Lung cancer: A comorbidity of COPD

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박 혜 윤

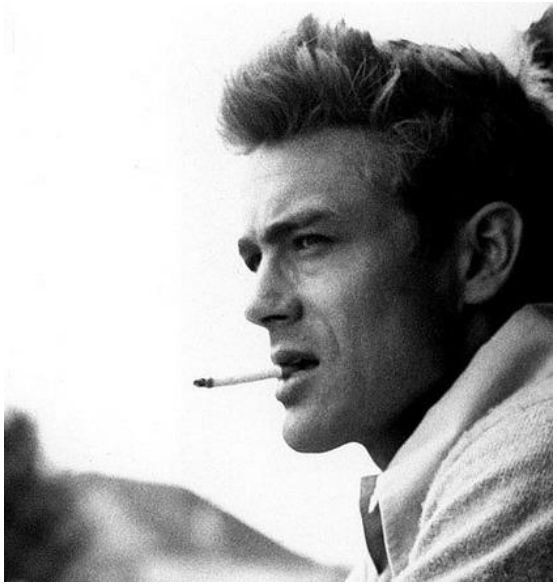
2011, COPD 종합평가

- 폐기능
- 증상
- 급성 악화
- 동반 질환

→ 치료 결정

Lung Health Study: AIM

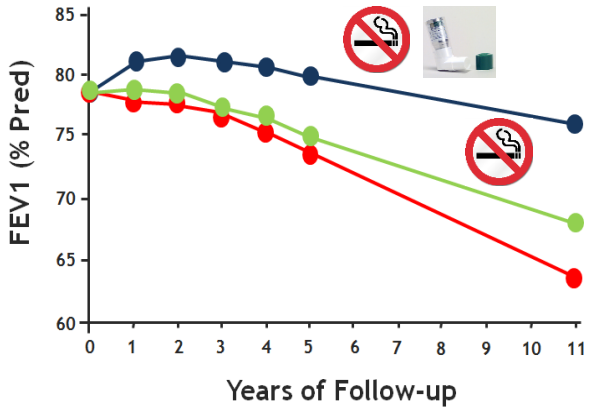
Mild to Moderate COPD Smokers (n=5887)



SMOKING INTERVENTION

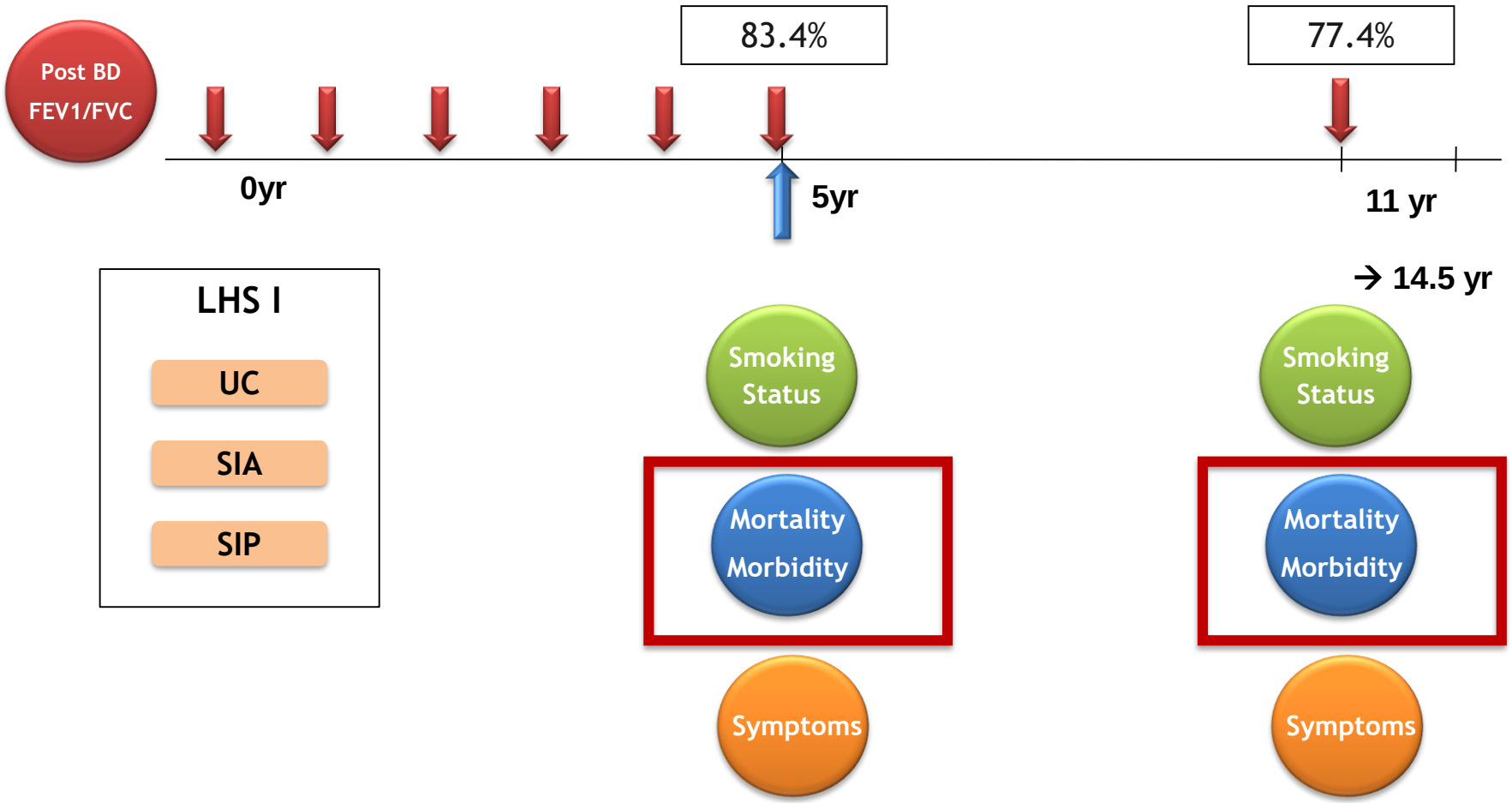
INHALED BRONCHODILATOR

Lung Function Decline?



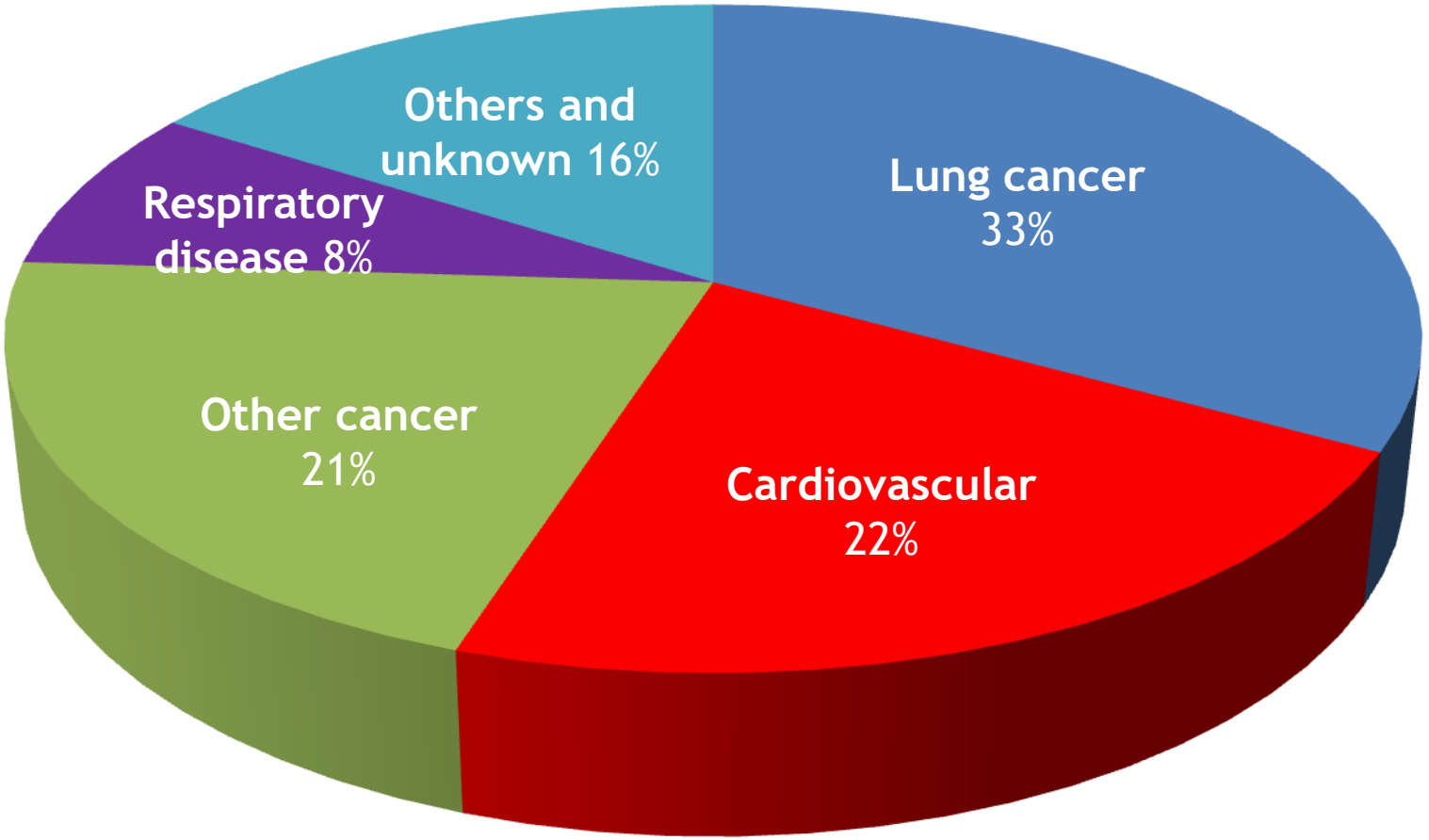
National Heart, Lung, and Blood Institute

LHS III



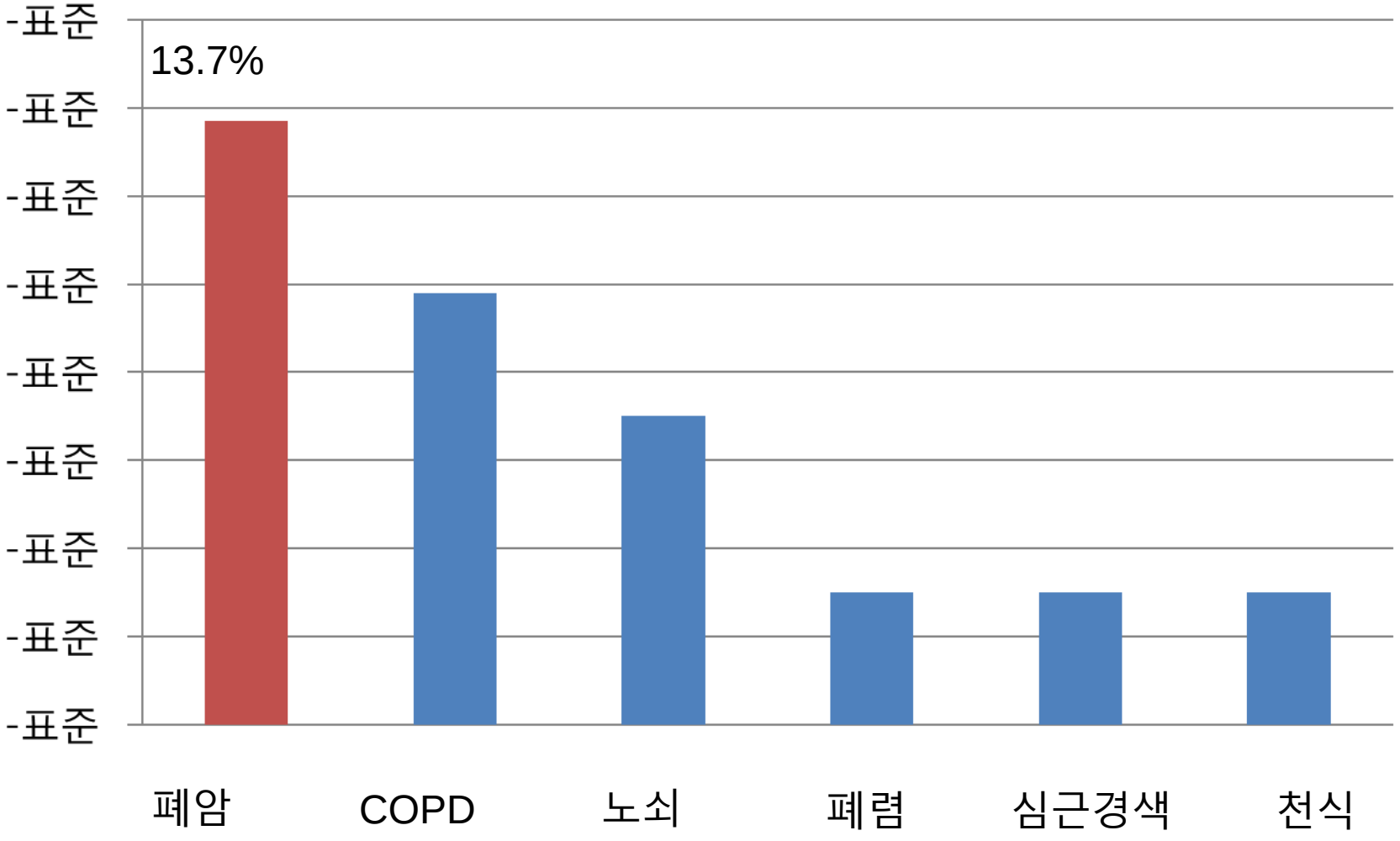
Causes of death in mild-to-moderate COPD

12.4% mortality after up to 14.5 years of follow-up



Anthonisen et al. Ann Intern Med 2005;142:233-9

Causes of death in Korean COPD (건강보험공단)



COPD & Lung Cancer

위험 인자

예후 인자

폐암 진단 시 COPD와 치료 효과

COPD & Lung Cancer

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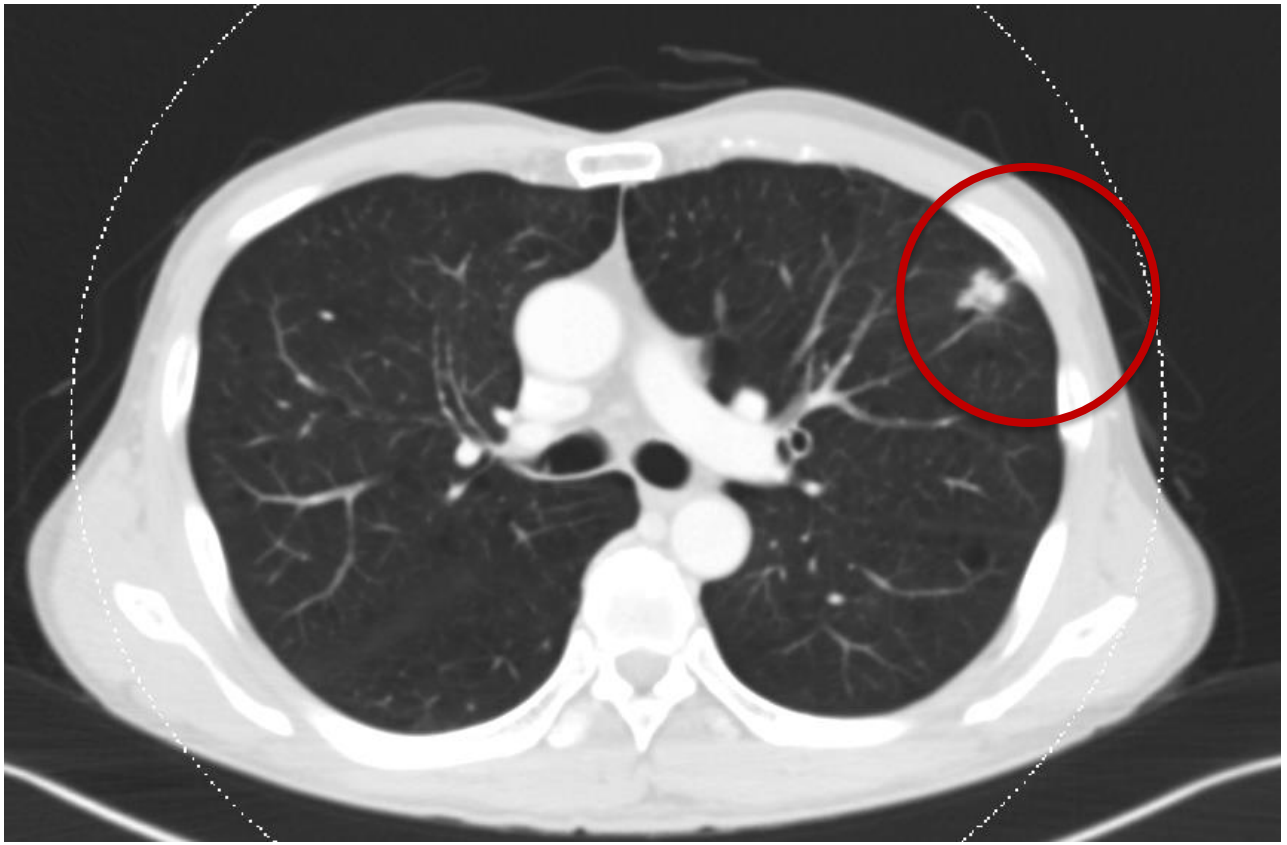
예후 인자

M/65

Ex-smoker, 150 pack-yr, quit smoking 7yrs ago
mMRC Gr II
post-BD FEV_1 2.50L, 77%

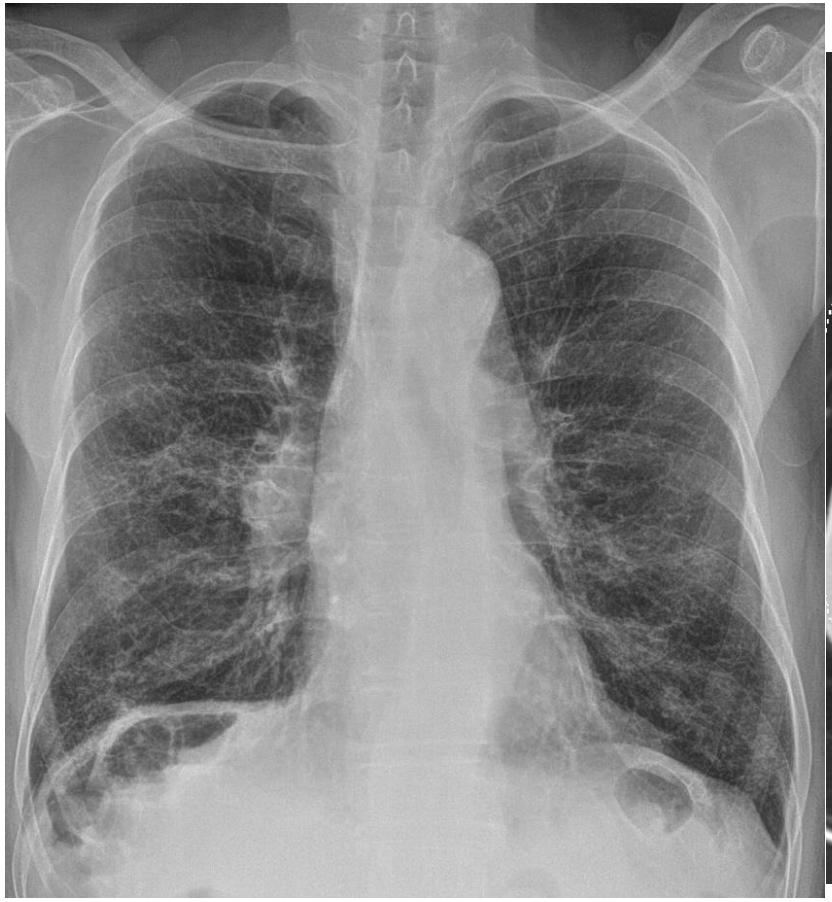
Adenocarcinoma

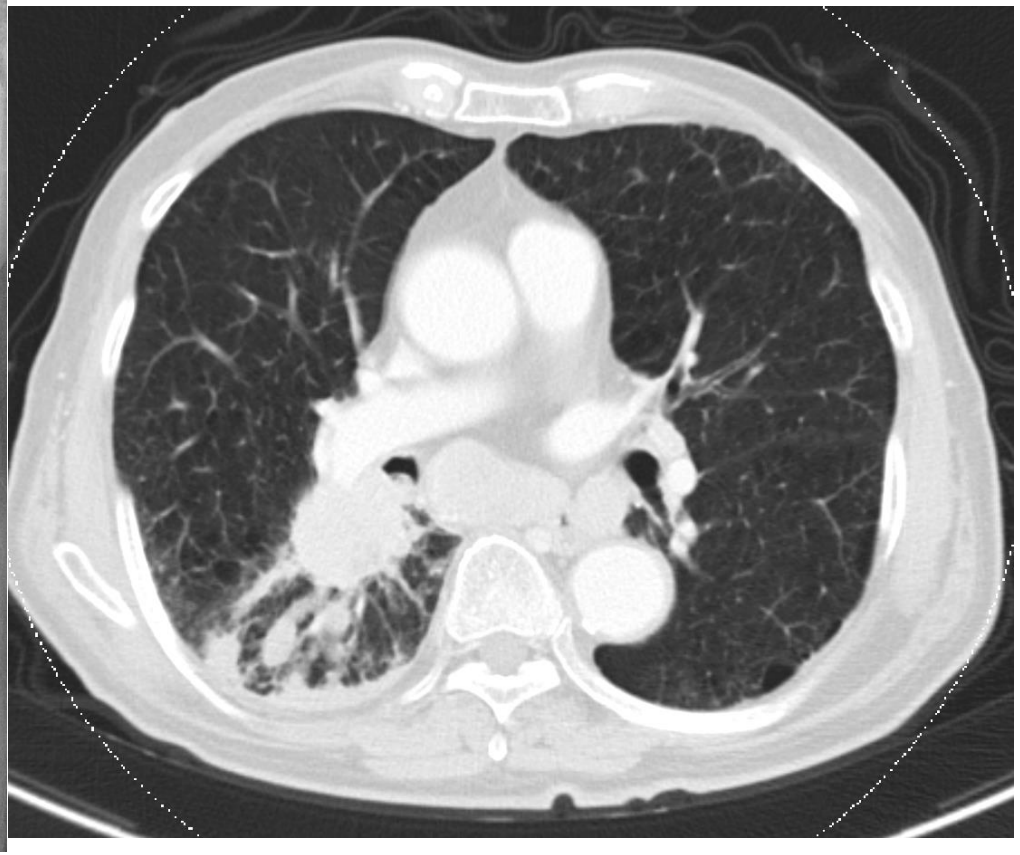


M/83

current-smoker, 50 pack-yr, mMRC Gr II
post-BD FEV_1 1.70L, 68%

Squamous CA





Diagnosis of lung cancer in COPD

- Assessment of concomitant chronic diseases
  - The existence of COPD may actually increase the risk for other diseases; this is particularly striking for COPD and lung cancer.

2017 GOLD guideline

Up to 5-fold higher risk of lung cancer than that of smokers without COPD

COPD ⇄ **Lung cancer**

6-fold increased prevalence in COPD than matched smokers in newly diagnosed lung cancer cases

Tockman et al. Ann Intern Med 1987; 106: 512-518.
Young et al.Eur Respir J 2009; 34: 380-386.

Airflow obstruction and Emphysema

Airflow obstruction

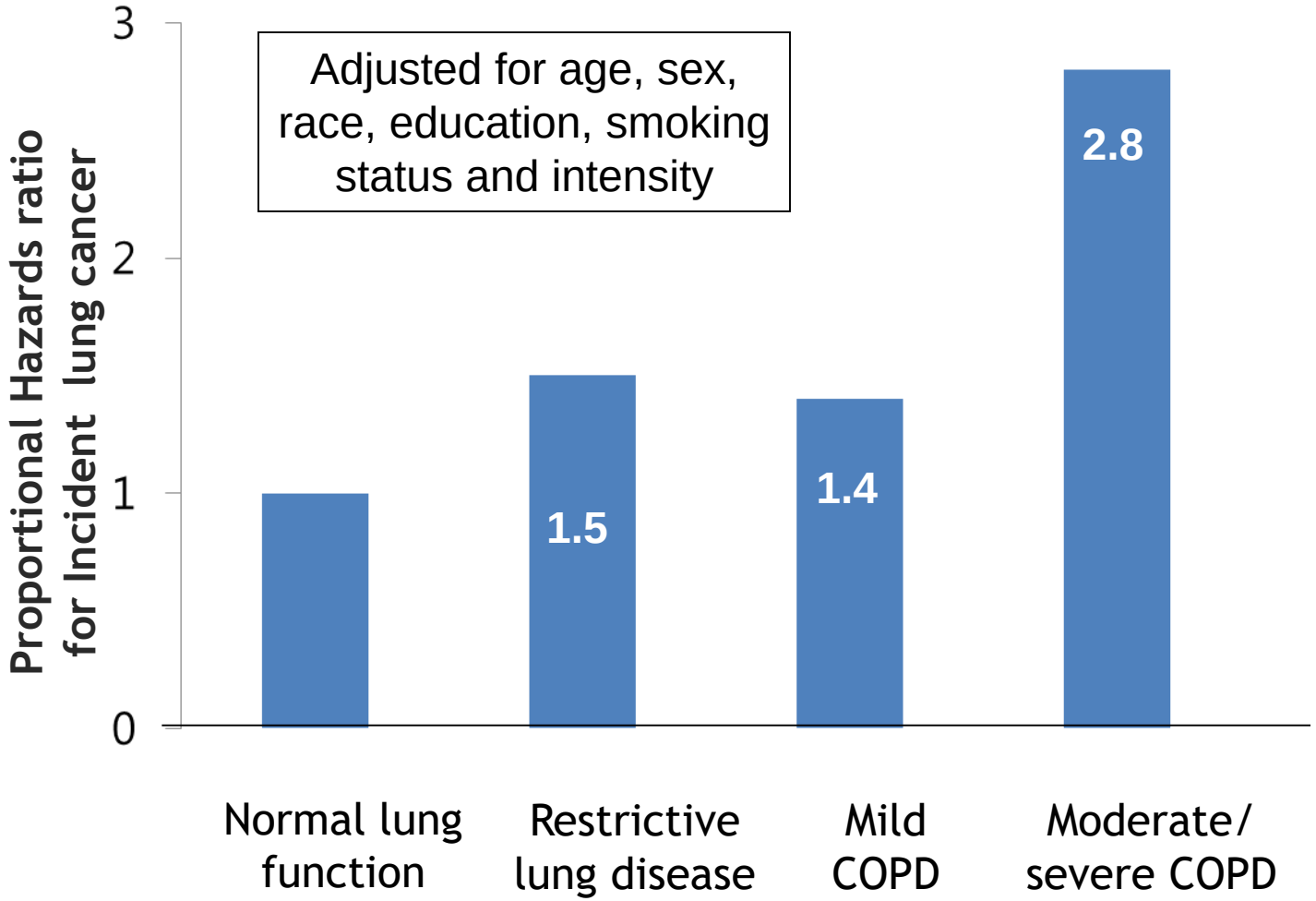
$FEV_1/FVC < 70\%$
FEV_1

Emphysema

DLco or CT scan

Degree of airflow limitation

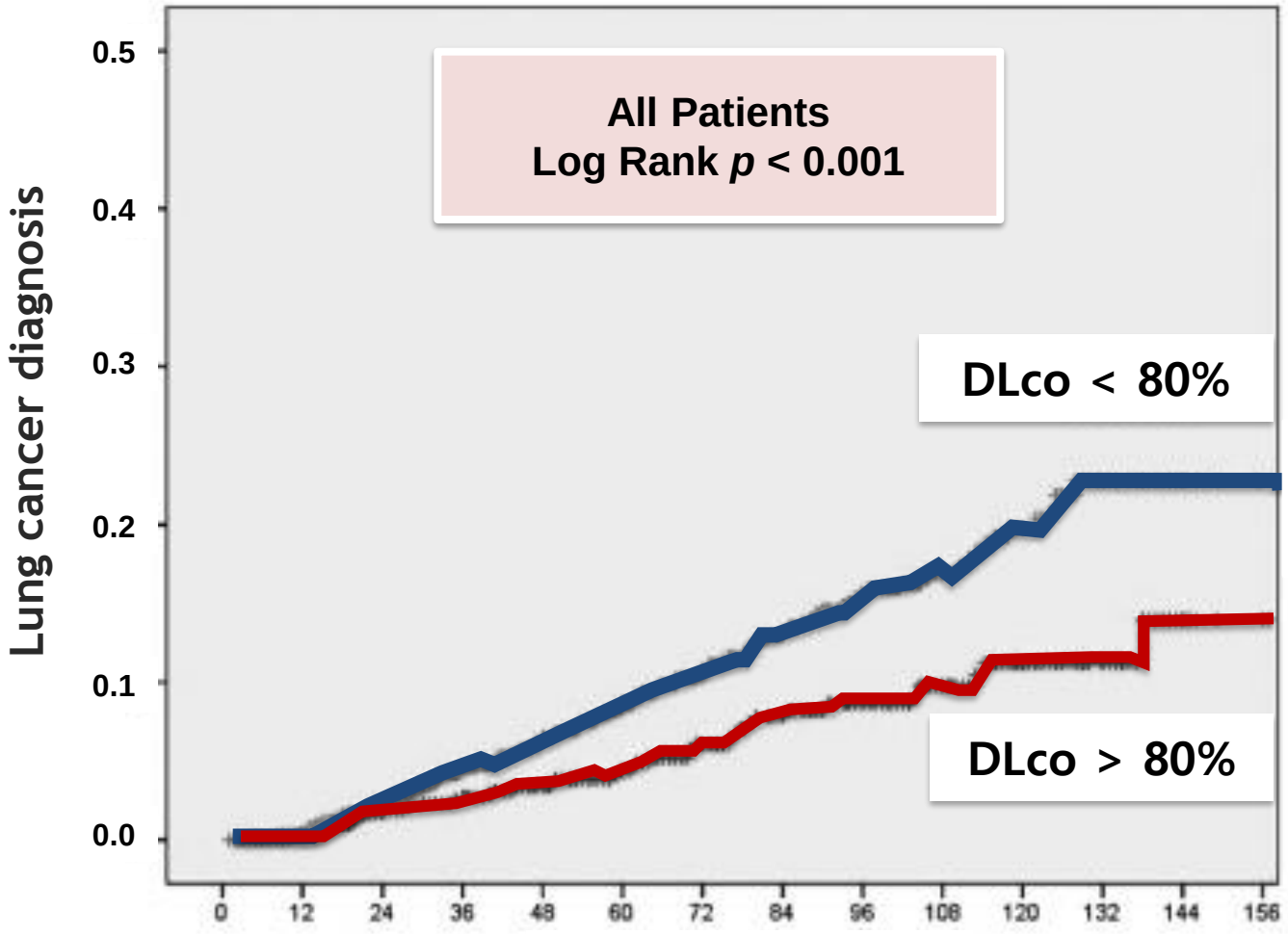
1st NHANES, who had up to 22 years of follow up (n=113/5,402)



Mannino et al. Arch Inter Med 2003;163:1475-80

Decreased DLco

BODE COPD observation study with more than 5 years f/u (n = 2,507 pts)



de-Torres, et al. AJRCCM 2011;184:913-19

Emphysema >> Airflow obstruction in association of lung cancer

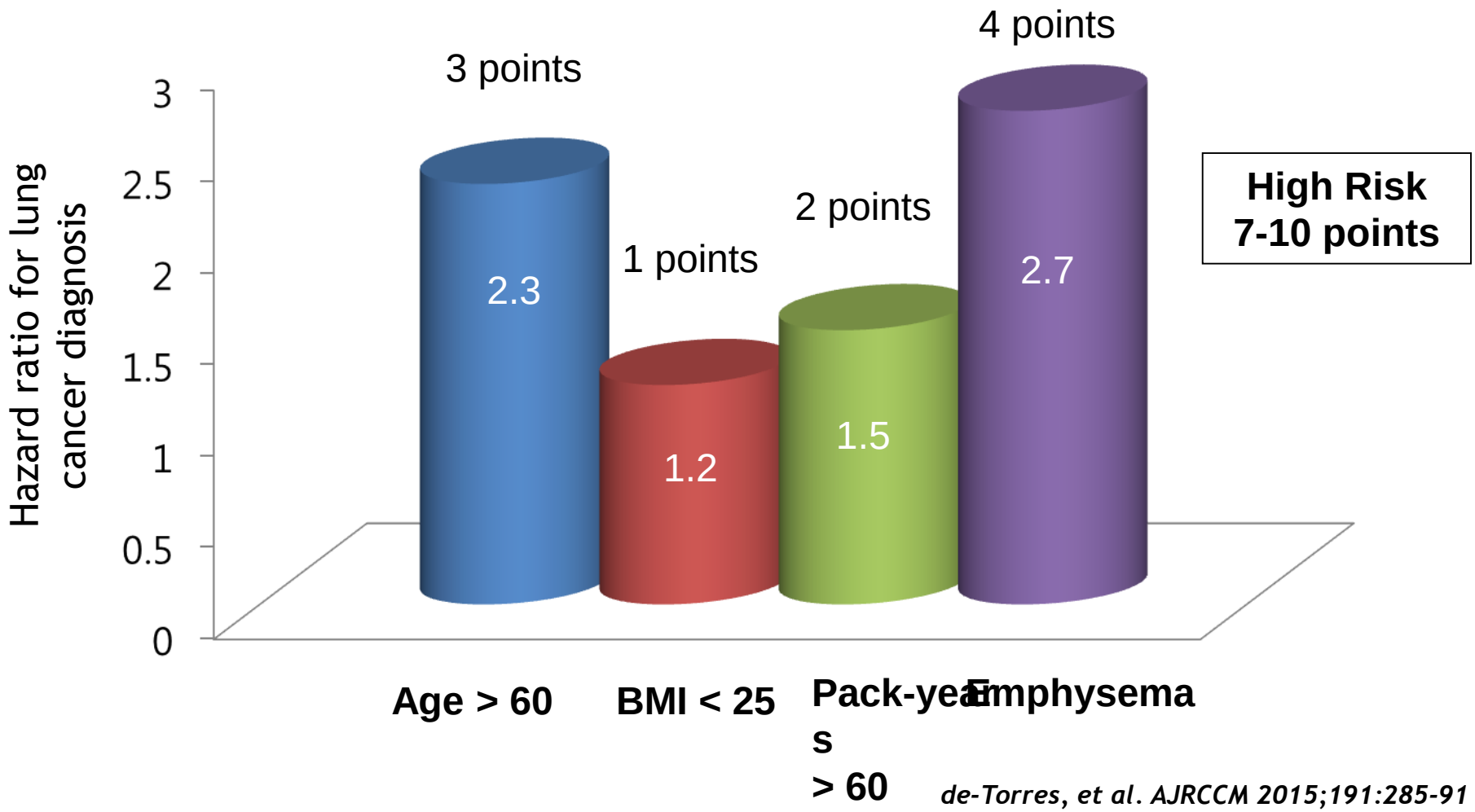
Prospective cohort for lung cancer screening using LDCT, up to 5 years (n=1,166) : visual assessment of emphysema (grade 0 – 4, ≥ 1)
Adjusted association between COPD and lung cancer (RR, (CI))
(age, sex, and No. of pack-years of smoking)

Model 1	Model 2	Model 3
2.89 (1.14-7.27)	3.13 (1.32-7.44)	2.51 (1.01-6.23)
		2.10 (0.79-5.58)
Airflow obstruction vs. No airway obstruction	**Emphysema vs. No emphysema**	**Emphysema Airway obstruction**
Without emphysema	**Without airway obstruction**	

de-Torres, et al. CHEST 2007;132:1932-38

Emphysema (A predictive score for LC in COPD)

Pittsburgh Lung Screening Study (factors with age, sex, BMI, pack-years, active smoker, years of former smoker, family history, GOLD I-II vs. III-IV and emphysema)



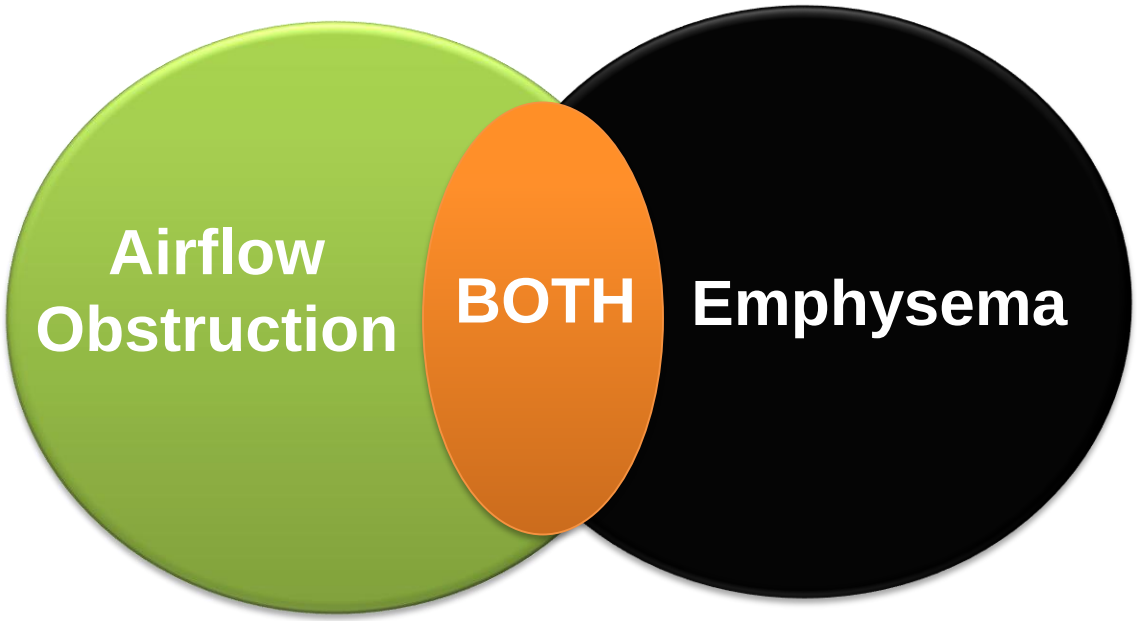
de-Torres, et al. AJRCCM 2015;191:285-91

Airflow obstruction and Emphysema

Airflow obstruction

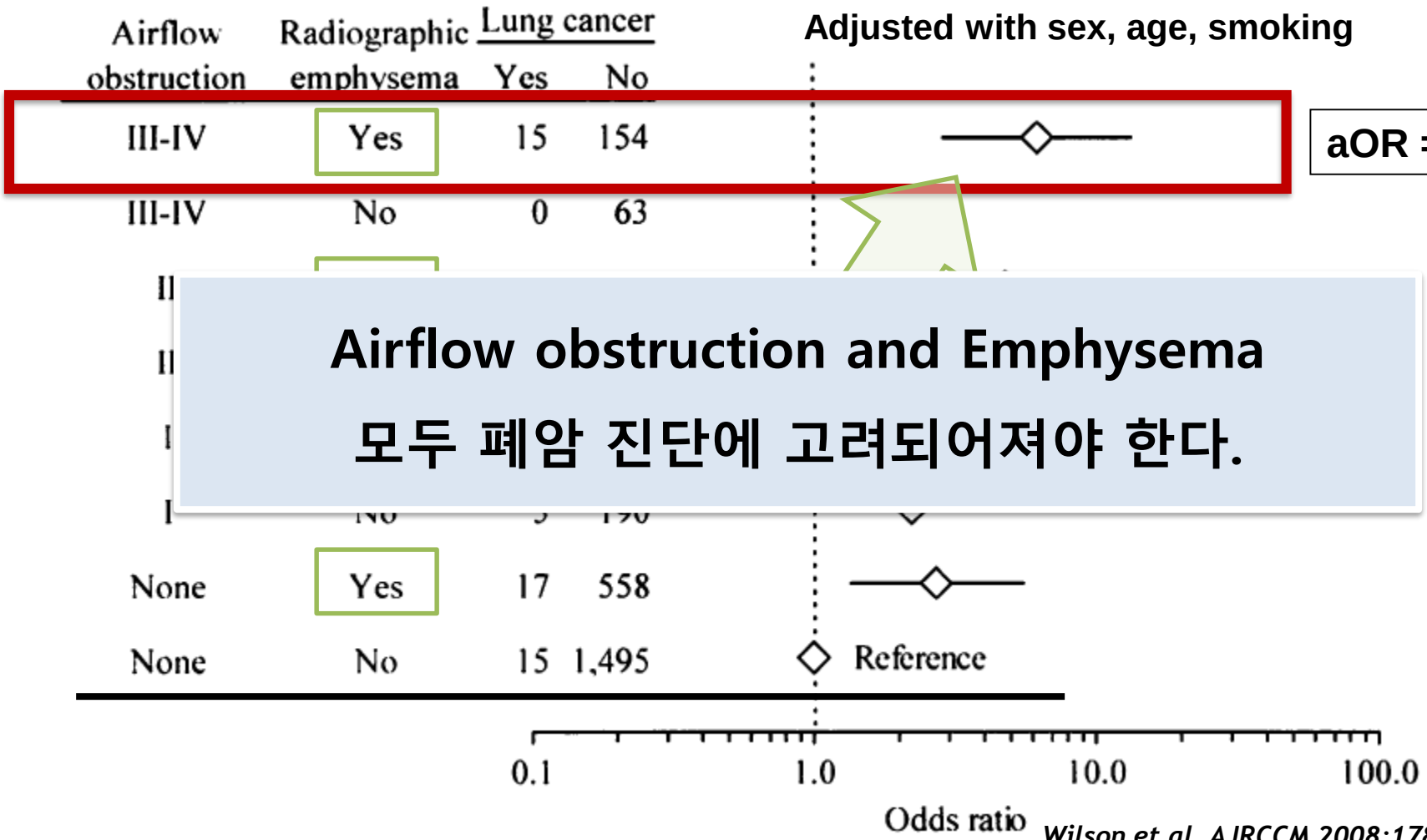
Emphysema

Airflow obstruction and Emphysema



Emphysema and Airflow obstruction severity

Pittsburgh Lung Screening Study (n=3,638, 3.7 yrs f/u)



Airflow obstruction and Emphysema

모두 폐암 진단에 고려되어져야 한다.

Wilson et al. AJRCCM 2008;178:738-44

COPD & Lung Cancer

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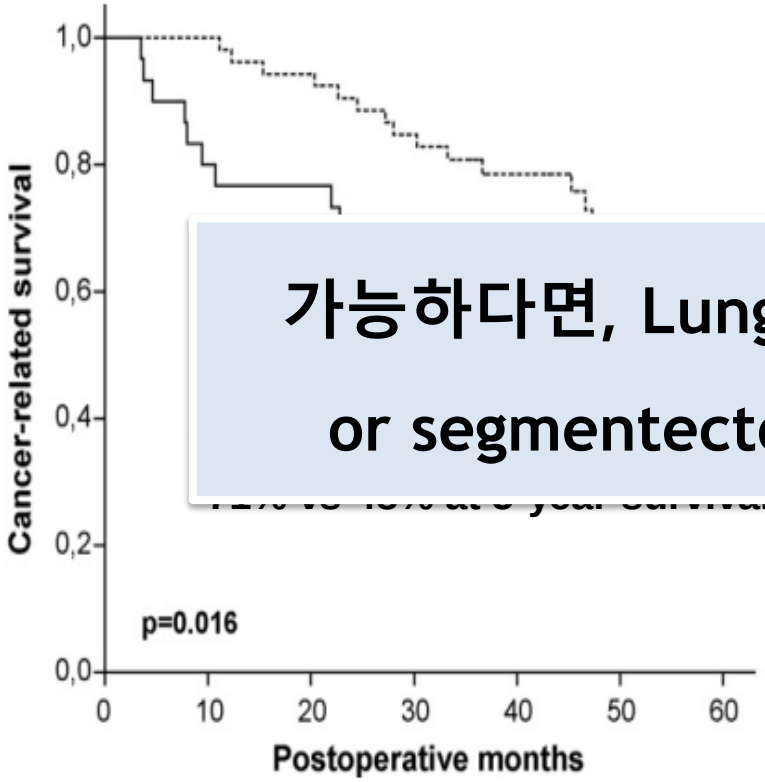
예후 인자

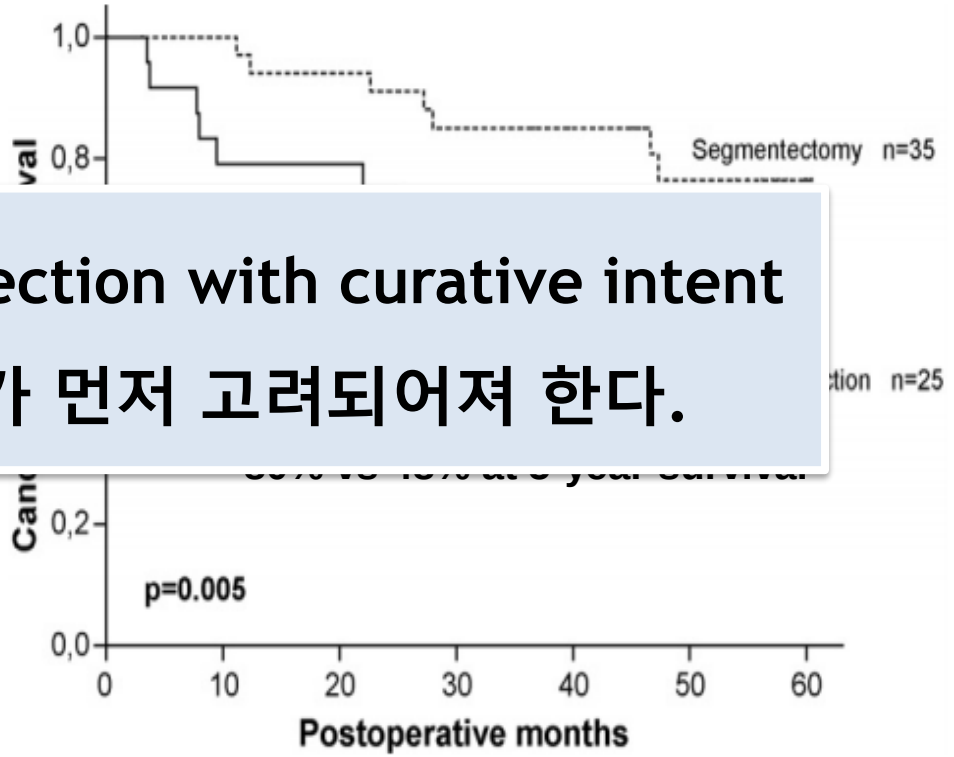
Surgical methods (IA NSCLC) segmentectomy Vs. Wedge resection

Limited PFT or severe cardiac comorbidity

Stage IA NSCLC

Tumor size less than 2cm



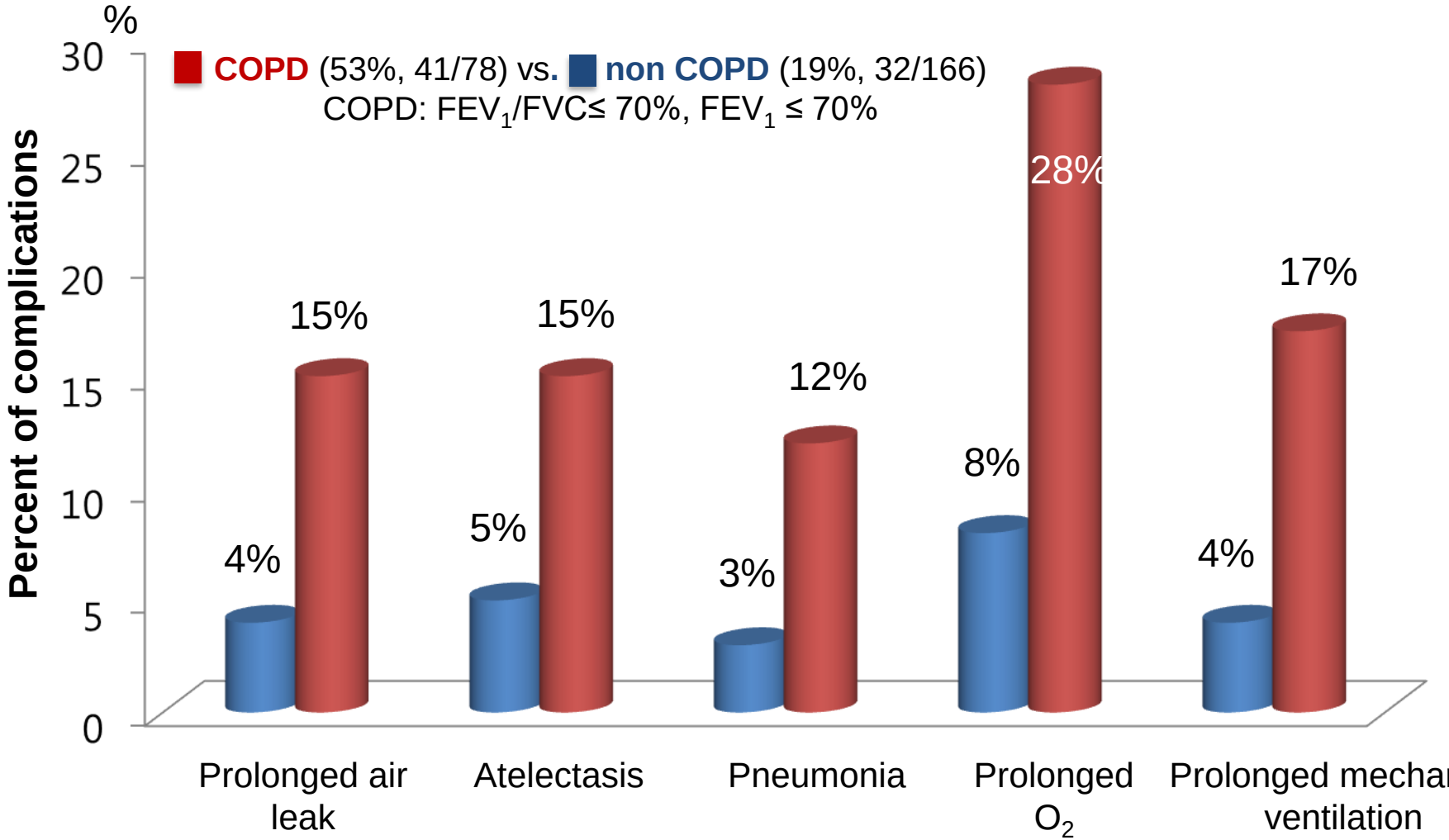


가능하다면, Lung resection with curative intent or segmentectomy가 먼저 고려되어져 한다.

Wulf Sienel et al. European Journal of Cardio-thoracic Surgery 2008;33:728-34

Postoperative pulmonary complications

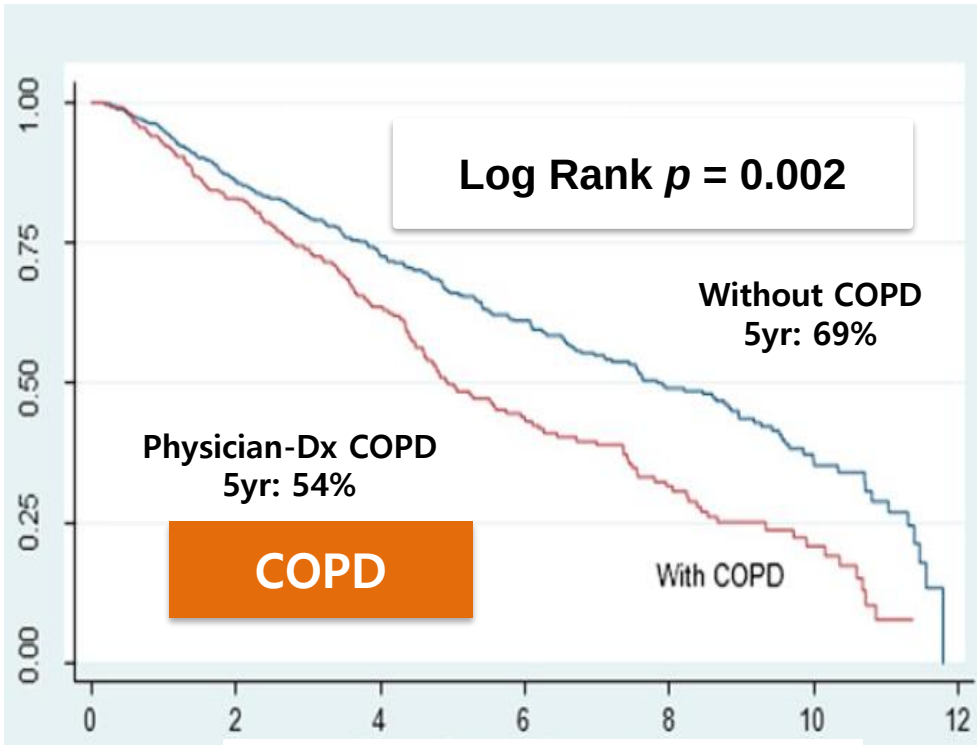
Retrospective study with 244 NSCLC pts undergoing curative surgery



Sekine et al. Lung cancer 2002;37:95-101

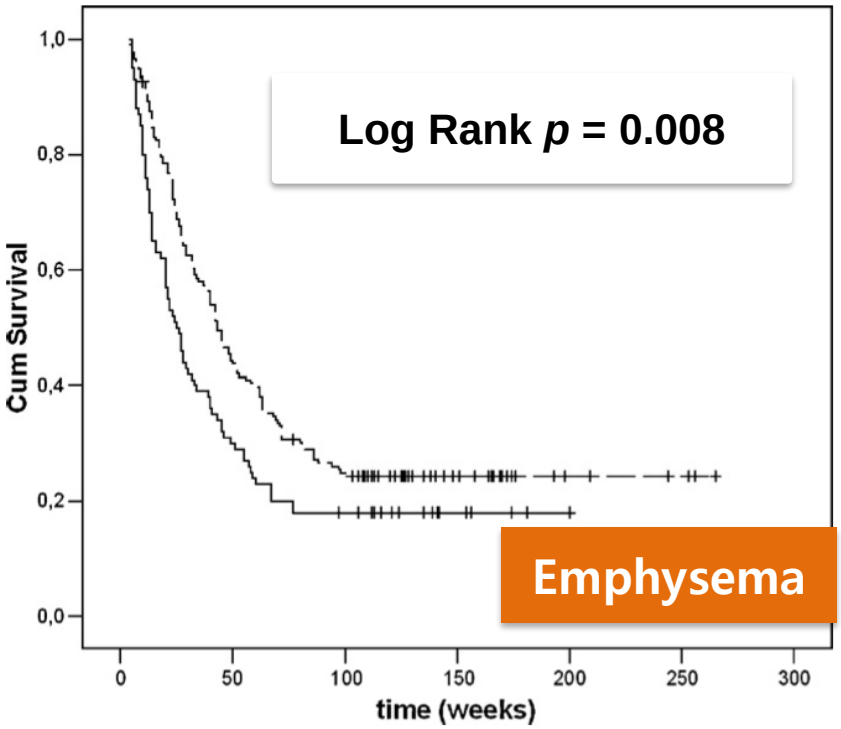
Overall Survival

A retrospective study,
902 pts with early stage IA-IIB & surgical resection
Overall survival



Rihong Zhai et al. CHEST 2014;145 (2):346-53

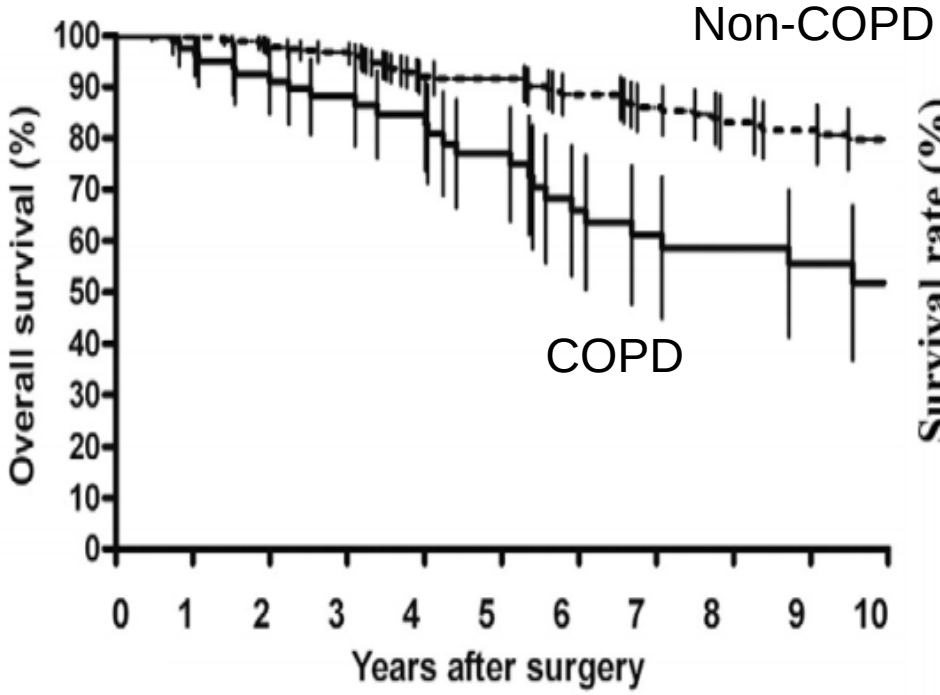
A prospective study
353 pts with all stages NSCLC
Survival at 2 yrs



Gullon et al. Lung Cancer 2011;71:182-5

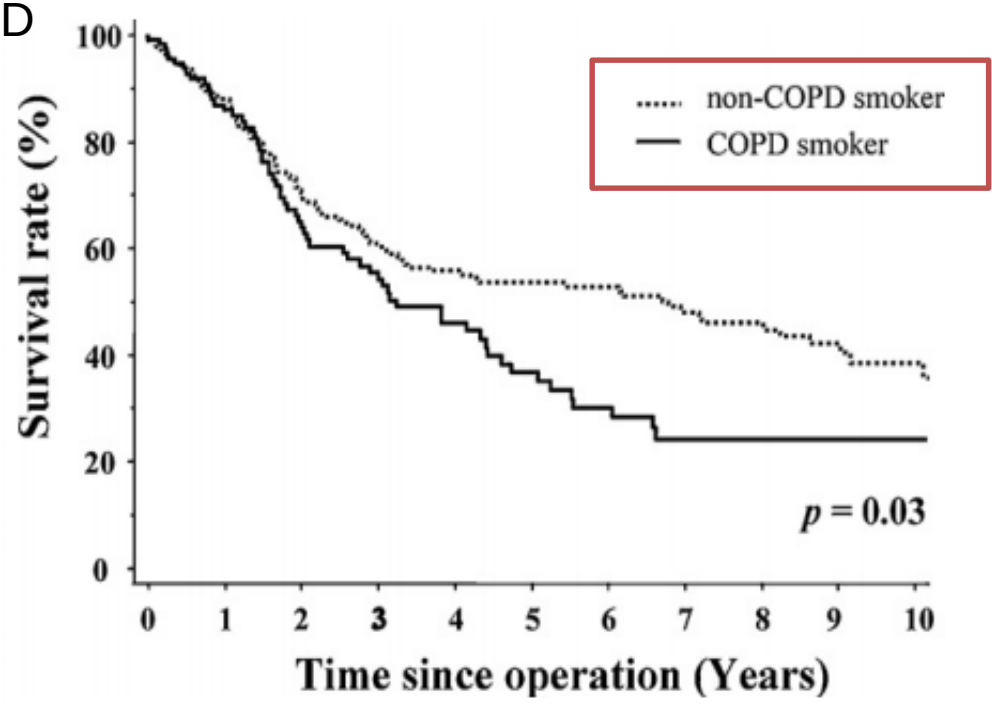
Overall Survival

A retrospective study, 442pts with NSCLC
Stage IA
Overall Survival



Sekine et al. Ann Thorac Surg 2007;84:946-51

A retrospective study, 1037 pts with NSCLC
Current or former smoker/COPD Gr I and II
Overall Survival with age > 65 yrs

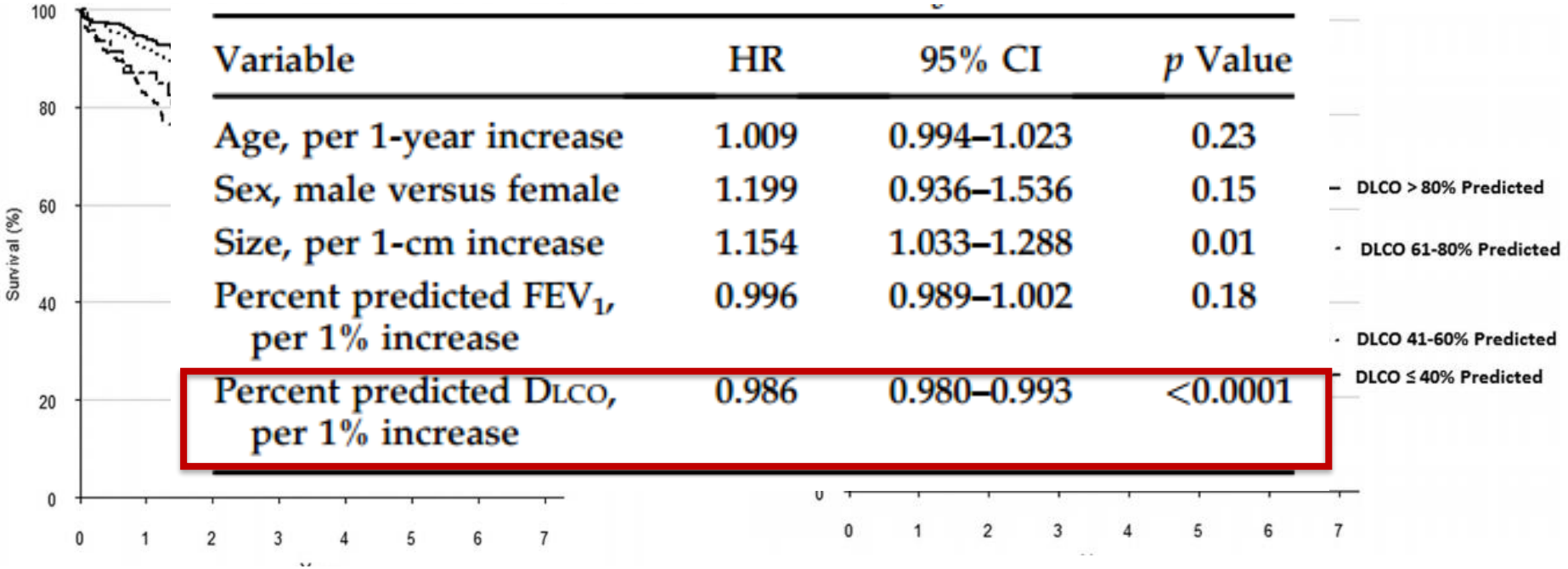


Kondo et al. European Journal of Cardio-thoracic Surgery 2011;40:1439-43

Emphysema >> Airflow obstruction as prognostic factor

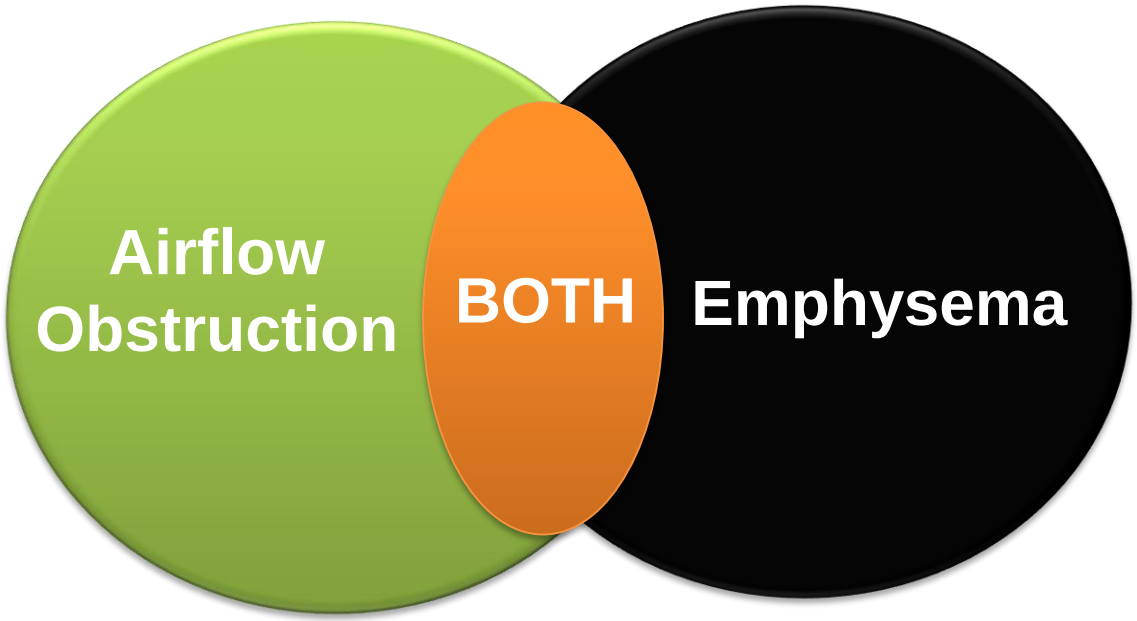
A retrospective study, **972** pts with NSCLC Stage IA who underwent lobectomy
Median f/u of 43 months

Variable	HR	95% CI	*p* Value
Age, per 1-year increase	1.009	0.994–1.023	0.23
Sex, male versus female	1.199	0.936–1.536	0.15
Size, per 1-cm increase	1.154	1.033–1.288	0.01
Percent predicted FEV_1, per 1% increase	0.996	0.989–1.002	0.18
Percent predicted DLCO, per 1% increase	0.986	0.980–0.993	<0.0001



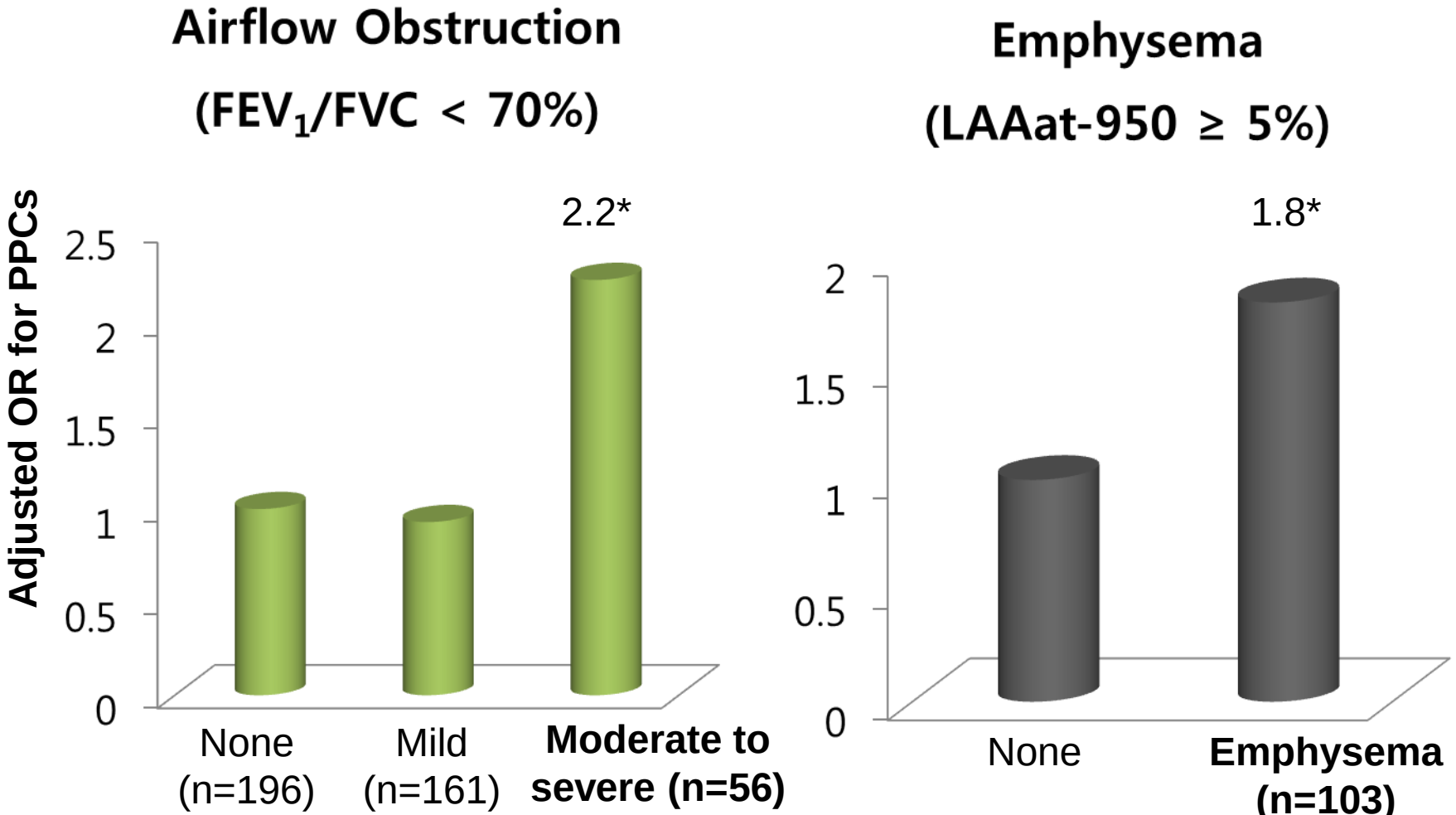
Berry et al. Ann Thorac Surg 2015;100:271-7

Airflow obstruction and Emphysema



Postoperative pulmonary complications

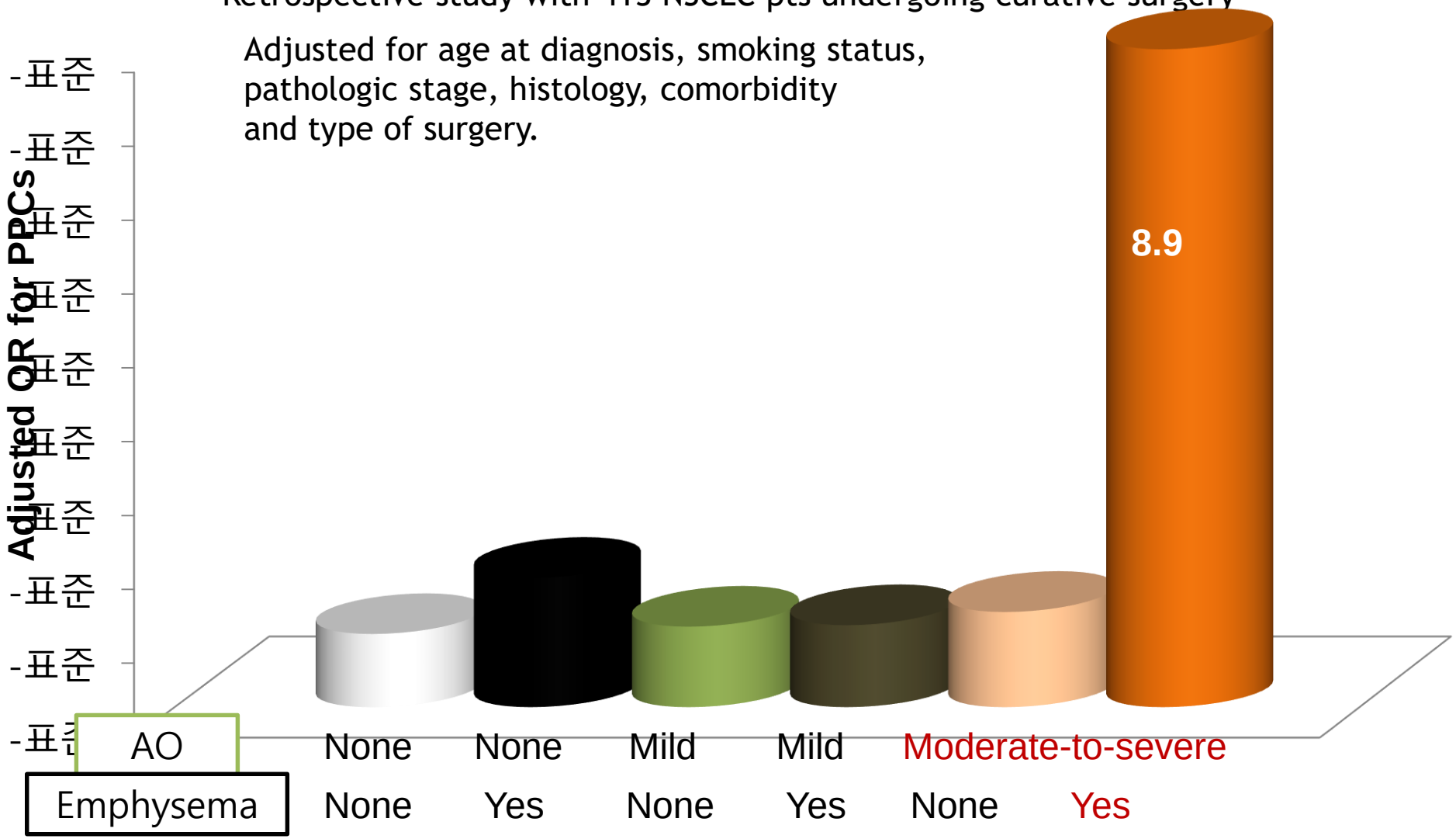
Retrospective study with 413 male NSCLC pts undergoing curative surgery (I-IIB)
Adjusted for age at diagnosis, smoking status, pathologic stage, histology, comorbidity and type of surgery. (n=2007-2009)



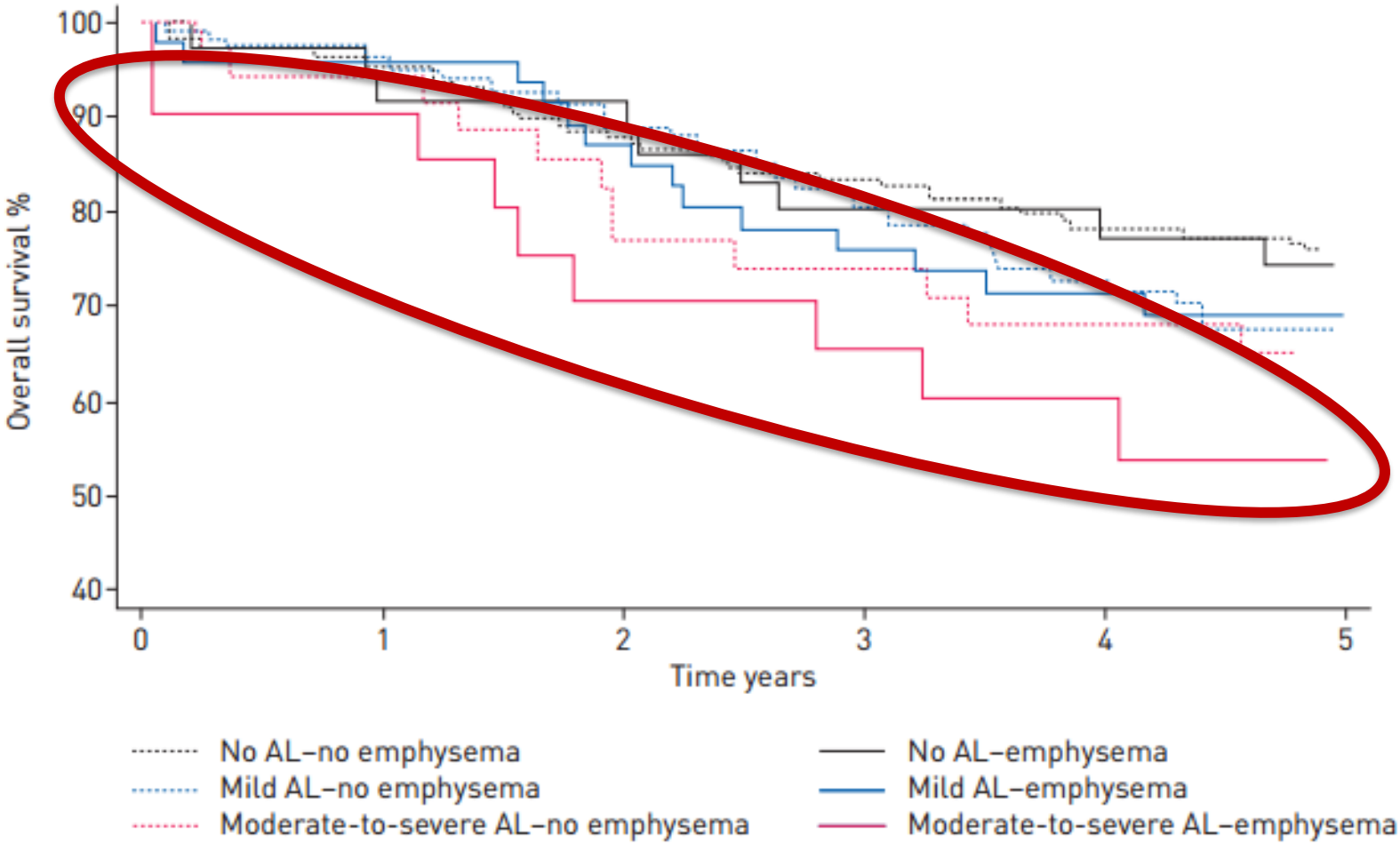
Joint effect for Postoperative pulmonary complications

Retrospective study with 413 NSCLC pts undergoing curative surgery

Adjusted for age at diagnosis, smoking status, pathologic stage, histology, comorbidity and type of surgery.



Overall survival



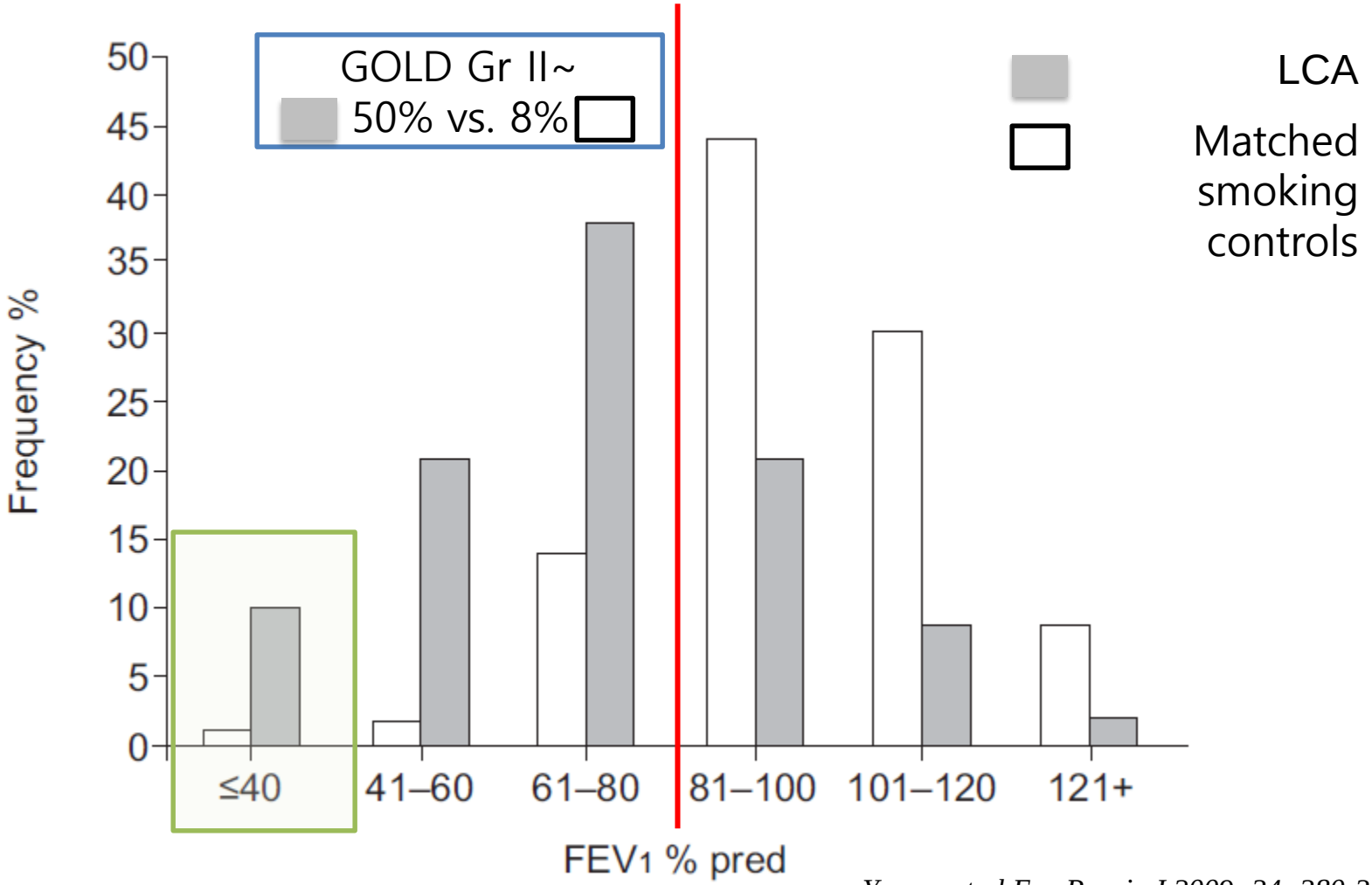
Shin et al. ERJ 2016; 48: 1743-1750

COPD & Lung Cancer

폐암 진단 시 COPD와 치료 효과

Distribution of FEV1 % pred LCA vs. matched smoking controls

N=446, matched with age, sex and smoking Hx (randomly recruited community control)



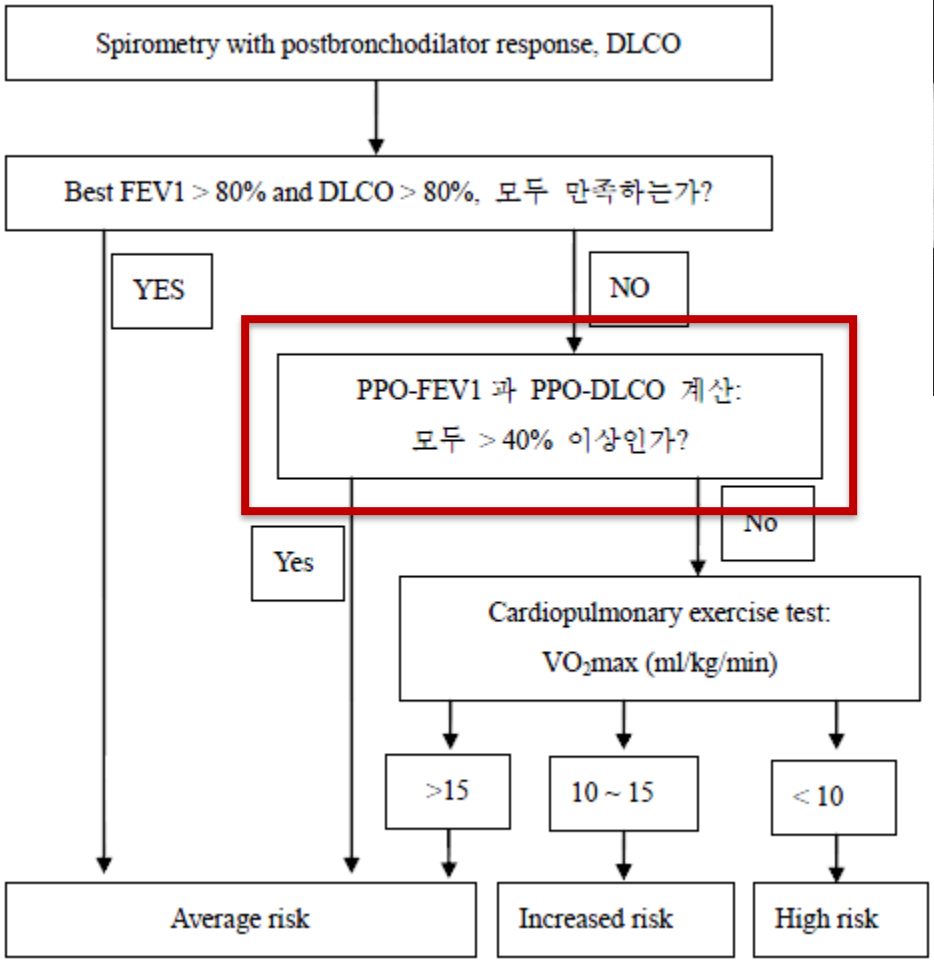
Young et al.Eur Respir J 2009; 34: 380-386.

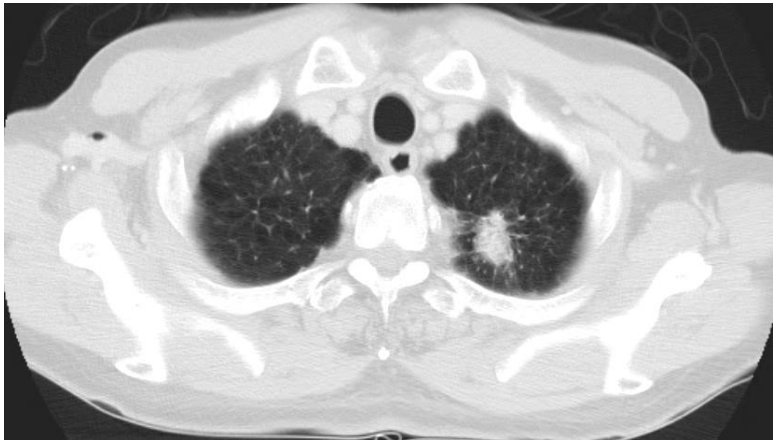
Criteria for tolerance of anatomic surgical resection

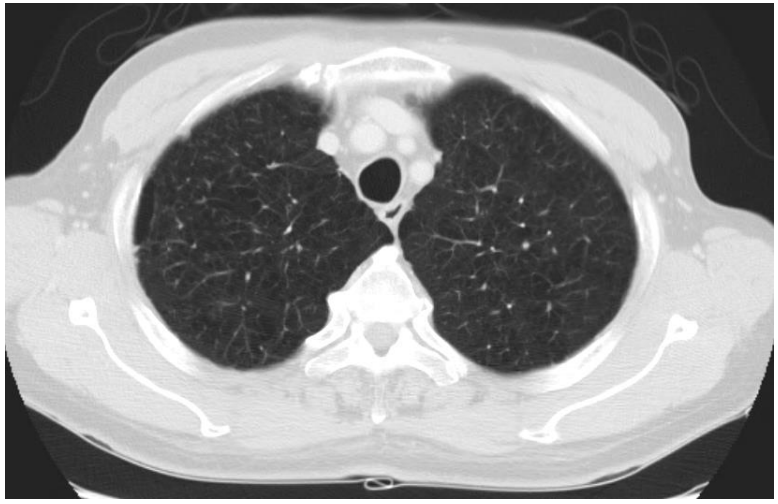
- Surgical Interventions
  - Lung Surgery
    - The risk of postoperative complications from lung resection appears to be increased in patients with decreased **predicted postoperative pulmonary function** (**FEV_1 or DLco < 30~40% predicted).**

2017 GOLD guideline

Criteria for tolerance of anatomic surgical resection





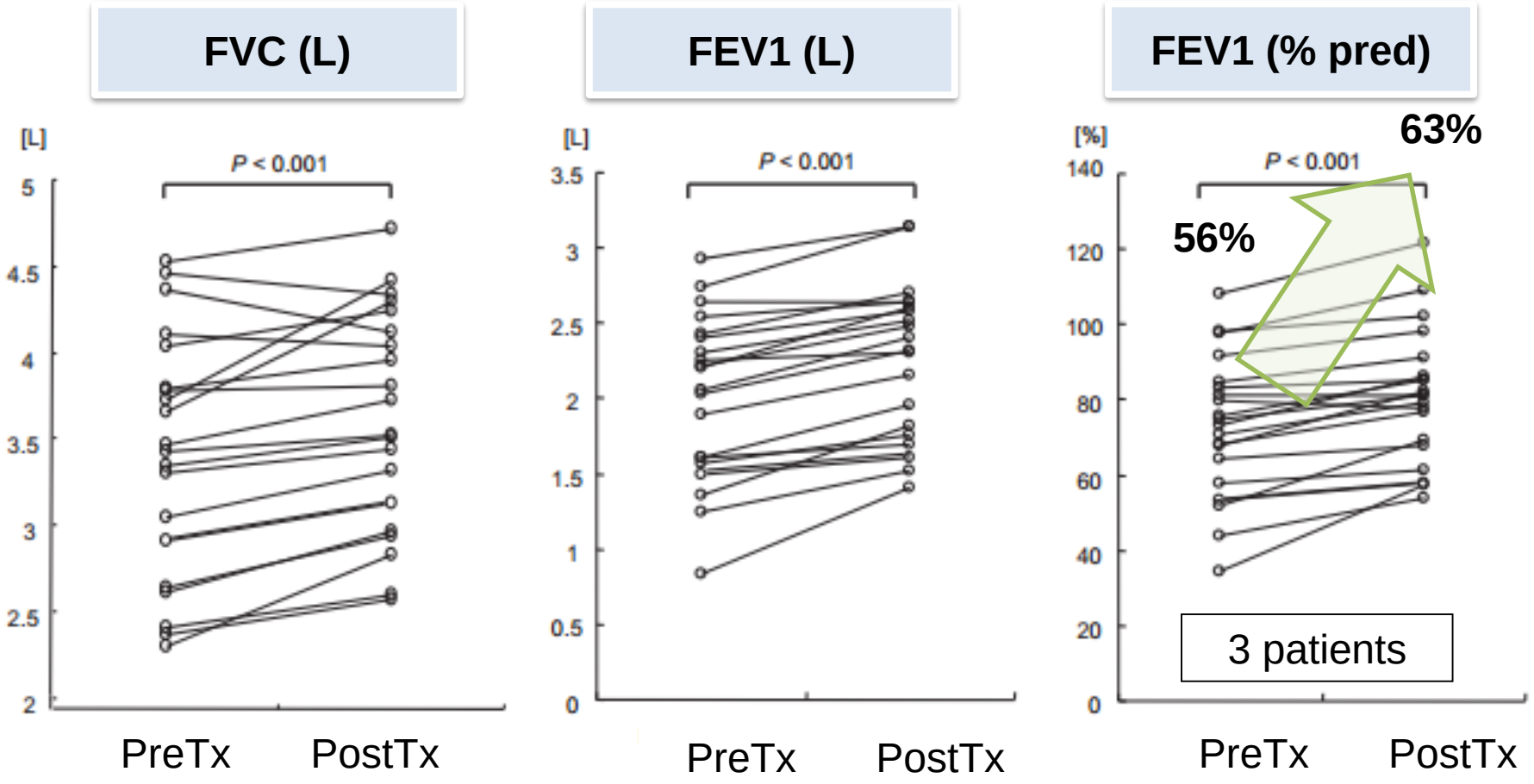


PPO*=predicted postoperative

BTS/ACCP guideline

Effect of Tiotropium in LCA patients with untreated COPD

Two-week preoperative treatment with TIOT
(n=21, newly diagnosed COPD)



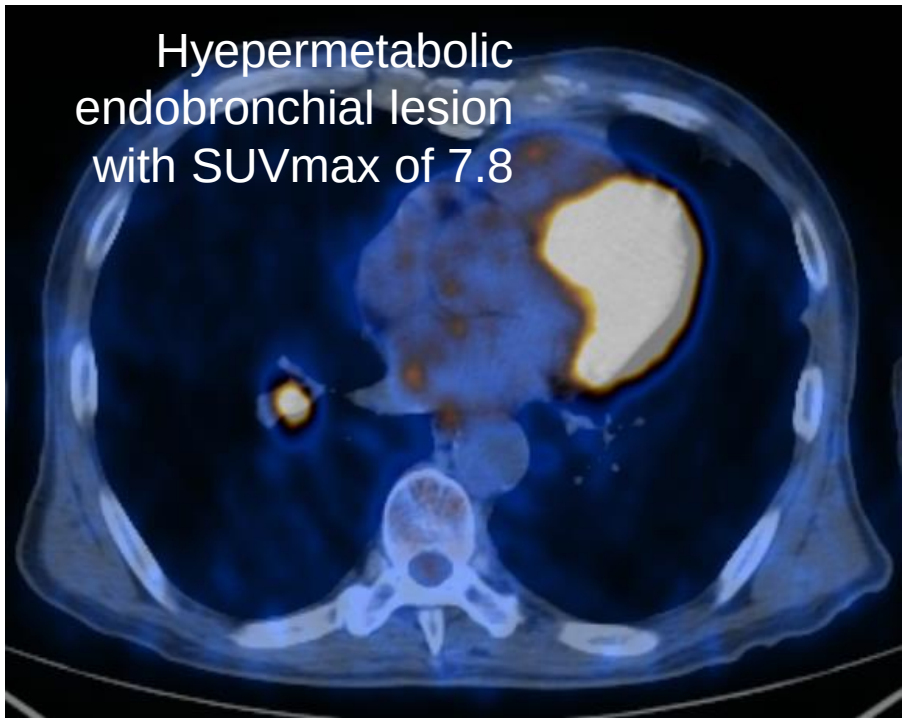
Kobayashi et al. Respirology 2009;14:675-79

COPD & LCA in RLL (M/66)

2월 23일

	POST	%PRED	%Chg
FVC (L)	3.04	73	24
FEV.5 (L)	0.51	27	2
FEV.5/FVC (%)	17		
FEV1 (L)	0.76	25%	12
FEV1/FVC (%)	25		

Ex-smoker (67 pack-yr),
he quit smoking 6-month ago



Lung Perfusion Result

(Counts)	Left	Right
Upper	082K	120K
Middle	081K	243K
Lower	014K	031K
Total	177K	394K

(% Ratios)	Left	Right
Upper	14.29	20.96
Middle	14.25	42.52
Lower	2.50	5.48
Total	31.03	68.97

COPD & LCA (M/66)

2월 23일

	POST	%PRED	%Chg
FVC (L)	3.04	73	24
FEV.5 (L)	0.51	27	2
FEV.5/FVC (%)	17		
FEV1 (L)	0.76	25%	12
FEV1/FVC (%)	25		

FULL Inhaler Therapy
for COPD for 2 weeks

3월 6일

	POST	%PRED
FVC (L)	4.81	114
FEV.5 (L)	0.96	50
FEV.5/FVC (%)	20	
FEV1 (L)	1.49	48%
FEV1/FVC (%)	31	

	AVG	%PRED
DLCO (mL/mmHg/min)	10.0	48
DLCO/VA (mL/mHg/min/L)	1.75	46

Predicted postoperative lung function
FEV1 % pred: 45.6%
DLco: 45.6%

VATS RLLobectomy

Prolonged air leakage

요약

- COPD, 특히 폐기종은 폐암의 위험인자이며 동시에 폐암 치료 후 예후와 관계 있는 인자이다.
- 폐쇄성 기류 제한과 폐기종이 동시에 있을 때, 각각 있을 때보다 폐암의 발생률이 훨씬 더 높고 치료 후 예후도 좋지 않다.
- 적절한 흡입기 사용, 호흡 재활, 금연 등을 포함한 수술 전에 최적화된 COPD 치료가 폐암 수술 전에 반드시 필요하다.

경청해 주셔서
감사합니다.

In What Patients Should We Screen Chest CT scan?

The National Lung Screening Trial (NLST)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

53,454 patients at high risk for lung cancer.
Low dose CT vs. PA CXR

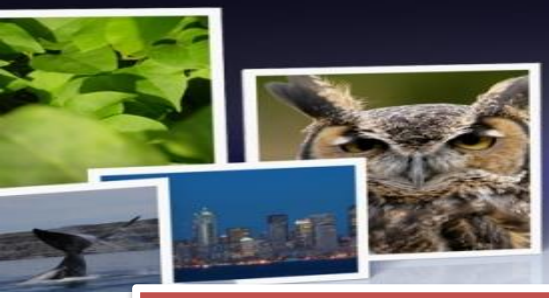
In What Patients Should We Screen Chest CT scan?

The National Lung Screening Trial (NLST)

There were 247 deaths from lung cancer per 100,000 person-years in the low-dose CT group and 309 deaths per 100,000 person-years in the radiography group, representing a relative reduction in mortality from lung cancer with low-dose CT screening of 20.0% (95% CI, 6.8 to 26.7; P=0.004). The rate of death from any cause was reduced in the low-dose CT group, as compared with the radiography group, by 6.7% (95% CI, 1.2 to 13.6; P=0.02).

CONCLUSIONS

Screening with the use of low-dose CT reduces mortality from lung cancer. (Funded by the National Cancer Institute; National Lung Screening Trial ClinicalTrials.gov number, NCT00047385.)



In What Patients Should We Screen Chest CT scan?

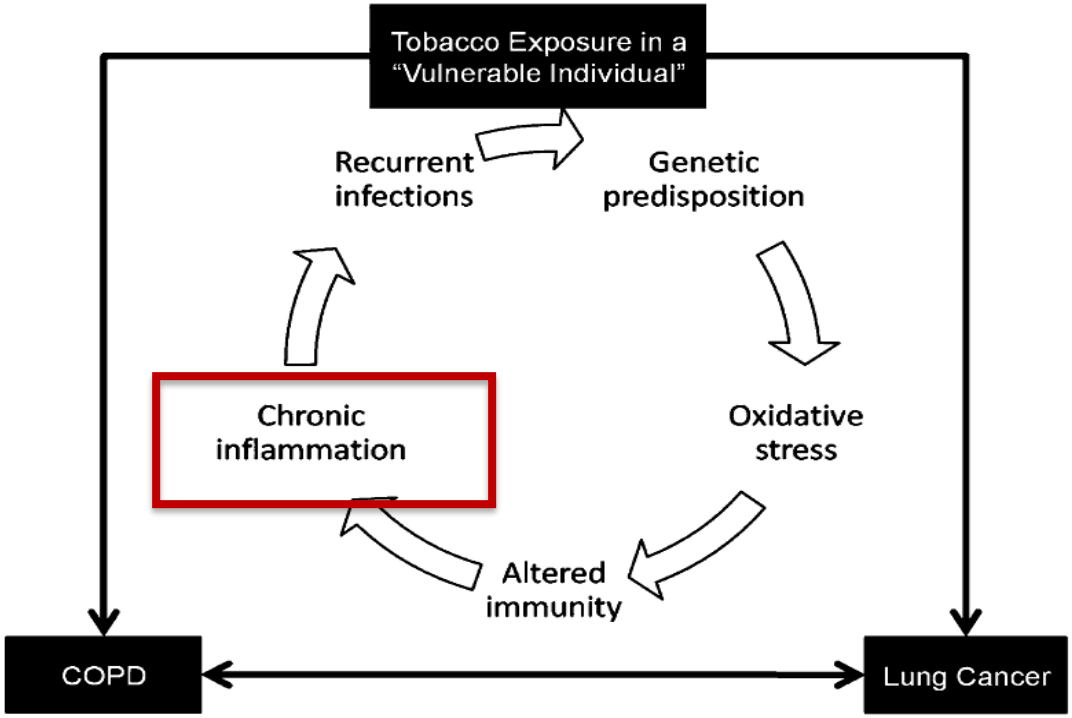
Recommendation of LDCT in US, 우리나라

- Eligible Participants
  - Age : 55-74 years
  - Smoking status
    - At least 30 pack-years
    - Continue to smoke or have quit within the previous 15 years

Possible Mechanisms

Smoking → Chronic inflammation
→ Repeated injury and repair, stimulating cell turnover and potential genetic errors
→ Lung cancer

Impaired mucocillarly clearance in COPD → carcionogens from the smoke in the mucous blanket to have longer exposure time at these sites



Stacy et al. AJRCCM 2011;183:1138-46

Possible Mechanisms

Smoking → Chronic inflammation
→ Repeated injury and repair, stimulating cell turnover and potential genetic errors
→ Lung cancer

Impaired mucocillarly clearance in COPD → carcionogens from the smoke in the mucous blanket to have longer exposure time at these sites

1. Patients with emphysema may have increased susceptibility to smoking-related biological damage, including damage to the DNA, which ultimately determines the aggressiveness of the tumor cells

2. tumor progression is enhanced in emphysematous lungs where matrixmetalloproteinases are rich

COPD and lung cancer
- Share underlying host susceptibility foactors
- 1. an exaggerated or maladaptive response to smoking → induced airway inflammation

Stacy et al. AJRCCM 2011;183:1138-46

Possible Mechanisms

COPD and lung cancer

- Share underlying host susceptibility foactors
- 1. an exaggerated or maladaptive response to smoking → induced airway inflammation : alpha5 subunit of the nicotinic acetylcholine receptor gene, previously implicated in smoking-induced lung inflammation
- 2.

Stacy et al. AJRCCM 2011;183:1138-46