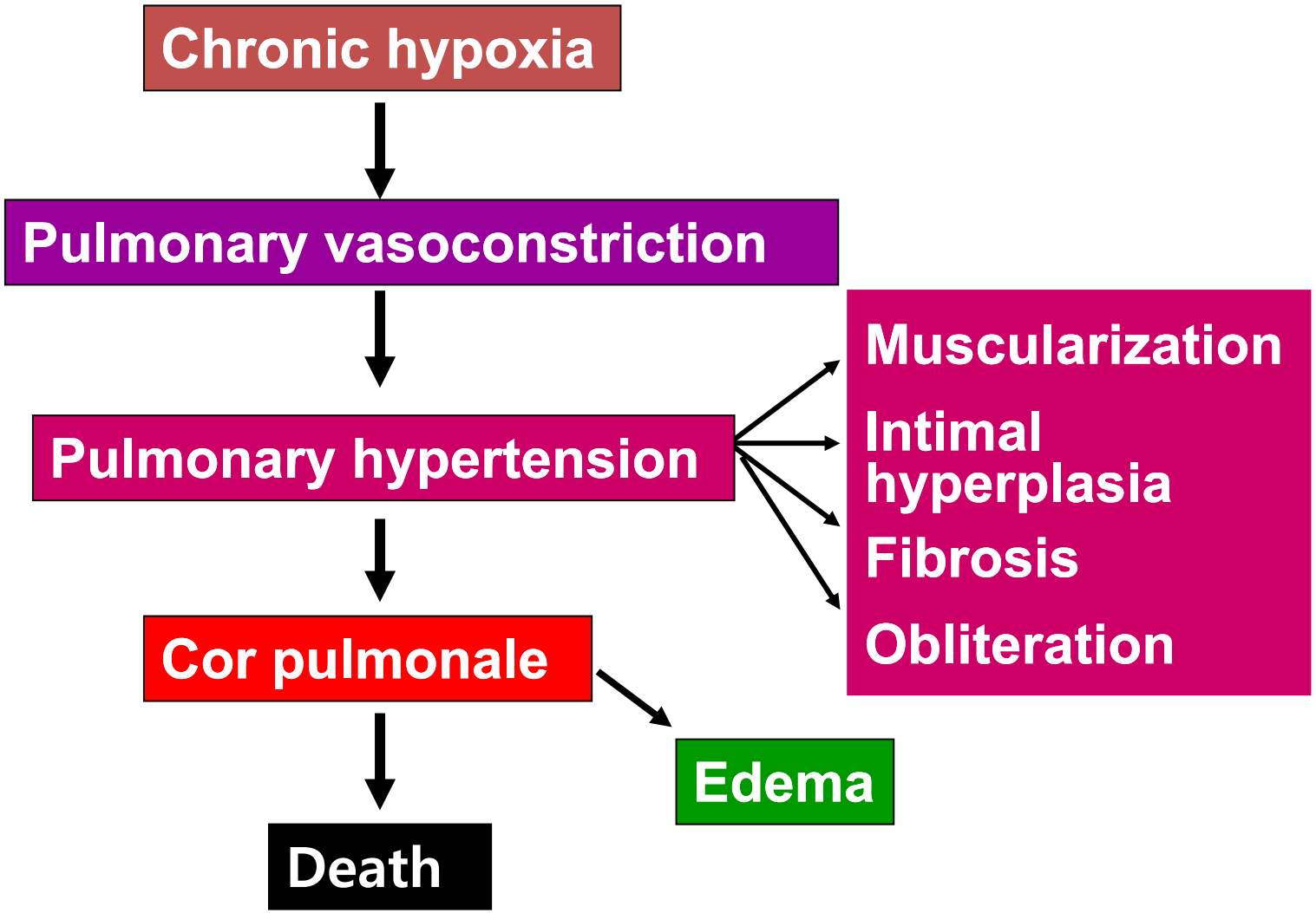
Gas Exchange

- The PaO_2 usually remains near normal until the FEV_1<50% of pred.
- The elevation of $PaCO_2$ is not expected until the FEV_1<25% of pred.
- Nonuniform ventilation and V/Q mismatching.-Ppr airway obstruction
- NO washout is delayed due to regions that are poorly ventilated.
- Emphysema: normal to dec PaO_2
- Chronic bronchitis: dec PaO_2

Pulmonary Hypertension in COPD



Pulmonary Hypertension in COPD



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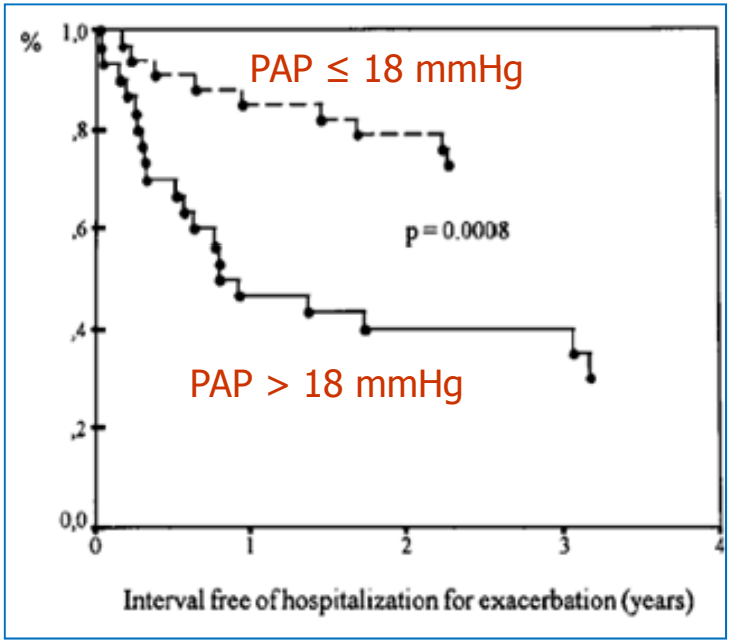
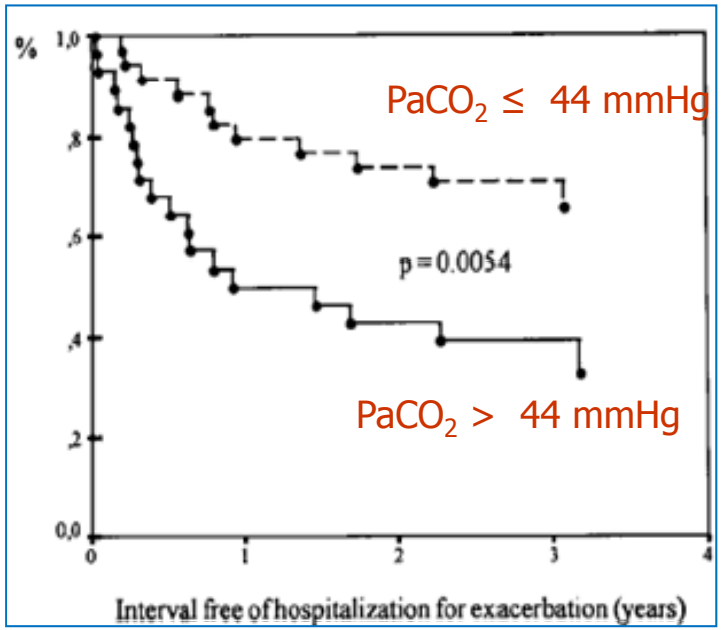
Common feature of PH in COPD

- **Exact incidence or prevalence is unknown**
- **Generally mild PH & slow progression**
  - 62/175 (35%) mod to severe COPD (mean FEV_1= 40.2%)
    mPAP = 19.8 ± 7.6 mmHg (*Weitzenblum et al. Thorax 1981*)
  - 109/120 (91%) in NETT (mean FEV_1= 27%) for LVRS
    mPAP = 26.3 ± 5.2 mmHg (Scharf et al. AJRCCM 2002)
  - 108/215 (50%) severe COPD (mean FEV_1= 24.3%) for LT or LVRS mPAP = 26.9 ± 8.9 mmHg (*Thabut et al. Chest 2005*)
  - average rate of increase in PAP is 0.4 mmHg/yr
- **Prognostic impact**
  - reduced survival and increased exacerbation

Predictive Factors of Hospitalization for Acute Exacerbation in a Series of 64 Patients with Chronic Obstructive Pulmonary Disease





Adverse prognostic factor

- mean PAP > 18 mmHg ← Independent
- pCO_2 > 44 mmHg ← predictors
- pO_2 ≤ 65 mmHg
- BMI ≤ 20 kg/m2
- 6-min-walk ≤ 367 m

AJRCCM 1999;159:158

Distinctive features and worse prognosis of out-of-proportion pul HTN

- Distinctive features of 11 patients with mPAP ≥ 40mmHg
  - marked dyspnea (grade 4 or 5)
  - profound hypoxemia (median: 46mmHg)
  - hypocapnia (median: 32mmHg)
  - moderate obstruction (median FEV_1: 50% predicted)
  - very low DLco
  - significantly worse survival

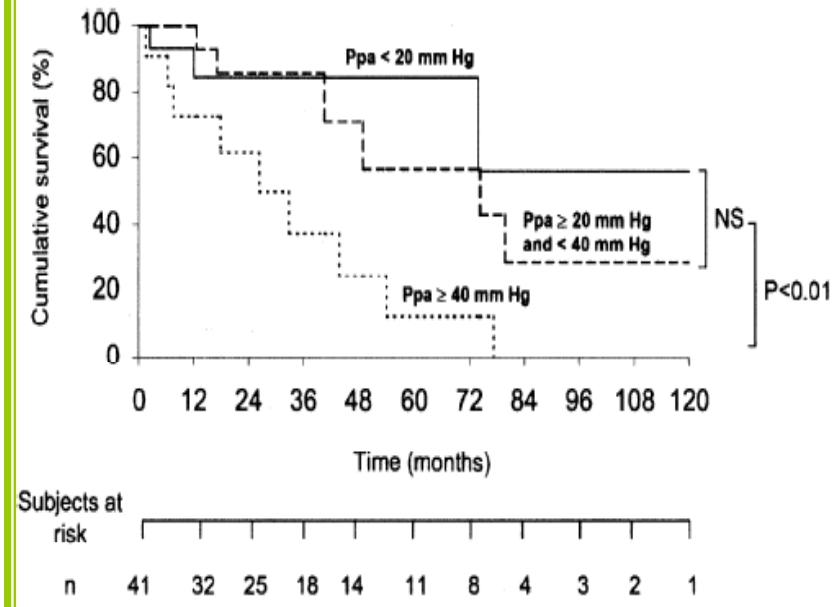


Figure 3. Survival of patients with COPD and no other detectable cause of pulmonary hypertension. The probability of survival of each group according to the Ppa was estimated using the Kaplan-Meier method and compared using the log-rank test. Eleven patients with a Ppa of 40 mm Hg or greater, 16 patients with Ppa of less than 40 mm Hg and 20 mm Hg or greater, and 14 patients with Ppa less than 20 mm Hg were at risk at baseline. NS = not significant.

AJRCCM. 2005;172; 189

Working group recommendation summary
- Dx and assessment of PH in chronic lung dis -

- Majority of COPD-PH is mild to moderate
- Severe or out-of-proportion PH in COPD exhibit distinctive clinical pattern with reduced survival
- The underlying lung disease should be optimally treated according to the respective guidelines, including the use of long-term oxygen therapy in patients with chronic hypoxemia (E/A)
- There is no sufficient evidence that the drugs currently used for PAH are safe and effective in patients with PH associated with chronic lung disease (E/A)

JACC 2009;54; S85

Systemic Feature of COPD

- Cachexia: loss of fat free mass
- Skeletal muscle wasting: apoptosis, disuse atrophy
- Osteoporosis
- Depression
- Normochromic normocytic anemia
- Increased risk of CV disease: associated with increased CRP

Pathophysiology of COPD

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