

Interstitial Lung Abnormalities (ILA)

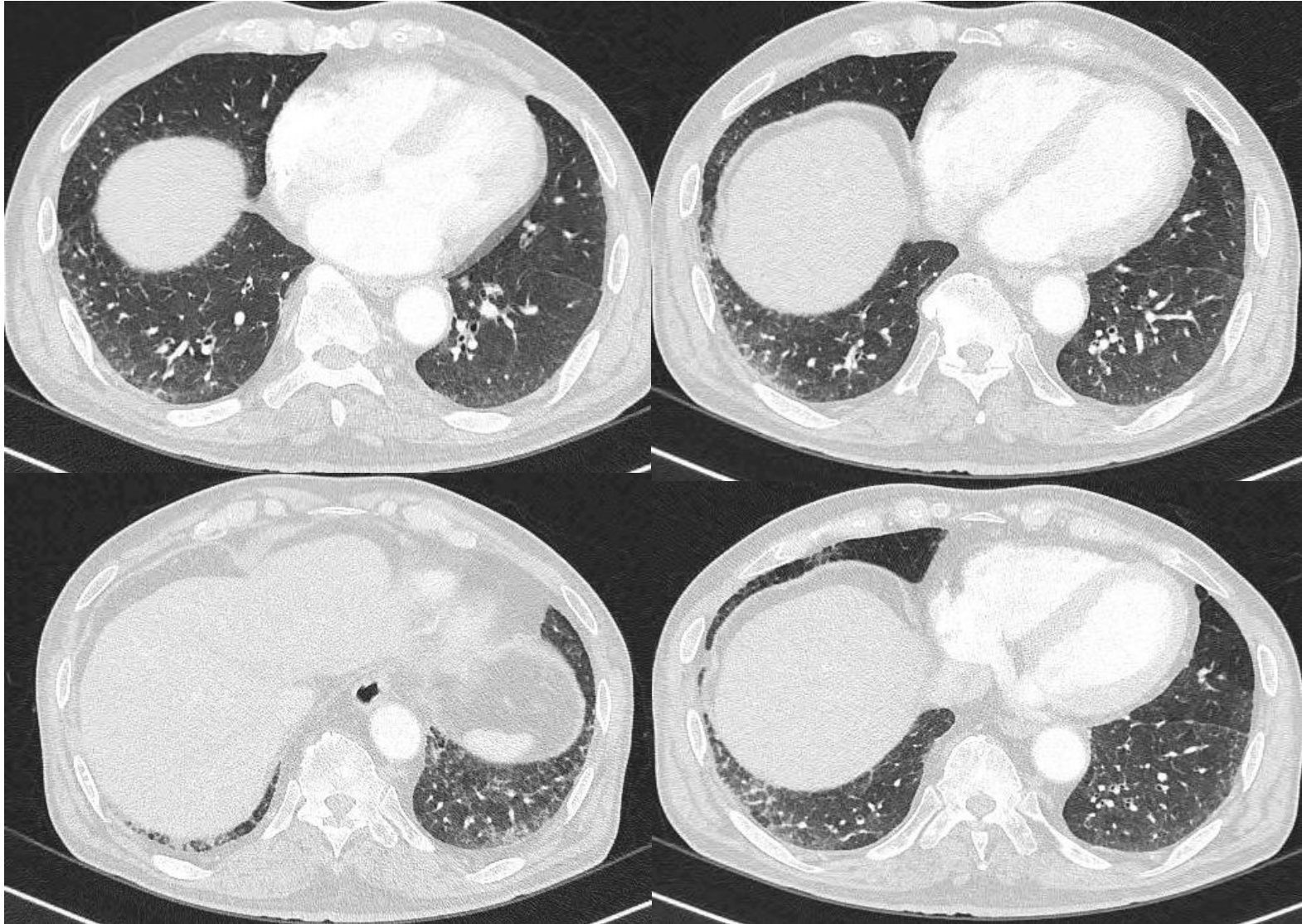
2020.7.25

인제의대 부산백병원 호흡기,알레르기내과

이 현 경



CASE : 82/M, admitted due to acute stroke at neurology dept.
Referred to pulmonology div. due to **suspected ILD**.



No respiratory symptom
No prior history of ILD

Questions..

- 진단은?
- 추적이 필요한가?
- 치료가 필요한가?

Definition of Interstitial Lung Abnormalities (ILA)

ILA on CT scans are defined as nondependent changes affecting more than **5% of any lung zone** including any combination of nondependent **identified in participants with no prior history of ILD**

- ground-glass or reticular abnormalities
- diffuse centrilobular nodularity
- nonemphysematous cysts
- honeycombing, or traction bronchiectasis.

Emergence of the concept of ILA

- *background*

- **Familial IPF**로 진단된 환자의 가족들 중 증상이 없는 사람들을 대상으로 HRCT 시행 시 ILD가 흔하게 관찰됨

- **General population**을 대상으로 한 대규모 연구 코호트에서 흉부 CT를 시행한 결과 subclinical ILD 소견이 흔하게 관찰됨
 - COPDGene : smokers (HRCT)
 - MESA-Lung study : participant without cardiovascular disease (cardiac CT)
 - FHS (Framingham Heart Study)

- **Lung cancer screening** 과정에서 ILA 소견이 흔하게 관찰됨

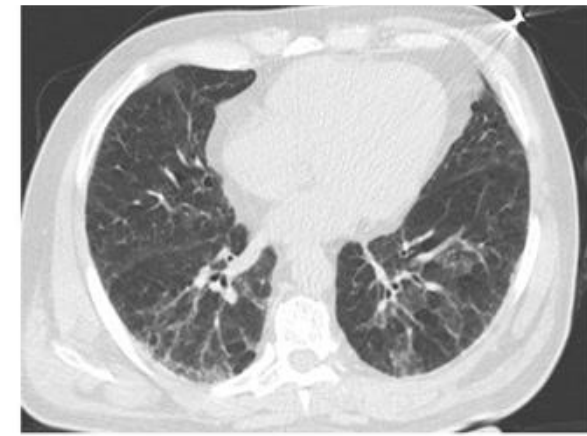
Questions regarding ILA

- 과연 ILA가 독립된 질환군인가? ILD의 early and/or mild form인가?
- ILA발생과 관련된 요인들에는 어떤 것이 있을까?
- ILA는 어떤 임상적 특성을 보이고 clinical ILD와 유사한 특성을 보이는가?
- ILA의 자연경과는 어떠한가?
- ILA를 치료하면 IPF로의 진행을 억제 또는 늦출 수 있나?

Contents

- Problems unsolved during the diagnosis of ILA
- Clinical characteristics of ILA
- Prevalence of ILA
- Natural history of ILA
- Clinical relevance of ILA

Problems unsolved during the diagnosis of ILA



Technical differences in obtaining and interpreting CT images

- **Factors potentially affecting the diagnosis of ILA**
 - **Different CT techniques : low dose, HRCT, prone view etc.**
 - **Different performances of CT**
 - **Different methods of reading CT images : reading algorithm, number of readers, qualitative reading vs automated reading by AI**
 - **Poor center-to-center and expert-to-expert reproducibility**

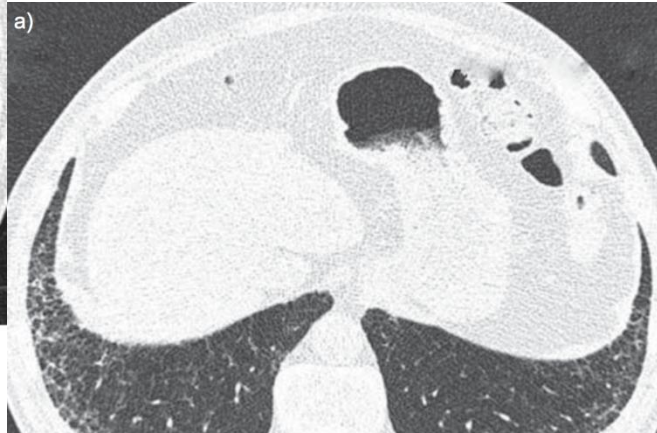
The spectrum of radiologic abnormalities in ILA



NORMAL

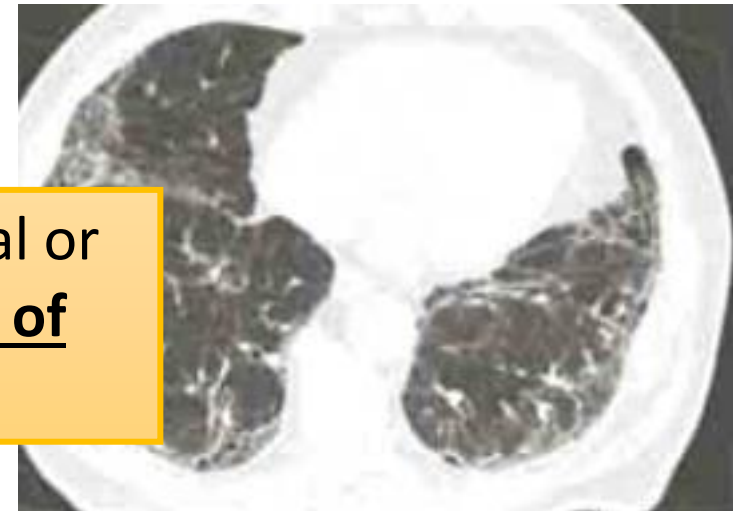


INDETERMINATE



ILA with RB-ILD

CTs with either **focal** or **unilateral** ground-glass attenuation, focal or **defined as pulmonary parenchymal architectural distortion** **of** diagnostic of fibrotic lung disease



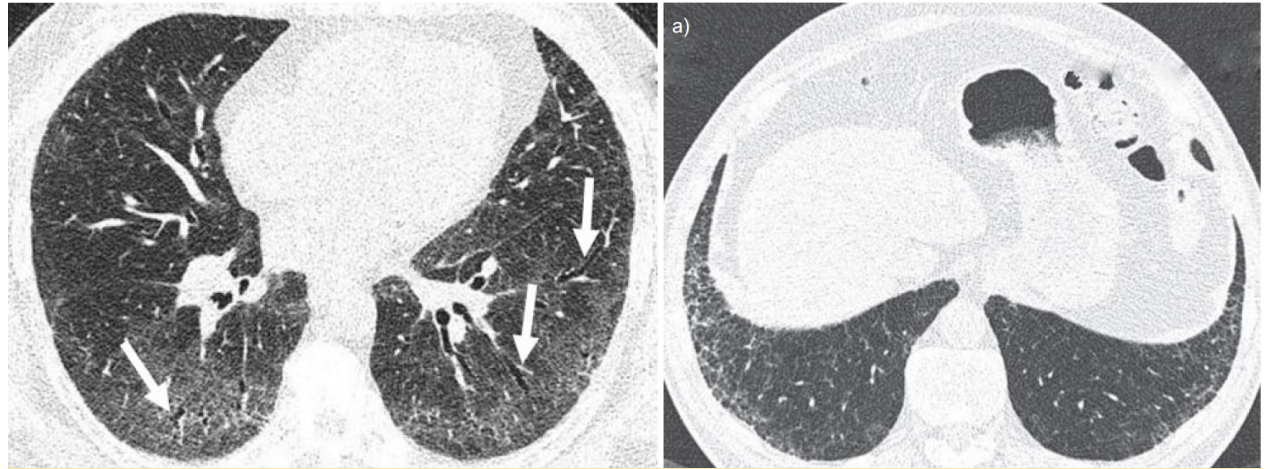
ILA with fibrosis

Different **subtyping** from different studies

- *MILD (Multicentric Italian Lung Detection) Project*



UIP-like pattern



**Chronic interstitial pneumonia (OCIP)-like pattern
(NSIP, DIP)**



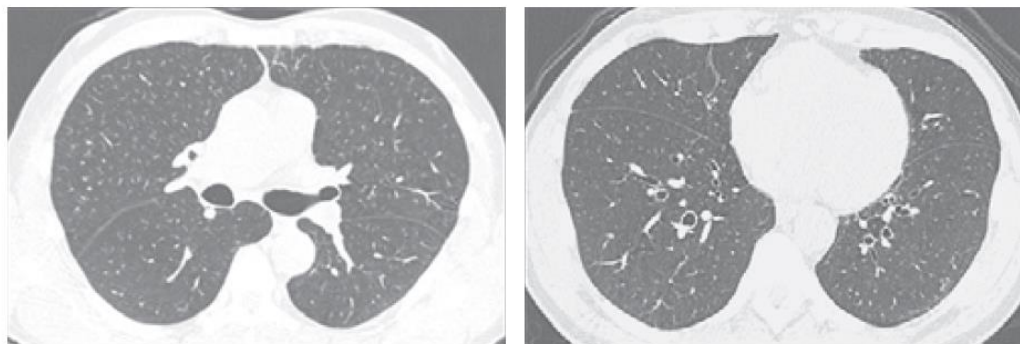
RB-like pattern



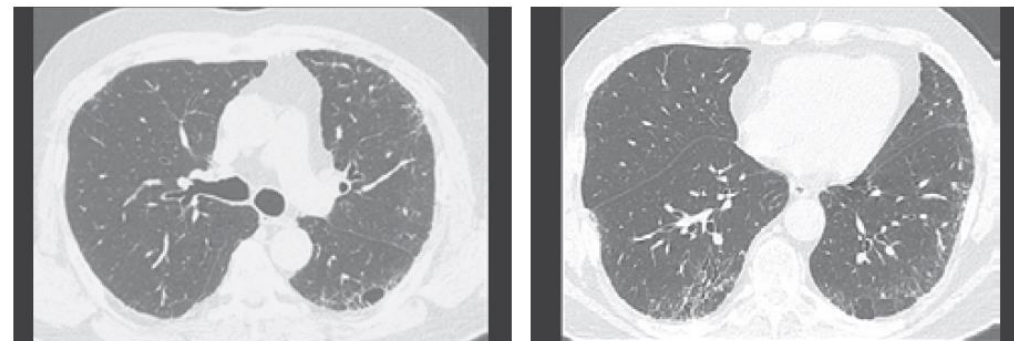
Indeterminate pattern

Different **subtyping** from different studies

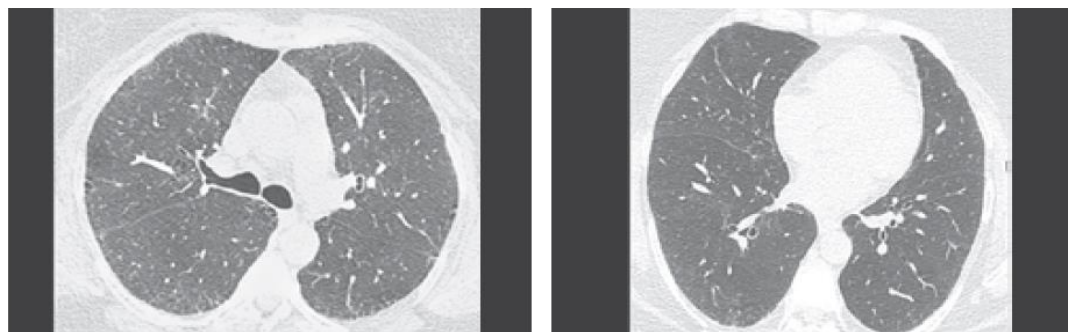
- *COPDGene study*



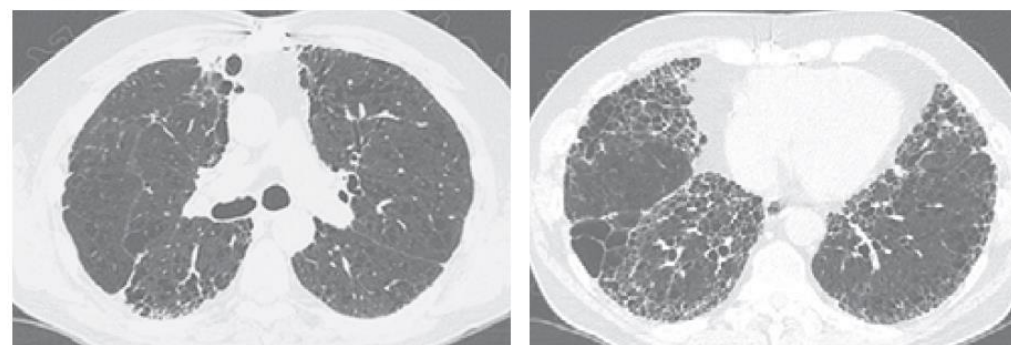
Centrilobular ILA



Subpleural ILA



Mixed (centrilobular+subpleural) ILA



Radiographic ILD

Rate of discrepancy among subtypes of ILA

CT reviewed by 3 readers (2 radiologists and 1 pulmonary physician) using a sequential reading method.

discrepancy between **normal and ILA** : 1%-5%
(58 in AGES-Reykjavik and 9 in The ECLIPSE).

NORMAL

ILA

ILA with definite fibrosis

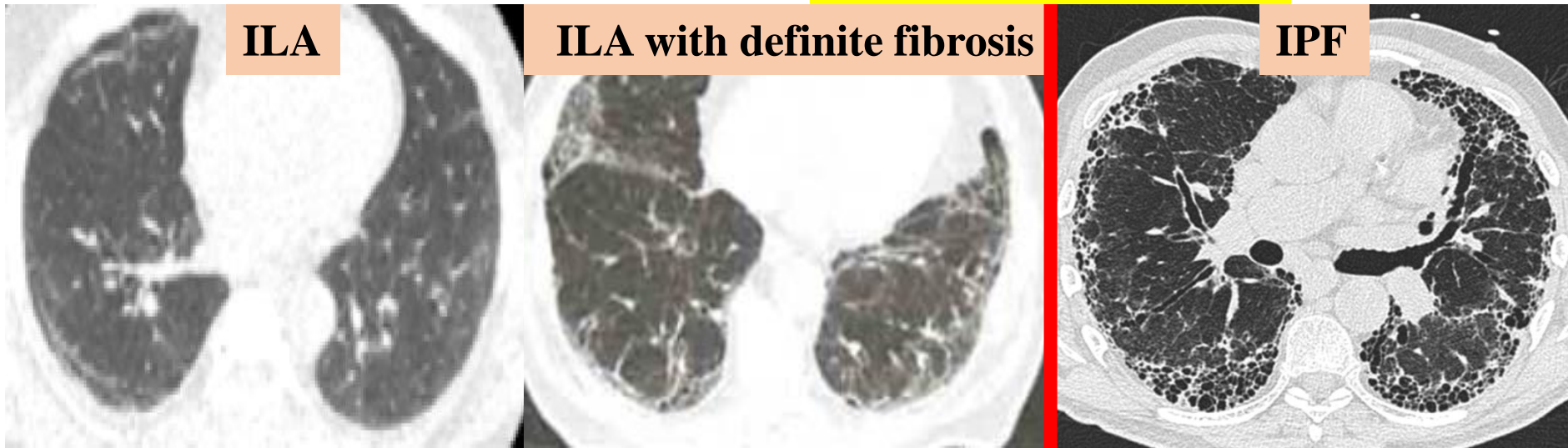
57% and 66% were concordant reads
(1623/2836 in the AGES-Reykjavik cohort, and
1240/1868 in the ECLIPSE cohort).

**95% and 98% of the discordant reads involved one
indeterminate read** (1155/1213 in the AGES-Reykjavik and
617/628 in the ECLIPSE)

INDETERMINATE

How to discriminate ILA from IPF ?

Where is the boundary?

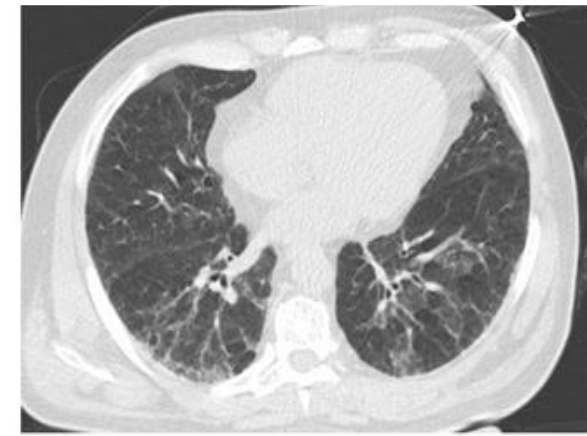


Summary : Problems unsolved during the diagnosis of ILA

- ILA is not a disease, but a **radiologic (CT) entity**, so standardized CT technique, diagnostic criteria and reporting system is required.
- Distinction of ILA from **indeterminate cases** may be challenging.
- The **boundaries** between ILA and fibrotic lung disease (particularly IPF) are unclear.

Clinical Characteristics of ILA

- **Respiratory symptoms**
- **Physiological**
- **Functional**
- **Histopathological**
- **Genetic and genomic**
- **Aging and ILA**
- **Smoking and ILA**



ILA and respiratory symptom

Health screening for lung cancer (Nagano)

- 흡연력 관계없이 검사 시행
- LDCT로 1차 검사
- ILD의심 -> HRCT 시행

Table 1 Characteristics of normal and abnormal subjects clarified by low-dose CT scan and HRCT scan.

	(A) Normal subject (n = 2981)	(B) Abnormal subject (n = 80)	P value (A) vs. (B)
Age (years)	53.8 ± 10.3	61.7 ± 9.4	<0.0001
Sex, M/F	1738/1243	59/21	0.002
Smoking history			
No. of subjects (%)	1531 (51.4)	56 (70.0)	<0.0001
Current smokers (%)	969 (32.5)	36 (45.0)	0.014
Pack-year	29.7 ± 9.9	46.0 ± 19.3	<0.0001
Former smokers (%)	562 (18.9)	20 (25.0)	0.110
Pack-year	20.5 ± 12.5	43.7 ± 25.9	<0.0001
Never smokers (%)	1450 (48.6)	24 (30.0)	0.001

ILA군은 No ILA군과 비교하여...

- 나이가 많았고, 남자가 많았고, ever smoker 비율이 높았고, 흡연량이 많았다
- **Shortness of breath** 호소 비율이 높았다

Impact of ILA on lung function (1)

- *ILA and lung function in smokers (COPDGene)*

- 결론 : ILA는 restrictive physiology와 관련이 있다

COPDGene Study

- 45-80yrs / 10pyrs smoker
- Spirometry
- HRCT measured TLC / emphysema
- Compared with ILA to without ILA

			P Value
Median age	60 (52-67)	64 (56-72)	<0.001
Median BMI	27 (24-31)	28 (25-33)	0.06
Median pack-yr	40 (29-54)	44 (31-63)	0.01
COPD (\geq GOLD 2), no. (%)	561 (41)	63 (32)	0.02
Spirometric restriction, no. (%)	414 (30)	81 (42)	0.002
Chest CT % emphysema	4.1 (1.3-12.4)	2.2 (0.7-6.0)	<0.001
TLC (% pred)	107 (91-120)	95 (81-109)	<0.001

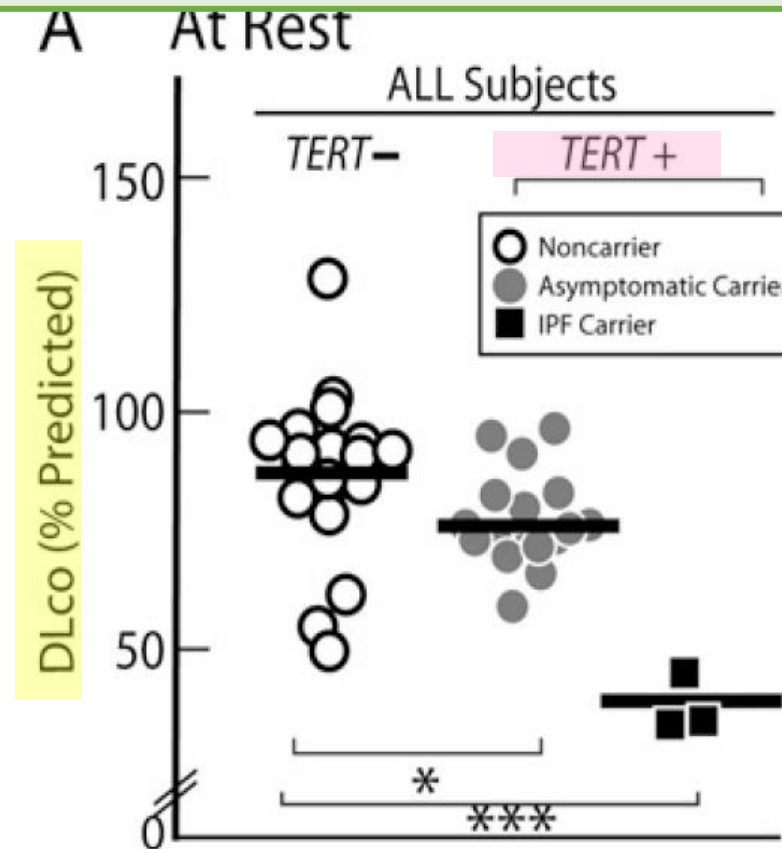
Impact of ILA on lung function (2)

- ILA and lung function (**DLCO**)

- 결론 : TERT(+)에서 ILA 비율이 높았고 DLCO가 감소되어 있었다

Subjects from Familial PF

- TERT(+) vs TERT (-)
- Spirometry, lung volume, DLCO, CPX
- HRCT



ILA and exercise capacity

- 결론 : ILA는 6분 걷기거리(6MWD)의 의미 있는 감소와 연관되어 있다

COPDGene Study

- 45-80yrs / 10pyrs smoker
- Excluding active lung ds other than asthma, emphysema, COPD

2416명에서 6MWT를 시행하여 ILA군과 비 ILA 군을 비교함.

- ILA중 250m미만 걸은 비율 : 19%

- Mean 6MWD
 - ILA : 386 m
 - IPF : 373-392 m
 - Advanced IPF : 246-268 m

OR (95% CI)
P Value

OR (95% CI)
P Value

CE (95% CI)
P Value

0.16

0.01

0.04

ILA and histopathologic findings

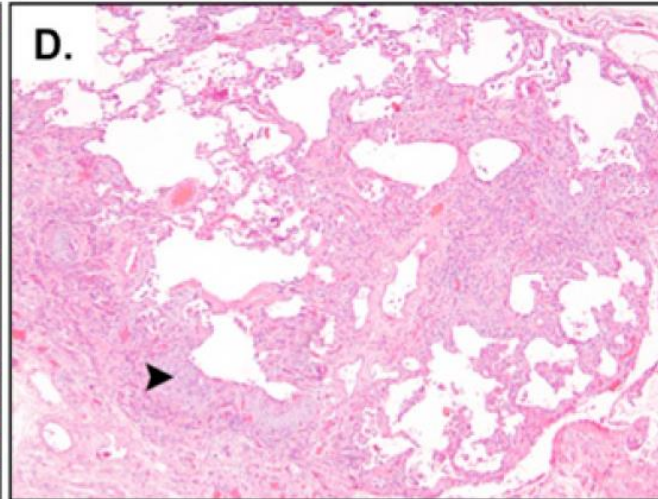
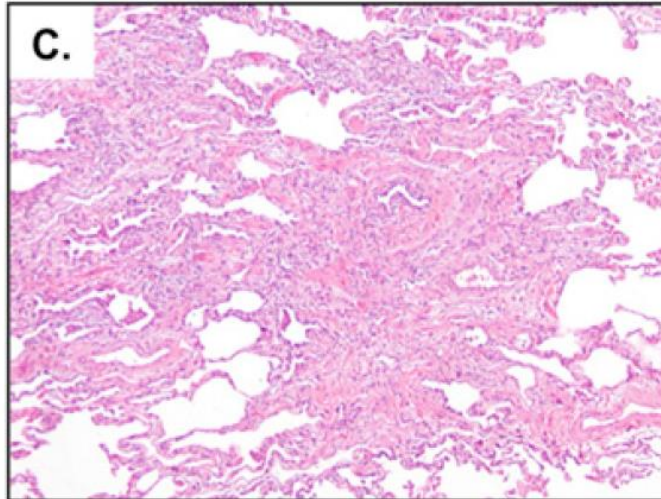
Population

Familial pulm

Connective ti

Smokers

Postoperative

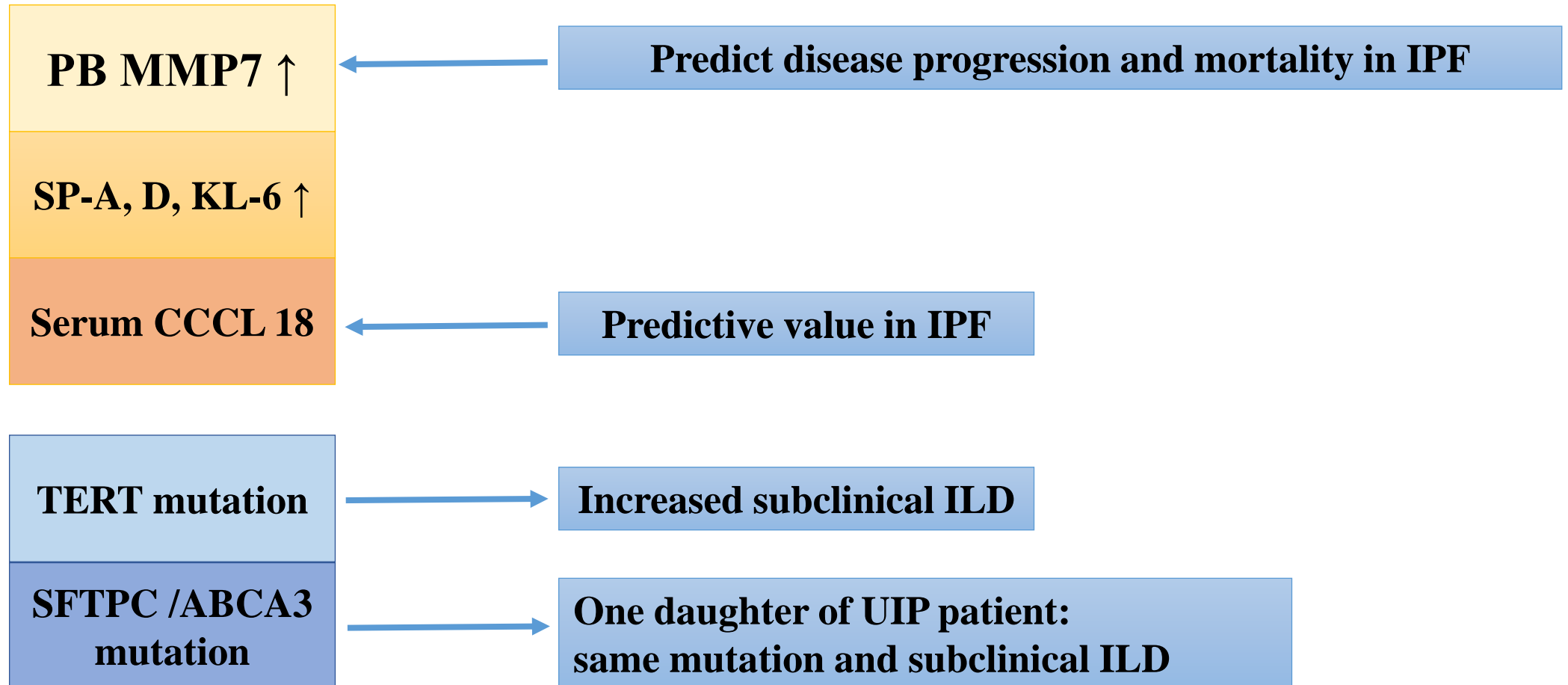


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Genetic association between ILA and clinical ILD (1)

Subclinical ILD



Genetic association between ILA and clinical ILD (2)

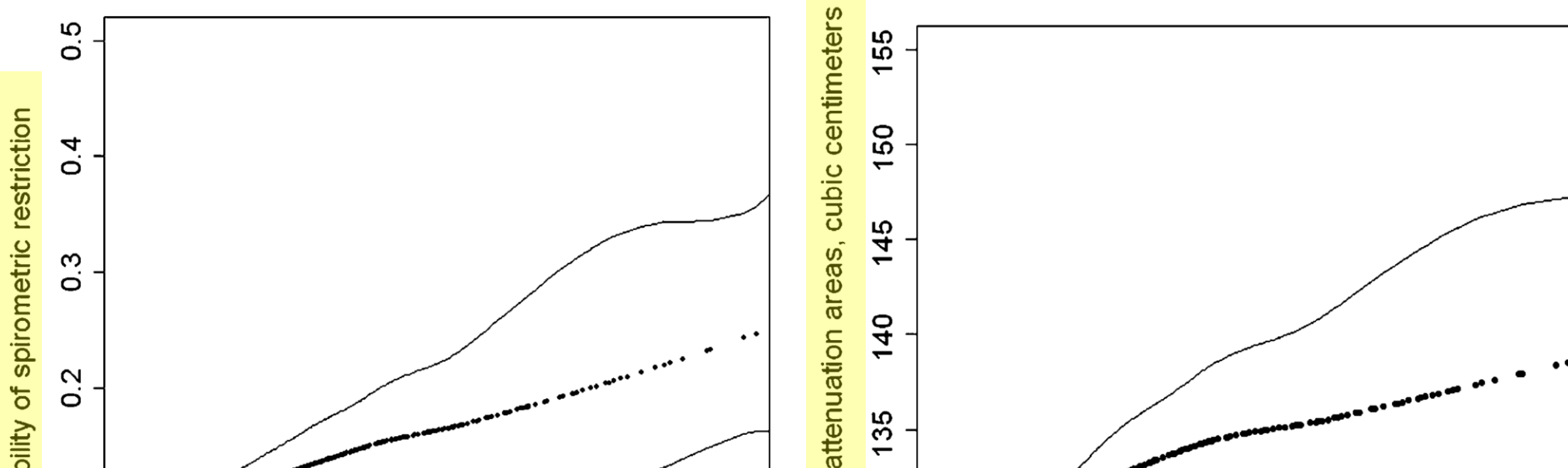
- *MUC5B* variant and ILA in FHS

- The *MUC5B* promoter polymorphism은 general population에서 ILD와 연관이 있었다

Status of Interstitial Lung Abnormalities	No. of Patients	<i>MUC5B</i> Genotype (rs35705950)			Adjusted Odds Ratio (95% CI) [†]	P Value	Ratio With Covariates (95% CI) [‡]	P Value
		G/G	G/T	T/T				
Absence of interstitial lung abnormalities	1370	1113 (81)	247 (18)	10 (<1)	1.0	1.0		
Presence of interstitial lung abnormalities	177	115 (65)	56 (32)	6 (3)	2.3 (1.6–3.1)	<0.001	2.8 (2.0–3.9)	
Definite fibrosis§	47	26 (55)	20 (43)	1 (2)	3.0 (1.8–5.0)	<0.001	6.3 (3.1–12.7)	

ILA and Smoking

MESA-Lung Study



- MESA-Lung, FHS, NLST, Familial PF 연구 등에서 흡연량 또는 흡연력은 ILA 발생과 의미 있는 연관성이 있었다

Cigarette packyears

Cigarette packyears

ILA and Aging

- asymptomatic volunteer **over 75** vs **under 55** years

Table 3

Prevalence of CT Features in Older Group versus Younger Group

CT Feature	Older Group (<i>n</i> = 40)*	Younger Group (<i>n</i> = 16)*	<i>P</i> Value
Reticular pattern	24 (60)	0 (0)	<.001 [†]
Cysts	10 (25)	0 (0)	.02 [‡]
Bronchial dilation	24 (60)	1 (6)	<.001 [†]
Bronchial wall thickening	22 (55)	1 (6)	<.001 [†]
Ground glass opacity	0 (0)	1 (6)	NS [‡]
Interlobular septal thickening	7 (18)	0 (0)	NS [‡]
Centrilobular emphysema	2 (5)	0 (0)	NS [‡]

ILA are frequently seen in asymptomatic elderly individuals and may not necessarily represent clinically relevant.

χ² test.

‡ Fisher exact test.

*** Median age 80.6 yo ± 4.2 and 39.4 yo ± 7.5**

Figure 1



Figure 1: Axial prone thin-section CT image of a 92-year-old woman who had normal pulmonary function shows a subtle bilateral subpleural basal reticular pattern of limited extent (grade 2). This individual was a nonsmoker and had been a city dweller for 76 years.

Summary : Clinical Characteristics of ILA

- Subjects with ILA have
 - more shortness of breath
 - restrictive physiology and decreased gas exchange
 - decreased exercise capacity
- ILA and IPF share genetic background especially MUC5B.
- Aging and smoking are associated with development of the ILA

Prevalence of ILA



Prevalence of ILA

Health screening for lung cancer (Nagano)

- 흡연력 관계없이 검사 시행
- LDCT로 1차 검사
- ILD의심 -> HRCT 시행

Familial IP Study

- FIP 가족 내 구성원을 recruit
- 병력청취, 폐기능, HRCT, BAL, TBLB, SLBx 등 시행

COPDGene Study

- 45-80yrs / 10pyrs smoker
- Excluding active lung ds other than asthma, emphysema, COPD
- HRCT performed

Rheumatoid arthritis

- 기침, 호흡곤란이 없는 RA 환자
- HRCT, PFT 시행

3%
(80/ 3079)

무증상자의
22%
(31/ 143)

ILA: 8%
194/2416

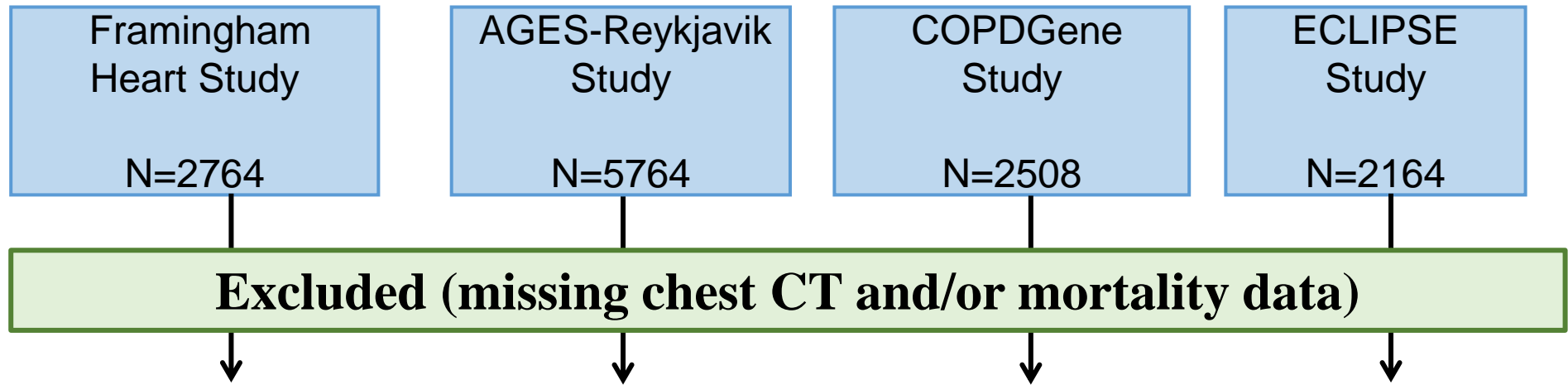
ILA: 33%
21/64

Prevalence of ILA in 4 prospective cohort study

Total : 11,691 participants

- **2633** from the **FHS (Framingham Heart Study; 2008-2011)**, to identify risk factors for cardiovascular d. in the general population.
- **5320** from the **AGES-Reykjavik Study** (Age Gene/Environment 2002-2006), longitudinal birth cohort from Reykjavik Study.
- **2068** from the **COPDGene Study** (2007-2010), to identify risk factors for COPD (all smokers, with and without COPD, any GOLD stage; participants with lung disease other than asthma, emphysema or COPD were excluded).
- **1670** from **ECLIPSE** (2005-2006), Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (2,180 COPD, GOLD II-IV and 500 controls smokers and non-smokers).

Prevalence of **ILA** in 4 studies



Included	95% (N=2633)	92% (N=5320)	782% (N=2068)	77% (N=1670)
ILA	7% (N=177)	7% (N=378)	7.5% (N=156)	9% (N=157)
Indeterminate	41% (N=1086)	23% (N=1726)	36% (N=739)	59% (N=985)
No ILA	52% (N=1370)	61% (N=1173)	56.5% (N=3216)	32% (N=528)

Prevalence of **definite fibrosis** in 4 studies

	Framingham Heart Study N=2633	AGES-Reykjavik Study N=5320	COPDGene Study N=2068	ECLIPSE Study N=1670
ILA	7% (N=177)	7% (N=378)	7.5% (N=156)	9% (N=157)
DEFINITE FIBROSIS	44	129	32	28
% vs ILA	25%	34%	21%	18%
% vs TOTAL	1.6%	2.4%	1.5%	1.6%

Prevalence of **ILA** and **IPF**

Variable	Percent or Median/Means Where Appropriate and Noted						
	Research Subjects with ILA						
	MESA*	Nagano, Japan†	COPDGene‡	MILD§	FHS	NLST¶	Patients with IPF**
Prevalence of ILA, %	2	3	8	4	7	10	0.01–0.04

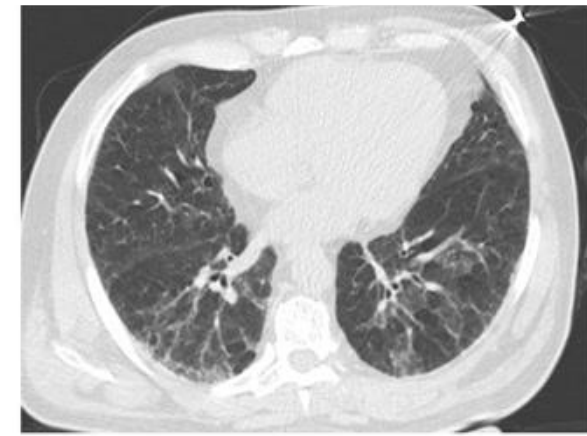
ILA prevalence 2~10 %

Summary : ILA prevalence

- **ILA** are present in \approx 2 to 10% of research participants and **7% of the general population.**
- **Definite fibrosis** is present in each cohort in \approx **2%** of cases.
- There is a **large discrepancy** between the prevalence of ILA and the prevalence of IPF and ILDs (\approx 0.002%-0.04% of the general population).

Natural history of ILA

- progression of ILD**
- ILA and mortality**



CT Follow-up study of ILA

- result from longitudinal studies (*NLST*)

NLST Trial

- 55-74 yrs, 30PYRs, within 15yrs after quitting
- 890 participants randomly reselected from 1846
- Participants with ILA (86) at baseline had 2-yr fu CT

Nonfibrotic

GGO
Mosaic attenuation
consolidation

Fibrotic ILA

GGO with reticular abnormality
Pure reticular abnormality
honeycombing

- result from longitudinal studies (**NLST**)

Table 1

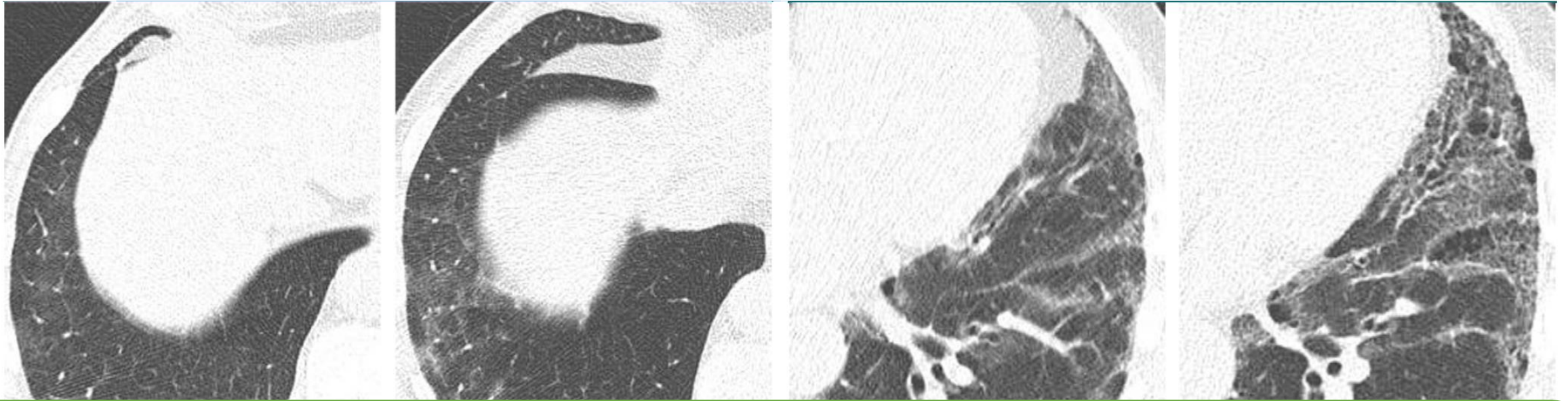
Demographic Data of Study Participants

Characteristics	Overall	No ILA	Equivocal ILA	ILA	PValue*
No. of participants	884	696 (78.7)	102 (11.5)	86 (9.7)	...
No. of men	524 (59.3)	401 (57.6)	61 (59.8)	62 (72.1)	.011
Age (y) [†]	61.5 ± 5.1	61.4 ± 5.0	62.3 ± 5.8	61.6 ± 5.2	.829
No. 55–59 years	37 (42.4)	297 (42.7)	43 (42.2)	35 (40.7)	...

ILA군은 No ILA군과 비교하여:

남자가 많았고, current smoker 비율이 높았고, 흡연량이 많았다

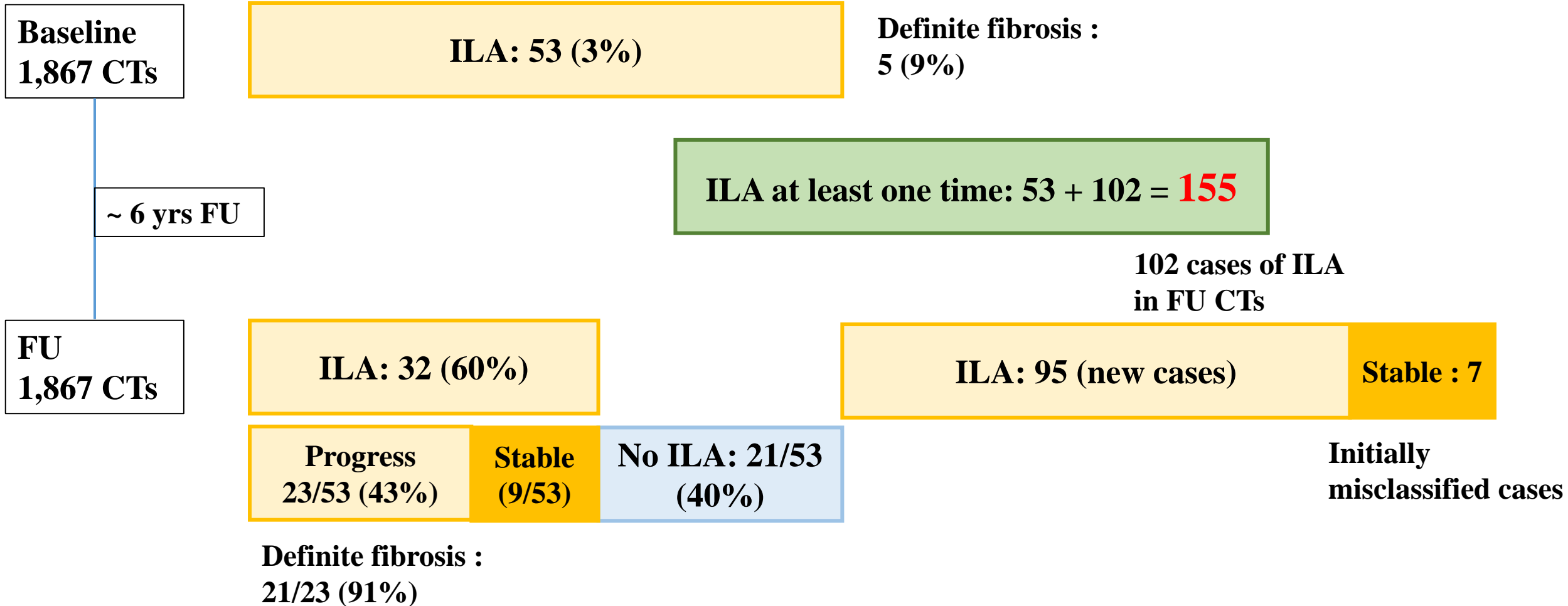
- result from longitudinal studies (**NLST**)



- Nonfibrotic ILA의 약 50%는 호전을 보였다
- ILA 중 fibrotic pattern은 2%에서 발생했다.
- Fibrotic ILA는 호전되지 않았으며 약 1/3에서는 진행했다.

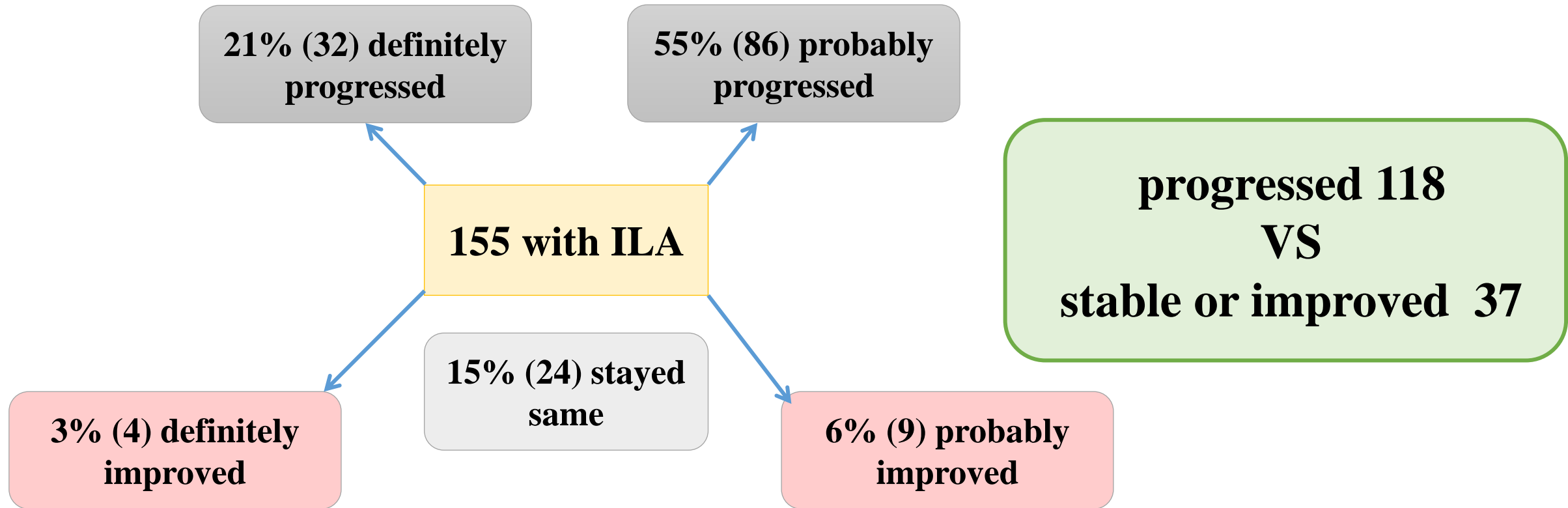
CT Follow-up study of ILA

- result from 6 yrs of longitudinal studies (*FHS*)



CT Follow-up study of ILA

- result from 6 yrs of longitudinal studies (*FHS*)



ILA progression in FHS :

Increasing age and increasing copies of the **MUC5B** promoter polymorphism were associated with ILA progression

	No ILA (n = 660; 35%) (1)	ILA without Progression (n = 37; 2%) (2)	ILA with Progression (n = 118; 6%) (3)	P Values			
				All [†]	1 vs. 2 [‡]	1 vs. 3 [§]	2 vs. 3
Age, yr	49 ± 10	58 ± 11	65 ± 11	<0.0001	<0.0001	<0.0001	<0.0001
Sex, female, n (%)	296 (45)	20 (54)	53 (45)	0.6	0.3	0.96	0.3
Race, white, n (%)	660 (100)	37 (100)	118 (100)	—	—	—	—
Body mass index	28 ± 6	30 ± 6	28 ± 5	0.01	0.006	0.91	0.005
Pack-years smoking	16 ± 16	26 ± 19	24 ± 21	<0.0001	0.003	0.0001	0.7
Current smokers, n (%) [¶]	48 (7)	9 (25)	6 (5)	0.004	0.001	0.2	0.07
Former smokers, n (%)	263 (40)	14 (39)	61 (52)				
Never smokers, n (%)	349 (53)	13 (36)	51 (43)				
MUC5B genotype, n (%)							
G/G	529 (80)	27 (73)	78 (66)	0.0003	0.5	<0.0001	0.1
G/T	125 (19)	10 (27)	36 (31)				
T/T	6 (1)	0	4 (3)				

ILA progression was associated with a **greater FVC decline**

	ILA with Progression Compared with No ILA				ILA with Progression Compared with ILA without Progression			
	Unadjusted Analysis	P Value	Adjusted Analysis [†]	P Value	Unadjusted Analysis	P Value	Adjusted Analysis [†]	P Value
FEV ₁ decline, ml/yr	13 ± 4	0.005	14 ± 5	0.005	9 ± 9	0.3	14 ± 10	0.2
FVC decline, ml/yr	29 ± 5	<0.0001	20 ± 6	0.0005	22 ± 11	0.04	25 ± 11	0.03
FEV ₁ /FVC, change, %	-0.2 ± 0.07	0.004	-0.06 ± 0.07	0.4	-0.1 ± 0.1	0.3	-0.08 ± 0.16	0.6

FVC mean decrease per year:

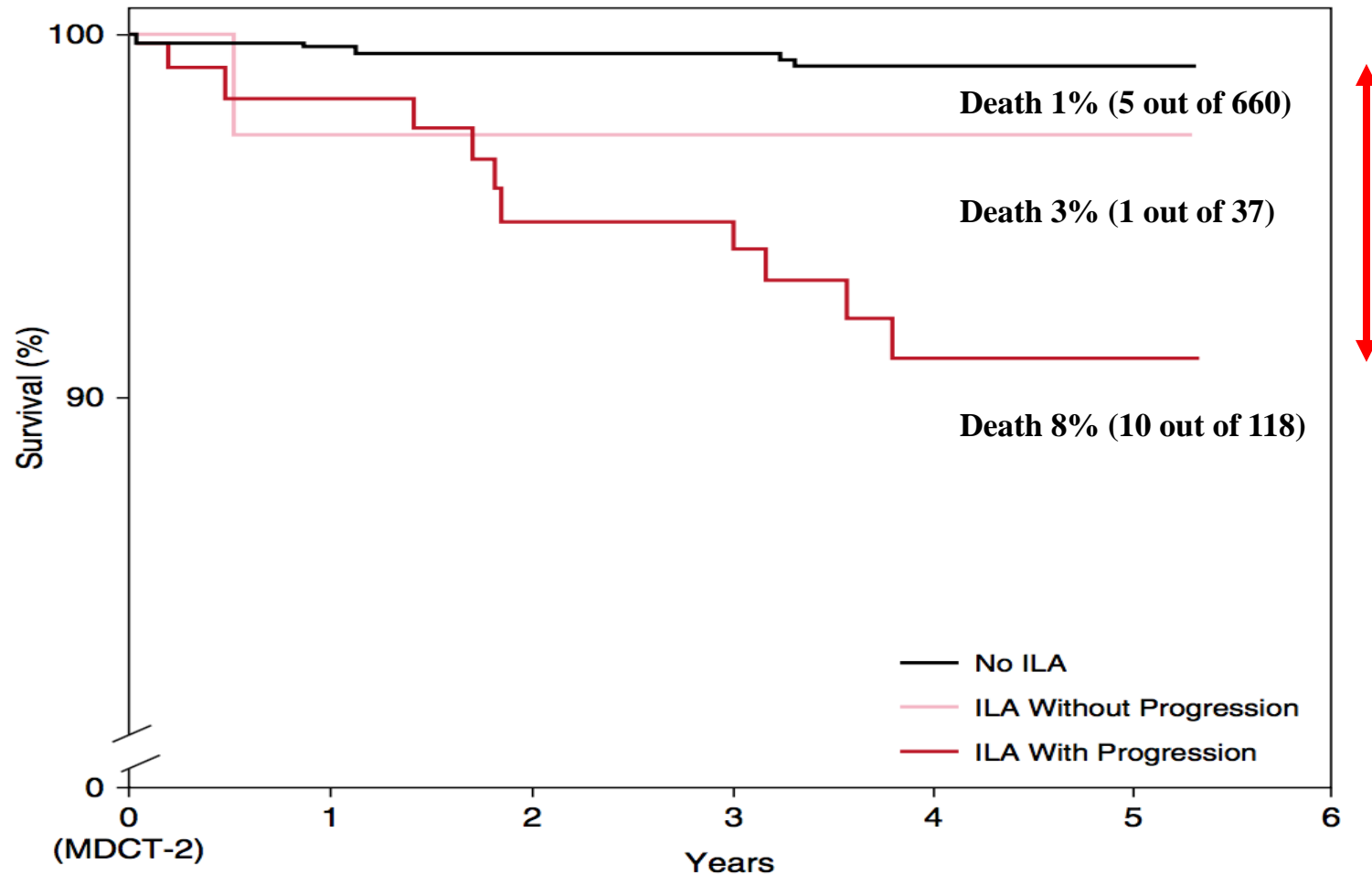
- 35 ml (SD 44 ml) participants without ILA
- 40 ml (SD 44 ml) ILA without progression
- **64 ml (SD 51 ml) ILA with progression**

Are ILA associated in increased **rate of mortality** ?

- 4개의 연구 코호트에서 ILA 존재와 all-cause mortality 증가와의 관련성을 연구함.

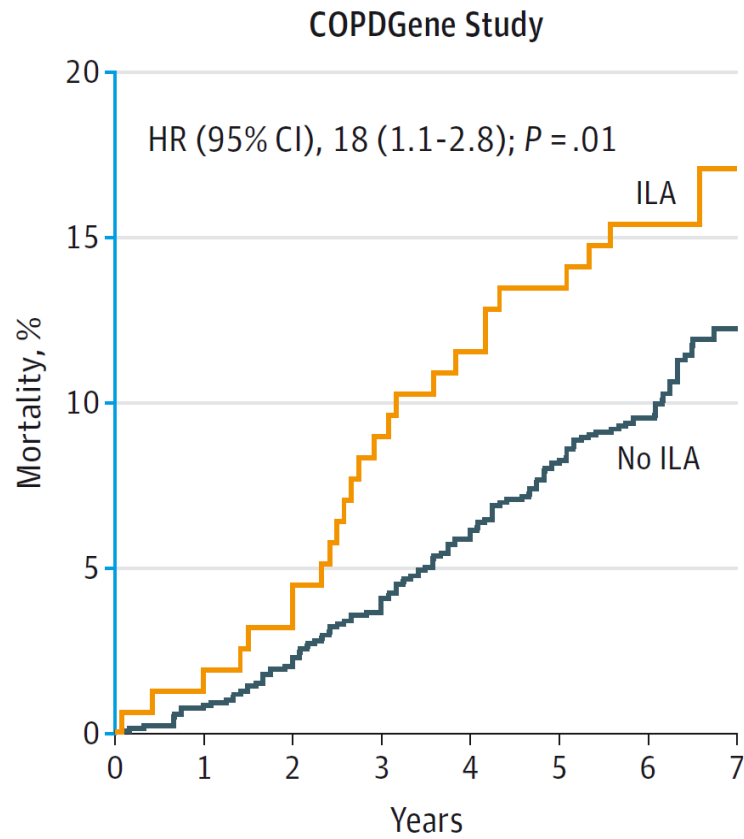
	FHS (N = 2633)	AGES-Reykjavik (N = 5320)	COPDGene (N = 2068)	ECLIPSE (N = 1670)
Median follow-up time, (IQR), y	4.0 (3.3 to 4.6)	8.9 (6.7 to 9.9)	6.5 (6.2 to 6.7)	2.9 (2.9 to 2.9)
Mortality, No. (%)				
No ILA	12 (1)	1065 (33)	133 (11)	27 (5)
ILA	12 (7)	210 (56)	25 (16)	18 (11)
Mortality difference % (95% CI)	6 (2 to 10)	23 (18 to 28)	5 (-1 to 11)	6 (1 to 11)

ILA progression is associated with an increase **in the risk of death** (hazard ratio, **3.9**; 95% CI 1.3–10.9; P = 0.01)

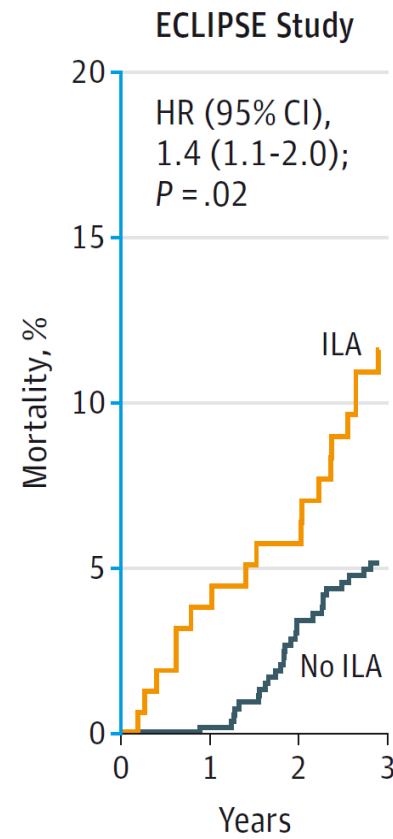


Comparison of mortality between ILA and no ILA

- 나이, 성별, 인종, BMI, 흡연량, 흡연상태, COPD GOLD stage를 보정



at risk							
ILA	156	153	149	142	138	135	131
No ILA	1173	1163	1146	1125	1104	1079	1062



No. at risk			
ILA	156	151	145
No ILA	528	525	505

ILA and Increased rate of **respiratory death**

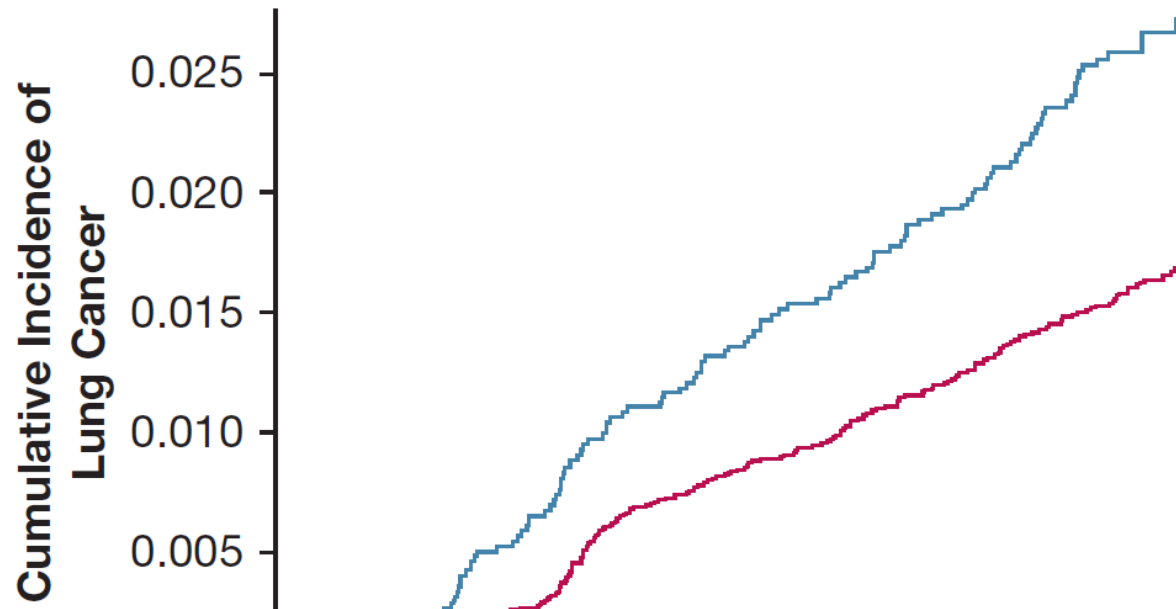
- *AGES-Reykjavik Study*

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

After adjusting for age, sex, race, BMI, pack-years of smoking, current smoking status, **ILA had a higher OR of death from a respiratory cause (OR, 2.4 [95% CI, 1.7-3.4]; P < .001)** compared with No-ILA. Results were similar when comparing participants with ILA with those indeterminate.

ILA and lung cancer incidence / mortality

- NLST, 25,041 LDCT arm participant, 6.6 yrs FU



ILA vs no ILA 2.4% vs 1.5%
Incidence rate ratio : 1.6

	Lung Cancer Deaths, No. (%)	P Value	Lung Cancer Deaths per 100,000 Person-Years (95% CI)	Unadjusted HR (95% CI)
ILA	68 (1.3)	< .01	217 (171-275)	1.82 (1.37-2.42)
No ILA	151 (0.8)		120 (103-141)	Reference

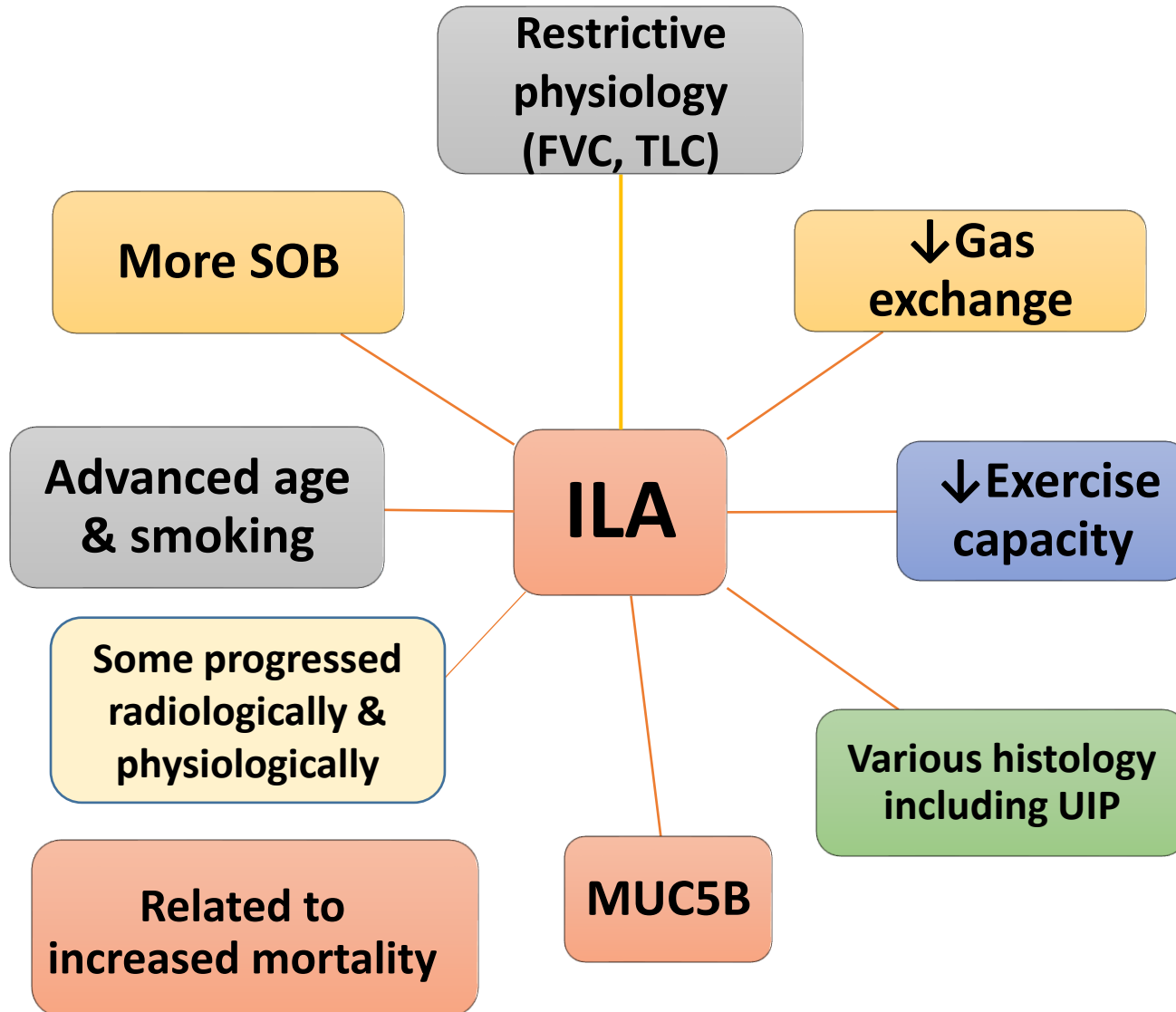
Summary : natural history of ILA

- Some of ILA, especially **fibrotic pattern** progressed even to definite fibrosis and/or UIP.
- Increasing **age** and **MUC5B** were associated with the progression of ILD.
- Subjects with ILD progression showed **greater FVC decline**.
- ILA showed **increased rate of mortality and death** from respiratory causes.
- ILA showed higher **incidence of lung cancer and death** from lung cancer

Clinical relevance of ILA

- **ILA and IPF**
- **Goals and action items of ILA**

Similarities between ILA and IPF



**In some cases,
ILA may be
an early stage of
pulmonary fibrosis**

Comparison between ILA and IPF

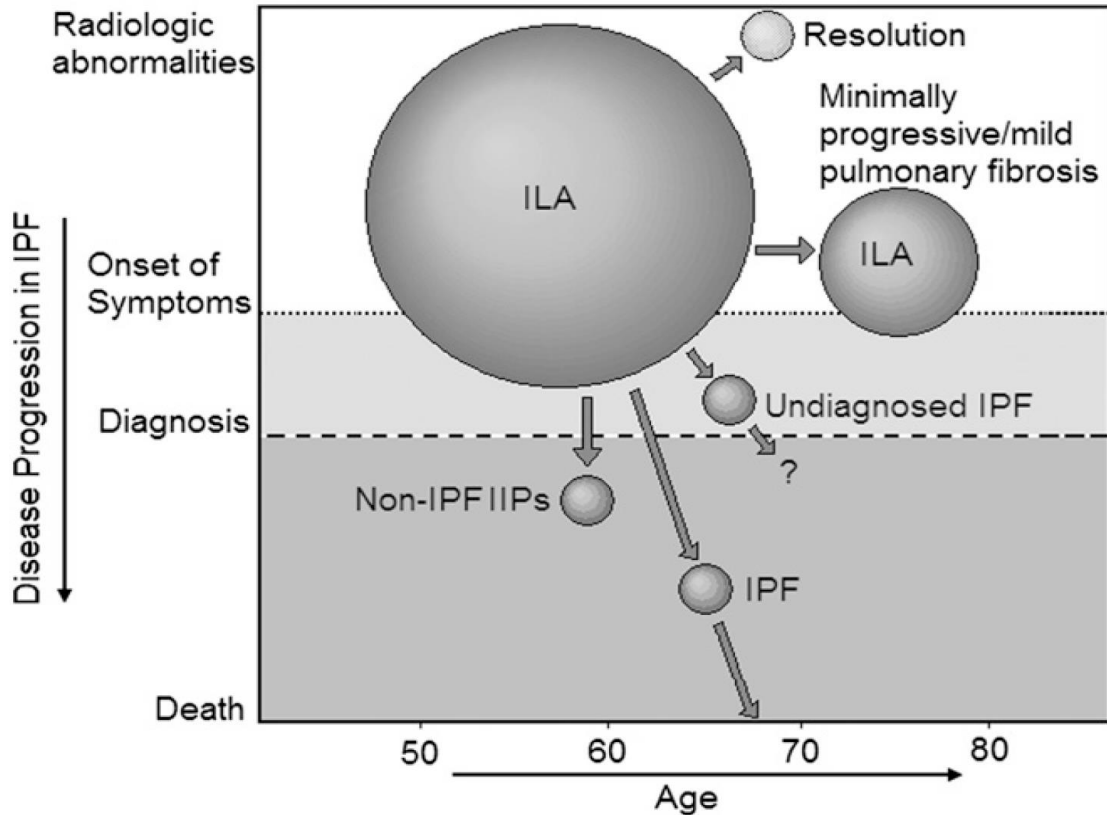
Percent or Median/Means Where Appropriate and Noted

Research Subjects with ILA

Variable	Research Subjects with ILA						Patients with IPF**
	MESA*	Nagano, Japan†	COPDGene‡	MILD§	FHS	NLST¶	
Prevalence of ILA, %							0.01–0.04
Radiologic features, %							
Reticular markings							
Ground glass							
Centrilobular nodules							
Sex, female, %							
History of smoking, current or former, %							
Respiratory symptoms, %							
Chronic cough, yes							
Chronic shortness of breath, yes							
Physical examination findings							
Fine crackles, %							
Pulmonary physiologic testing							
FVC % predicted							
Total lung capacity % predicted							
Diffusion capacity of carbon monoxide, % predicted							
6-min walk distance, m							
Radiologic progression, %, follow-							
Improvement							
Unchanged							
Overall progression	—	40, 4 yr	—	75, 3 yr	—	47, 2 yr	Median survival of IPF patients is 3 yr
Progression to UIP pattern	—	46, 4 yr	—	25, 3 yr	—	20, 2 yr	
		5, 4 yr	—	8, 3 yr	—	—	

IPF: much lower prevalence and radiologic abnormalities

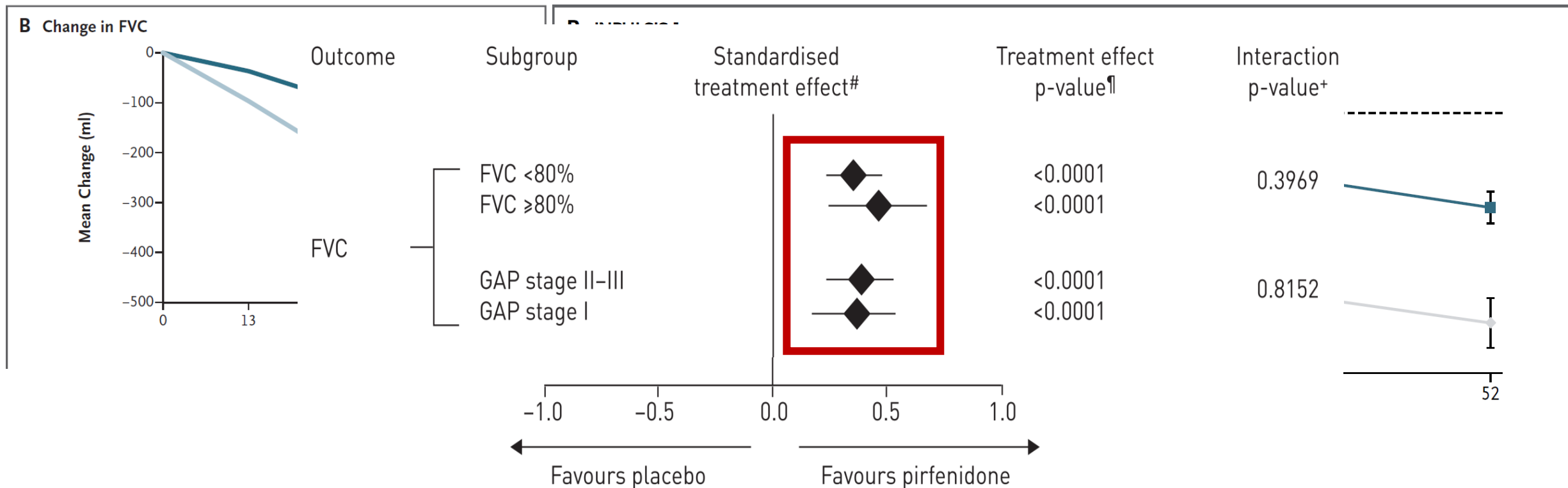
More symptoms and radiologic testing



Potential outcome of ILA

0.01–0.04
 onal
 41–49
 60–72
 73–86
 t in most patients
 t in most patients
 68–89
 46–78
 46–61
 373–392
 Median survival of IPF patients is 3 yr

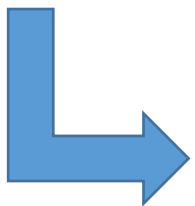
Why is the ILA interested more than before? - background



Antifibrotics (pirfenidone, nintedanib) slowed the rate of FVC decline in IPF patients.

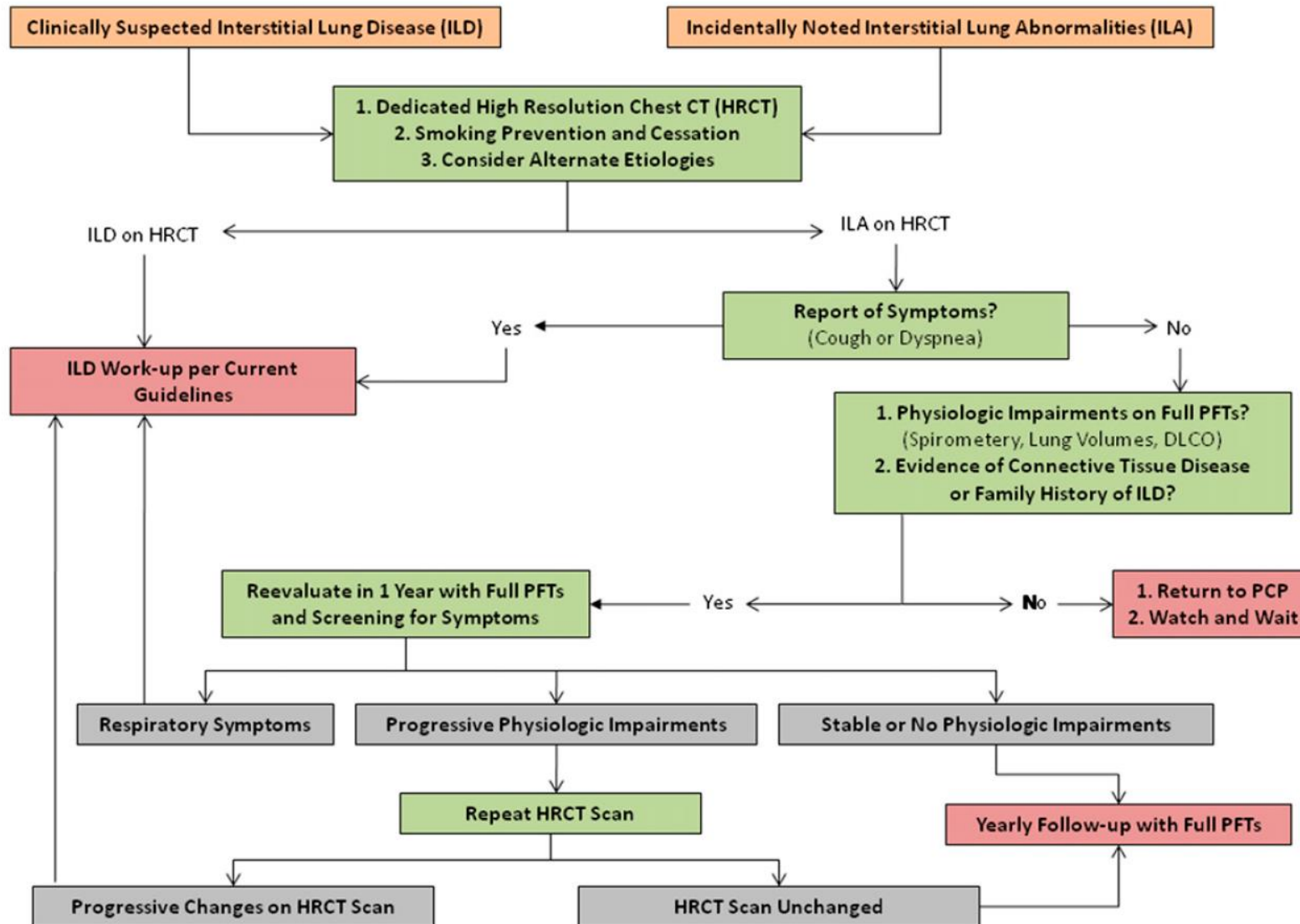
Facts supportive the ILA screening

- 일부 ILA는 IPF나 기타 ILD로 진행된다
- IPF는 조기발견, 조기 refer, 조기치료가 예후향상을 위해 필수적이다
- IPF의 자연경과에 영향을 줄 수 있는 약제가 개발되었고 개발 중이다
- ILA를 진행되게 하는 잠재적 위험인자에의 노출(흡연, 환경 등)을 줄일 수 있다



아직까지 evidence가 부족하다

Suggested algorithm of ILA diagnosis and follow-up



Goals and Action items in ILA

GOALS

To develop radiological standards on reporting ILA

To develop consensus statements when an imaging abnormality constitutes a disease

To develop effective screening programs in high-risk groups

To conduct secondary prevention trial in patients with early stage of pulmonary fibrosis

Action items

Studies needed to identify specific radiological patterns help predict adverse outcomes in ILA

Evidence based consensus guidelines and position statements

Studies actively participating in screening efforts

Early discussions should be undertaken to consider how to define reasonable endpoints and how to appropriately power trials in those with early stages of pulmonary fibrosis

Summary and Conclusion



Summary

- ILA는 영상의학적으로 정의되며, 진단부분에서 명확히 해야 할 부분들이 있다.
- ILA는 발생의 risk가 있는 군과 general population에서 흔하게 발생한다 (유병율 2-10%).
- 일부 ILA특히 fibrotic pattern을 보이는 경우 진행할 확률이 높고, 진행할 경우 mortality 특히 호흡기질환에 의한 mortality 증가를 보인다.
- IPF와 risk factors, symptom, physiology, functional, genetic, natural history and prognosis 에서 유사점을 가지나 차이점도 보인다. ILA중 일부 환자에서는 clinical ILD의 early or mild form 이라 할 수 있다

Conclusions

For ILA Dx

Predict progression

Predict prognosis

**Development of BIOMARKER
(blood, radiologic, genetic, etc.)**

**To define more precisely
the natural history of ILA**

**Longer and larger LONGITUDINAL
Studies**

- **Whom to and how to screen ?**
- **Whom to follow?**
- **How to follow**
- **Whom to treat ?**



**Establishment of clinical practice
guideline for physicians**

**THANK YOU FOR YOUR
KIND ATTENTION !!**

