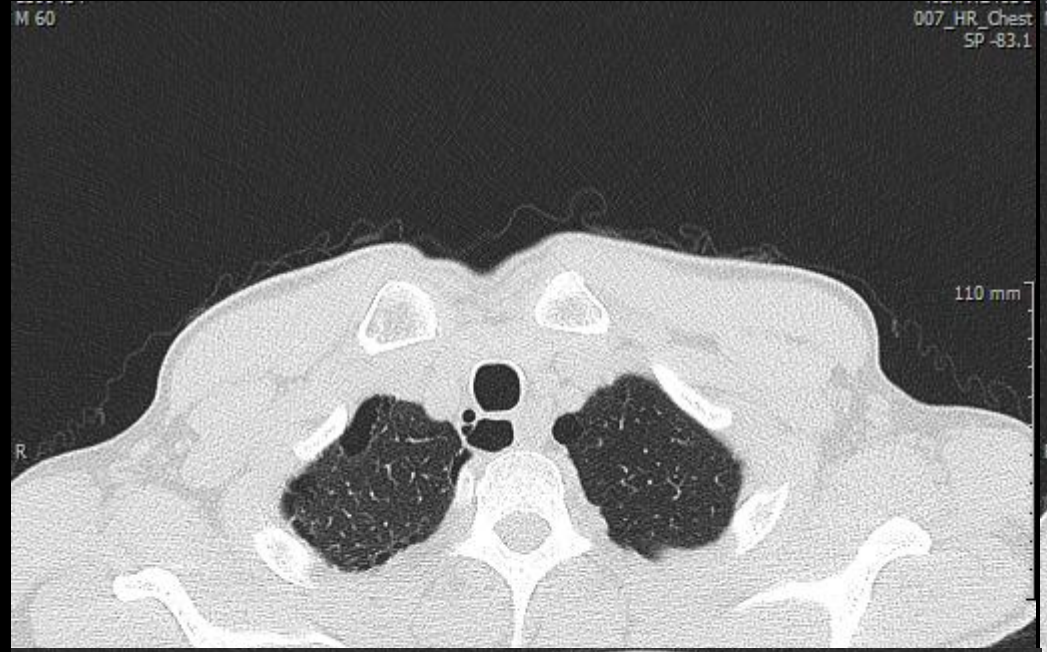
Lung fibrosis in COPD

가톨릭의대 김 용 현

2018 COPD school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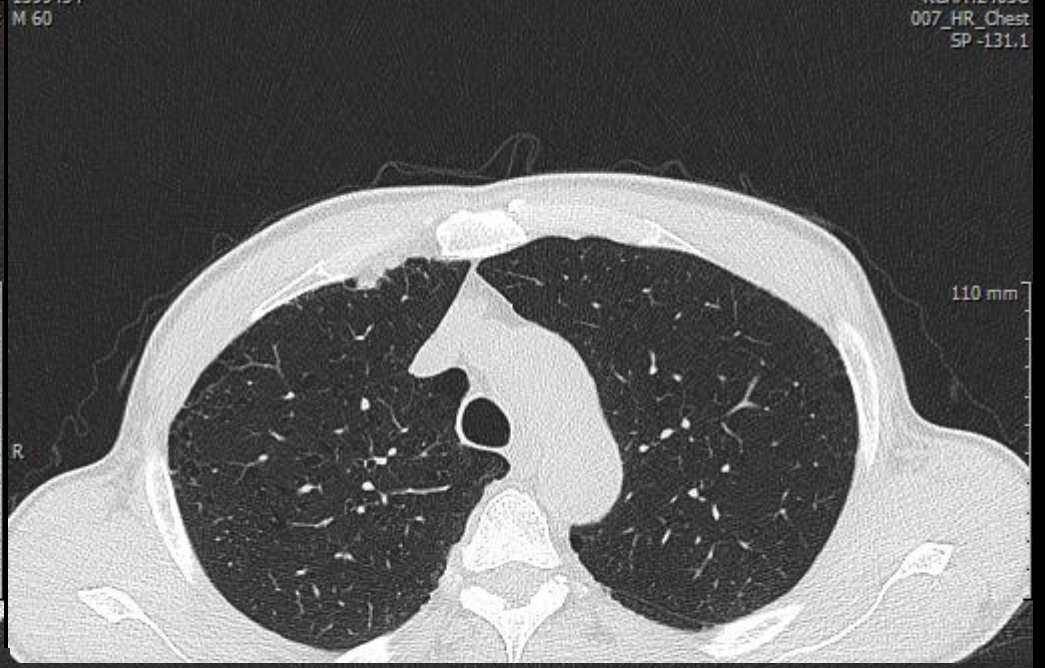
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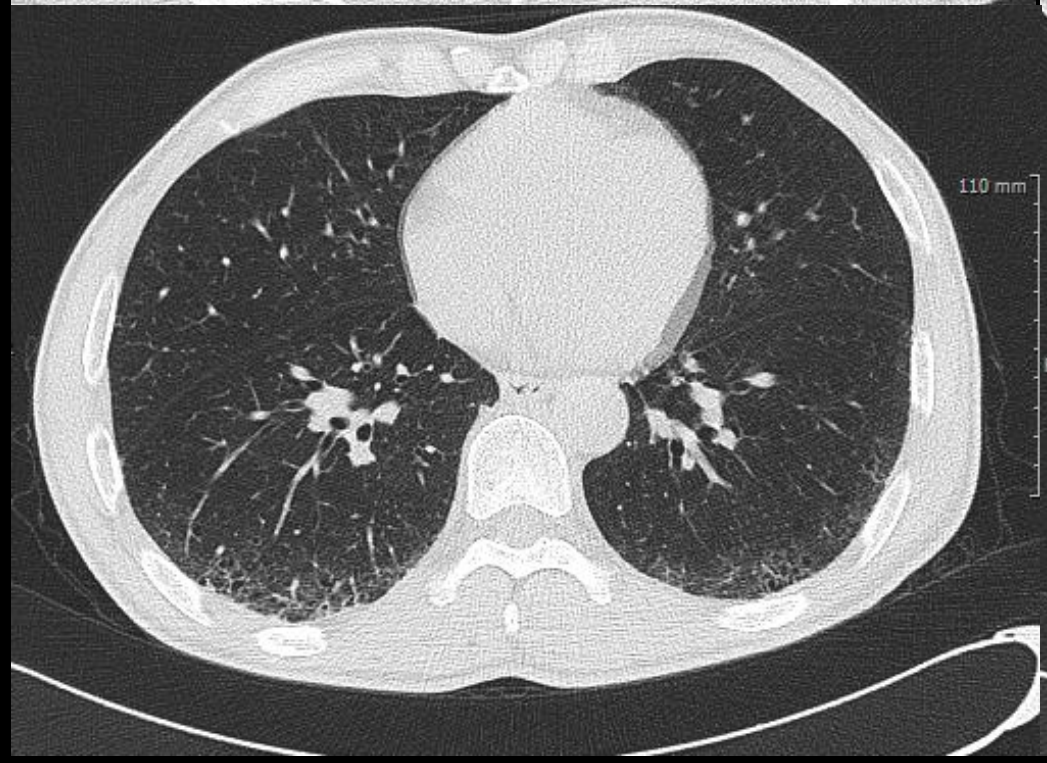
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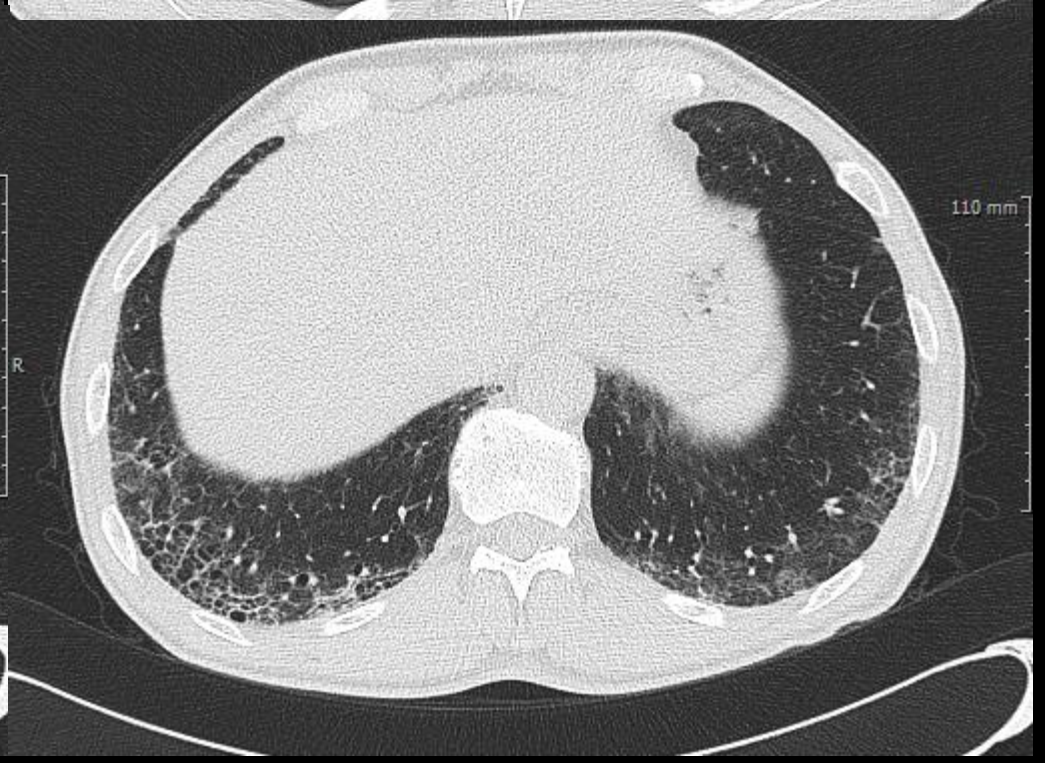
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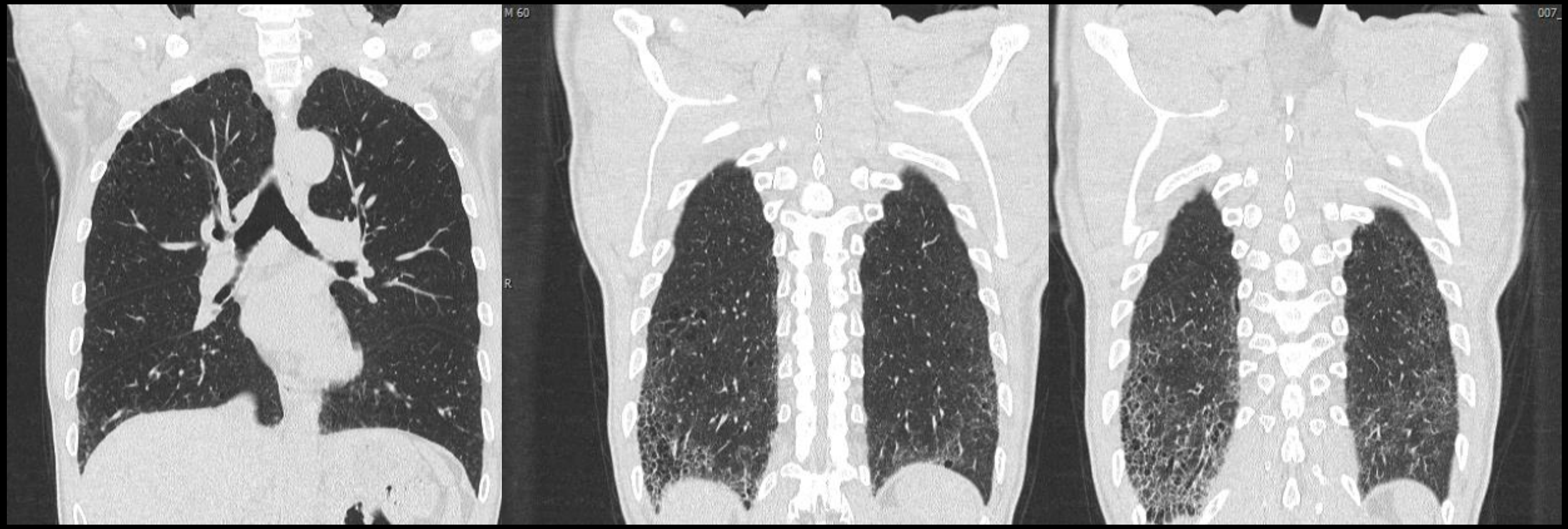
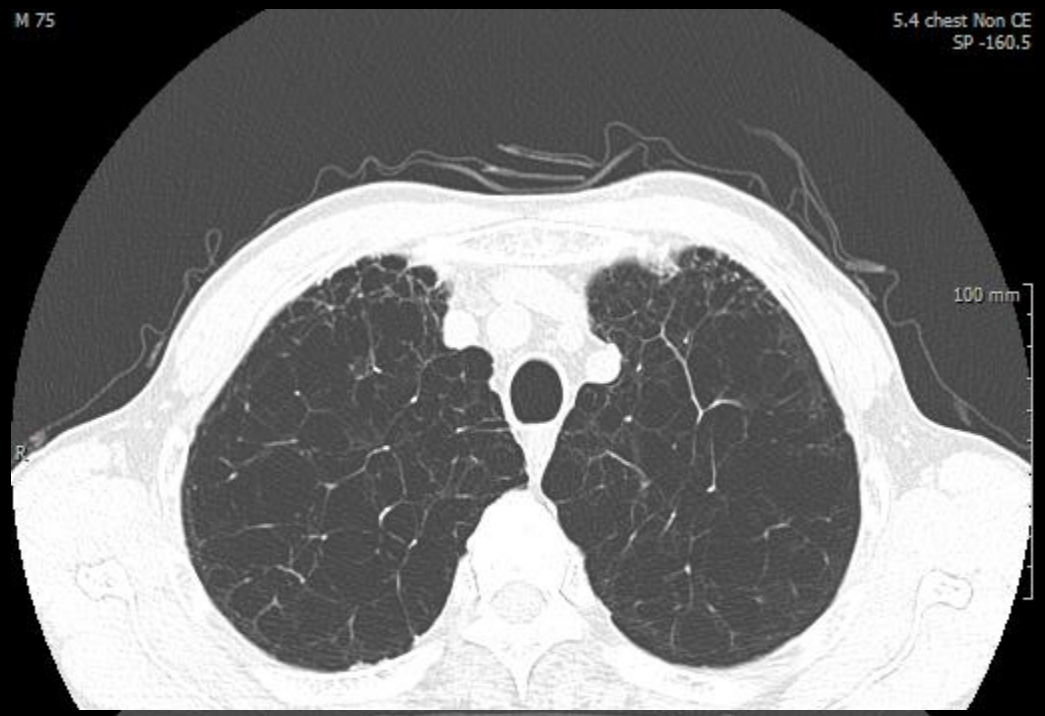


Combined pulmonary fibrosis and emphysema (CPFE)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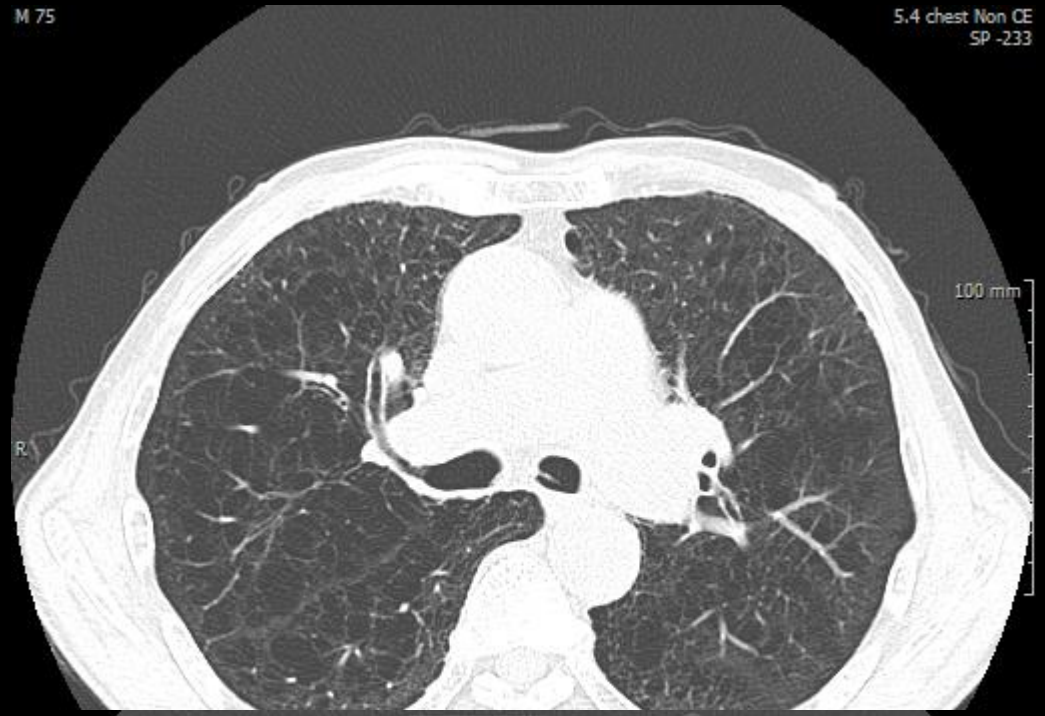
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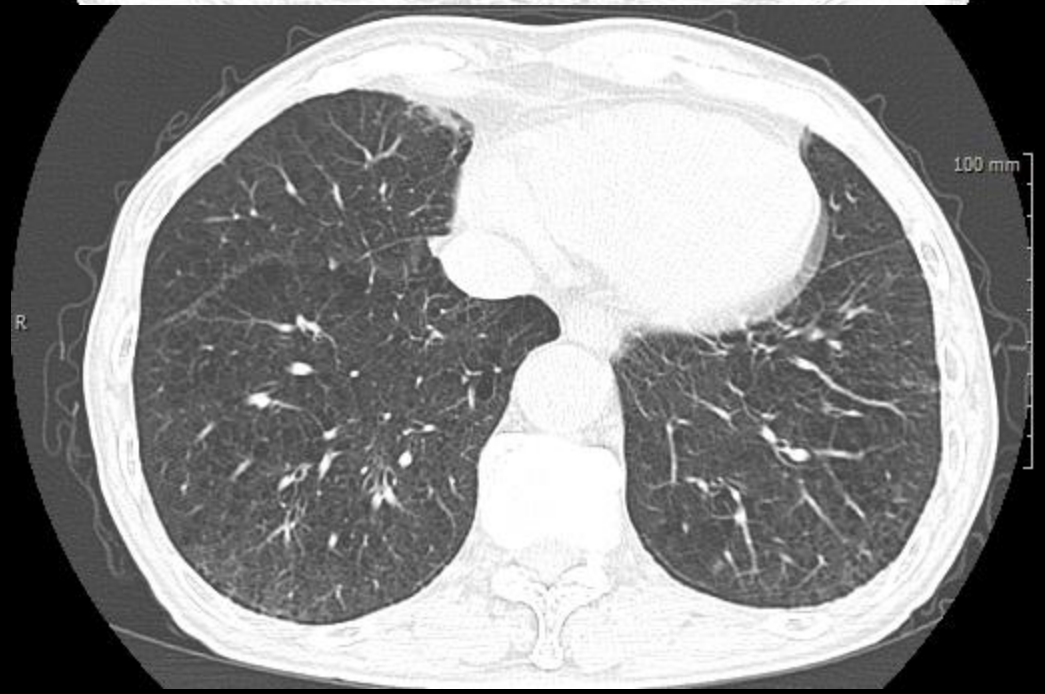
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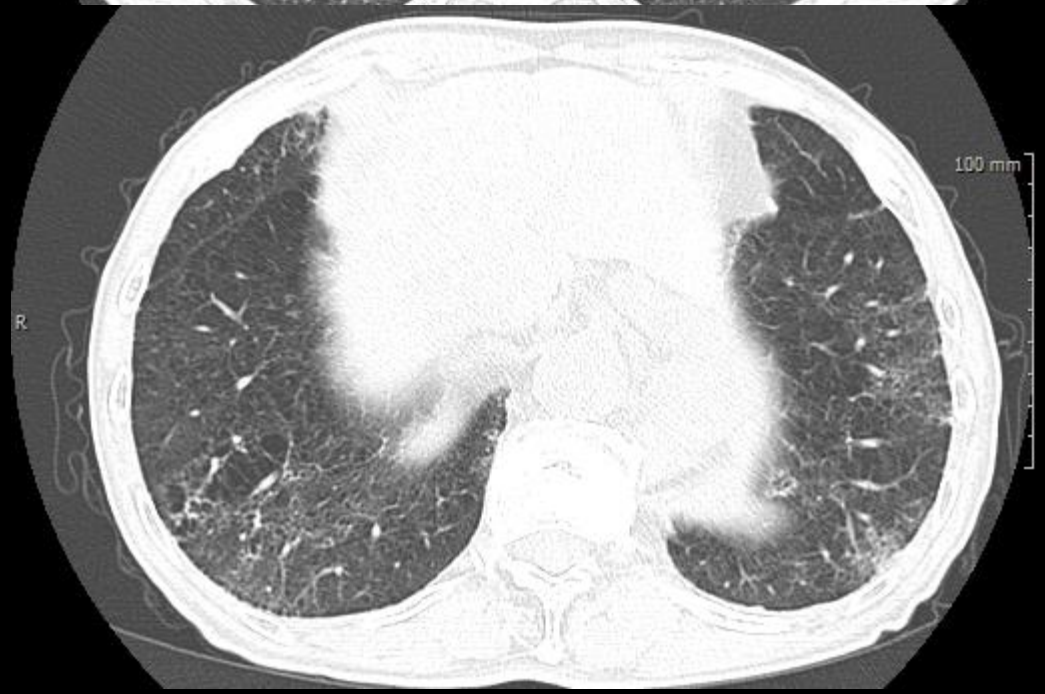
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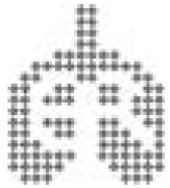
Eur Respir J 2005; 26: 586–593
DOI: 10.1183/09031936.05.00021005

CLINICAL FORUM

Combined pulmonary fibrosis and emphysema: a distinct underrecognised entity



61 patients with both emphysema of the upper zones and diffuse parenchymal lung disease with fibrosis of the lower zones of the lungs

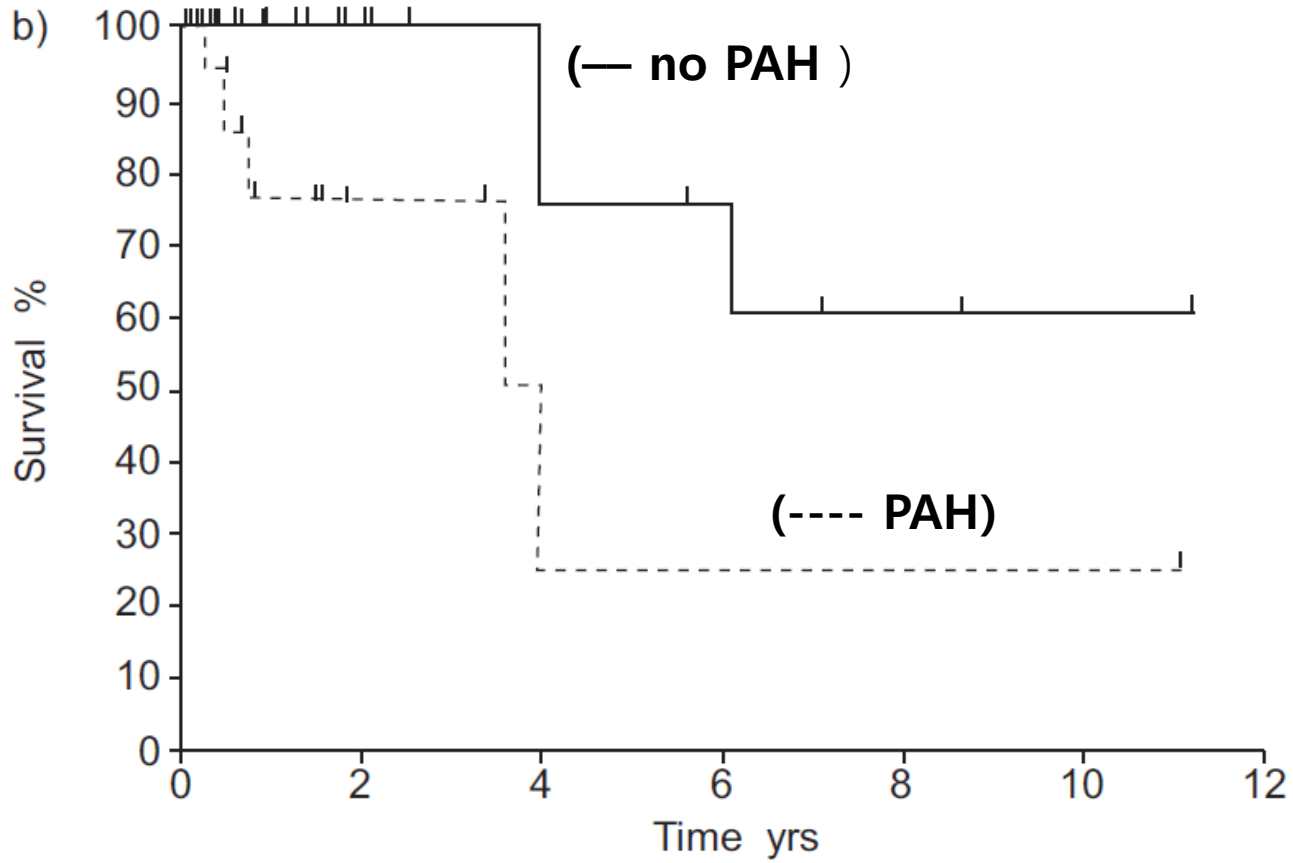
Patient characteristics	
Sex M/F n	60/1
Age yrs	65.2±10.2 (36–84)
Body mass index kg·m^{-2}	26±3 (19–32)
Current/ex-/never-smokers	19/42/0
Pack-yrs smoking	46±27 (5–120)
Current smokers	57±27 (8–120)
Ex-smokers	41±25 (5–110)
Asthenia	14 (23)
NYHA grade of dyspnoea	
Grade 1	10 (16)
Grade 2	23 (38)
Grade 3	23 (38)
Grade 4	5 (8)

Test	Patients tested n	
FVC % pred	61	90±18 (47–125)
FEV_1 % pred	61	80±21 (33–123)
Post-bronchodilator improvement in FEV_1 L	36	0.06±0.13 (-0.35–0.3)
FEV_1/FVC %	61	69±13 (30–94)
$FEF_{25-75\%}$ % pred	57	51±26 (15–118)
TLC % pred	56	88±17 (44–132)
RV % pred	56	90±32 (35–188)
$T_{L,CO}$ % pred	57	37±16 (10–80)
K_{CO} % pred	57	46±19 (8–84)

Combined pulmonary fibrosis ?

CT finding	
Fibrotic changes	
Honeycombing	58 (95)
Reticular opacities	53 (87)
Traction bronchiectasis	42 (69)
Ground-glass opacities	40 (66)
Architectural or bronchial distortion	24 (39)
Emphysema	
Centrilobular emphysema	59 (97)
Paraseptal emphysema	57 (93)
Bullae	33 (54)

Data are presented as n (%).



No PAH, systolic arterial pulmonary pressure <45 mmHg,
5-yr survival 75%

PAH, systolic arterial pulmonary pressure ≥45 mmHg,
5-yr survival 25%

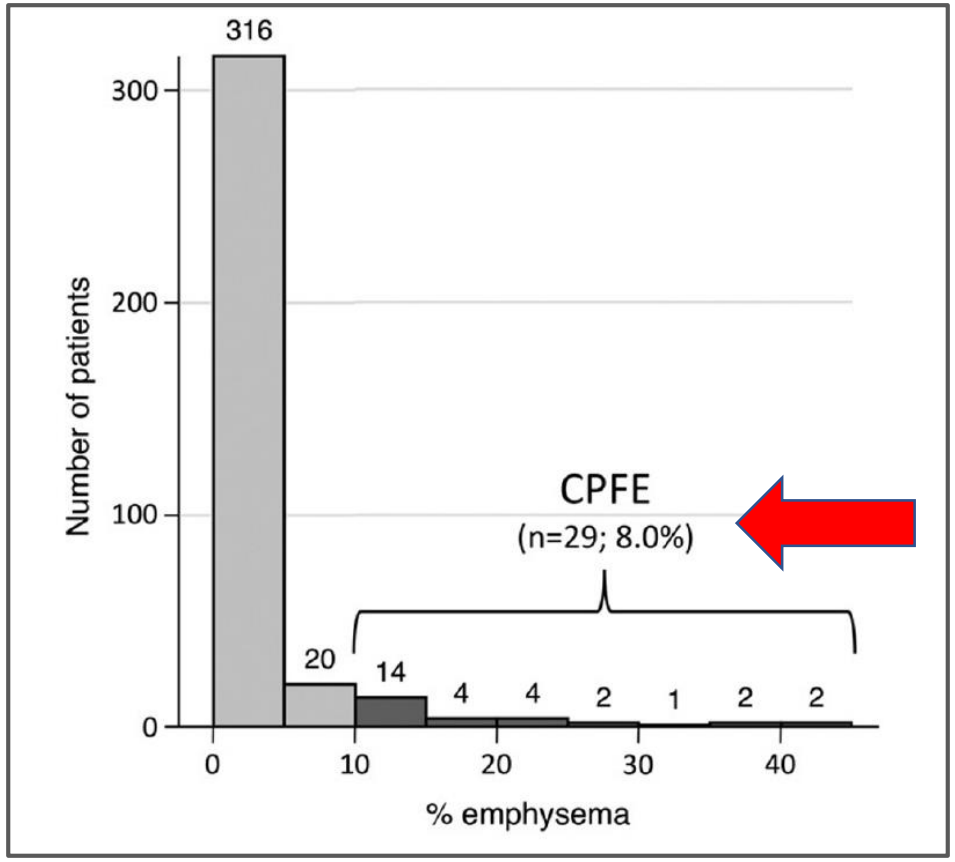
Characteristics of CPFE

- Almost exclusively males
- Strong association with smoking (current or ex-smoker)
- Preserved lung volumes
- Severely impaired carbon monoxide diffusing capacity
- Pulmonary arterial hypertension is a critical determinant of prognosis

CHEST
Original Research
DIFFUSE LUNG DISEASE

Clinical Features and Outcomes in Combined Pulmonary Fibrosis and Emphysema in Idiopathic Pulmonary Fibrosis

CPFE was defined as ≥10% emphysema

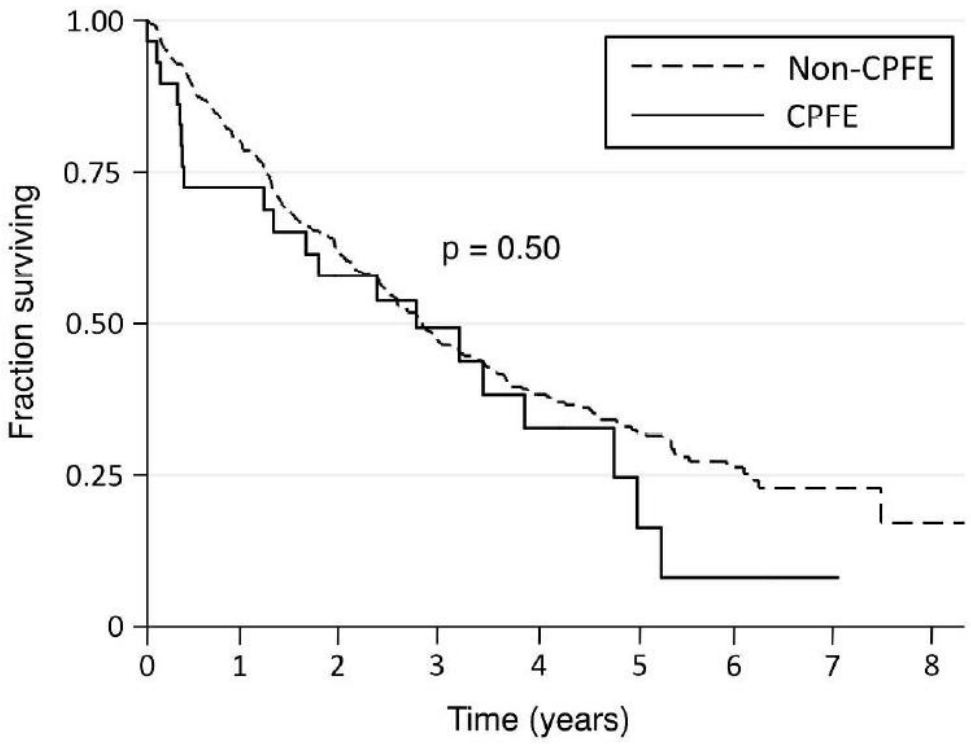


CHEST 2013; 144(1):234–240

Baseline Patient Characteristics

Variable	Non-CPFE (n = 336)	CPFE (n = 29)	P value
Age, years at baseline	69.0 (8.6)	69.9 (8.7)	0.59
Male sex	71%	69%	0.83
Body mass index, kg/m^2*	28.1 (4.8)	28.0 (5.4)	0.91
Smoking history			
Current or former smoker	71%	100%	0.007
Pack-years*	16.1 (23.5)	46.4 (15.3)	< 0.001
Measures of disease severity			
Dyspnea score*	9.3 (5.6)	10.7 (6.3)	0.33
Long-term oxygen therapy	25%	55%	0.001
Pulmonary arterial pressure			
Echo SPAP, mmHg*	39.6 (12.7)	56.6 (20.3)	0.008
Pulmonary function			
FVC, % predicted	65.0 (16.9)	79.8 (15.7)	< 0.001
FEV_1, % predicted	71.4 (17.5)	80.3 (16.8)	0.01
FEV_1/FVC ratio*	0.83 (0.07)	0.74 (0.06)	< 0.001
TLC, % predicted	66.0 (12.9)	78.9 (14.4)	< 0.001
RV, % predicted*	66.2 (22.8)	73.8 (29.7)	0.24
DLCO, % predicted	44.4 (14.7)	37.1 (14.0)	0.02
HRCT fibrosis score	22.6 (11.4)	16.8 (10.3)	0.003

No significant difference in mortality



CHEST 2013; 144(1):234–240

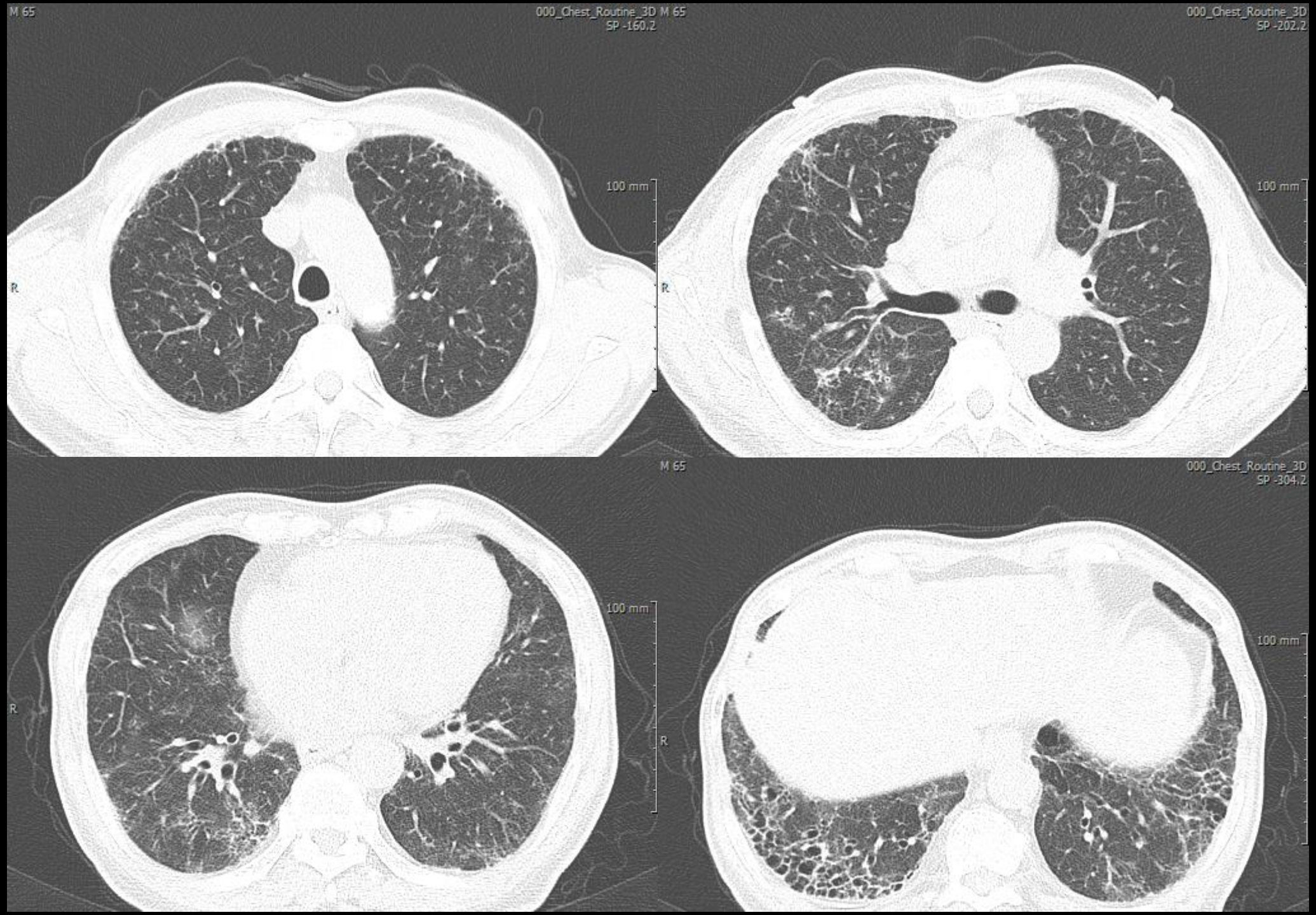
Diagnosis and Management of Emphysema at Presentation

Variable	Non-CPFE (n = 175)	CPFE (n = 17)	P value
Diagnosis			
Physician-reported diagnosis of COPD/emphysema	17 (10%)	14 (82%)	< 0.001
Self-reported diagnosis of COPD/emphysema	41 (24%)	13 (76%)	< 0.001
Management			
Inhaled bronchodilator	52 (30%)	9 (53%)	0.0496
Short-acting β-agonist	31 (18%)	8 (47%)	0.004
Short-acting anticholinergic	13 (7%)	5 (29%)	0.003
Long-acting β-agonist	27 (15%)	3 (18%)	0.81
Long-acting anticholinergic	13 (7%)	4 (24%)	0.03
Inhaled corticosteroid	29 (17%)	4 (24%)	0.47
Not on inhaled bronchodilator or corticosteroid	120 (69%)	8 (47%)	0.07

CHEST 2013; 144(1):234–240

Questions to be answered

- Whether CPFE is a phenotype of IPF, or a more general condition occurring in lung fibrosis of any cause (ie, not just IPF) ?
- CPFE could alternatively be regarded as a phenotype of emphysema ?
- Why some smokers develop emphysema, some IPF, and some CPFE ?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R
000_Chest_Routine_3D
SP -202.2
100 mm
R
100 mm
R
M 65
000_Chest_Routine_3D
SP -304.2
100 mm
R

Subclinical ILD / Interstitial lung abnormalities (ILA)

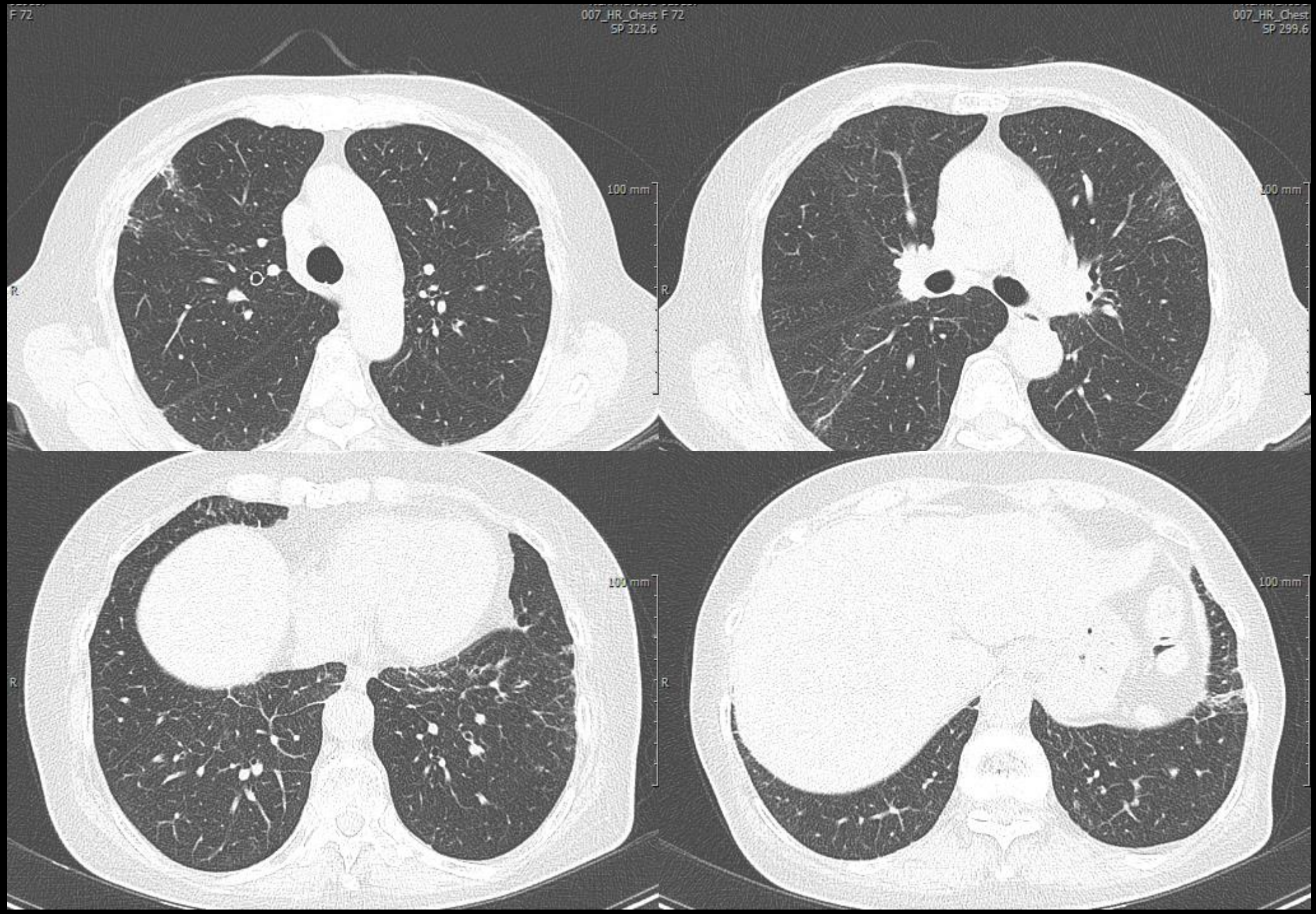
- First described in families affected with interstitial pneumonia

- Recent studies
  - some individuals at risk for ILD (e.g., members of families affected with pulmonary fibrosis, **smokers**, and individuals with connective tissue diseases)
  - a subset of these patients over time could develop ILD

Definition of ILA

- Specific patterns of increased lung density on chest CT identified in who with no prior history of interstitial lung disease

- ILA – defined as nondependent change affecting more than 5% of any lung zone
  1) Reticular or ground-glass abnormalities
  2) Diffuse centrilobular nodularity
  3) Nonemphysematous cyst
  4) Honeycombing or taction bronchiectasis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R
100 mm
R
100 mm
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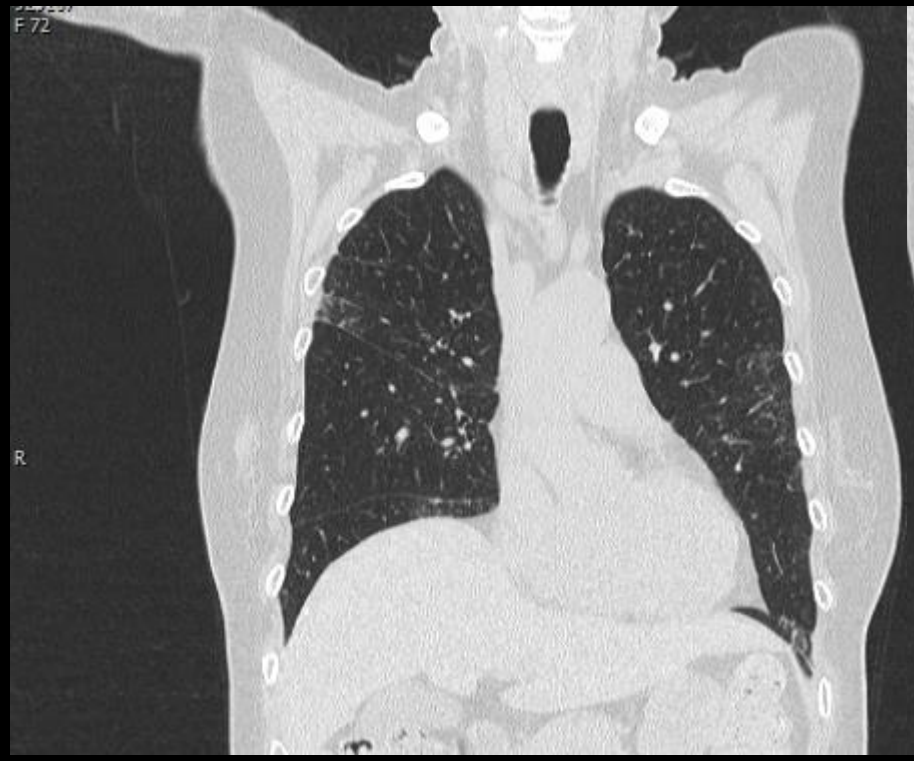
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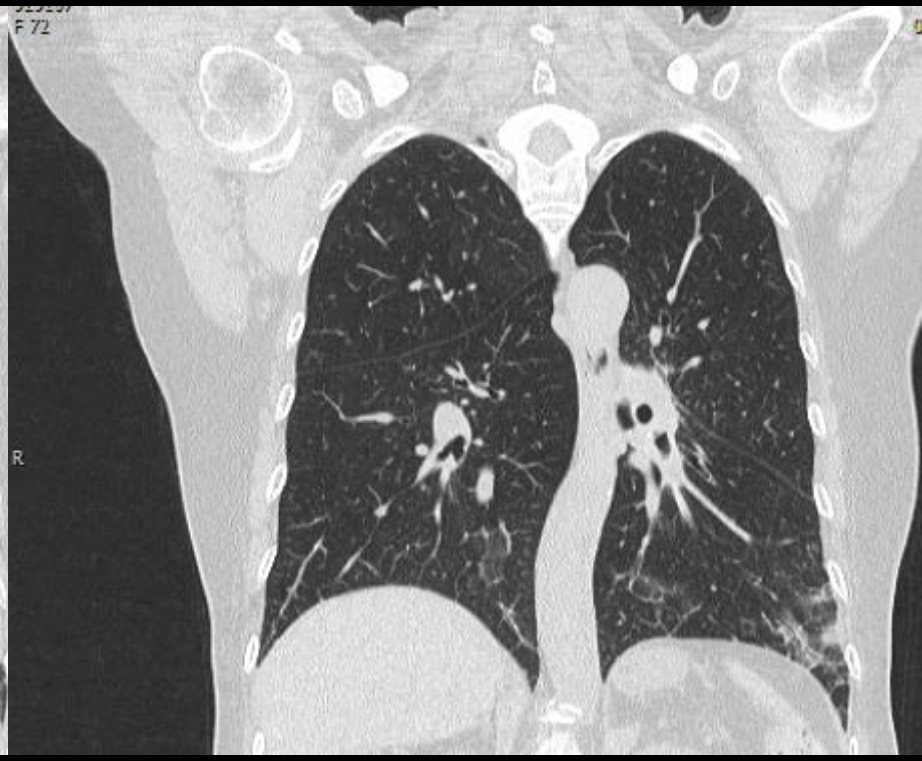
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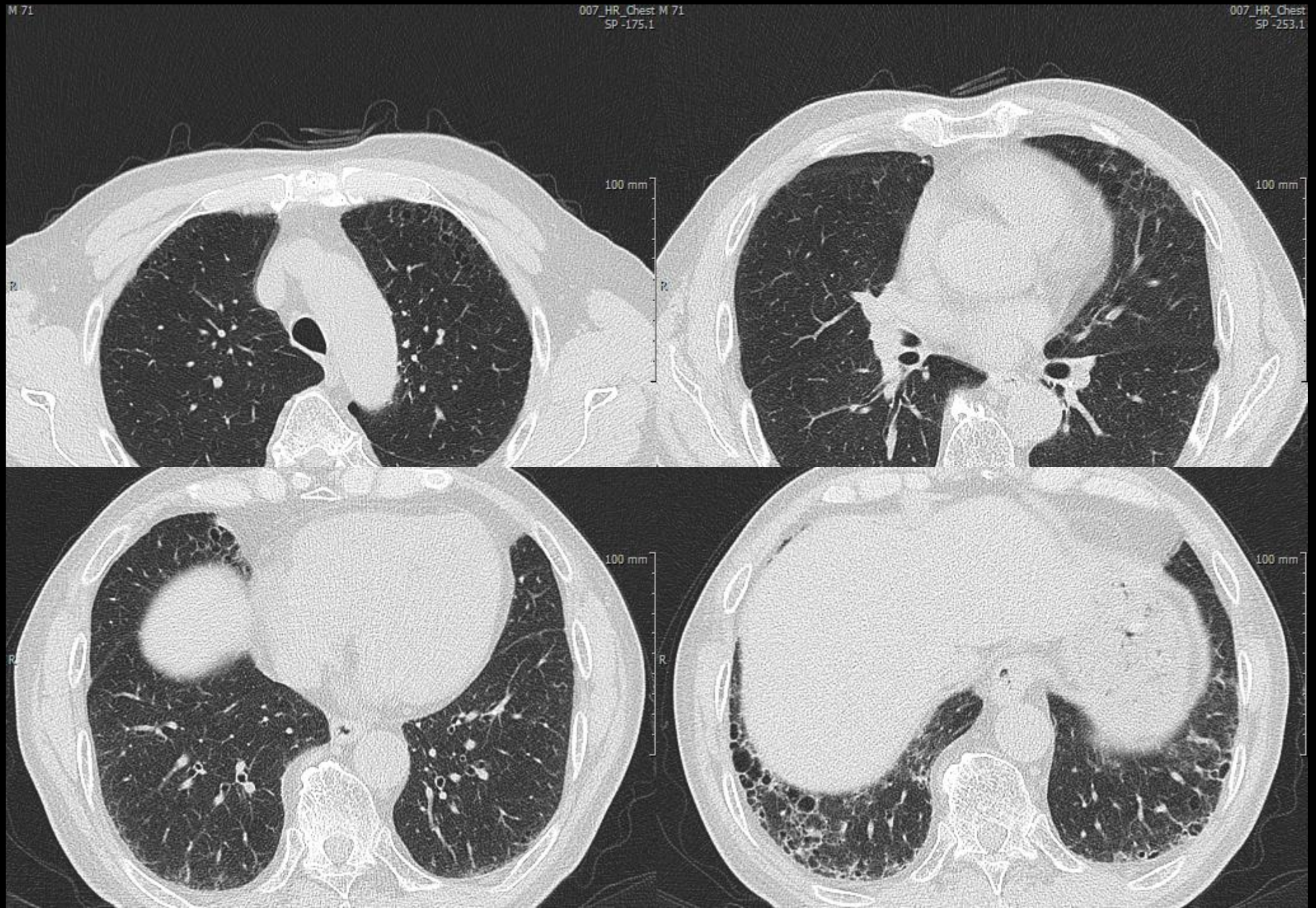
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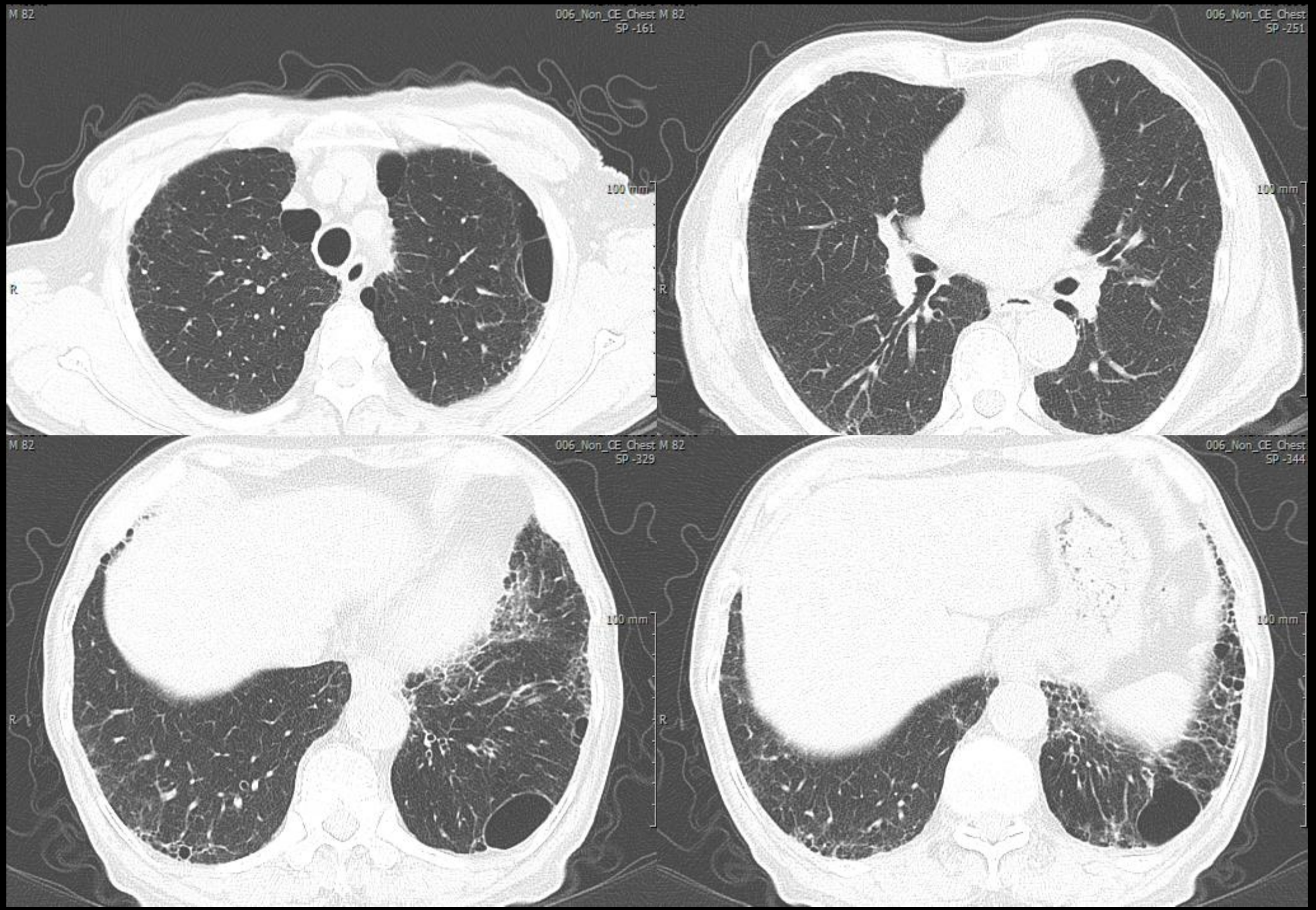
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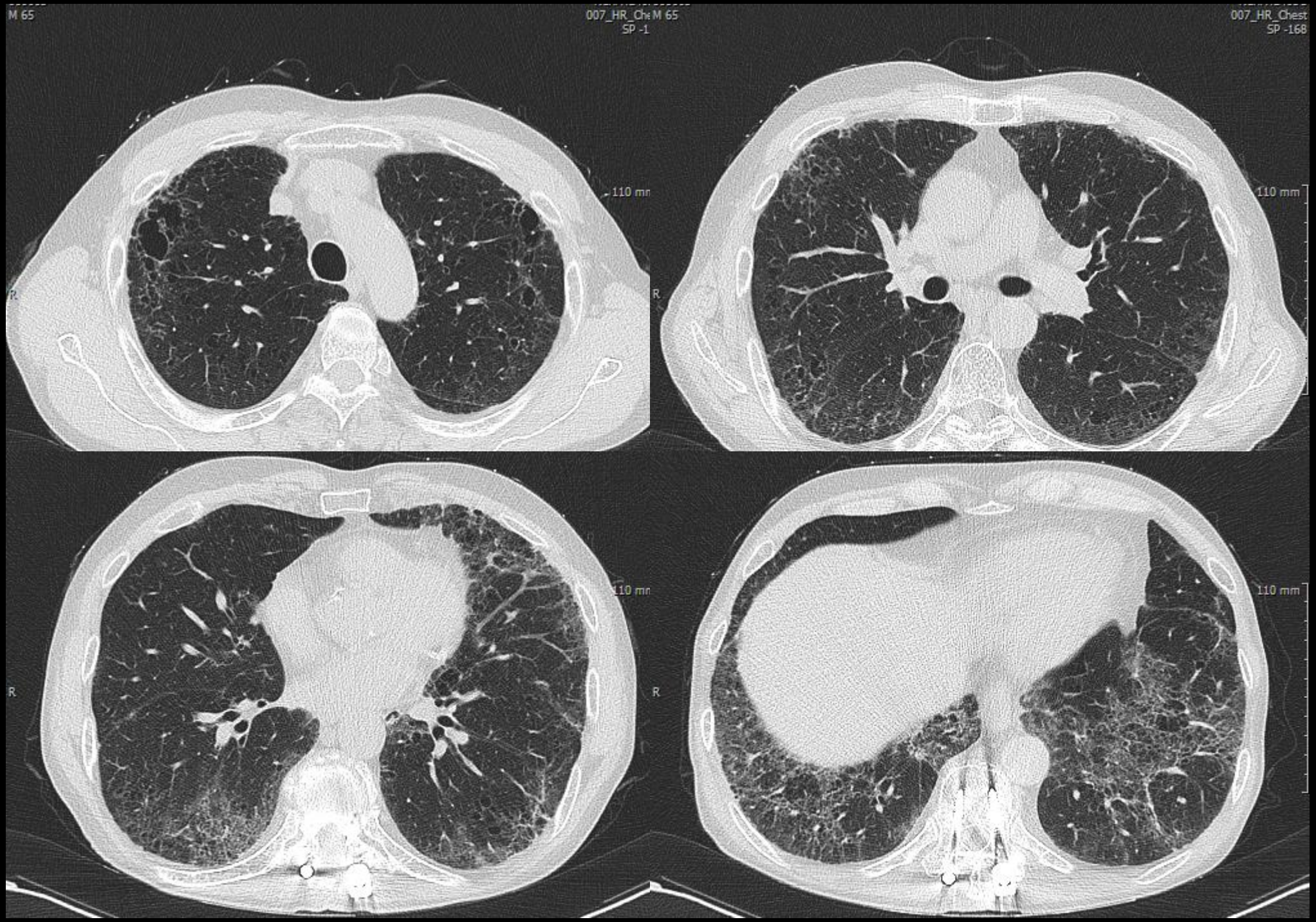
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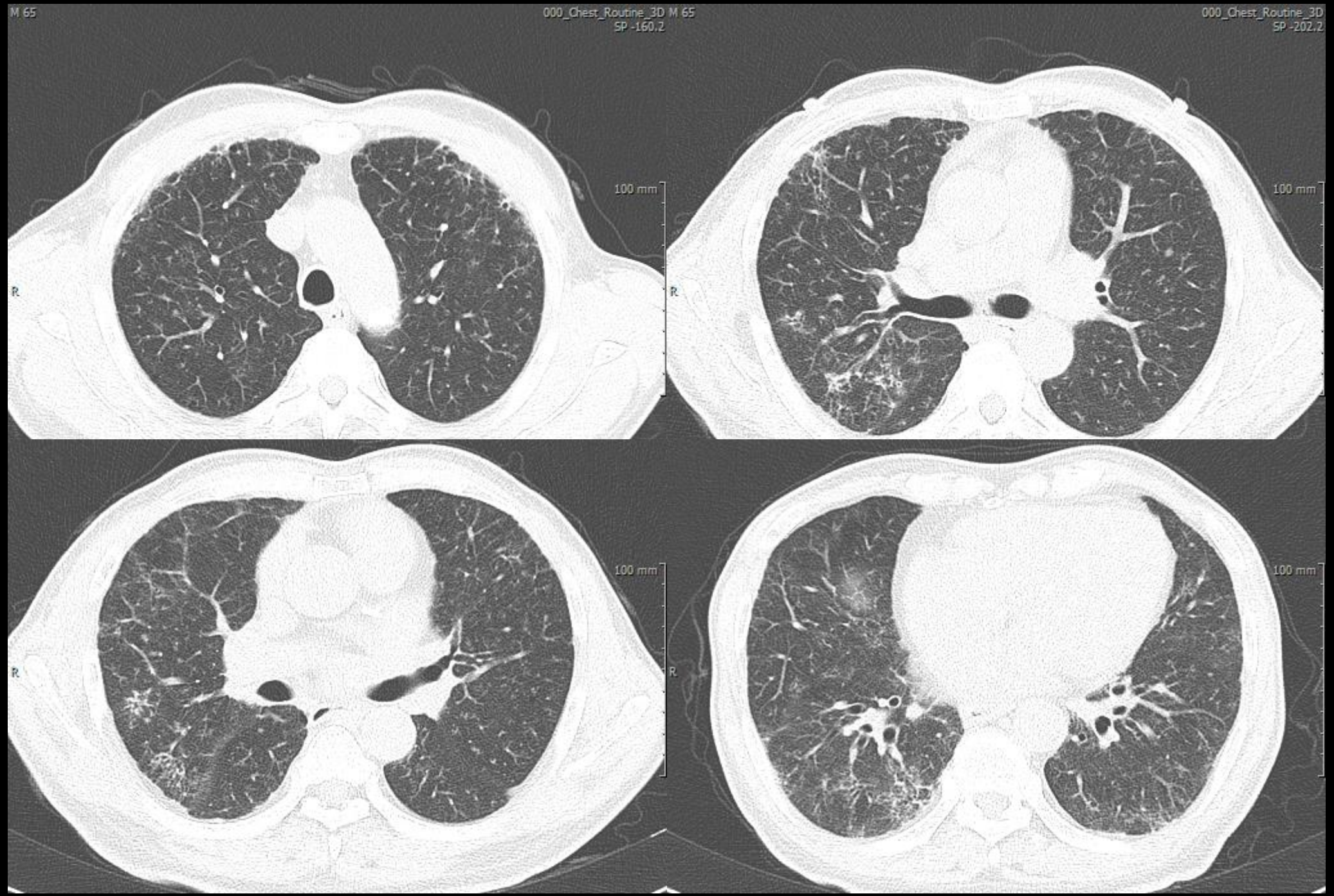
M 65
000_Chest_Routine_3D M 65
SP -160.2
000_Chest_Routine_3D
SP -202.2
100 mm
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Cigarette Smoking Is Associated with Subclinical Parenchymal Lung Disease

The Multi-Ethnic Study of Atherosclerosis (MESA)–Lung Study

- 2,563 adults without airflow obstruction or clinical cardiovascular disease in a population-based cohort

- measured spirometric restriction and regions of high attenuation area (HAA) on CT imaging

AJRCCM Vol 180. pp 407–414, 2009

The prevalence of spirometric restriction was 10.0% and increased relatively by 8% for each 10 cigarette pack-years

The median volume of high attenuation areas was 119 cm^3 and the volume of high attenuation areas increased by 1.6 cm^3 for each 10 cigarette pack-years

	Cigarette Pack-Years				*P* for Trend	Effect Estimate per 10 Pack-Years (95% CI)	*P* Value
	0	1–10	11–20	>20			
No. of subjects	1,444	432	235	452		2,563	
Prevalence of spirometric restriction	9%	8%	9%	16%	<0.001		
Prevalence ratios for spirometric restriction							
Age, sex, and race/ethnicity-adjusted	1 (Ref)	0.8	0.9	1.6	0.003	1.10 (1.07–1.14)	<0.001
Age, sex, race/ethnicity, smoking status, and urine cotinine-adjusted	1 (Ref)	0.8	0.9	1.5	0.02	1.09 (1.05–1.14)	<0.001
Full multivariate model	1 (Ref)	0.8	0.8	1.4	0.08	1.08 (1.03–1.12)	<0.001
HAA volume, cm^3*	122	130	131	140	<0.001		
Mean increase in HAA volume, cm^3*							
Age, sex, and race/ethnicity-adjusted	0 (Ref)	2.4	5.0	14.0	<0.001	2.5 (1.8–3.3)	<0.001
Age, sex, race/ethnicity, smoking status, and urine cotinine-adjusted	0 (Ref)	2.1	3.7	10.9	<0.001	2.0 (1.2–2.8)	<0.001
Full multivariate model	0 (Ref)	1.0	3.3	9.2	<0.001	1.6 (0.9–2.4)	<0.001

Suggestion

- **Smoking may cause subclinical parenchymal lung disease (ILA) even among a generally healthy cohort**

The NEW ENGLAND JOURNAL of MEDICINE

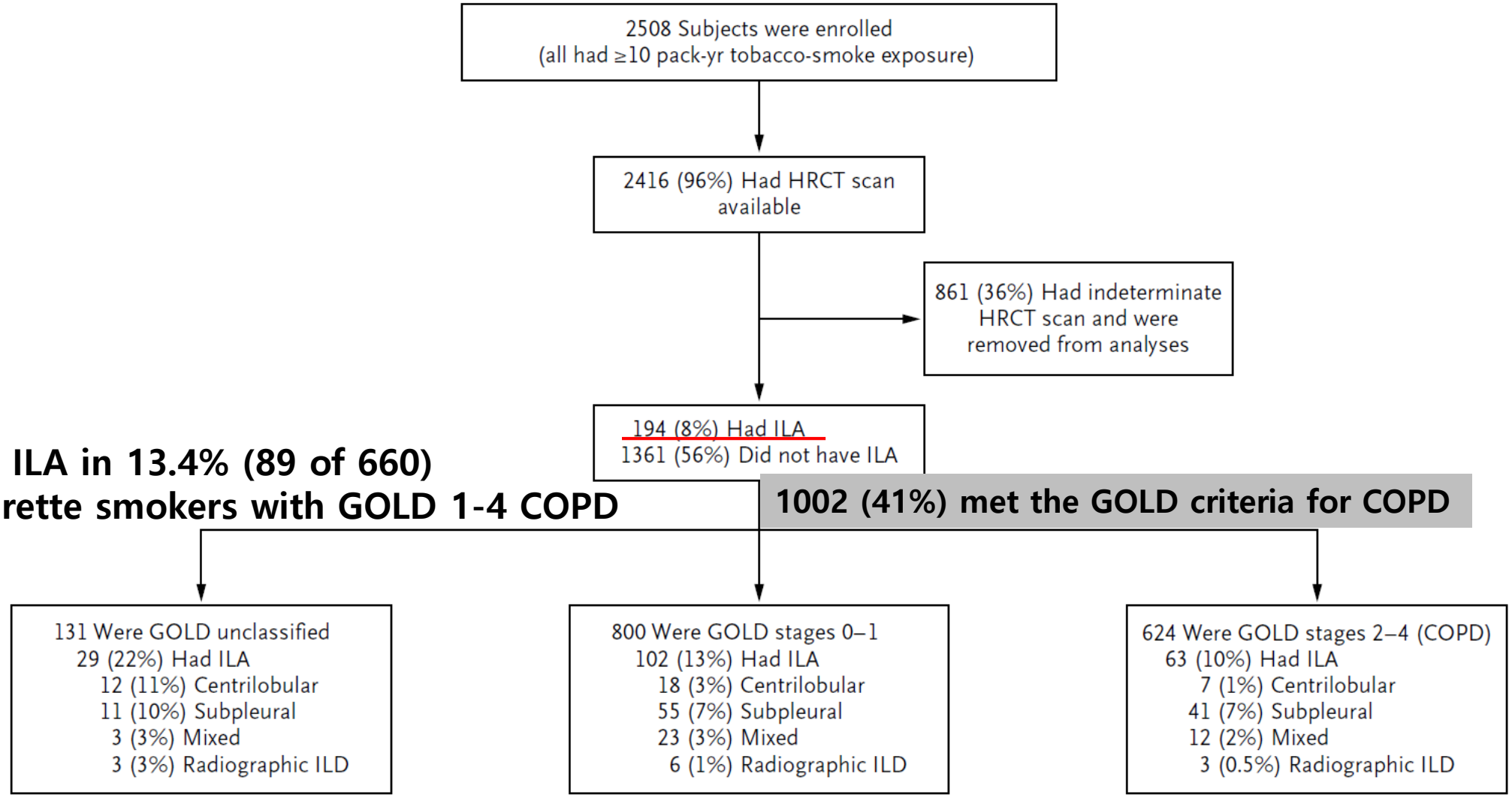
ESTABLISHED IN 1812 MARCH 10, 2011 VOL. 364 NO. 10

Lung Volumes and Emphysema in Smokers with Interstitial Lung Abnormalities

George R. Washko, M.D., M.M.Sc., Gary M. Hunninghake, M.D., M.P.H., Isis E. Fernandez, M.D., Mizuki Nishino, M.D., Yuka Okajima, M.D., Tsuneo Yamashiro, M.D., James C. Ross, M.S., Raúl San José Estépar, Ph.D., David A. Lynch, M.D., John M. Brehm, M.D., M.P.H., Katherine P. Andriole, Ph.D., Alejandro A. Diaz, M.D., Ramin Khorasani, Ph.D., Katherine D'Aco, M.S., Frank C. Sciurba, M.D., Edwin K. Silverman, M.D., Ph.D., Hiroto Hatabu, M.D., Ph.D., and Ivan O. Rosas, M.D., for the COPDGene Investigators*

N Engl J Med 2011;364:897-906

Study population and groups

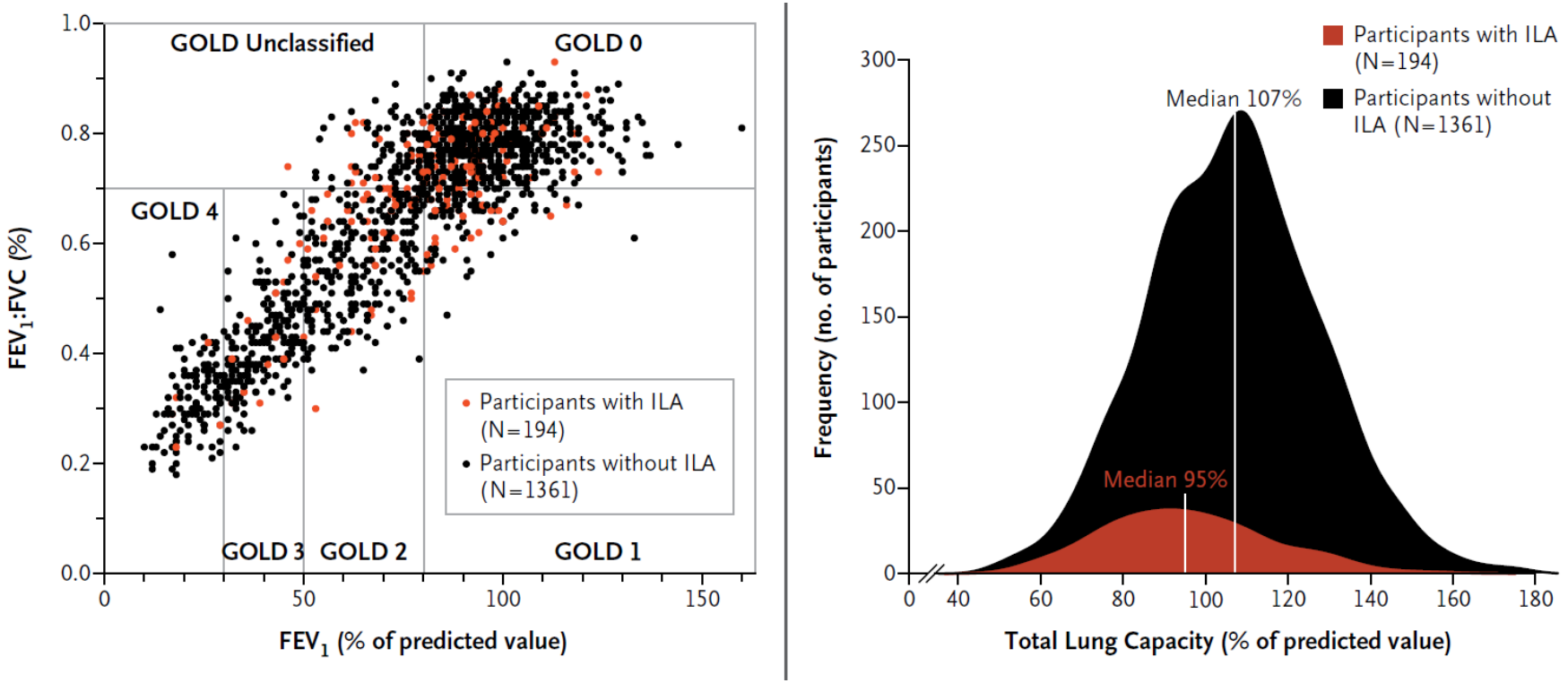


Definit ILA in 13.4% (89 of 660) of cigarette smokers with GOLD 1-4 COPD

Baseline Characteristics

Variable	Participants without ILA	P Value	Participants with Indeterminate HRCT Scans	P Value	Participants with ILA	P Value
Median FEV_1 — % of predicted‡	80 (52–97)	0.02	77 (55–92)	0.03	82 (67–93)	0.15
Median FVC — % of predicted‡	88 (75–100)	0.08	87 (74–99)	0.30	88 (77–98)	0.80
Median FEV_1:FVC %‡	70 (51–79)	0.04	68 (53–76)	0.01	71 (61–77)	0.32
Spirometric restriction — no. (%)§	414 (30)	0.82	266 (31)	0.004	81 (42)	0.002
Chest CT findings						
Median % emphysema¶						
–950 HU	4.1 (1.3–12.4)	<0.001	3.3 (0.9–9.7)	<0.001	2.2 (0.7–6.0)	<0.001
–910 HU	30 (15–47)	<0.001	23 (10–41)	<0.001	14 (7–29)	<0.001
Total lung capacity‖						
Median volume at full inspiration — liters	5.70 (4.80–6.78)	<0.001	5.21 (4.38–6.27)	0.08	5.02 (4.15–5.96)	<0.001
Median % of predicted value	107 (92–120)	<0.001	100 (84–112)	0.04	95 (81–109)	<0.001
<80% of predicted value — no. (%)	134 (10)	<0.001	169 (20)	0.77	40 (21)	<0.001
Median lung volume at relaxed exhalation — liters	3.13 (2.51–3.98)	0.06	3.04 (2.48–3.84)	<0.001	2.67 (2.23–3.44)	<0.001
Unclassified	102 (7)	0.007	94 (11)	0.17	28 (14)	0.002
0	599 (44)		306 (36)		76 (39)	
1	99 (7)		83 (10)		26 (13)	
2	260 (19)		201 (23)		46 (24)	
3	186 (14)		121 (14)		12 (6)	
4	115 (8)		56 (7)		5 (3)	

Study Enrollment and Findings



Participants with ILA were less likely to have COPD, were more likely to have spirometric values that could not be classified according to the GOLD criteria

ILA were associated with a lower percentage of emphysema
Participants with ILA had a 47% decrease in their odds of having COPD

Table 2. Univariate and Multivariate Analyses of the Association between Interstitial Lung Abnormalities and Metrics of Restrictive and Obstructive Lung Disease.*

Analysis	Restrictive Lung Disease								Obstructive Lung Disease			
	TLC		% of Predicted TLC		<80% of Predicted TLC		% Emphysema, −950 HU†		% Emphysema, −910 HU†		COPD‡	
	CE (95% CI)	P value	CE (95% CI)	P value	OR (95% CI)	P value	CE (95% CI)	P value	CE (95% CI)	P value	OR (95% CI)	P value
	liters											
Unadjusted	−0.655 (−0.869 to −0.441)	<0.001	−11 (−14 to −8)	<0.001	2.38 (1.61 to 3.51)	<0.001	−4 (−6 to 3)	<0.001	−13 (−16 to −10)	<0.001	0.69 (0.50 to 0.95)	0.02
Adjusted§	−0.444 (−0.596 to −0.292)	<0.001	−9 (−11 to −6)	<0.001	2.29 (1.43 to 3.68)	<0.001	−3 (−4 to −2)	<0.001	−10 (−12 to −8)	<0.001	0.53 (0.37 to 0.76)	<0.001

Suggestions of the study

- Emphysema and ILA have opposing effects on lung volume
- Inverse association between ILA and the severity of COPD/emphysema
- Patient who does not have characteristic abnormalities on PFT may be not disease-free, in fact the patient could be affected by two of the consequences of smoking

Interstitial Lung Abnormalities and Reduced Exercise Capacity

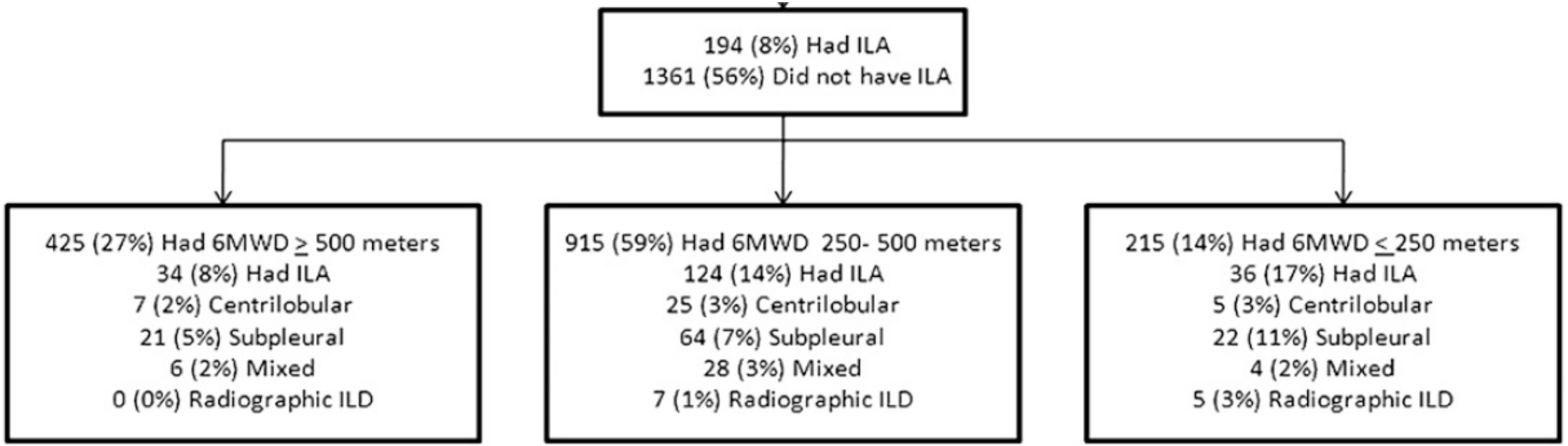
Tracy J. Doyle[1], George R. Washko[1], Isis E. Fernandez[1], Mizuki Nishino[2,3], Yuka Okajima[2], Tsuneo Yamashiro[2,3], Miguel J. Divo[1], Bartolome R. Celli[1], Frank C. Sciurba[4], Edwin K. Silverman[1,5], Hiroto Hatabu[2,3], Ivan O. Rosas[1], and Gary M. Hunninghake[1,5], for the COPDGene Investigators

Subjects in COPDGene study (>10 PY smokers)

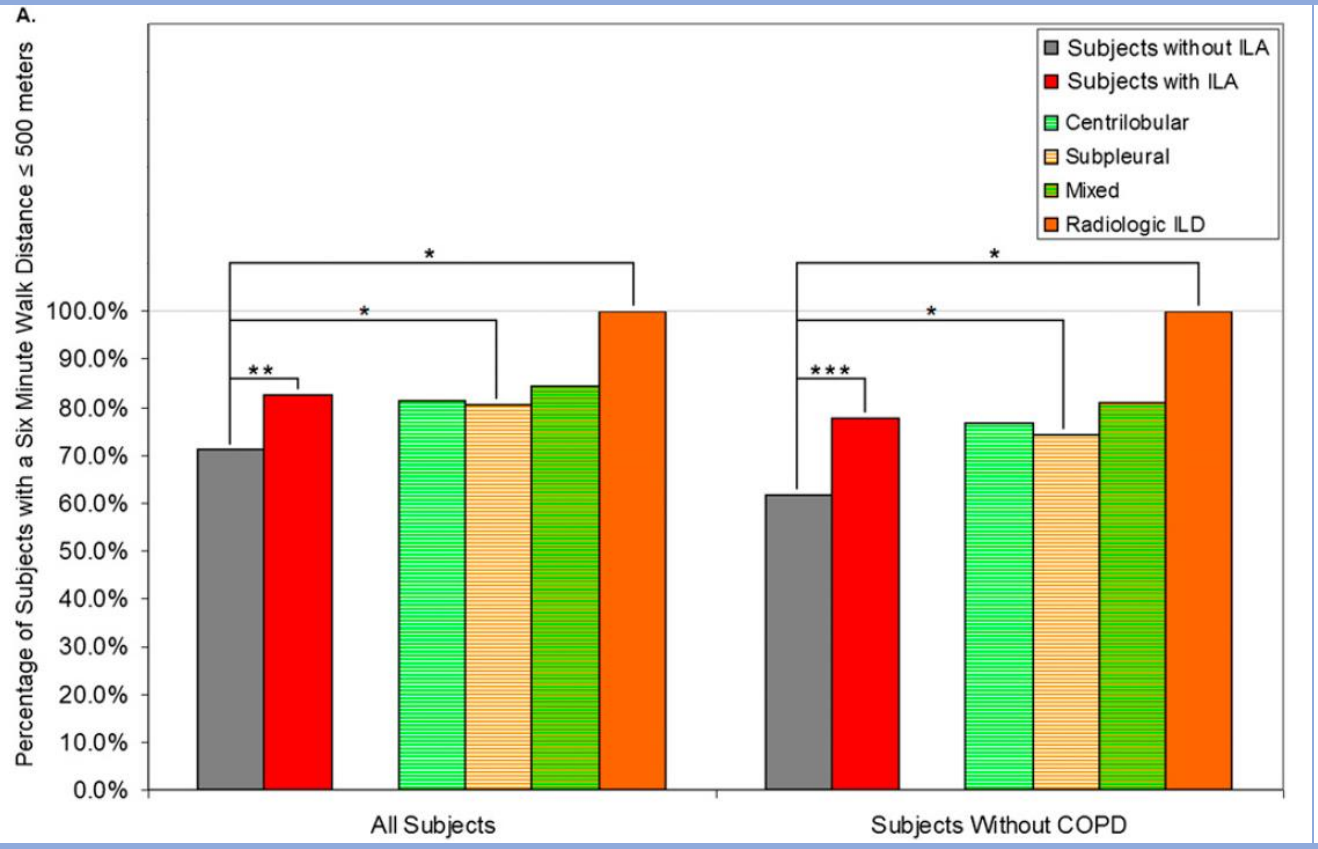
To examine the association between ILA and exercise capacity (6MWD)

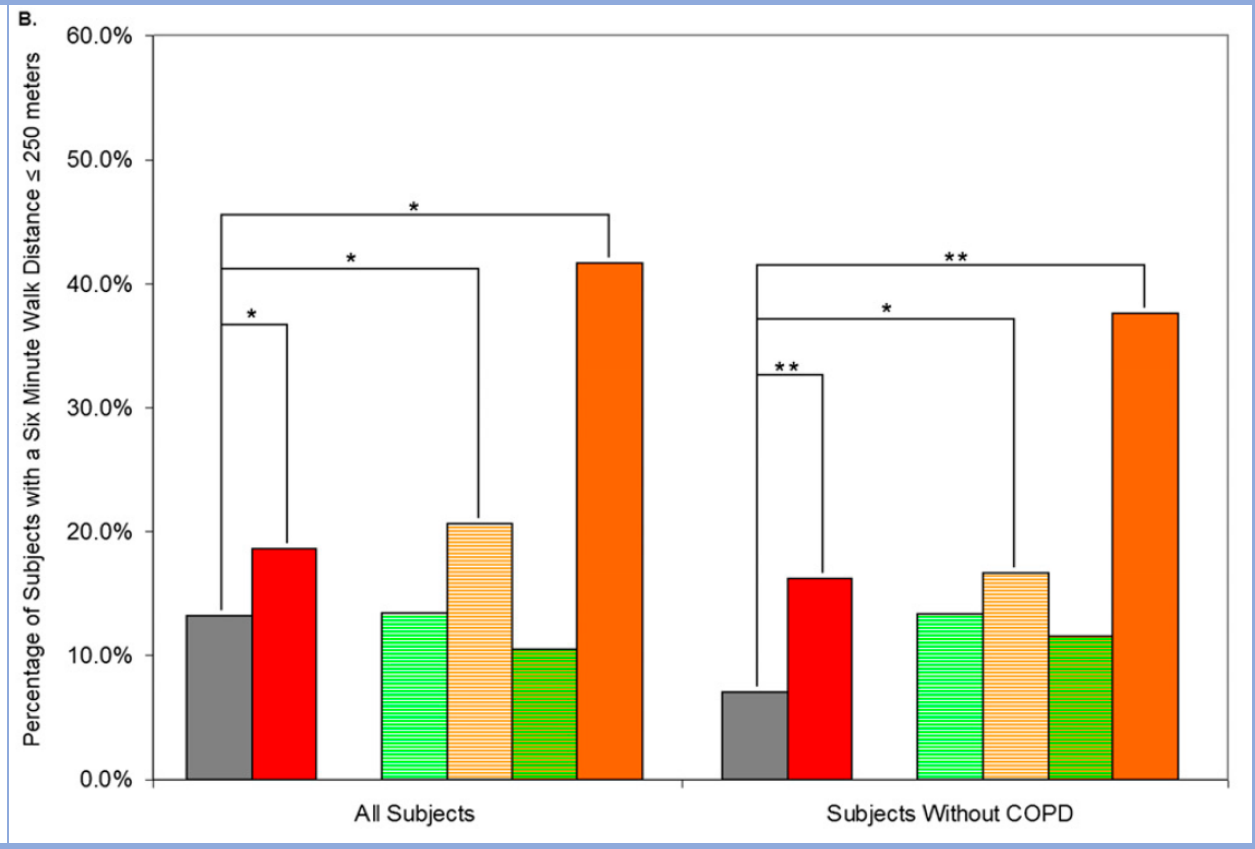
AJRCCM Vol 185, Iss. 7, pp 756–762, Apr 1, 2012

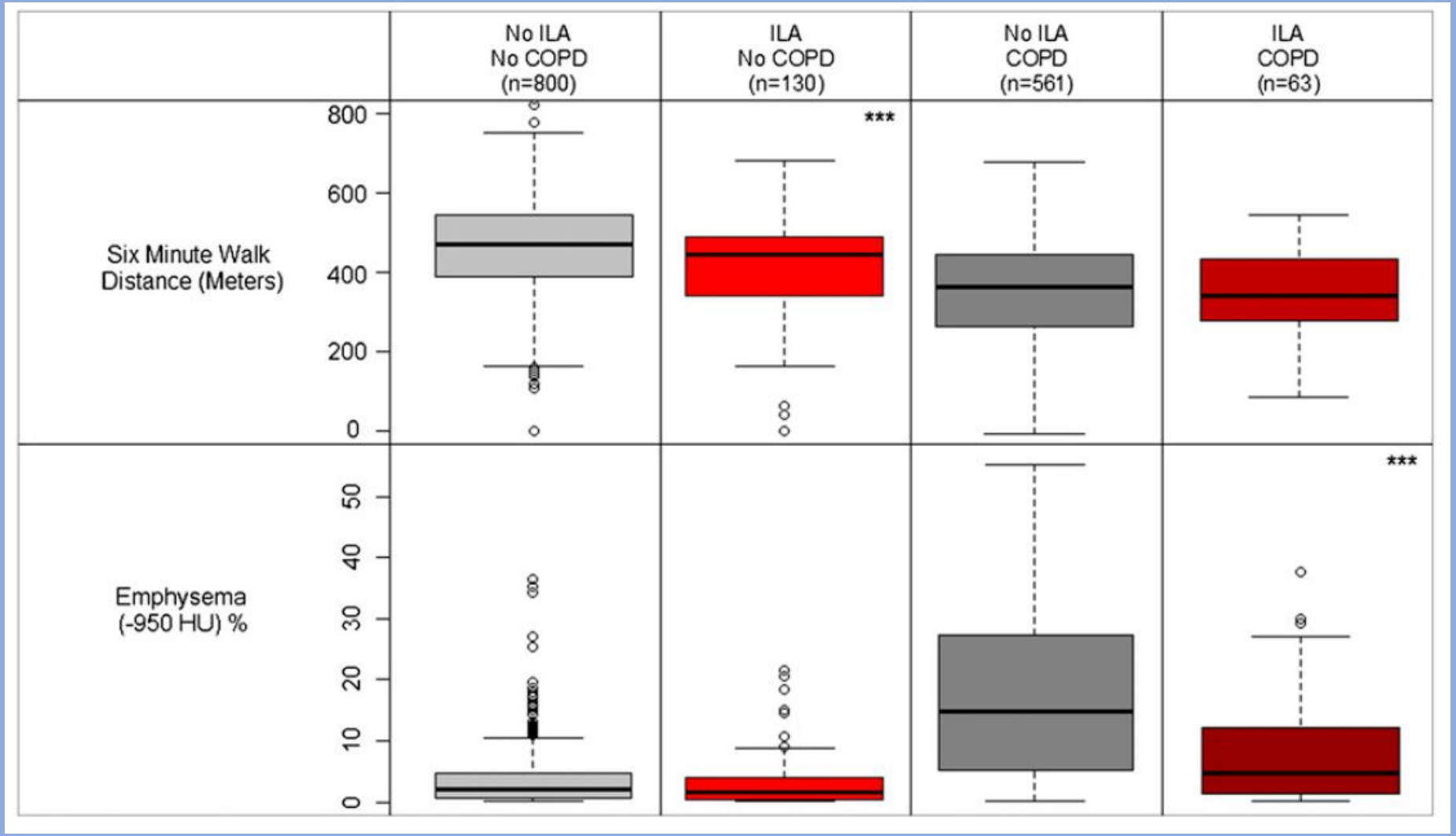
A flow diagram of study enrollment divides participants into three groups according to 6-minute walk distance



Bar graphs represent the % of all subjects and subjects without COPD who had a 6 MWT





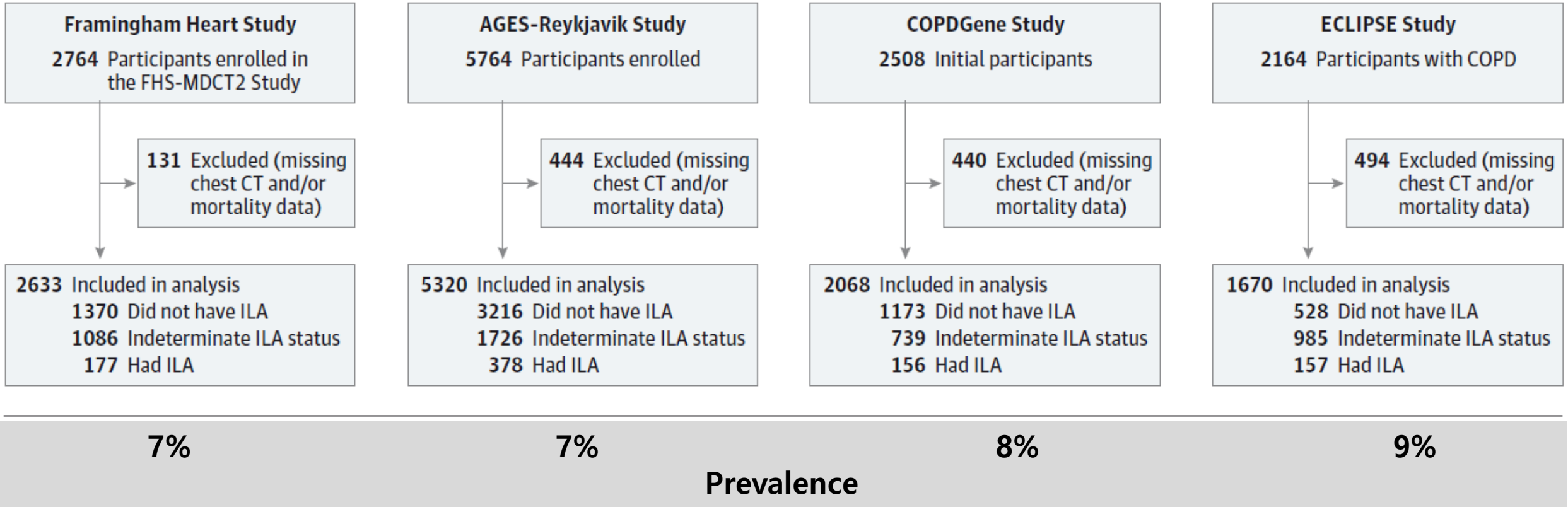

No ILA
No COPD
(n=800)
ILA
No COPD
(n=130)
No ILA
COPD
(n=561)
ILA
COPD
(n=63)
Six Minute Walk
Distance (Meters)
800
600
400
200
0
***
Emphysema
(-950 HU) %
50
40
30
20
10
0
***

Compared with subjects without ILA, subjects with ILA had an 80% and 77% increase in their odds to have a walk distance limited to less than or equal to 500 and 250 m, respectively

	All Subjects ($n = 1555$)			Subjects without COPD ($n = 930$)		
	6MWD ⩽ 500 m	6MWD ⩽ 250 *m*	6MWD (*m*)	6MWD ⩽ 500 m	6MWD ⩽ 250 m	6MWD (*m*)
	OR (95% CI) *P* Value	OR (95% CI) *P* Value	CE (95% CI) *P* Value	OR (95% CI) *P* Value	OR (95% CI) *P* Value	CE (95% CI) *P* Value
Unadjusted	1.90 (1.30 to 2.80) 0.001	1.51 (1.01 to 2.23) 0.04	−30 (−50 to −10) 0.004	2.19 (1.42 to 3.39) <0.001	2.56 (1.49 to 4.39) <0.001	−50 (−72 to −27) <0.001
Adjusted*	1.80 (1.12 to 2.89) 0.02	1.77 (1.04 to 3.03) 0.04	−19 (−33 to −5) 0.008	1.48 (0.86 to 2.55) 0.16	2.67 (1.23 to 5.80) 0.01	−18 (−35 to −1) 0.04

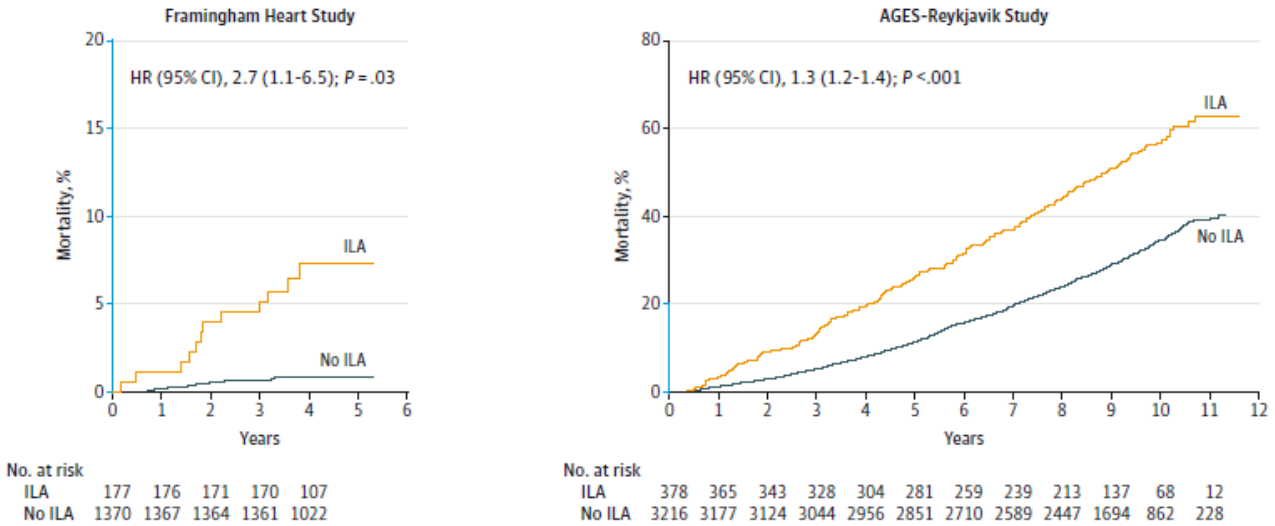
Original Investigation

Association Between Interstitial Lung Abnormalities and All-Cause Mortality



JAMA. 2016;315(7):672-681

Interstitial lung abnormalities were associated with a greater risk of all-cause mortality



JAMA. 2016;315(7):672-681

Mortality, ILA, and Cause of Death for the AGES-Reykjavik Study

	No. (%)[a]			
	ILA	Indeterminate	No ILA	Overall
No. of participants	378	1726	3216	5320
Deaths				
Total	115 (100)	382 (100)	468 (100)	965
Cardiovascular[b]	48 (42)	161 (42)	204 (44)	413
Cancer[c]	29 (25)	111 (29)	151 (32)	291
Respiratory[d]	15 (13)	22 (6)	20 (4)	57
Pulmonary fibrosis	7	1	0	8
Other	8	21	20	49
Other[e]	23 (20)	88 (23)	93 (20)	204

Open Access Full Text Article

ORIGINAL RESEARCH

Are interstitial lung abnormalities associated with COPD? A nested case–control study

Predominant LDCT pattern	LDCT features
Definite UIP pattern	Predominant lower lung zone subpleural reticular opacities and honeycombing With or without traction bronchiectasis/bronchiolectasis and signs of architectural distortion (eg, lung fissure displacement) Focal ground glass
Possible UIP pattern	Predominant lower lung zone subpleural reticular opacities With or without traction bronchiectasis/bronchiolectasis and signs of architectural distortion (eg, lung fissure displacement) Focal ground glass
RB	Predominant upper middle lung zone fluffy centrilobular nodules with or without GGO
Indeterminate	Any combination of features that do not fit UIP or RB patterns and do not consist of AEF (eg, bilateral GGO and predominant upper lung zone subpleural reticular opacities)

International Journal of COPD 2016:11 1087–1096

457 COPD cases / 914 control
Subjects with any ILA – more frequently men and current smokers

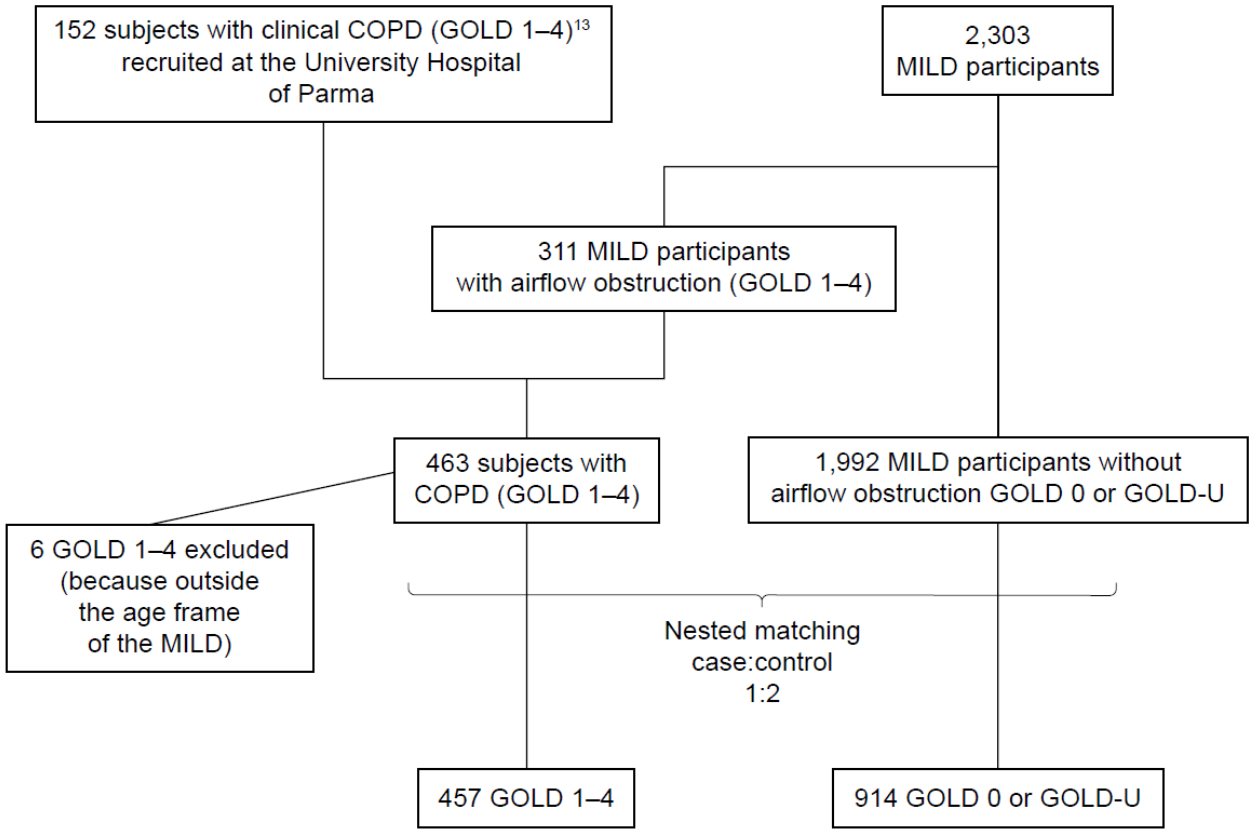
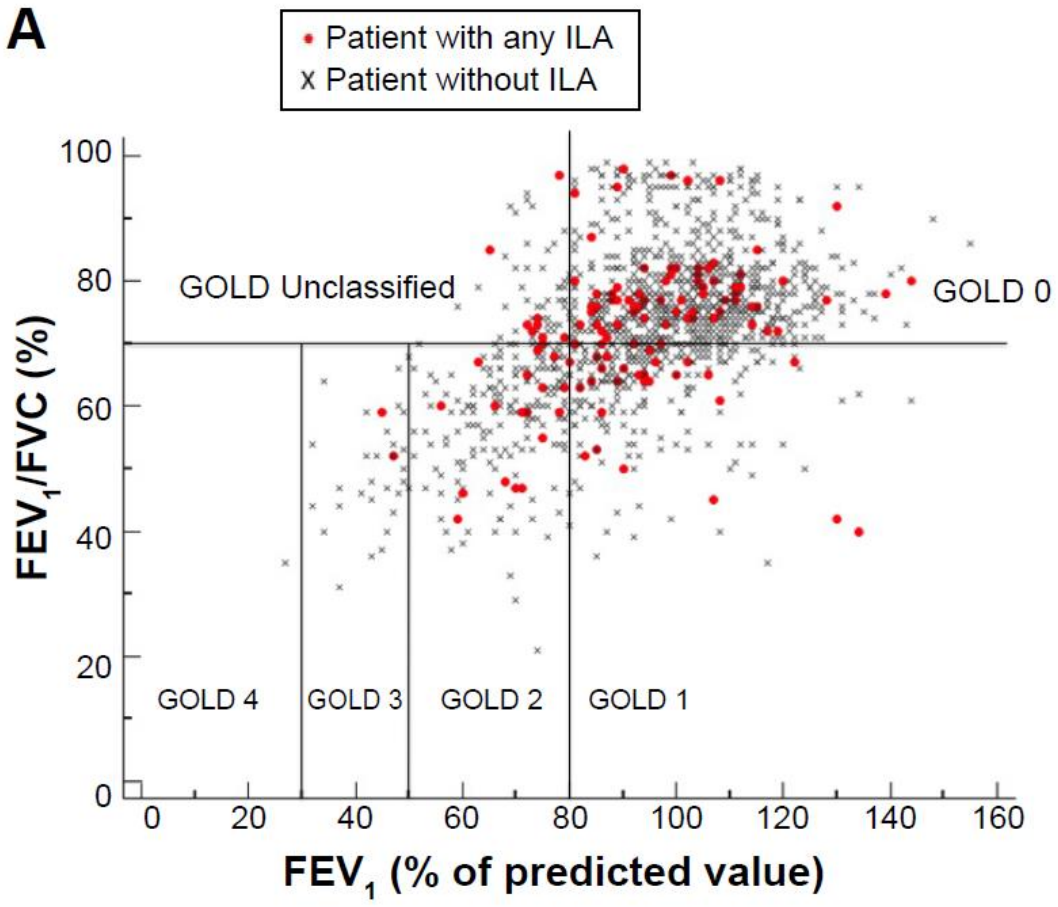
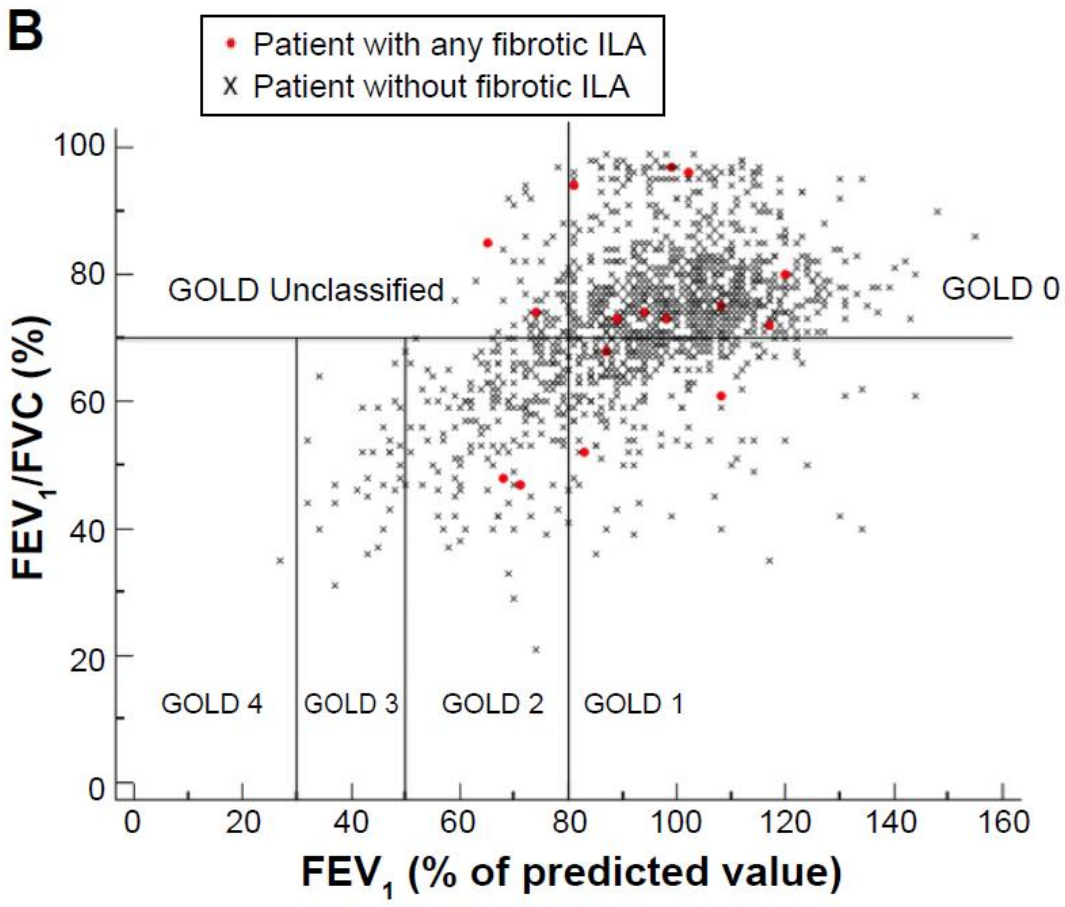


Table 4 Characteristics of subjects stratified for the presence of ILA

Variables	Subjects with any ILA (n=129)	Subjects with no ILA (n=1,242)	*P*-value
Sex (n)			
Female	33	427	0.04
Male	96	815	
Age, years (mean ± SD)	59.8±7.6	59.6±7	0.8
BMI (mean ± SD)	25.9±3.6	26.3±4.2	0.07
Smoking status (n)			
Current	109	791	<0.0001
Former	20	433	
Pack-years of smoking (mean ± SD)	49.5±24	44.9±21.7	0.03
FEV_1% (mean ± SD)	92.8±17.8	94.6±18.9	0.3
FVC% (mean ± SD)	102.7±17.8	104.8±17.4	0.6
FEV_1/FVC (mean ± SD)	71.8±12	72.8±12.5	0.7

Any ILA did not differ in terms of frequency across GOLD stages





The presence of airflow obstruction was not associated with definite ILA

Table 5 Univariate and multivariate logistic regression models predicting the likelihood of definite ILA

Variables	Univariate					Multivariate				
	β	SE	OR	95% CI	*P*-value	*β*	SE	OR	95% CI	*P*-value
Age, years	−0.018	0.014	0.982	0.955–1.010	0.208					
Sex										
Female	–	–	1	–	–					
Male	0.293	0.216	1.341	0.877–2.049	0.175					
FEV_1, % of predicted	−0.003	0.005	0.997	0.987–1.008	0.621					
BMI, kg/m^2	−0.036	0.025	0.965	0.919–1.013	0.148					
Smoking status										
Former	–	–	1	–	–	–	–	1	–	–
Current	1.456	0.301	4.289	2.380–7.731	**<0.001**	1.476 (1.400)[a]	0.302 (0.309)[a]	4.377 (4.054)[a]	2.422–7.910 (2.214–7.421)[a]	**<0.001 (<0.001)[a]**
Pack-years	0.010	0.004	1.010	1.003–1.018	**0.009**	0.012 (0.014)[a]	0.004 (0.004)[a]	1.012 (1.014)[a]	1.004–1.020 (1.005–1.022)[a]	**0.004 (0.001)[a]**
Airflow obstruction										
Absent	–	–	1	–	–					
Present	−0.226	0.220	0.798	0.519–1.227	0.303					

Conclusion

- No association between ILA and COPD in smokers
- COPD is not a risk factor for ILA
- It is still not clear which proportions of emphysema and ILA are required to produce either predominant obstructive or predominant restrictive functional pattern

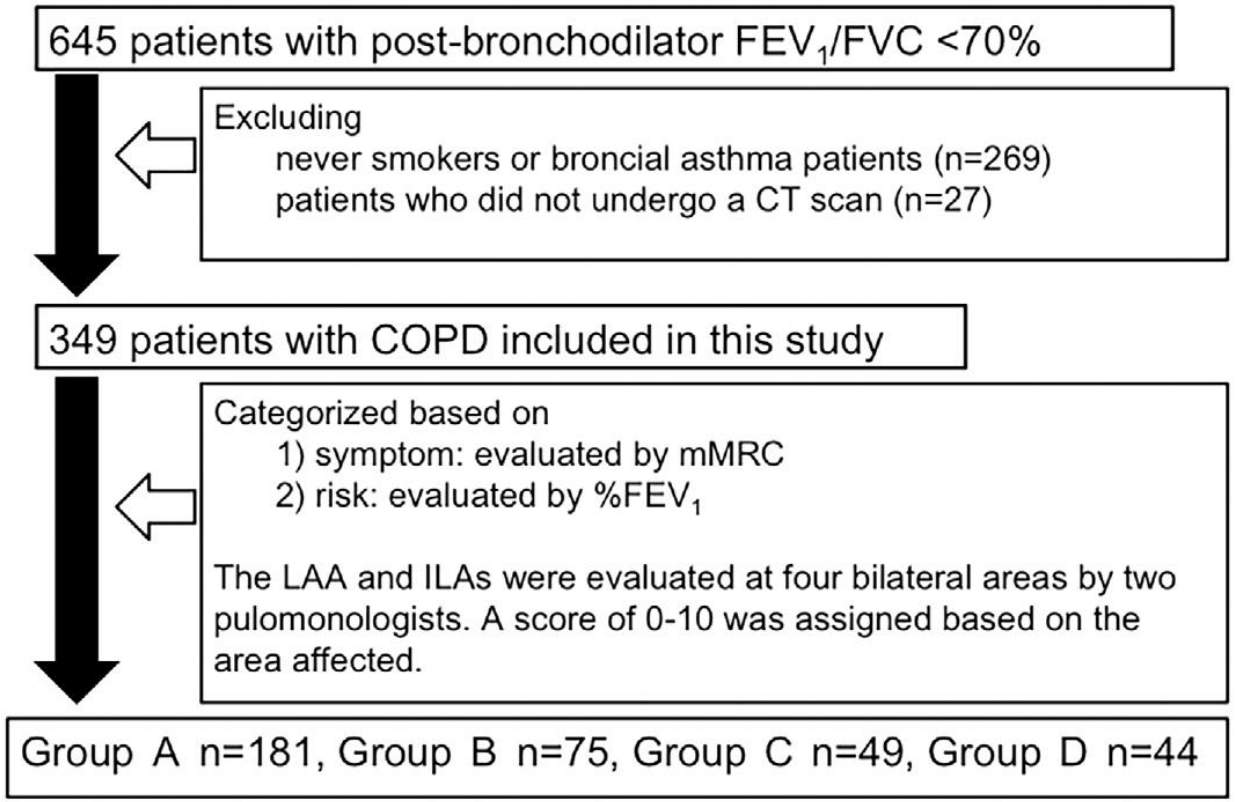
【 ORIGINAL ARTICLE 】

The Evaluation of Interstitial Abnormalities in Group B of the 2011 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Classification of Chronic Obstructive Pulmonary Disease (COPD)

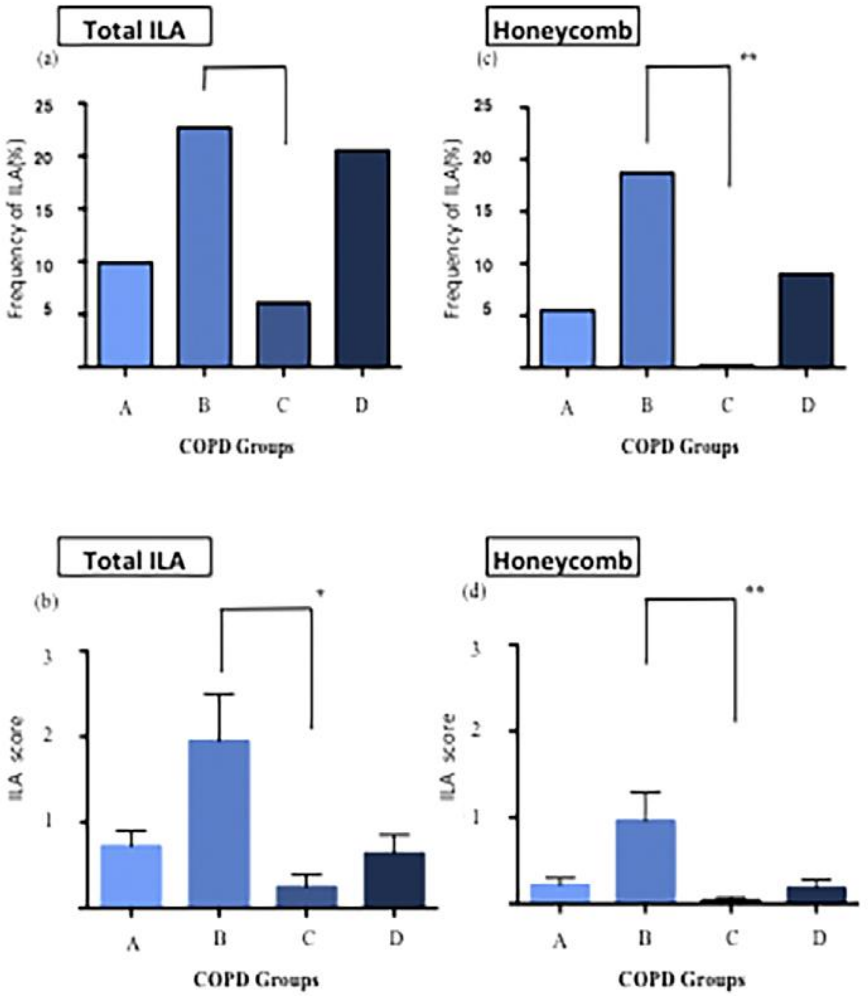
Intern Med 56: 2711-2717, 2017

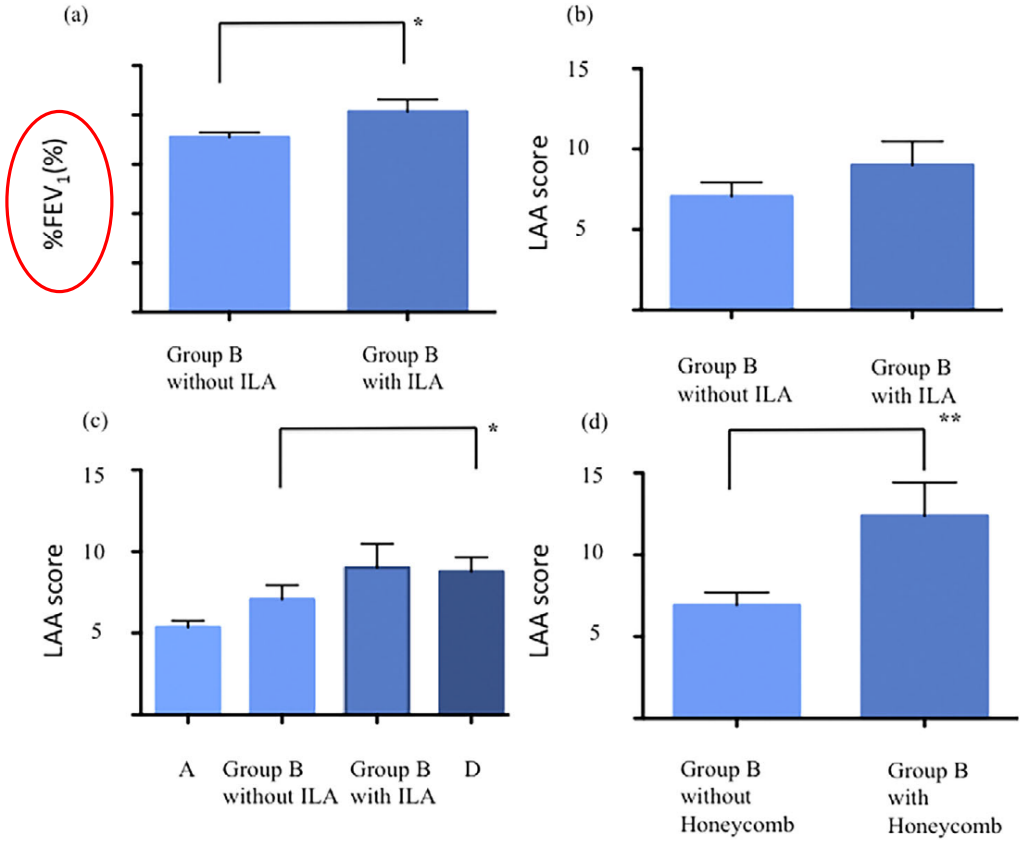
▪ The aim of study

Test the hypothesis that ILAs are more prevalent in Group B than Group C and that they may be responsible for the higher mortality in Group B



In Group B, the frequency and the area of ILAs was significantly higher in comparison to Group C





Conclusion

- ILAs were detected
  - ✓10.3% of the patients in Group A , 22.5% of the patients in Group B
  - ✓5.6% of the patients in Group C, 23.1% of the patients in Group D
- COPD patients with ILAs, especially those with honeycombing, tended to show better %FEV1 values
- ILA, if present in emphysematous lungs, contributed to the preserved %FEV1, the dyspnea score and possibly to the poorer prognosis of the patients in Group B

Annual changes in pulmonary function in combined pulmonary fibrosis and emphysema: Over a 5-year follow-up

Yoshiaki Kitaguchi [a], Keisaku Fujimoto [b,*], Ryoichi Hayashi [c], Masayuki Hanaoka [a], Takayuki Honda [d], Keishi Kubo [a]

Aim

To compare the yearly dynamics of pulmonary function parameters in CPFE patients with those in COPD patients

Respiratory Medicine (2013) 107, 1986-1992

CPFE vs COPD groups

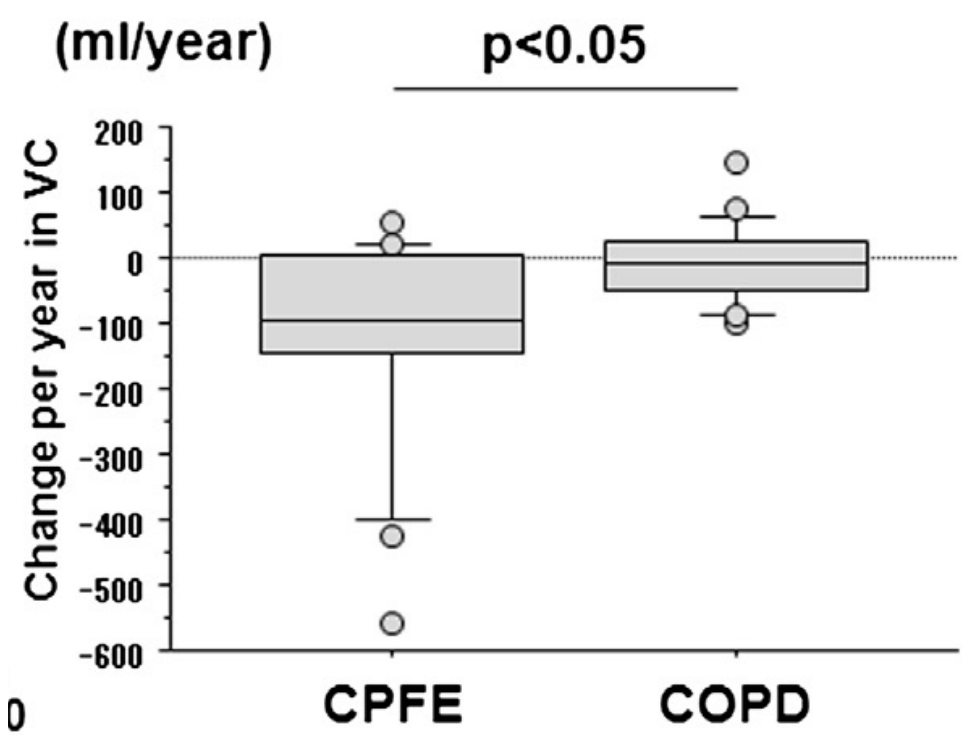
Clinical characteristics during the F/U

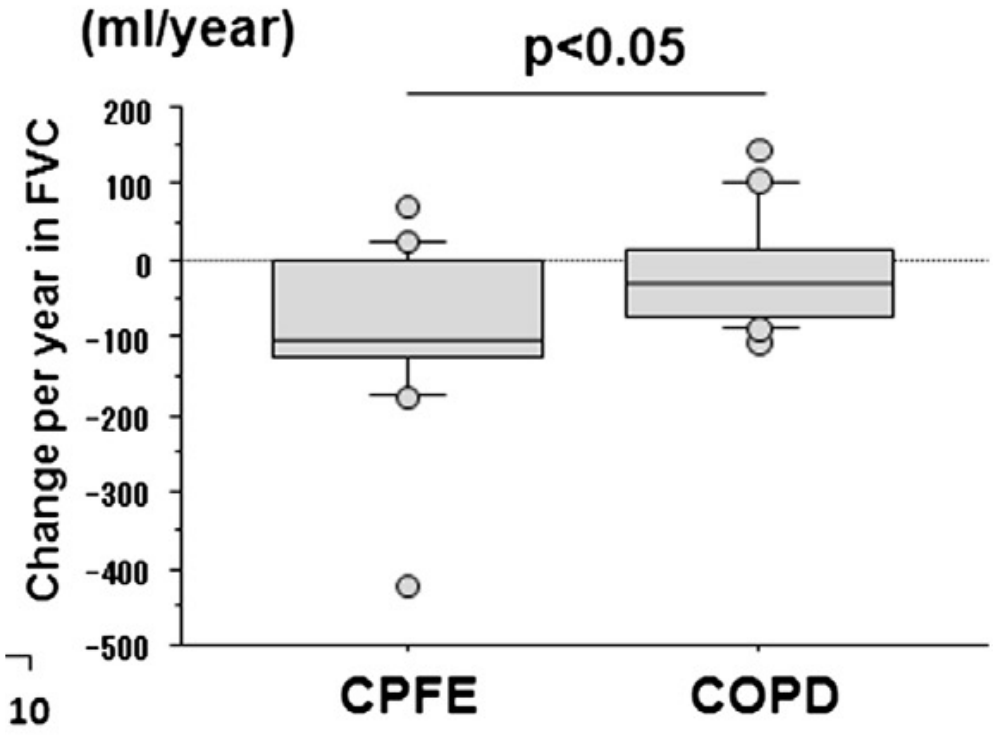
	CPFE (n = 16)	COPD (n = 19)
Follow-up period, years	6.47 ± 0.38	6.92 ± 0.30
Smoking status*		
Continuous smoker, n(%)	1(6.3)	1(5.3)
Intermittent smoker, n(%)	0(0)	0(0)
Former smoker, n(%)	15(93.8)	18(94.7)
Medication for COPD**		
Any medication, n(%)	7(43.8)††	19(100)
LAMA, n(%)	4(25.0)††	15(78.9)
LABA, n(%)	3(18.8)††	13(68.4)
ICS, n(%)	1(6.3)	5(26.3)
Theophyllline, n(%)	3(18.8)†	11(57.9)

Annual changes in pulmonary function

	CPFE (n = 16)	COPD (n = 19)
VC, ml/year	−113.5 ± 41.3†	−11.0 ± 13.9
FVC, ml/year	−88.2 ± 28.5†	−15.6 ± 16.6
FEV_1, ml/year	−57.7 ± 26.7	−34.8 ± 8.8
FEV_1, % predicted/year	−0.98 ± 0.91	−0.76 ± 0.34
FEV_1/FVC, %/year	0.31 ± 0.45†	−0.94 ± 0.24
FRC, ml/year	−20.9 ± 29.2	−57.3 ± 20.8
RV, ml/year	9.5 ± 36.1	−41.0 ± 22.8
TLC, ml/year	−93.7 ± 37.4	−61.3 ± 16.4
DLco, ml/min/mmHg/year	−1.15 ± 0.22††	−0.51 ± 0.10
DLco/VA, ml/min/mmHg/l/year	−0.22 ± 0.05††	−0.06 ± 0.03

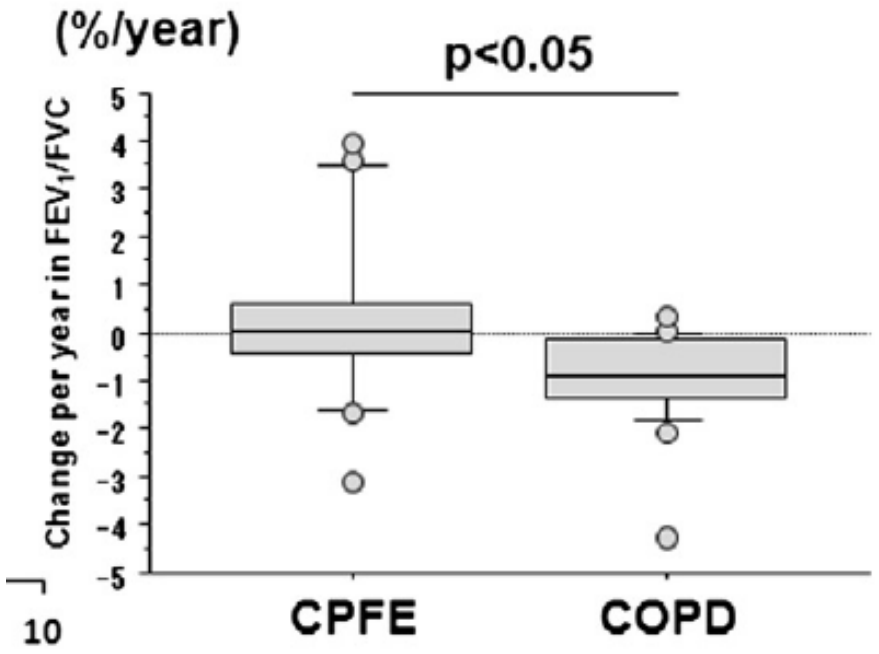
Annual decreases in VC and FVC in the CPFE group were significantly higher than COPD group

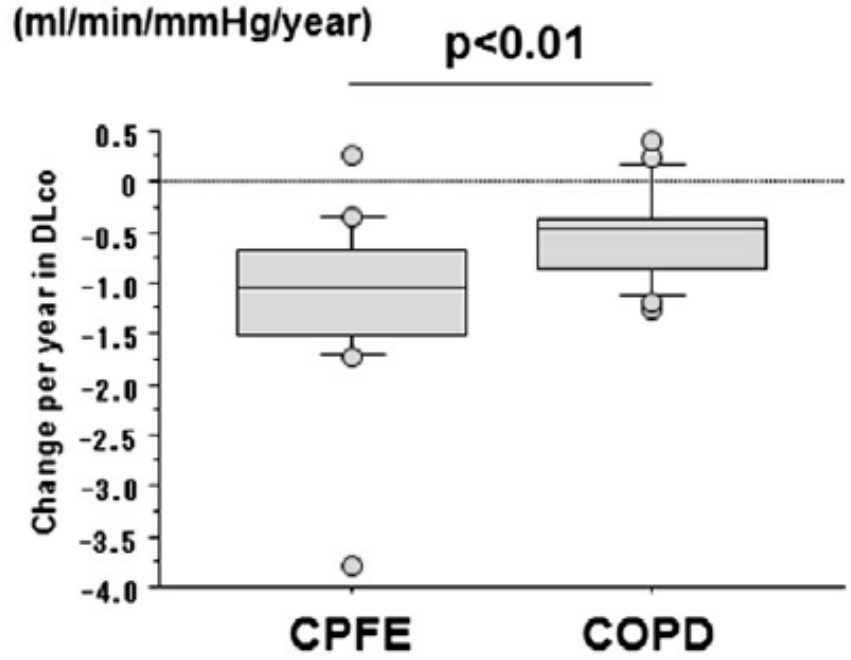


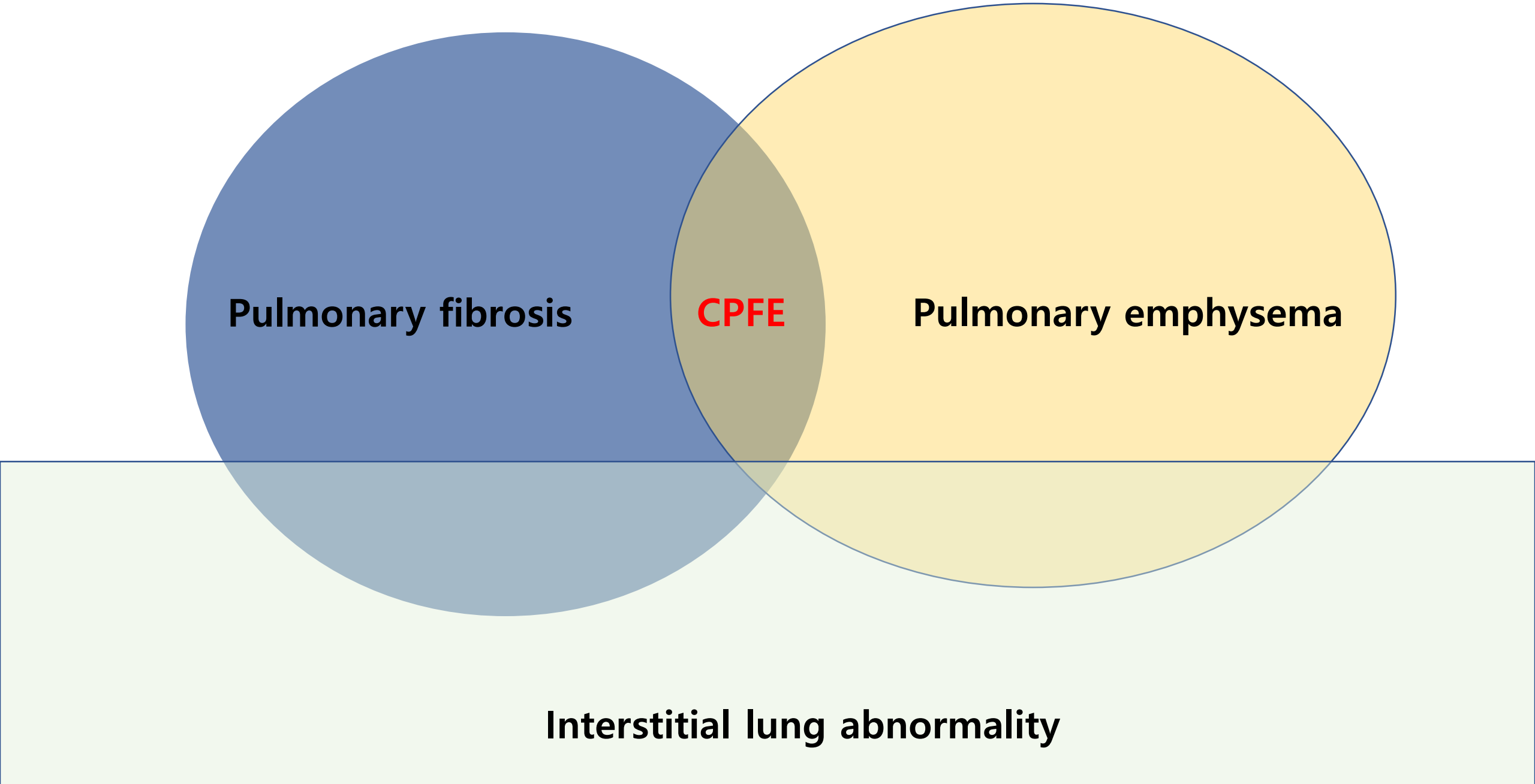


Annual decrease in FEV1/FVC in the COPD group was significantly higher

Annual decreases in DLco and DLco/VA in the CPFE group were significantly higher






Pulmonary fibrosis
CPFE
Pulmonary emphysema
Interstitial lung abnormality

Summary

- An increasing recognition of the coexistence of emphysema and pulmonary fibrosis – especially smokers and old age
- Emphysema and ILD produce opposing effects on expiratory flow rates and lung volumes on PFT - Isolated reduction in DLCO
- The relationship between lung fibrosis and emphysema (COPD) is not yet clear
- The problem of underdiagnosis in both conditions
- No data for effective therapeutic strategies in clinical practice

Functional and radiological characteristics of IPF, CPFE and Emphysema

	IPF	CPFE	Emphysema
Pulmonary function tests			
FEV_1	↓	↓ or N	↓
FVC	↓	↓ or N	↓
FEV_1/FVC	↑	↓ or ↑ or N	↓
TLC	↓	↓ or ↑ or N	↑
FRC	↓	↓ or ↑ or N	↑
RV	↓	↓ or ↑ or N	↑
DLCO	↓	↓↓	↓
Desaturation during exercise	+	++	+
CT findings			
Emphysema	−	+	+
Fibrosis	+	+	−
Pathological findings	UIP	UIP or f-NSIP + Emphysema	Emphysema
Pulmonary Hypertension	+	++	+
Lung cancer risk	++	++	+

Questions to be answered

- Whether CPFE (or emphysema with ILA) is just a coincidence of two smoking-related lung diseases or a distinct clinical entity?
- The need for specific clinical diagnostic and classified criteria for CPFE – by phenotype ?
- Interactive impact between lung fibrosis and emphysema (COPD)
- Valuable parameters for predict clinical course and disease progression
- The predictors of mortality for CPFE (vs COPD or IPF) ?