2024.6.29
ILD school

ILD 환자의 다학제적 접근

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Contents

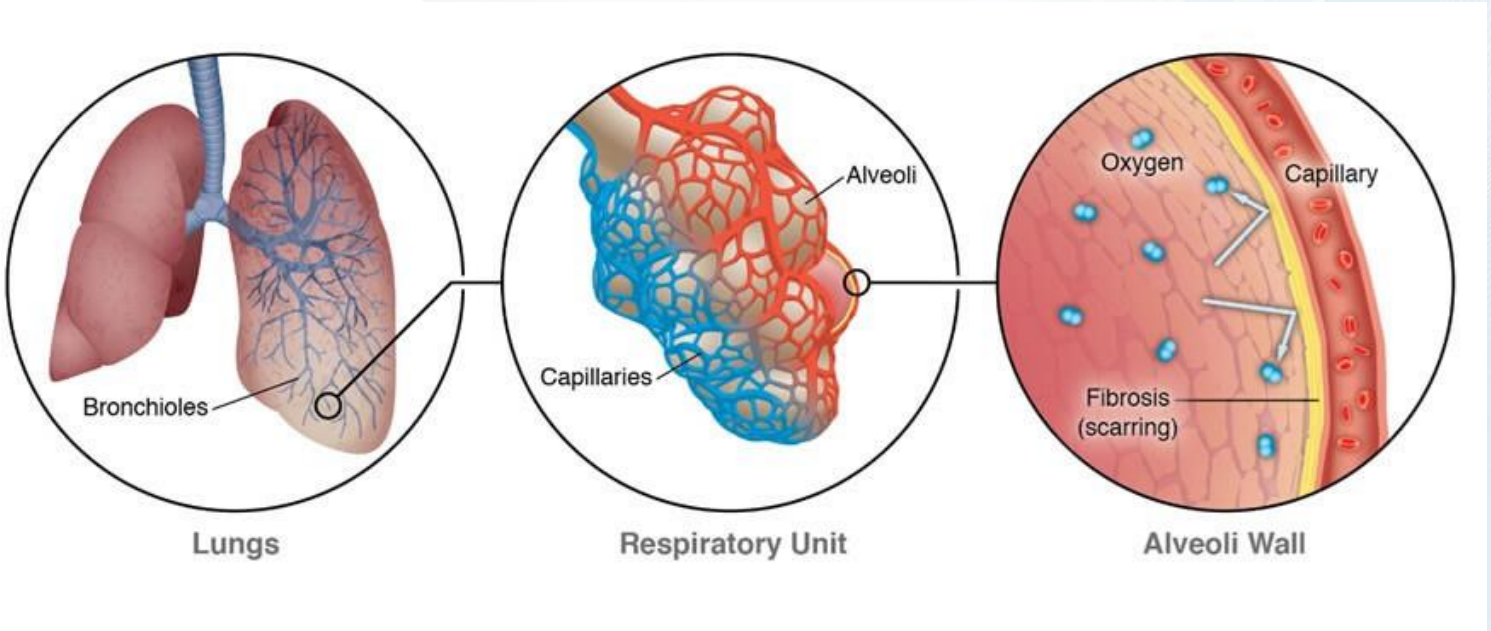
- Introduction
- Pulmonological Diagnostic Approaches
- Multidisciplinary Discussion
- MDD Cases
- Conclusion

Contents

간질(Interstitium)

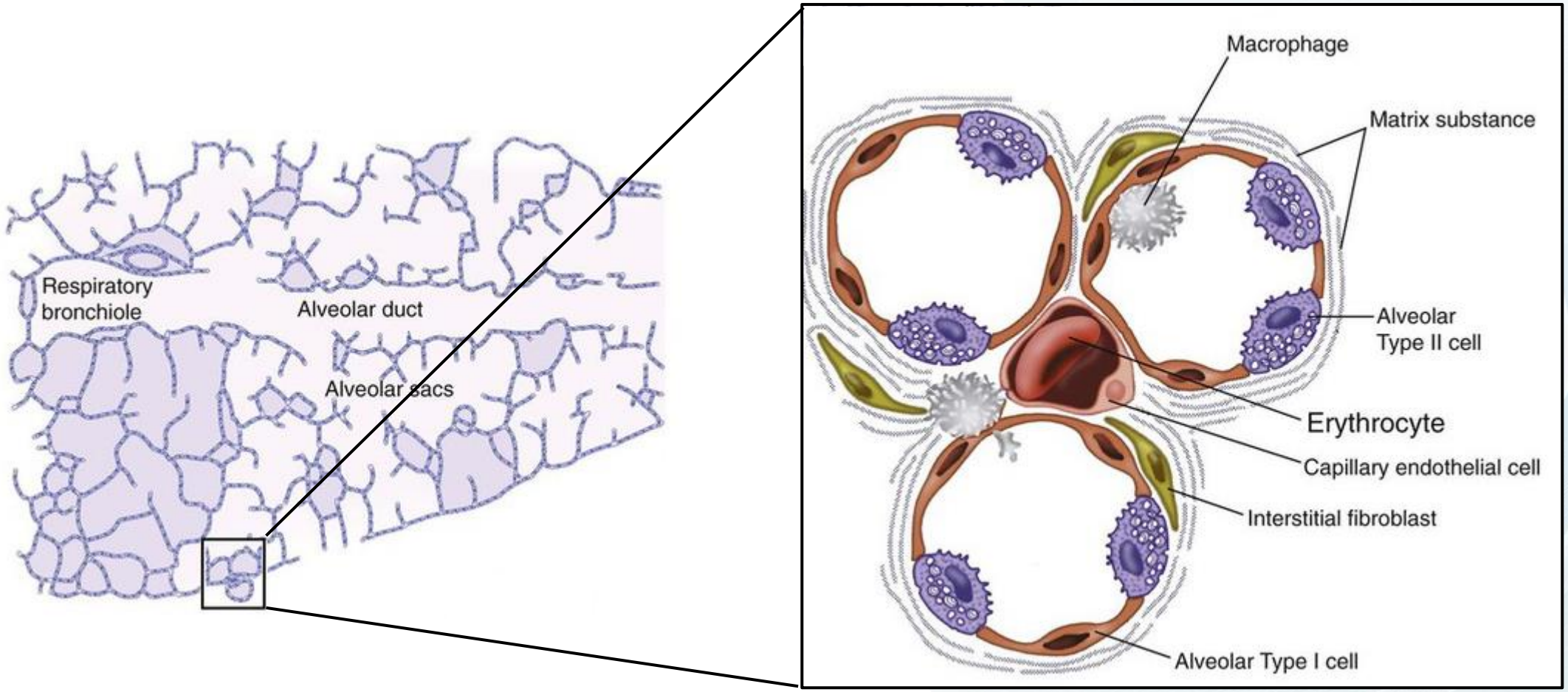
- Microscopic area within the walls of the alveoli between the **membrane of the alveolar epithelial** and the **membrane of capillary endothelial basement**.
- Gas exchange: from CO_2 to O_2

- Type I&II pneumocyte
- Endothelium
- Extracellular matrix
- Fibroblast
- Immune cells



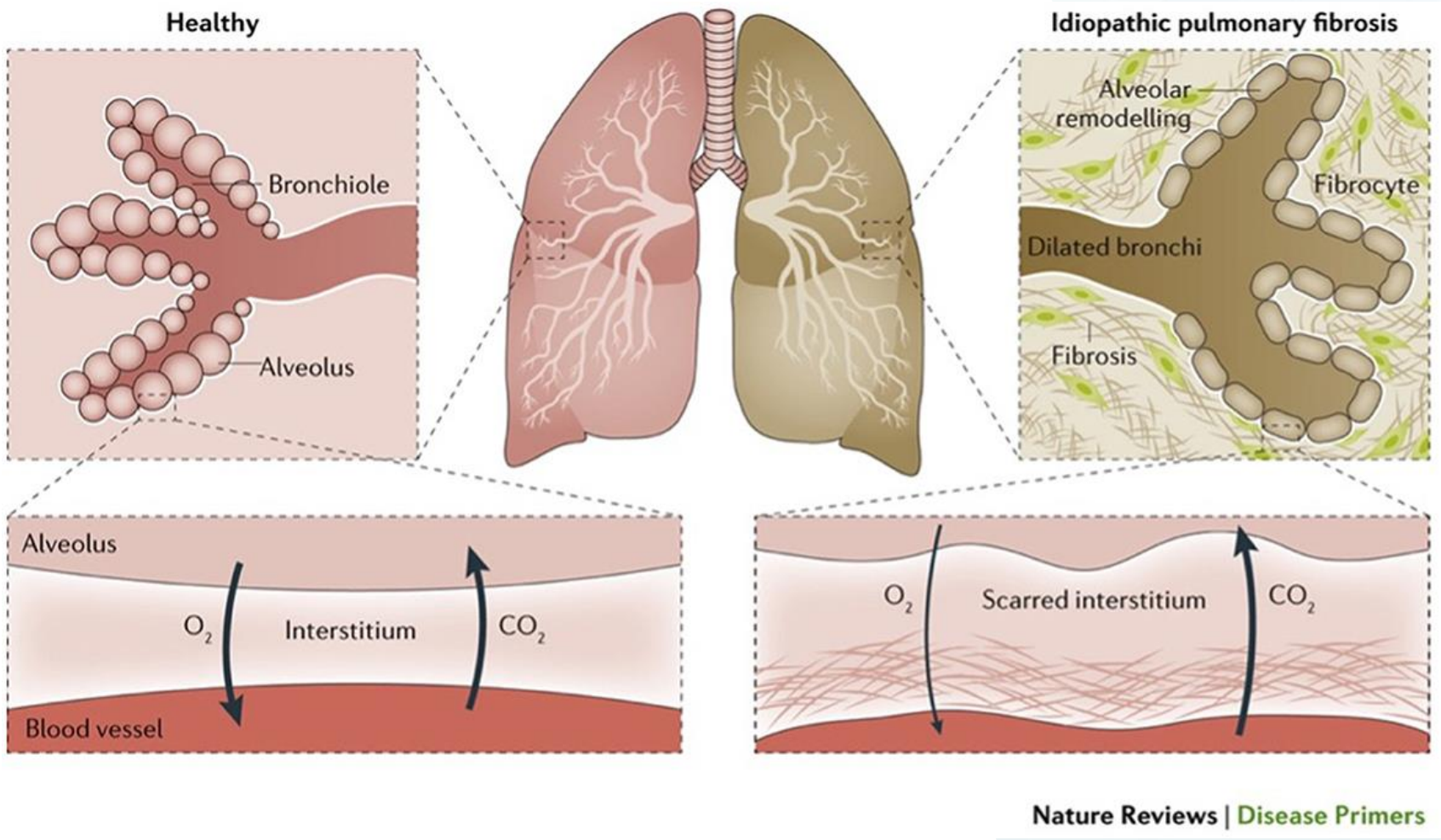
https://www.nationaljewish.org/

간질(Interstitium)



https://thoracickey.com/

간질성 폐질환(Interstitial lung disease, ILD)



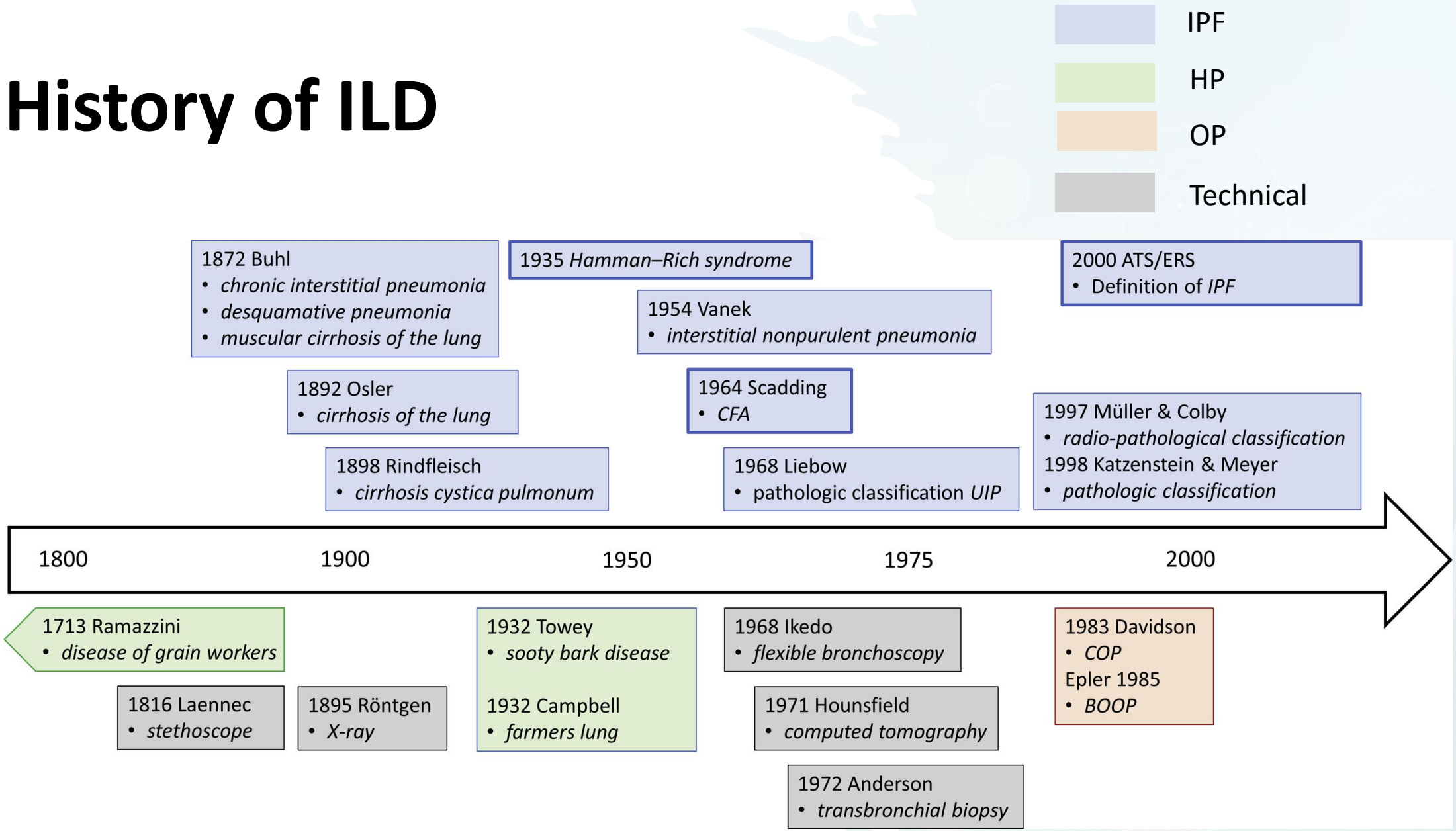
Front Med (Lausanne). 2024 Apr 18:11:129689

간질성 폐질환(Interstitial lung disease, ILD)

- A group of pulmonary disorder characterized clinically by

1. Radiologically **diffused infiltrates**
2. Histologically by **distortion of the gas exchanging units**
3. Physiologically by **restriction of lung volumes** and **impaired oxygenation**

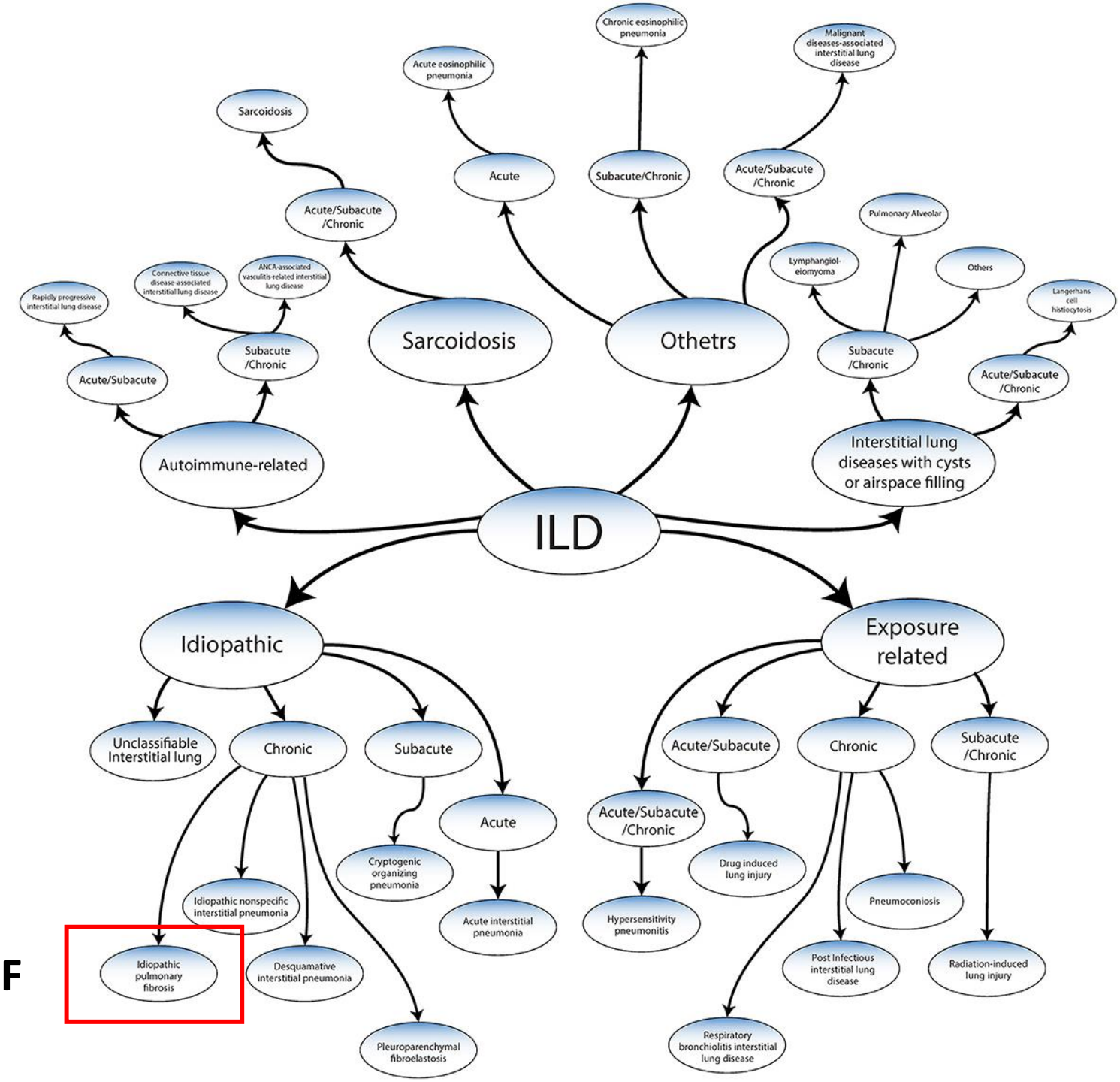
History of ILD



Clin Chest Med. 2021 Jun;42(2):229-239.

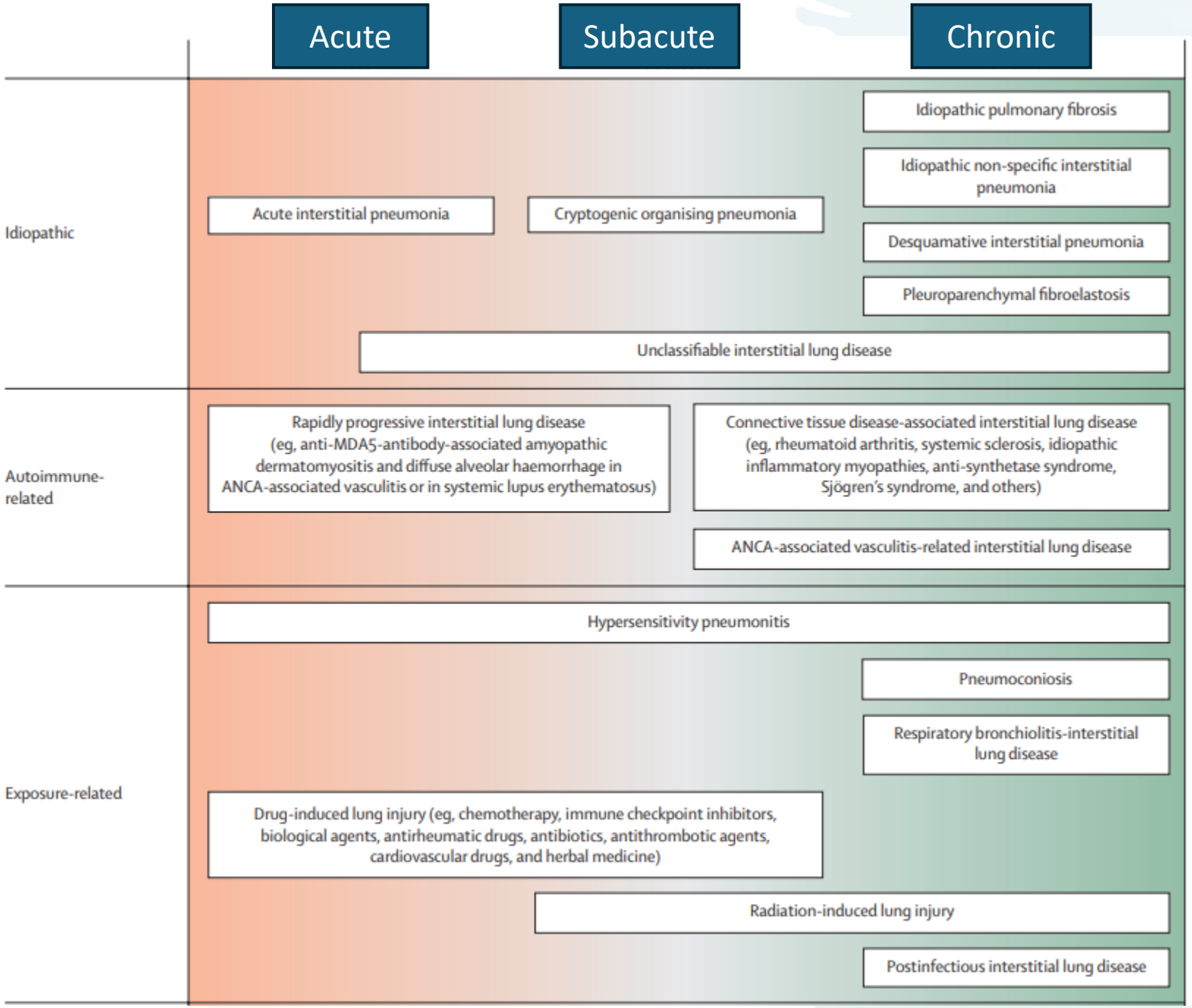
Classification of ILD

- IIP
- CTD-ILD
- Exposure
- Sarcoidosis
- Cystic
- Others

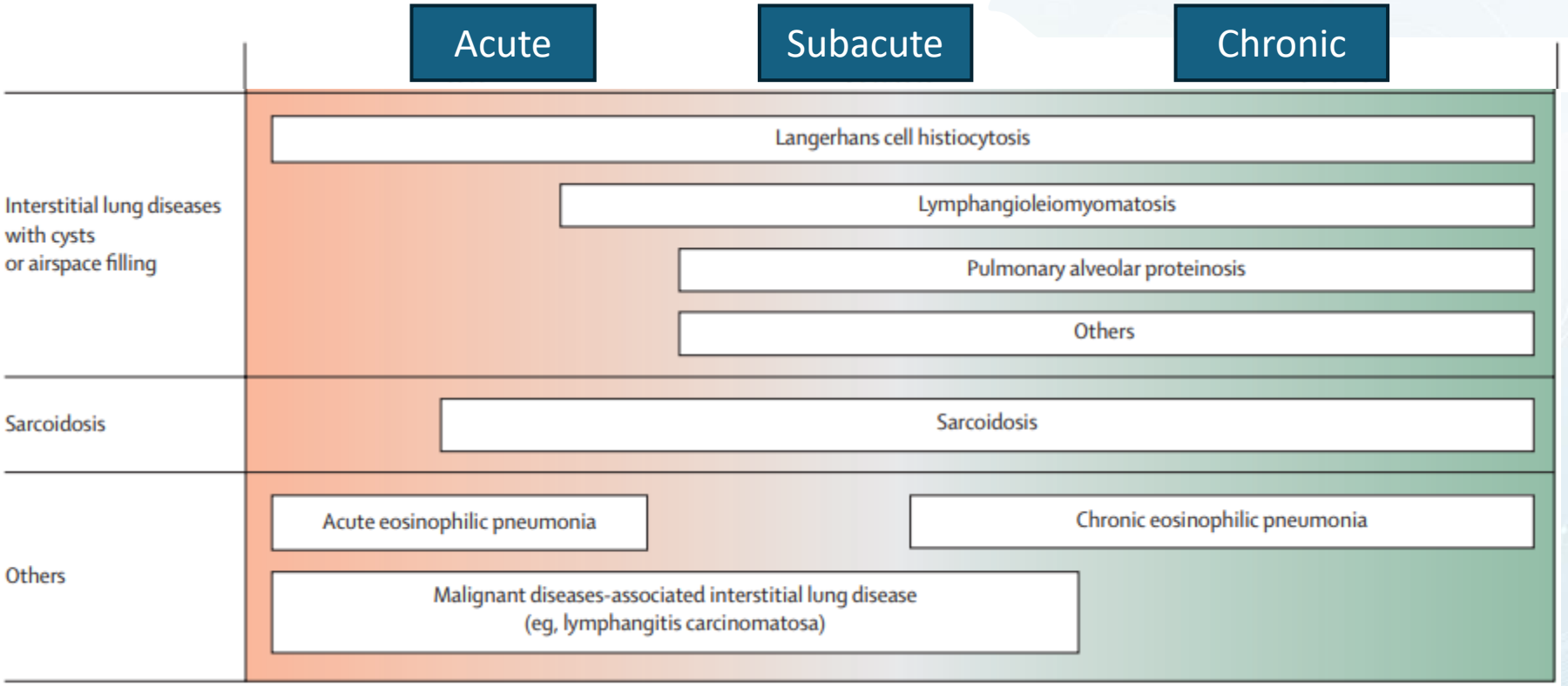


IPF

Front Med (Lausanne). 2024 Apr 18:11:129689



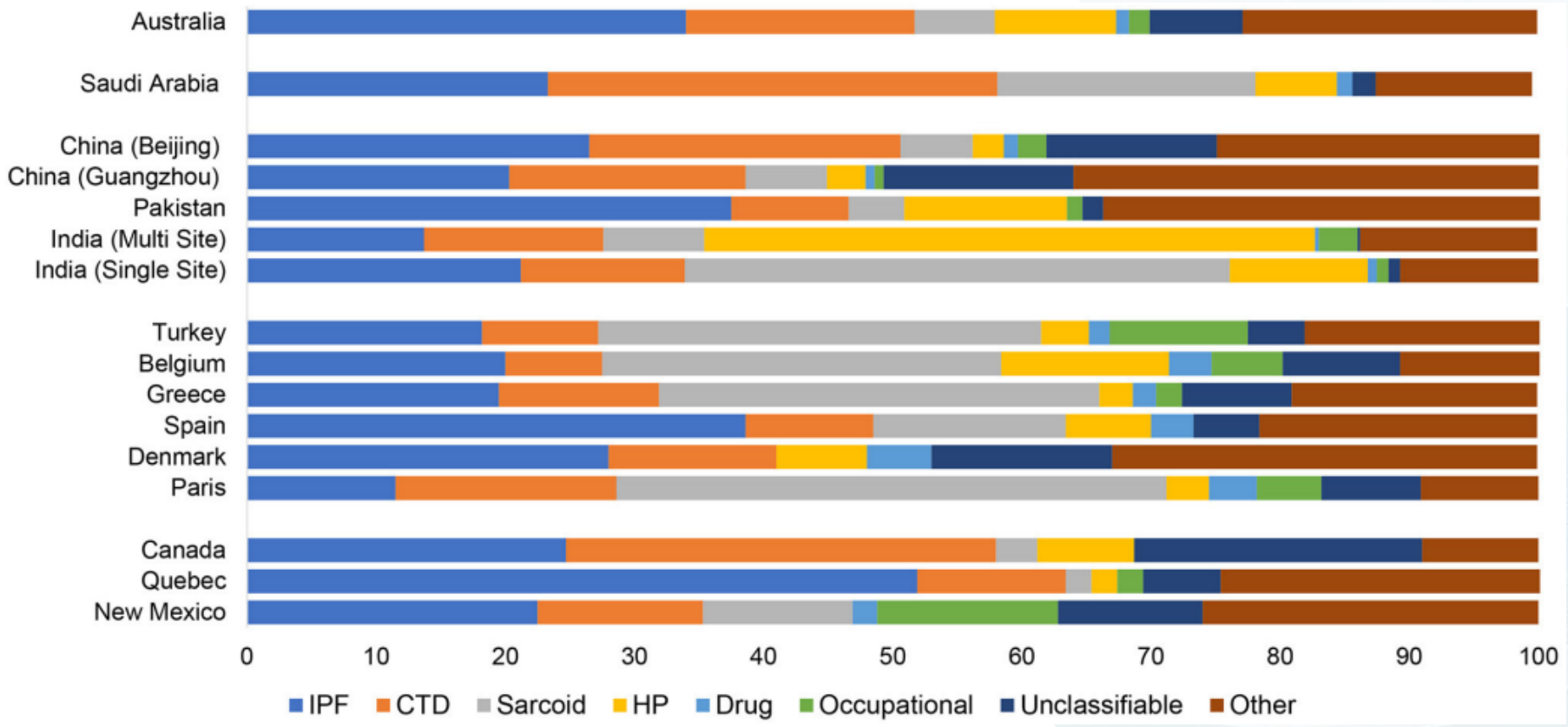
Lancet. 2022 Sep 3;400(10354):769-786.



Lancet. 2022 Sep 3;400(10354):769-786.

Epidemiology

- Varies according to the definition, study year, region…



Front Med (Lausanne). 2021; 8: 751181.

Epidemiology

- **Prevalence of IPF**

✓7 to1,650 per 100,000

- **Incidence of IPF**

✓2.3 to 331 per 100,000

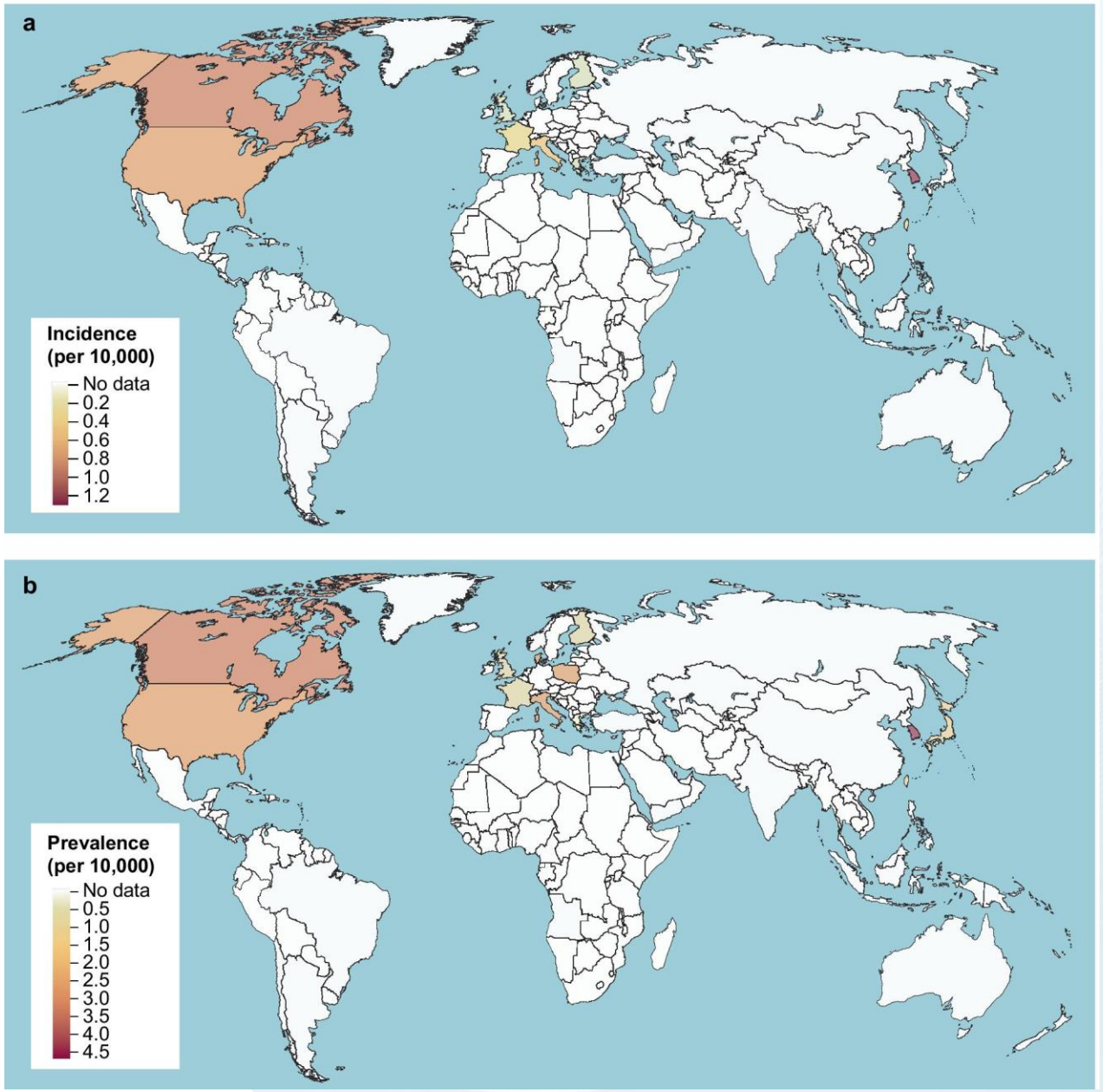
Case definitions	Prevalence estimate (per 100 000 persons)	Case descriptions	Country, author-published year
General/primary	36	► Patients with at least 1 hospitalisation or at least 1 outpatient visits with IPF diagnosis	Italy, Harari,[13] 2016
General/primary	13	► Patients with at least 1 claim with IPF diagnosis.	USA, Raghu,[2] 2016
Overall IPF	20	► Patients with at least 1 IPF inpatient claim, or 2 IPF outpatient claims with ICD code with no other ILD claim	USA, Raimundo,[14] 2016
Overall IPF	35	► IPF diagnostic K codes	South Korea, Lee,[15] 2016
Broad	1160	► Patients who had a code for IPF with no other ILD	USA, Zhang,[16] 2021
Broad	11	► Patients with code of ICD 516.3, patients excluded if they had a claim with code 515 after the last ICD code 516.3	USA, Raghu,[2] 2016
Broad	42	► Patients with code ICD code J84.1, cases with diagnosis of another ILD excluded	Canada, Hopkins,[17] 2016
Broad	22	► Patients with IPF code and no claims for other ILD diagnosis	Italy, Harari,[13] 2016
Broad	39	► Patients with Read codes: H563.00, H563.12, H563300, H563.13, H563100, H563200 and H563.11	UK, Strongman,[18] 2018
Narrow	13	► Patients that satisfied the broad definition ► Had 1> claim with procedure code for SLB, TLB or CT thorax	Italy, Harari,[13] 2016
Narrow	725	► Patients who had a code for IPF ► And if they did not have any other code for an alternative ILD ► And patients who had procedure code for an SLB or a thorax	USA, Zhang,[16] 2021
Narrow	7	► Patients with an ICD code of 516.3 and they were excluded if they had a claim with the ICD code 515 ► And further restricted by requiring a claim for an SLB, TLB or CT thorax	USA, Raghu,[2] 2016
Narrow	20	► Patients with ICD codes J84.1 with no other ILD and excluded cases that did not have chest CT, bronchus or SLB or bronchoscopy	Canada, Hopkins,[17] 2016

BMJ Open Respir Res. 2023 Jun;10(1):e001291

Epidemiology

- IPF
- 22 studies covering 12 countries

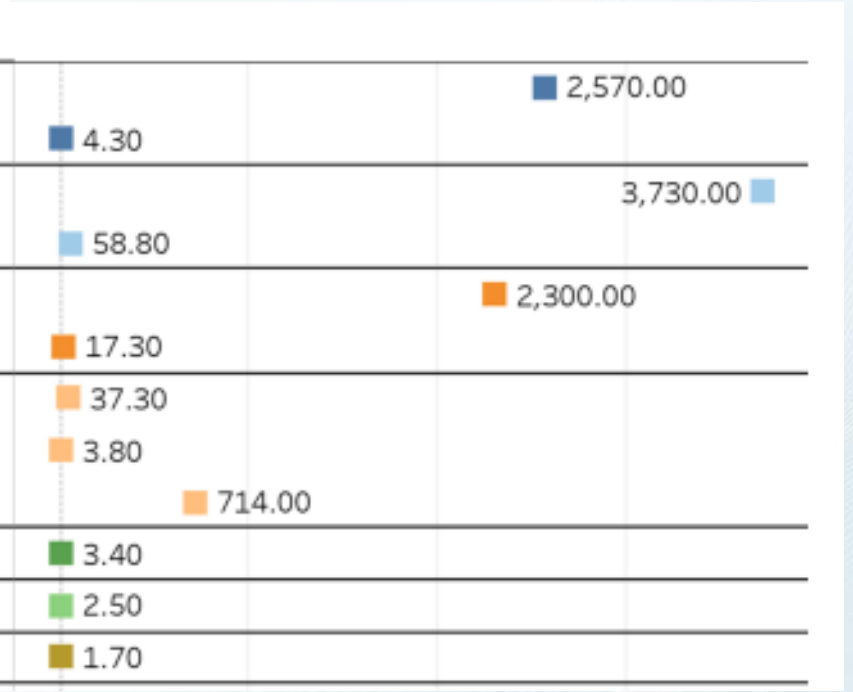
Region	Adjusted Incidence (per 100,000)	Adjusted Prevalence (per 100,000)
Asia-Pacific	3.5 – 13.0	5,7 – 45.1
Europe	0.9 – 4.9	3.3 – 25.1
North America	7.5 – 9.3	2.4 – 29.8



Respir Res. 2021 Jul 7;22(1):197.

ILD incidence

ILD condition	Unit for reporting	Author, Year	Year	Country
SSc ILD, overall	per 100,000 person years	Carton 2021 [39]	2018	Belgium
		Li 2021 [21]	2017	USA
SSc ILD, DcSSc	per 100,000 person years	Carton 2021 [39]	2018	Belgium
		Wangkaew 2016 [46]	2014	Thailand
SSc ILD, LcSSc	per 100,000 person years	Carton 2021 [39]	2018	Belgium
		Wangkaew 2016 [46]	2014	Thailand
RA ILD	% of study population	Zhang 2017 [29]	2013	China
	per 100,000 persons	Raimundo 2019 [22]	2013	USA
		Sparks 2021** [23]	2017	USA
Sjogren's ILD	% of study population	Roca 2017 [48]	2012	France
CTD ILD	% of study population	Olaosebikan 2021 [77]	2019	Nigeria
MCTD ILD	% of study population	Reiseter 2018 [73]	2008	Norway



BMJ Open Respir Res. 2023; 10(1): e001291.

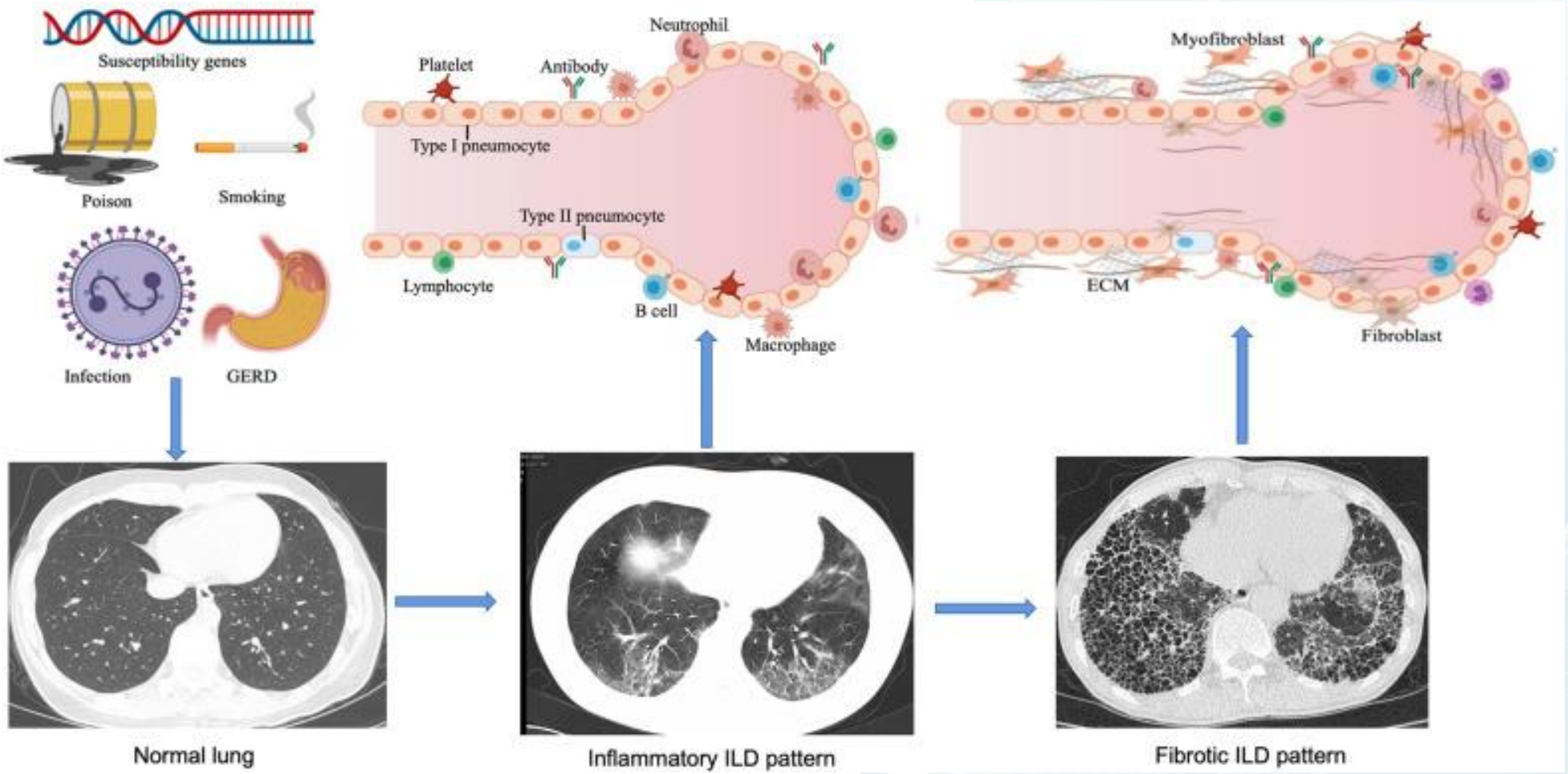
ILD incidence

Pneumoconiosis	% of study population	Cui 2015 [80]	2013	China, Datong	4.10
				China, Fuxin	1.40
				China, Kailuan	4.90
				China, Tiefa	0.30
	per 100,000 persons per year	Duchemann 2017 [72]	2012	France	0.80
Asbestosis	% of study population	DeBono 2021 [81]	2016	Canada	0.04
		Szeszenia-Dąbrowska 2.. [82]	1998	Poland	4.94
		Thomsen 2021 [83]	2012	Denmark	0.03
Radiation induced ILD	% of study population	Murofushi 2015 [84]	2008	Japan	1.40
		Sato 2018 [85]	2012	Japan	1.40
	per 100,000 persons per year	Duchemann 2017 [72]	2012	France	0.10
HP	per 100,000 persons	Perez 2018 [86]	2014	USA	1.94
	per 100,000 persons per year	Duchemann 2017 [72]	2012	France	0.90
IIP	per 100,000 persons	Lee 2016 [16]	2013	Korea	34.90
	per 100,000 persons per year	Duchemann 2017 [72]	2012	France	4.40
Pulmonary Sarcoid	per 100,000 persons per year	Duchemann 2017 [72]	2012	France	4.90
		Jeon 2020 [87]	2015	South Korea	0.48
LAM	per 100,000 persons per year	Duchemann 2017 [72]	2012	France	0.30
PLCH	per 100,000 persons per year	Duchemann 2017 [72]	2012	France	0.20
Progressive fibrosing ILD	per 100,000 persons	Nasser 2021 [88]	2016	France	4.70
		Olson 2021** [89]	2015	USA	32.55
Silicosis	per 100,000 persons	Casey 2019ǂ [90]	2014	USA	16.60
Unclassifiable ILD	per 100,000 persons per year	Duchemann 2017 [72]	2012	France	1.80

BMJ Open Respir Res. 2023; 10(1): e001291.

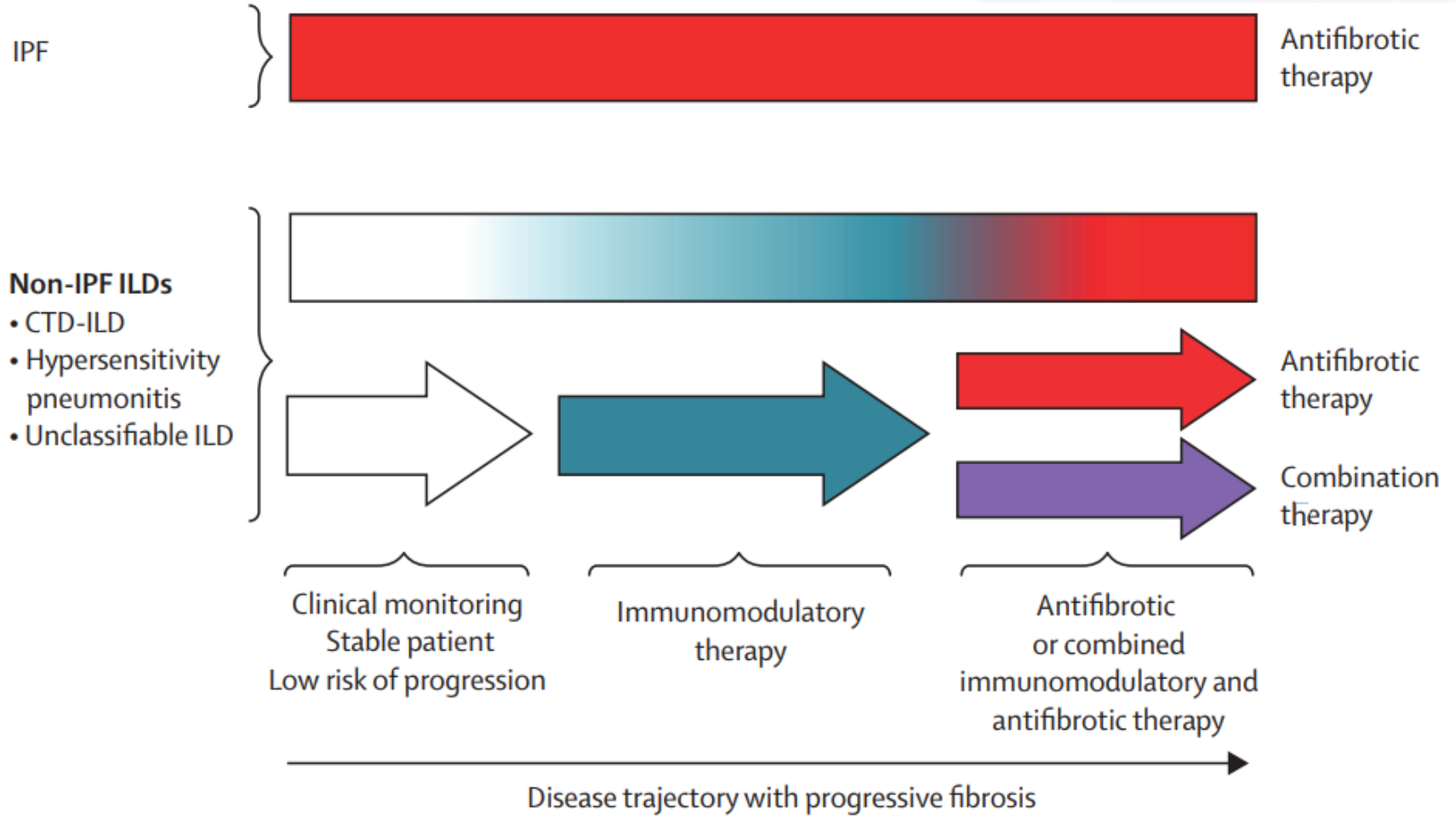
Pathogenesis

- Mixed Inflammation & Fibrosis



Nat Rev Rheumatol. 2014 Dec;10(12):728-39.

Inflammation vs. fibrosis



Lancet. 2022 Sep3;400(10354):769-786

Pathophysiology of IPF vs CTD-ILD

Feature	CTD-ILD	IPF
Primary Cause	Autoimmune diseases	Unknown, multifactorial (environment, genetics, aging)
Pathogenic trigger	Autoimmune reaction, chronic inflammation	**Repeated epithelial injury**, aging, genetic predisposition
Key immune mechanisms	**Autoantibody production** Activation of immune cells Cytokine release (TNF, IL-1, IL-6)	**Epithelial cell damage** Aberrant wound healing Myofibroblast activation
Inflammatory cells	T cells (CD4+), Macrophages, B cells	Alveolar epithelial cells, Fibroblasts
Fibrosis pathway	Cytokines promote fibrosis Specific autoantibodies influence patterns	**Senescence of epithelial cells** Imbalance of profibrotic and antifibrotic factors
Granuloma formation	**Present** in some CTD-ILDs	Not typical
Disease progression	Variable, based on underlying CTD	**Generally progressive**, leading to respiratory failure
Treatment Response	Immunosuppressants, Tailored to underlying CTD	Anti-fibrotics, Supportive care, lung translation

First step diagnosing ILD?

Physical Examination?

HRCT?

BFS & Biopsy?

Symptom Review?

Laboratory & Biomarker?

Detailed Medical History?

Consultation?

Contents

Common symptoms of ILD

- **Dyspnea**: progressive, often worsen with exertion
- **Chronic cough**: dry persistent
- **Fatigue:** persistent tiredness not relieved by rest.
- **Chest pain or discomfort**
  - ✓ Substernal chest pain: sarcoidosis
  - ✓Pleuritic chest pain: PLCH, LAM, tuberous sclerosis, neurofibromatosis
- **Hemoptysis:** diffuse alveolar hemorrhage (DAH), LAM, cancer
- **Other Symptoms:** fever, weight loss, Joint and muscle pain

Harrison's Principles of Internal Medicine 21th

Symptom patterns and triggers

- **Onset and Duration**
  - ✓Initial onset time
  - ✓Duration

Acute	Subacute	Chronic
Days to weeks	Weeks to months	Month to year
AIP, AEP, HP, DAH	COP, sarcoidosis, CEP, drug	IPF, pneumoconiosis, PLCH

- **Progression**
  - ✓worsening over time: gradual increase in severity.
  - ✓exacerbations
- **Triggers**
  - ✓environmental exposures: dust, mold, chemicals.
  - ✓physical activity
  - ✓infections

Harrison's Principles of Internal Medicine 21th

Medical History

- **Personal and family medical history**
  - ✓Sex: Female (LAM, CTD-ILD) vs. male (pneumoconiosis, PLCH, IPF)
  - ✓Previous respiratory conditions
  - ✓Chronic diseases: Autoimmune diseases
  - ✓Genetic predispositions: metabolic disorder, familiar IPF, sarcoidosis
- **Occupational and environmental exposures**
  - ✓ Exposure (asbestos, silica dust, organic dusts, chemicals) & job roles
  - ✓ Home environment & Hobbies: mold, pet birds, humidifiers (HP)
  - ✓Geographic location: high pollution areas, regions with known environmental risks.

Harrison's Principles of Internal Medicine 21th

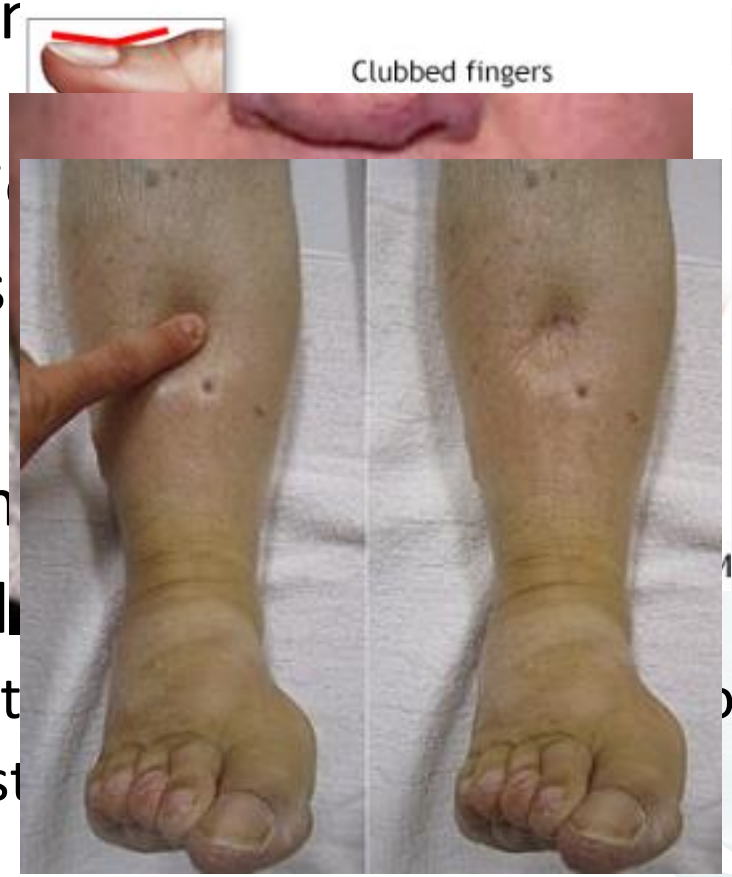
Medical History

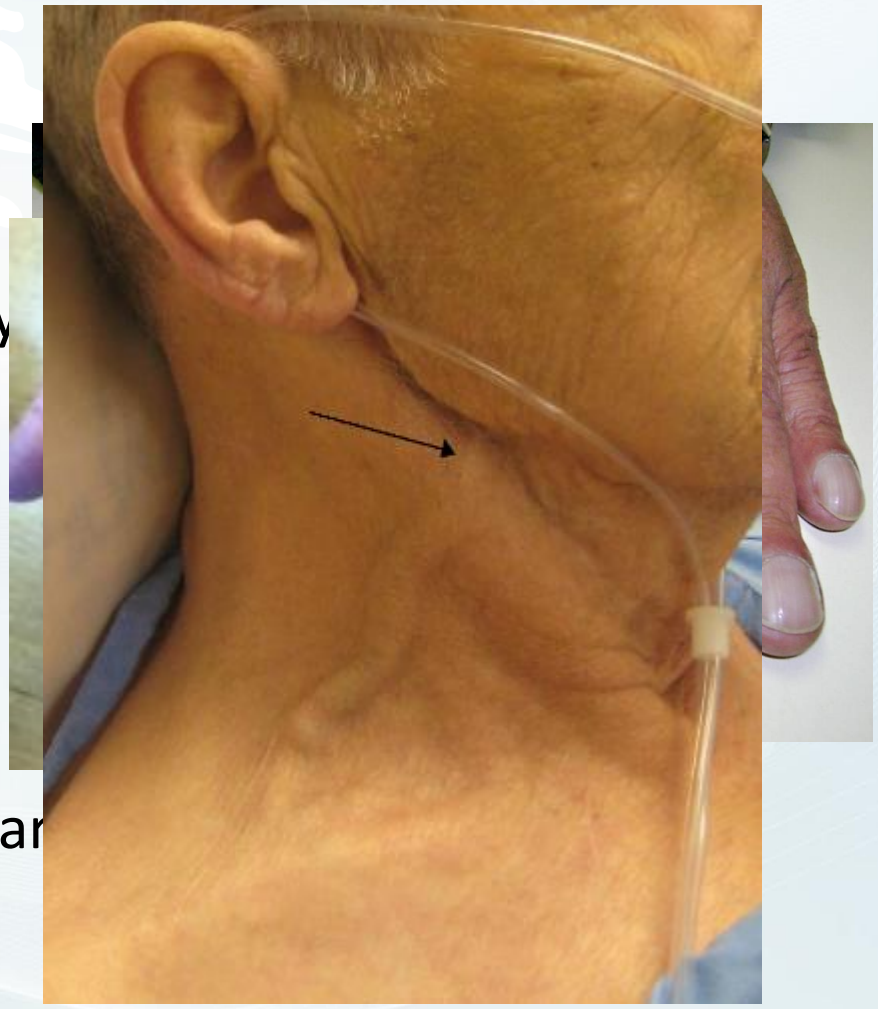
- **Smoking history**
  - ✓Current and past smoking status
  - ✓Duration and Intensity: number of pack-years, attempts to quit, exposure to secondhand smoke.
  - ✓PLCH(90%-smoking), RB-ILD, Goodpasture syndrome, asbestosis
  - ✓Non-smoker: sarcoidosis, HP
- **Medication and treatment History**
  - ✓Prescribed, over-the-counter, and herbal supplements.
  - ✓Previous treatments
  - ✓Adverse reactions: History of drug allergies or adverse effects.
- **Co-morbidities**

Harrison's Principles of Internal Medicine 21th

Physical examination

- Auscultation Findir
  - ✓ **Crackles (Rales)**
  - ✓ Wheezes: Chroni
- Clubbing of fingers
- Cyanosis
- Use of accessory m
- Additional physicall
  - ✓Edema: right heart
  - ✓Jugular venous dist

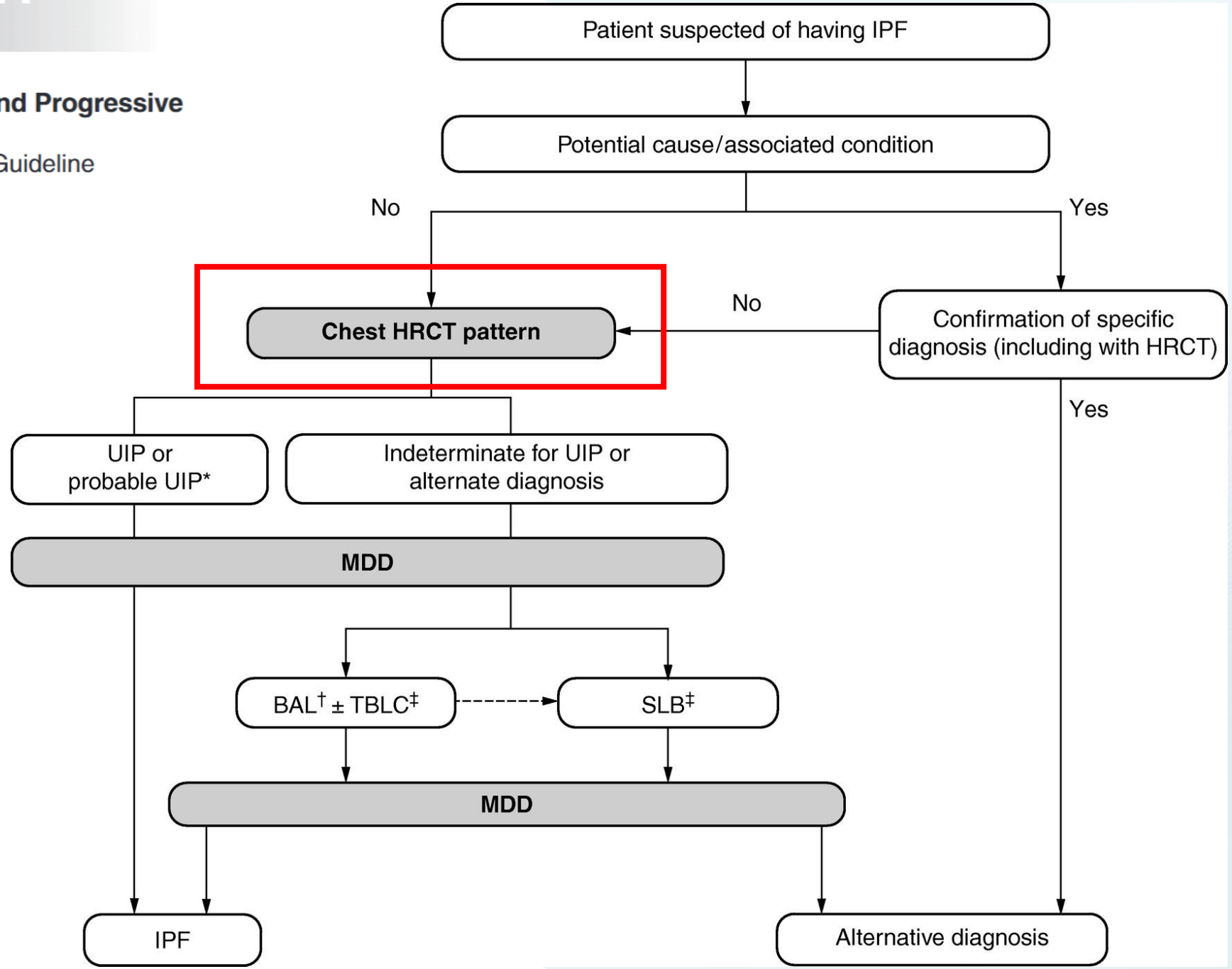




Wikipedia

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults

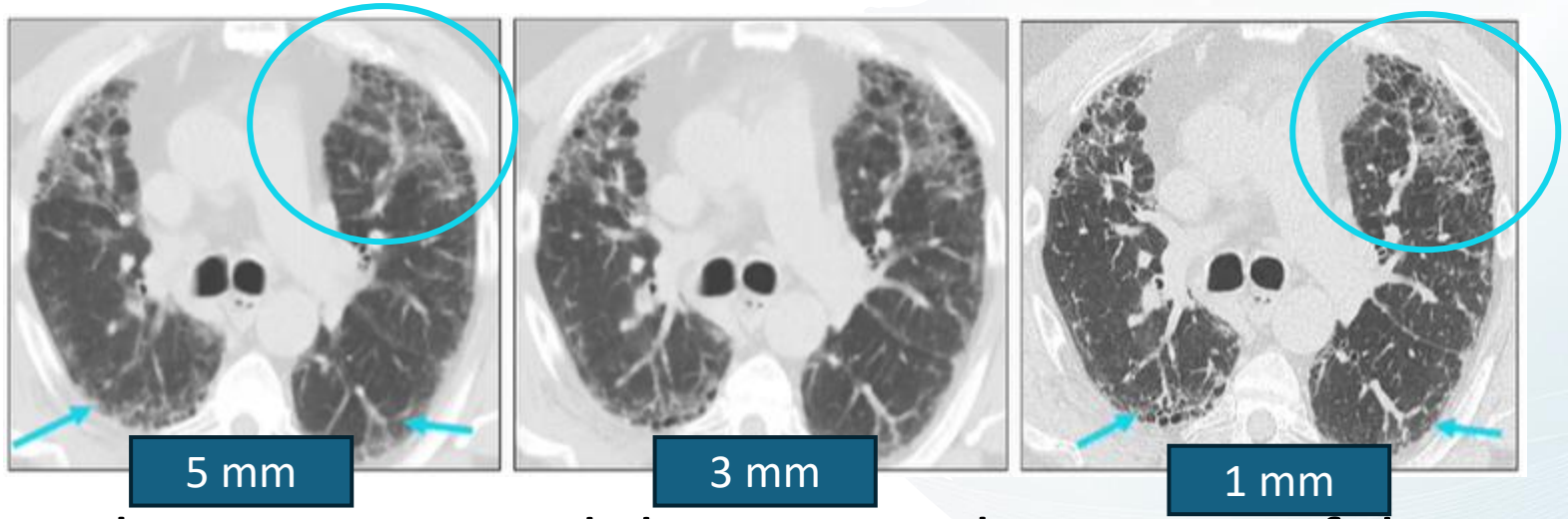
An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline



Am J Respir Crit Care Med. 2022 May 1;205(9):e18-e47.

HRCT (High-Resolution Computed Tomography)

- HRCT is the use of **thin section** CT images (0.625 to 2 mm slice thickness) often with a **high-spatial-frequency reconstruction algorithm**

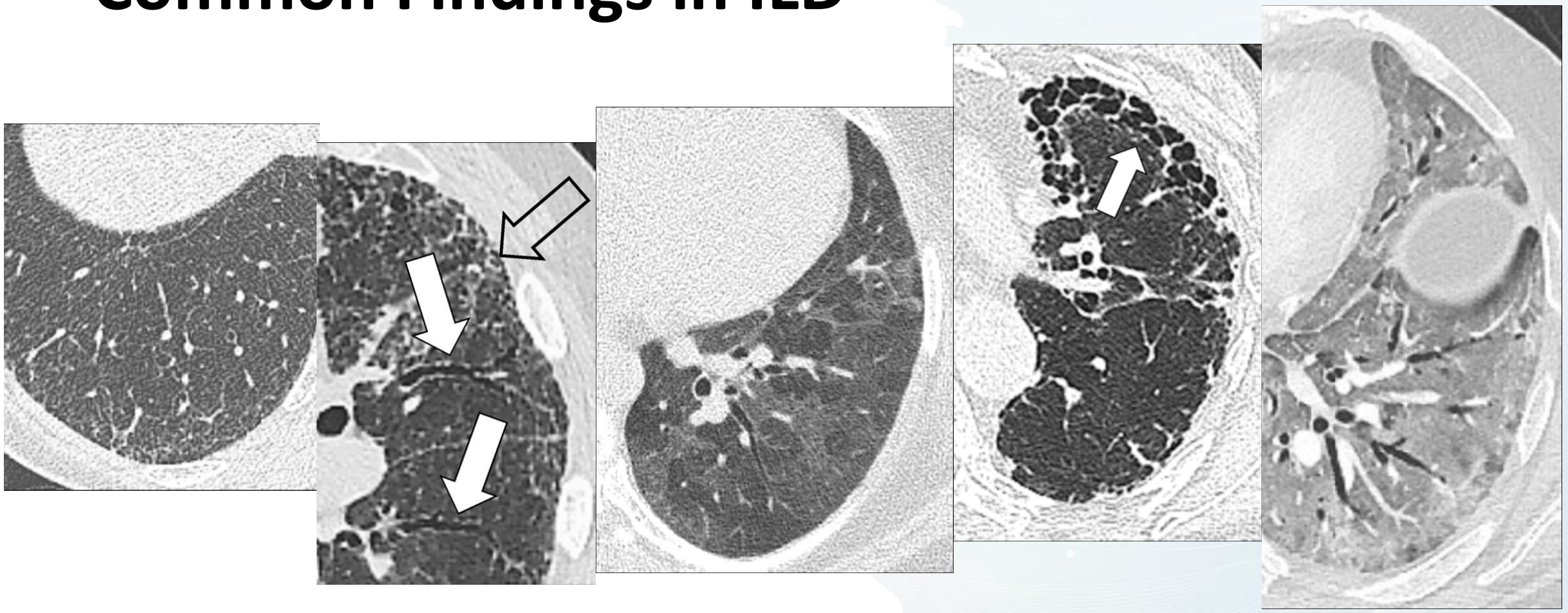


- To detect, characterize, and determine the extent of disease that involve the lung parenchyma and airway

HRCT: Role in diagnosis and management

- **High Resolution:** detailed images of lung structures, allowing for the identification of subtle changes.
- **Specificity:** aids in the initial diagnosis by **differentiating** between various types of ILD based on specific imaging patterns.
- **Non-Invasive:** minimal risk to the patient.
- **Disease monitoring:** Used to monitor disease progression and response to treatment.

Common Findings in ILD



Reticulation

Traction bronchiectasis

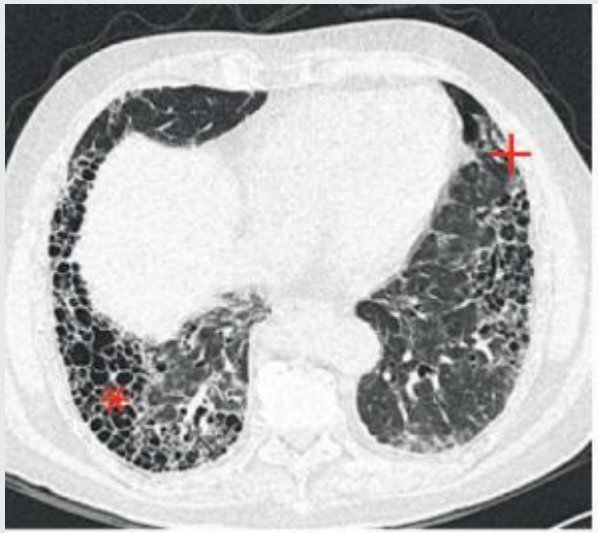
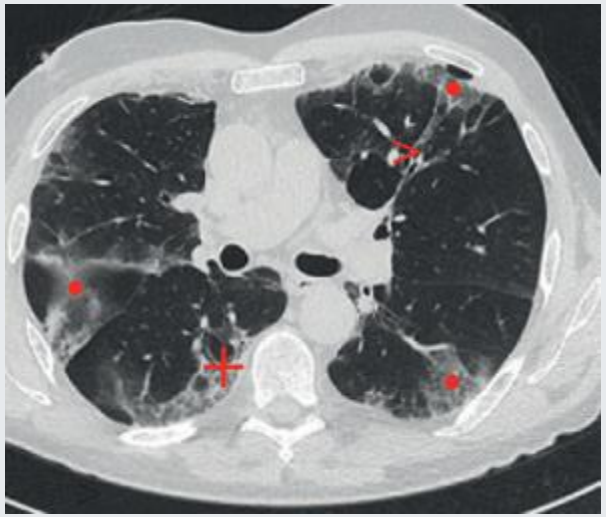
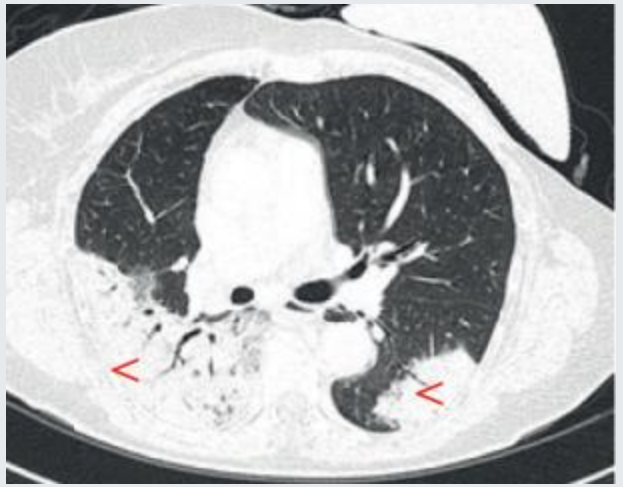
Mosaic attenuation

Honeycomb

GGO

Radiology. 2024 Feb;310(2):e232558.

HRCT Patterns in ILD

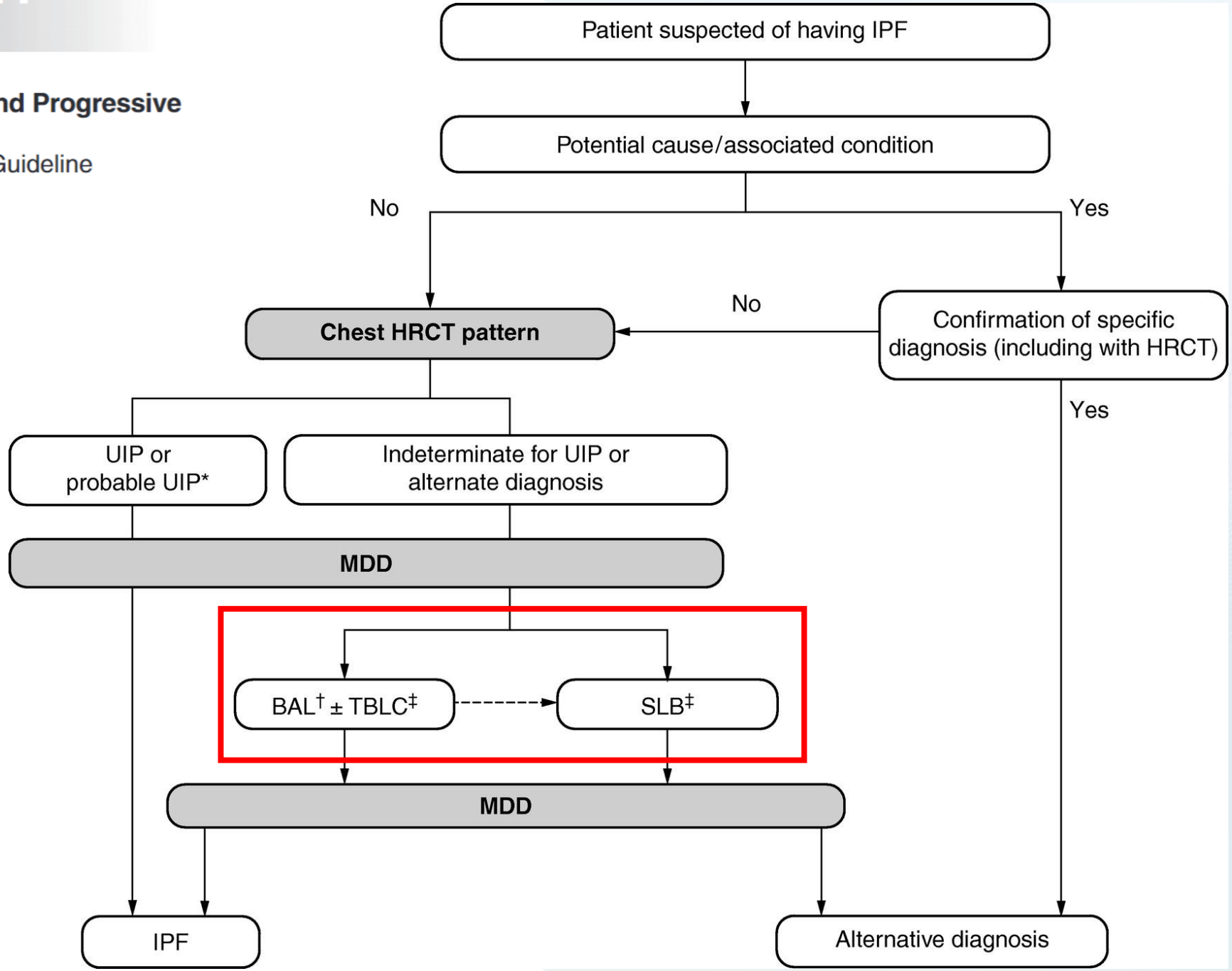
UIP	NSIP	OP
• Honeycombing, Reticulation, Traction bronchiectasis • Basal and subpleural predominance • IPF, RA-ILD	• Ground-glass opacities, fine reticulation, subpleural sparing • Predominantly lower lung zones • iNSIP, CTD-ILD	• Patchy consolidation, peribronchial and subpleural distribution, ground-glass opacities and nodules • Random, often peripheral • COP, CTD-ILD
		

Lancet. 2022 Sep 3;400(10354):769-786.

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults
An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

BAL may be appropriate in some patients with a probable UIP pattern.

‡Transbronchial lung cryobiopsy (TBLC) may be preferred to surgical lung biopsy (SLB) in centers with appropriate expertise and/or in some patient populations, as described in the text. A subsequent SLB may be justified in some patients with nondiagnostic findings on TBLC.



Am J Respir Crit Care Med. 2022 May 1;205(9):e18-e47.

Bronchoalveolar lavage (BAL)

정상 성인(비흡연자)		간질성폐질환		
세포	분율	림프구 증가형	호산구 증가형	호중구 증가형

- 세포성 NSIP, 과민성폐렴 또는 COP에서는 림프구가 증가하게 되어 주로 중성구가 증가 하는 IPF와 감별이 될 수 있다. 하지만 결과가 비특이적이기 때문에 진단적 가치는 별로 없어 모든 환자에서 다 시행할 필요는 없다. **흉부 HRCT에서 UIP 진단이 명확한 경우(definite UIP)에는 기관지폐포세척검사는 필요하지 않으나**, UIP인지 명확하지 않으면 기관지폐포세척검사를 통한 세포분석을 통해 타 간질성폐질환 감별에 도움이 될 수 있다.

- 간질성폐질환(ILD) 임상진료지침 (2023 년 1 차 개정판)

‡호중구 >50%는 급성폐손상, 흡인폐렴 또는 농성감염질환의 진단을 시사한다.

Bronchoalveolar lavage (BAL)

Finding	Disease association
Progressive increase in bloody fluid return with sequential lavages. Hemosiderin-positive alveolar macrophage.	Diffuse alveolar hemorrhage
Milky fluid. Positive periodic acid-Schiff staining and amorphous acellular debris	Pulmonary alveolar proteinosis
Macrophage predominance -smoking-related inclusions	Smoking-related interstitial lung diseases (DIP, RBILD, or PLCH)
Lymphocytosis (>25%)	Granulomatous diseases: sarcoidosis, HP, or chronic beryllium disease
Neutrophilia (>50%)	Acute lung injury, aspiration pneumonia, or suppurative infection
Eosinophilla (>25%)	AEP or CEP.
Cell differential count of more than 1% mast cells, more than 50% lymphocytes, and more than 3% neutrophils	Acute HP
CD4+/CD8 greater than 4	Sarcoidosis
CD1a positive cells at least 5%/Birbeck granules in macrophages (electron microscopy)	PLCH

AEP, acute eosinophilic pneumonia; CEP, chronic eosinophilic pneumonia; DIP, desquamative interstitial pneumonia; HP, hypersensitivity pneumonitis; PLCH, pulmonary langerhans cell histiocytosis; RBILD, respiratory bronchiolitis with interstitial lung disease.

Curr Opin Pulm Med. 2022 Jan 1;28(1):3-8.

Surgical lung biopsy: Indication

1. Identify treatable diseases:

- Distinguish between treatable and non-treatable diseases (e.g., HP vs. IPF).

2. Exclude infectious and neoplastic causes:

- Rule out infections and cancers that mimic chronic ILD.

3. Assess treatment response:

- Evaluate potential response to therapies with serious side effects (e.g., NSIP vs. IPF).

4. Specific diagnosis for therapy and prognosis:

- Obtain a precise diagnosis to guide treatment and prognosis.

5. Unexplained hypoxemia:

- Investigate unexplained low oxygen levels with strong suspected ILD based on PFT and negative workup for pulmonary vascular disease with normal HRCT.

Ann Am Thorac Soc. 2021 Oct;18(10):1601-1609.

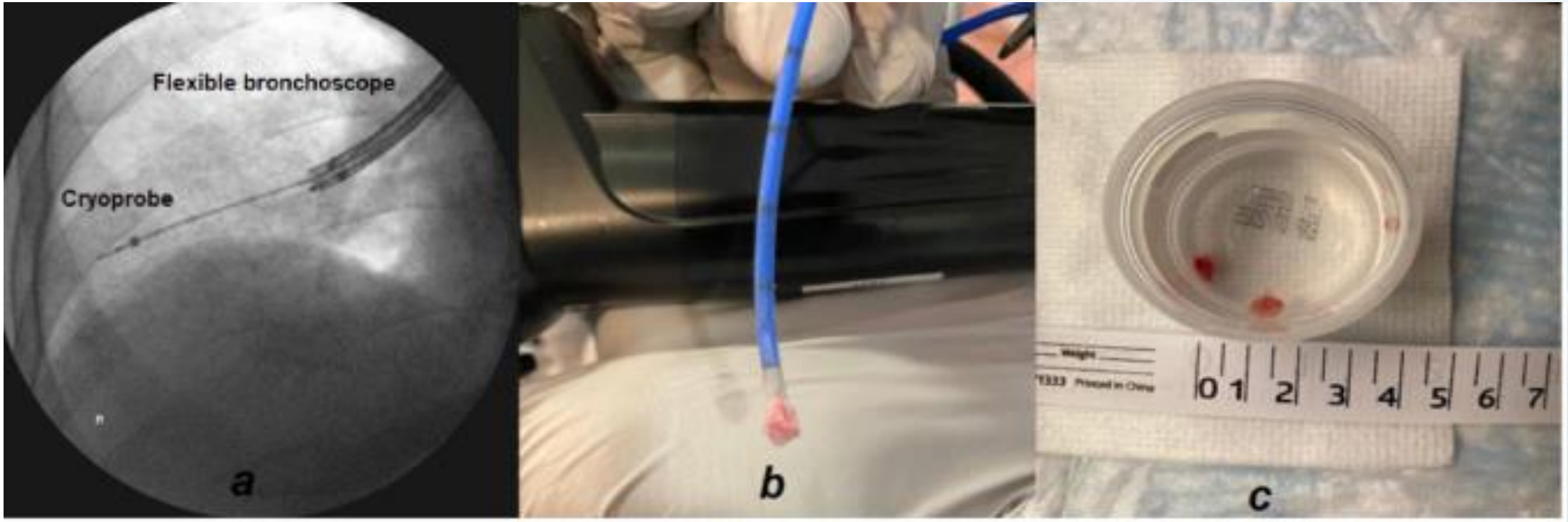
Surgical lung biopsy: High-risk

Table. Patient factors associated with increased risk of morbidity and mortality in the setting of SLB in ILD	
Increased age (e.g., >74 yr old)	Decreased pulmonary function (FVC < 50–55%; DL_{CO} < 35–40%)
Immunosuppression	Hypoxemic respiratory failure (i.e., need for supplemental oxygen)
Male sex	Nonelective procedure, hospitalized patient, rapidly progressive disease
Malignancy	Corticosteroid therapy (e.g., prednisone ⩾ 20 mg/d)
Comorbidities	Frailty, poor functional status
	Composite risk categorization based on age, sex, and comorbidities

Ann Am Thorac Soc. 2021 Oct;18(10):1601-1609.

Transbronchial cryobiopsy (TBLC)

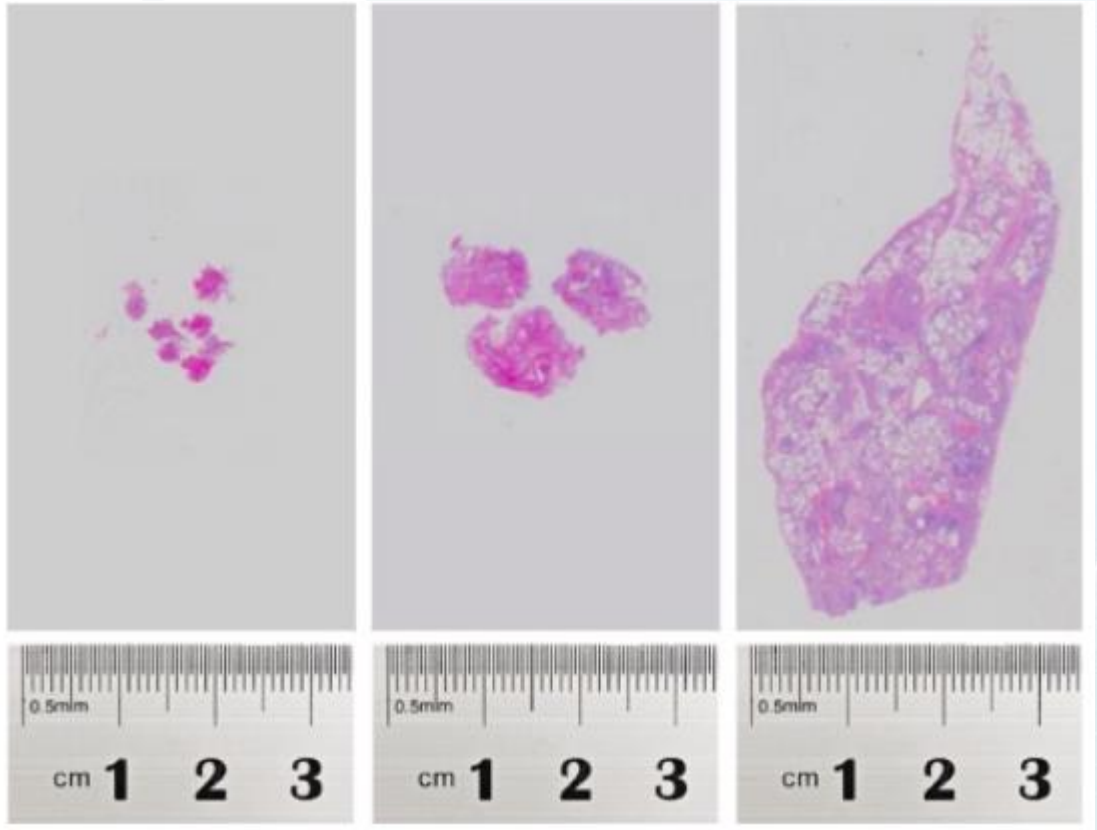
- A minimally invasive bronchoscopic technique used to obtain lung tissue samples for the diagnosis of ILD



Diagnostics (Basel). 2023 Sep 8;13(18):2886.

Transbronchial cryobiopsy (TBLC)

- High diagnostic accuracy: yield greater than 70%
- Low complications
- Minimally invasive
- Cost-effective
- Compatibility with **multidisciplinary discussion**
  - ✓high diagnostic agreement with MDD, especially with more samples
  - ✓improved diagnostic confidence



TBLB TBLC VATS

Heliyon. 2023 Mar 25;9(4):e14768

Transbronchial cryobiopsy (TBLC)

- Meta-analysis (n=30)

Table 2. Evidence profile for transbronchial cryobiopsy in patients with fibrotic interstitial lung disease

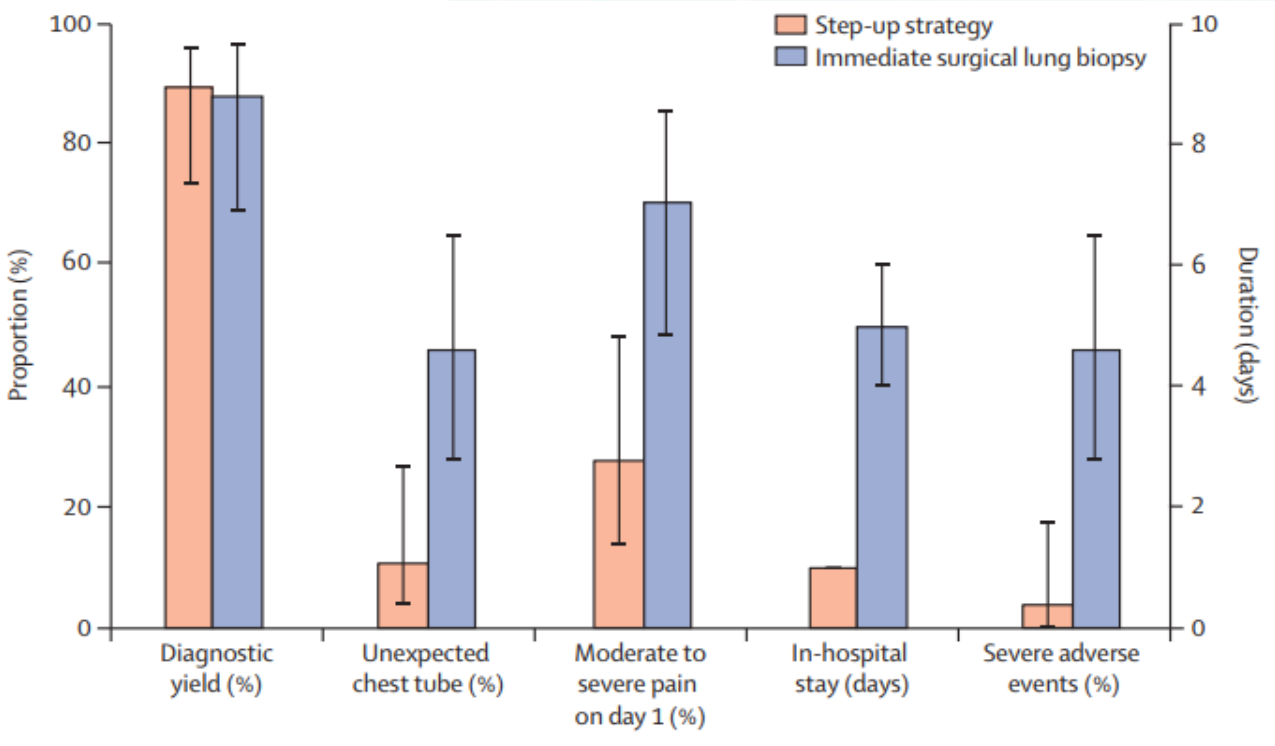
Quality Assessment							Summary of Findings			
Studies, *n*	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other	Patients	Effect after Outliers Removed (95% CI)	Quality	Importance
Diagnostic yield										
29*	Case series	Very severe†	Very Severe‡	None	None	None	1846	0.80 (0.76–0.83)	⊕OOO VERY LOW	CRITICAL
Mortality, 30-d										
20§										ORTANT
Bleeding, a										
12‖										ORTANT
Bleeding, s										
29¶										ORTANT
Pneumoth										
20**	Case series	None	Very Severe‡	None	None	None	1796	0.08 (0.06–0.11)	⊕OOO VERY LOW	IMPORTANT
Prolonged air leak										
6††	Case series	Very severe†	None	None	None	None	469	0.00 (0.00–0.00)	⊕OOO VERY LOW	IMPORTANT
Exacerbations										
14‡‡	Case series	Very severe†	Severe§§	None	None	None	1863	0.00 (0.00–0.00)	⊕OOO VERY LOW	IMPORTANT
Respiratory infections										
7‖‖	Case series	Very severe†	None	None	None	None	444	0.00 (0.00–0.00)	⊕OOO VERY LOW	IMPORTANT

High diagnostic yield & low adverse event!!

Ann Am Thorac Soc. 2022 Jul;19(7):1193-1202.

TBLC vs. surgical lung biopsy

- A multicentre, RCT in six hospitals across the Netherlands
- TBLC + sequential SLB (step-up) (n=28) vs. immediate SLB (n=27)



- More chest tube insertion, long total in-hospital stay, and pain in immediate SLB group, but similar diagnostic yield

Lancet Respir Med. 2024 Apr 16:S2213-2600(24)00074-2.

TBLC

Transbronchial Cryobiopsy for the Diagnosis of Interstitial Lung Diseases
CHEST Guideline and Expert Panel Report

- In patients with suspected ILD, we suggest **that TBLC can be used to provide histopathologic findings for multidisciplinary discussion diagnosis** (Weak Recommendation, Very Low-Quality Evidence).
  - ✓ Choose based on local expertise, risks, and patient preference. Nondiagnostic TBC may lead to SLB.
- In patients with suspected ILD undergoing TBLC, we suggest biopsy of **at least two different sites** (either different segments in the same lobe or different lobes) (Weak Recommendation, Very Low-Quality Evidence).
  - ✓ Increases pneumothorax risk but improves diagnostic yield.
- In patients with suspected ILD undergoing TBLC, we suggest biopsy with **the tip of the cryoprobe located 1cm from the pleura** (Ungraded Consensus-Based Statement).
  - ✓ Balances diagnostic yield with safety.

Chest. 2020 Apr;157(4):1030-1042

TBLC

Transbronchial Cryobiopsy for the Diagnosis of Interstitial Lung Diseases
CHEST Guideline and Expert Panel Report

- In patients with suspected ILD undergoing TBLC, we suggest the **use of fluoroscopy** (Ungraded Consensus Based Statement).
  - ✓ Enhances safety and accuracy
- In patients with suspected ILD undergoing TBLC, we suggest that TBLC be performed with a **bronchial blocker** either through an endotracheal tube or rigid bronchoscope (Ungraded Consensus-Based Statement)
  - ✓ Controls bleeding effectively.
- In patients with suspected ILD undergoing TBLC, we suggest the **use of a small cryoprobe (1.9 mm)** rather than a larger cryoprobe (2.4 mm) (Ungraded Consensus-Based Statement)
  - ✓ Easier to maneuver and safer.

Chest. 2020 Apr;157(4):1030-1042

Transbronchial biopsy (TBLB)

- **Diagnostic yield**

✓**Sarcoidosis:** up to 71%.

✓**Hypersensitivity Pneumonitis (HP):**

- Nonfibrotic HP: BAL cellular analysis + TBLB
- Fibrotic HP: TBLC

✓**IPF: <u>Not recommended</u>**, but the Envisia Genomic Classifier may enhance yield in probable UIP

✓Lymphangitic carcinomatosis, eosinophilic pneumonia, and alveolar proteinosis.

✓Infections: Often diagnosis with small samples.

Curr Opin Pulm Med. 2022 Jan 1;28(1):3-8.

Transbronchial biopsy (TBLB)

- **Safety Profile**

✓Pneumothorax: 0.7–2%, up to 10% in some studies

✓Bleeding: up to 4%

✓Mortality: <0.05%

- **Limitations**

✓**Small sample size**: Few millimeters, prone to crush artifacts

✓Patchy disease: May miss diagnosis

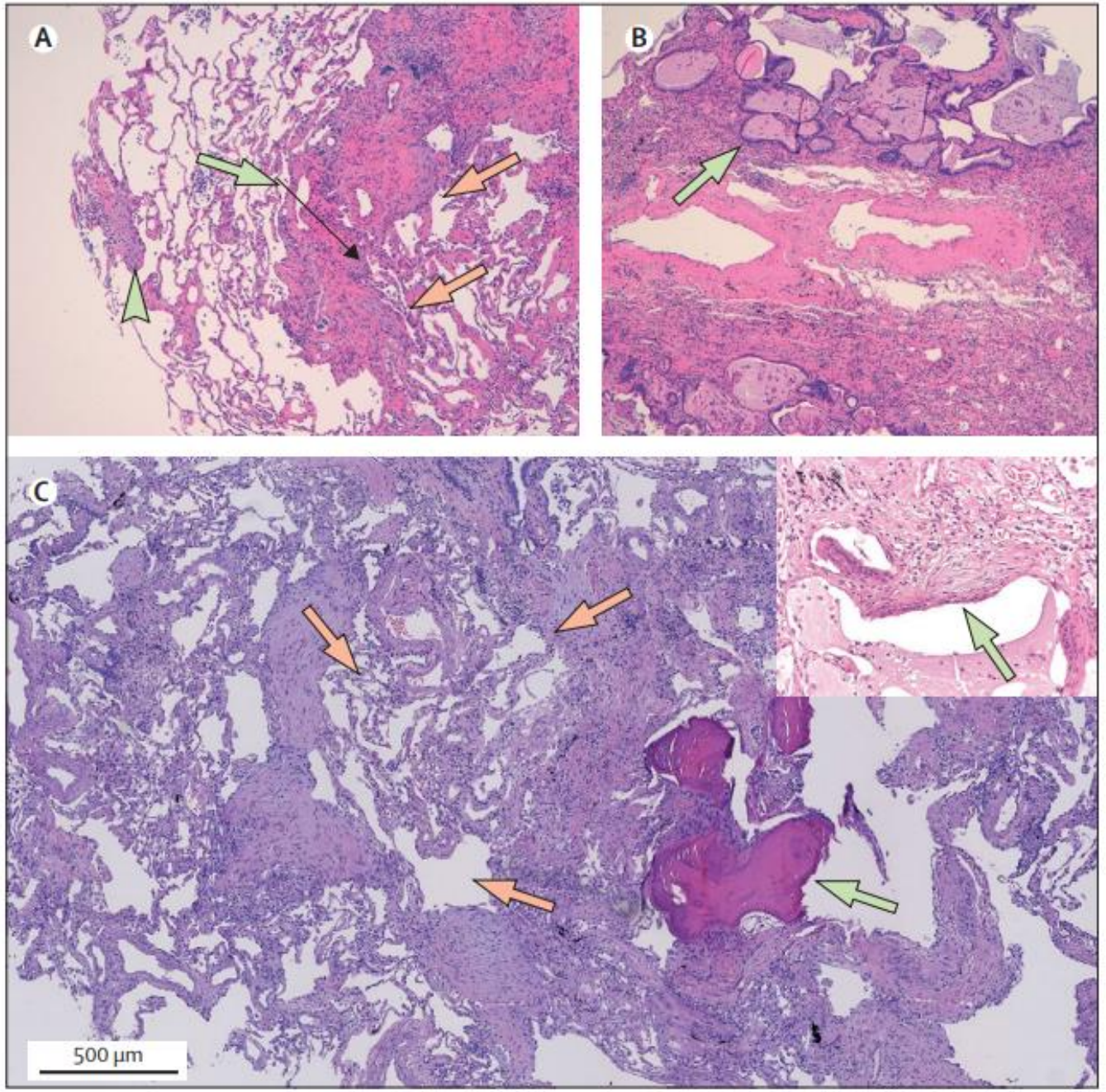
✓Specific ILDs: Less effective for UIP/IPF, useful in certain IIPs like **COP**

Curr Opin Pulm Med. 2022 Jan 1;28(1):3-8.

Histopathology: UIP

- **Usual interstitial pneumonia (UIP)**

✓ Dense fibrosis with architectural distortion
✓ **Honeycombing**
✓ Predominantly subpleural or paraseptal distribution, or both
✓ Patchy involvement
✓ **Fibroblastic foci**

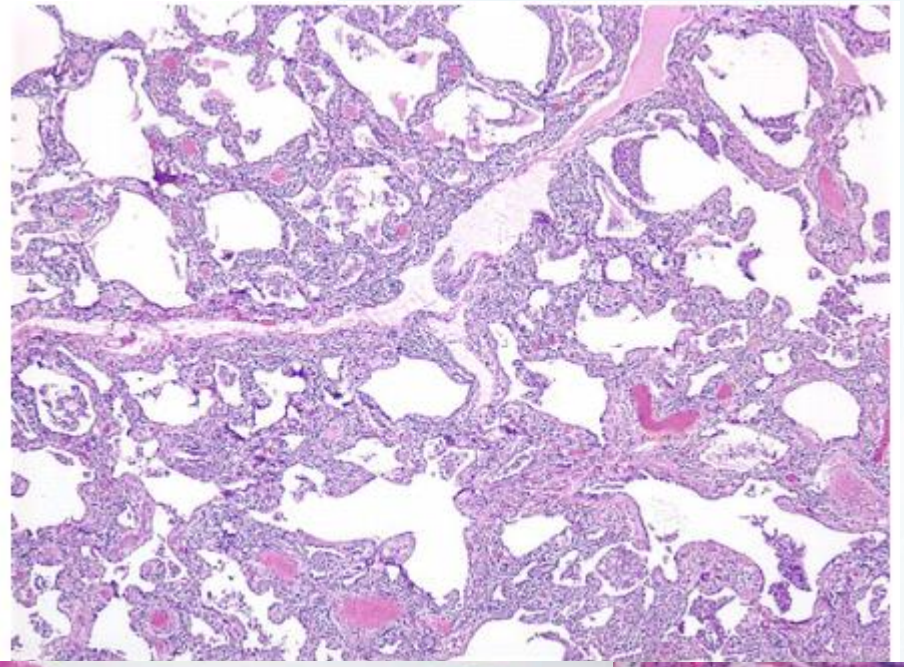


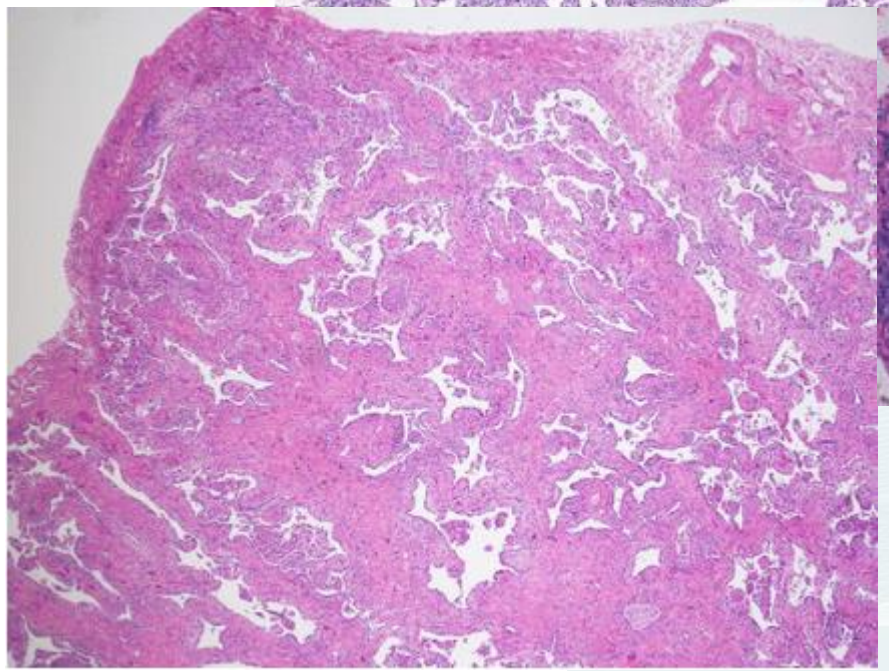
Lancet. 2021 Oct 16;398(10309):1437-1449.

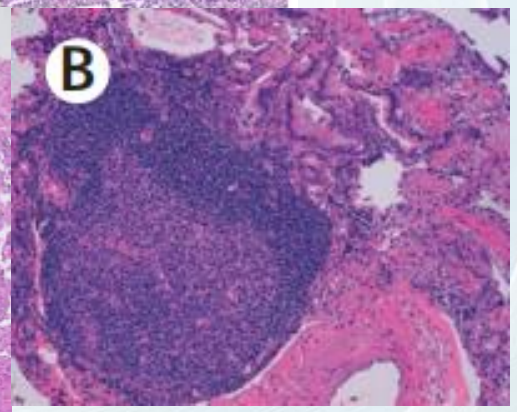
Histopathology: NSIP

- **Nonspecific interstitial pneumonia/fibrosis (NSIP)**

✓ **Homogeneous fibrosis** with varying degrees of inflammation
✓ Few if any fibroblastic foci
✓ Absence of honeycombing







Lymphoid follicles have germinal centres

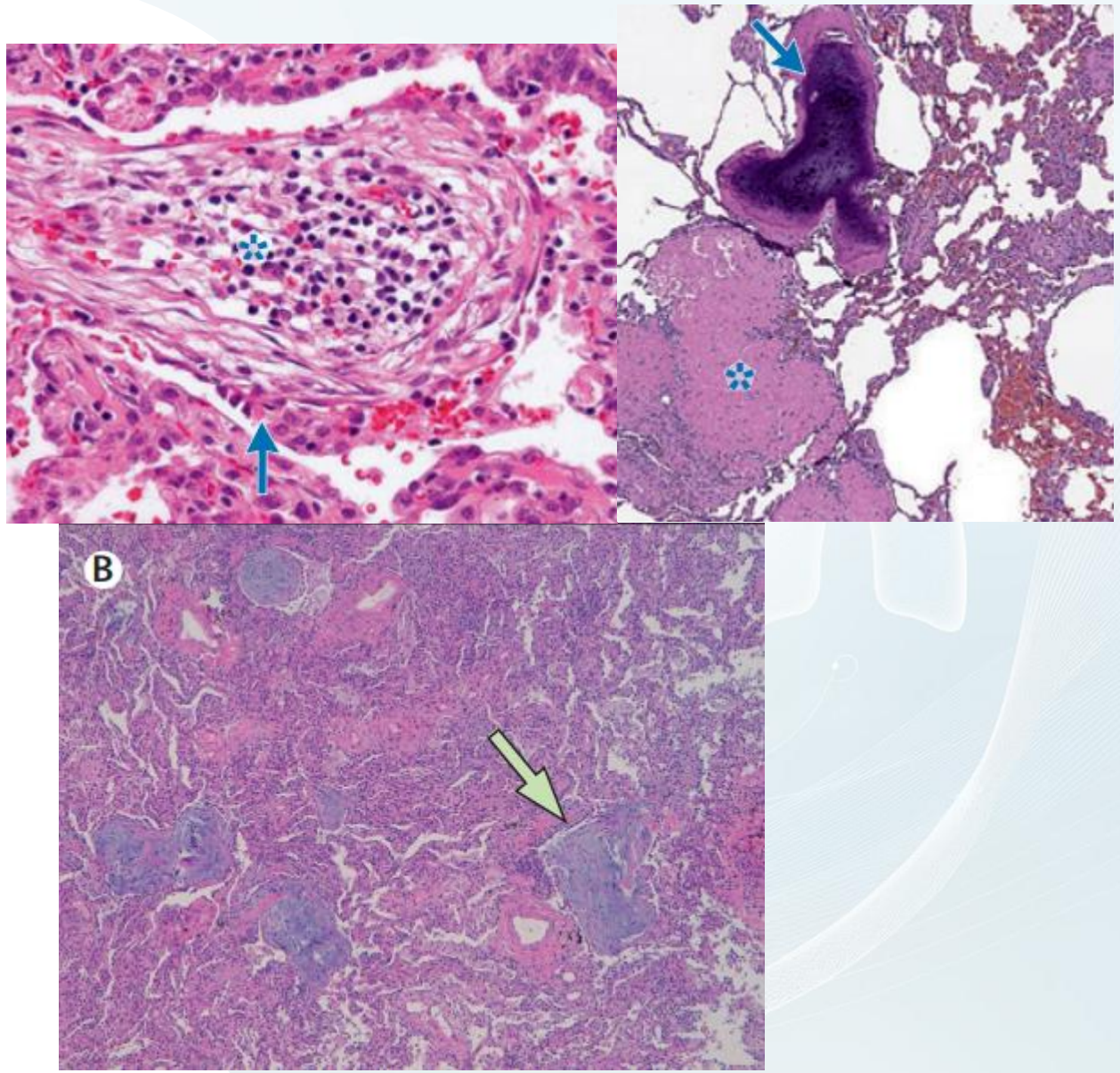
Proc Am Thorac Soc. 2006 Jun;3(4):322-9.
Lancet. 2021 Oct 16;398(10309):1437-1449.

Histopathology: OP

- **Organising pneumonia**

✓ Interstitial fibrosis with **buds of intra-alveolar granulation tissue** (Masson bodies)

metaplastic bone formation



NSIP overlaps

N Engl J Med. 2022 Mar 17;386(11):
Lancet. 2021 Oct 16;398(10309):1437-1449.

Serological tests

- **Autoantibodies**

✓Antinuclear Antibodies (**ANA**): CTD-ILD

✓Rheumatoid Factor (**RF**) and Anti-Cyclic Citrullinated Peptide (**Anti-CCP**): RA-ILD

✓anti-neutrophil cytoplasmic antibody (**ANCA)**: Vasculitis

- **Other Autoantibodies:**

✓Anti-Ro/SSA & Anti-La/SSB: Sjögren's syndrome

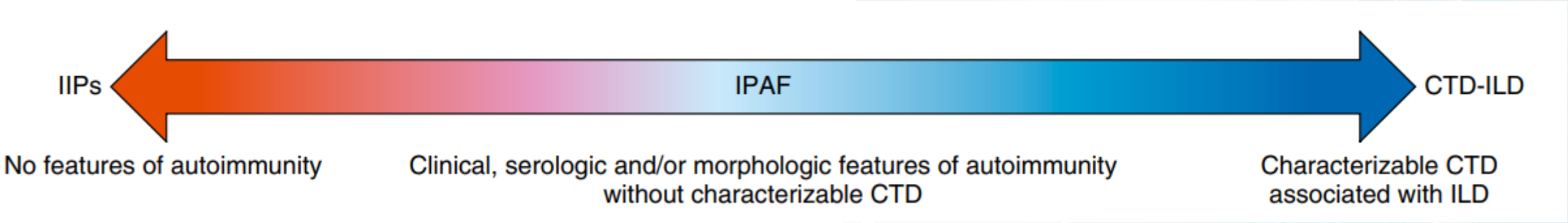
✓Myositis-Specific Antibodies (Anti-Jo-1): Polymyositis and dermatomyositis with ILD.

✓Anti-Topoisomerase I (Scl-70): Systemic sclerosis-ILD

Ther Adv Musculoskelet Dis. 2021; 13:

Interstitial pneumonia with autoimmune features (IPAF)

- IPAF is a clinical syndrome characterized by interstitial pneumonia accompanied by features **suggestive of an autoimmune process**, but which does not fully meet the criteria for a specific connective tissue disease.



Ann Am Thorac Soc. 2019 May;16(5):525-533.

Table 1. Classification criteria for interstitial pneumonia with autoimmune features

1. Presence of an interstitial pneumonia by HRCT or SLB *and*
2. Exclusion of alternative etiologies *and*
3. Does not meet criteria for a defined CTD *and*
4. At least one feature from at least two of the following domains:

A. Clinical domain	B. Serologic domain	C. Morphologic domain
1. Distal digital fissuring (i.e., "mechanic hands")	1. ANA ⩾ 1:320 titer, diffuse, speckled, homogeneous patterns *or*	1. Suggestive radiology patterns by HRCT:
2. Distal digital tip ulceration	a. ANA nucleolar pattern (any titer) *or*	a. NSIP
3. Inflammatory arthritis *or* polyarticular morning joint stiffness ⩾60 min	b. ANA centromere pattern (any titer)	b. OP
4. Palmar telangiectasia	2. Rheumatoid factor ⩾2 × upper limit of normal	c. NSIP with OP overlap
5. Raynaud phenomenon	3. Anti-CCP	d. LIP
6. Unexplained digital edema	4. Anti-dsDNA	2. Histopathology patterns or features by surgical lung biopsy:
7. Unexplained fixed rash on the digital extensor surfaces (Gottron sign)	5. Anti-Ro (SS-A)	a. NSIP
	6. Anti-La (SS-B)	b. OP
	7. Anti-ribonucleoprotein	c. NSIP with OP overlap
	8. Anti-Smith	d. LIP
	9. Anti-topoisomerase (Scl-70)	e. Interstitial lymphoid aggregates with germinal centers
	10. Anti-tRNA synthetase (e.g., Jo-1, PL-7, PL-12; others are: EJ, OJ, KS, Zo, tRS)	f. Diffuse lymphoplasmacytic infiltration (with or without lymphoid follicles)
	11. Anti–PM-Scl	3. Multicompartment involvement (in addition to interstitial pneumonia):
	12. Anti–MDA-5	a. Unexplained pleural effusion or thickening
		b. Unexplained pericardial effusion or thickening
		c. Unexplained intrinsic airways disease* (by PFT, imaging or pathology)
		d. Unexplained pulmonary vasculopathy

Definition of abbreviations: ANA = antinuclear antibody; CTD = connective tissue disease; HRCT = high-resolution computed tomography; LIP = lymphocytic interstitial pneumonia; NSIP = nonspecific interstitial pneumonia; OP = organizing pneumonia; PFT = pulmonary function testing; SLB = surgical lung biopsy.
*Includes airflow obstruction, bronchiolitis or bronchiectasis.
Adapted by permission from Reference 11.

Ann Am Thorac Soc. 2019 May;16(5):525-533.

IPAF: demographics

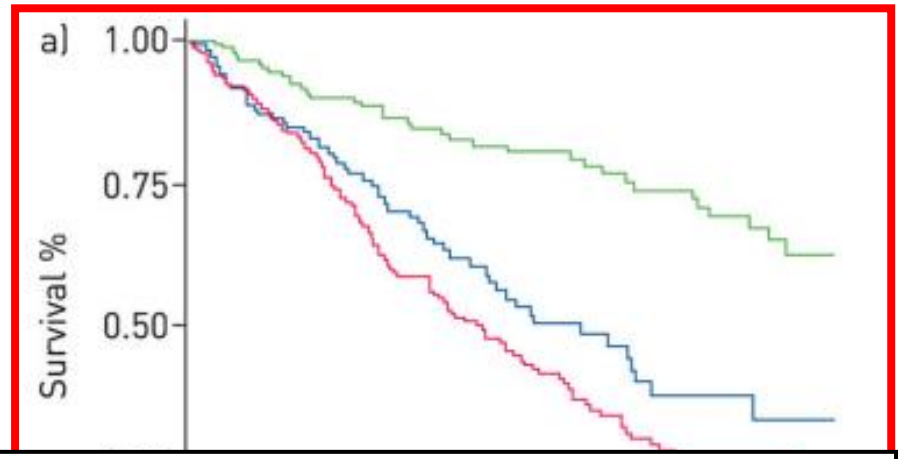
Study (Location)	n	Age, Years	Female, %	Smoking, %	FVC, % pred	DLCO, % pred	Clinical domain	Serologic	Morphology	UIP Pattern (%)
Dai et al. (Nanjing, China)	177	60.2 ± 12.8	56	19.2	N/A	N/A	Raynaud's (12.9)	ANA (49.2), anti-Ro (36.1)	NSIP (61.6)	UIP (4.5)
Li et al. (Xi'an, China)	147	64.2 ± 7.4	54	32	78.5 ± 13.5	65.5 ± 10.1	Raynaud's (1.4)	Anti-Ro (25.9), RF (17.7)	NSIP (57.1)	UIP (15.7)
Oldham et al.	144	63.2 ± 11	52.1	54.9	61.9 ± 18.3	45.3 ± 20.6	Raynaud's	ANA (77.6),	NSIP (31.9)	HRCT UIP (54.6) Histopathology
Xue et al. (Guangzhou, China)	65	51 ± 14.1	55.4	N/A	68.4 ± 13.8	59.9 ± 12.4	Raynaud's (18.5)	ANA (75.4), RF (43.1)	NSIP (N/A)	N/A
Ahmad et al. (Lyon, France)	57	64.4 ± 14.0	49.1	34	80.2	49.3	Raynaud's (74.1)	ANA (82.4), anti-tRNA (17)	NSIP (42.1)	UIP (28)
Chartrand et al. (Denver, USA)	56	54.6 ± 10.3	71.4	32.1	68.4 ± 16.0	52.2 ± 15.9	Raynaud's (39.3)	ANA (48.2), anti-Ro (42.9)	NSIP (57.1)	UIP (8.9)
Lim et al. (Bucheon-si, South Korea)	54	67.9 ± 10.5	64.8	27.8	81.8 ± 17.0	62.7 ± 21.0	Arthritis (76.5)	ANA (63.3), RF (28.6)	NSIP (63)	UIP (25.9)

Heterogeneity exists between published IPAF cohorts, with some resembling CTD-ILD and others similar to idiopathic interstitial pneumonias, including IPF.

Curr Opin Pulm Med. 2021 Sep 1;27(5):374-387.

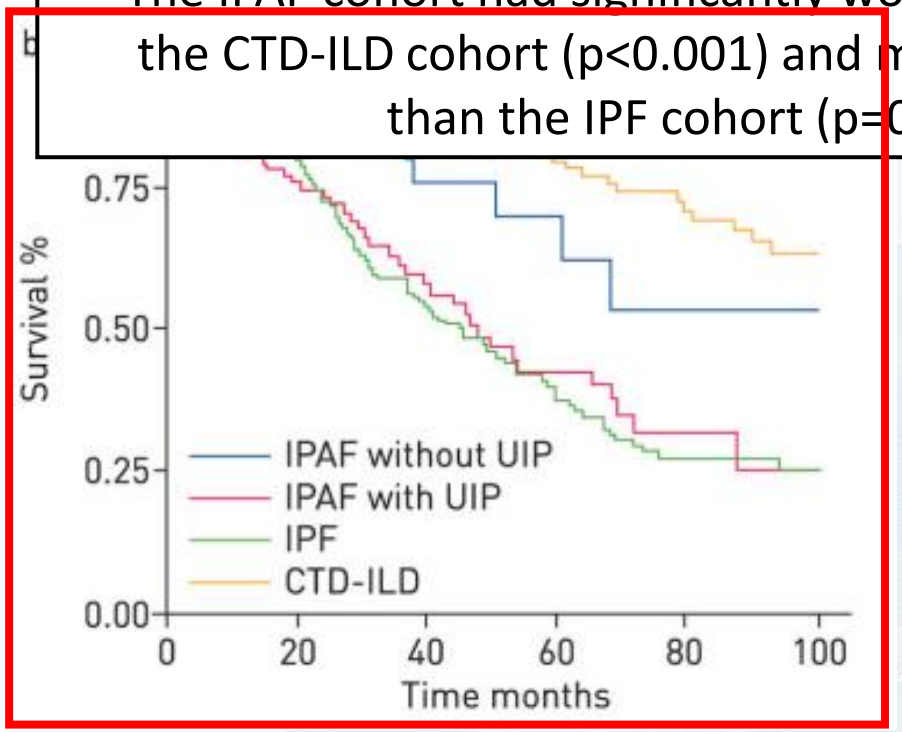
IPAF: prognosis

- Retrospective single center study
- N=422 (IPAF = 144)



- After stratification by the presence of a UIP pattern, IPAF patients without UIP had survival similar to CTD-ILD (p=0.45), while those with UIP had survival similar to IPF (p=0.51).

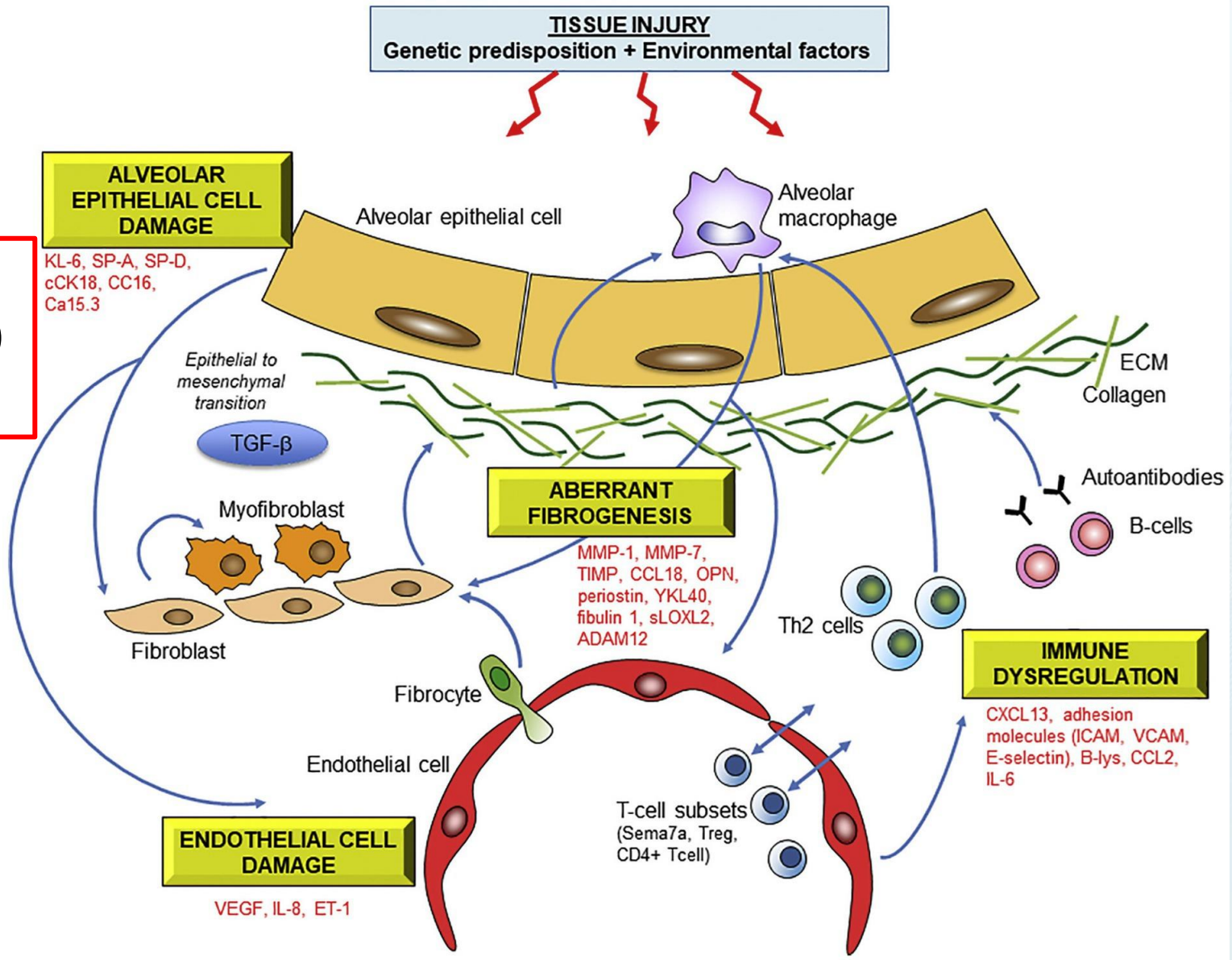
- The IPAF cohort had significantly worse survival than the CTD-ILD cohort (p<0.001) and marginally better than the IPF cohort (p=0.07)



Eur Respir J. 2016 Jun;47(6):1767-75.

Biomarker

- Krebs von den Lungen-6 (KL-6)
- Matrix Metalloproteinase-7 (MMP-7)
- cCK-18



Front Med (Lausanne). 2023; 10: 1174443.

Biomarker: Krebs von den Lungen-6 (KL-6)

- A high-molecular-weight glycoprotein expressed by regenerating alveolar type II cells.
- Indicate **alveolar epithelial cell damage**
- **Clinical Significance**

✓ **Elevated levels in various ILD**, including IPF, allergic pneumonia, CTD-ILD, and alveolar protein deposition disease

✓ Correlation with severity of ILD & prognosis

- **Clinical Utility**

✓ **Early detection**: Helps in early diagnosis of ILD

✓ **Monitoring disease activity:** tracks disease progression and treatment response

✓ **Guiding treatment decisions:** informs therapeutic adjustments

Biomark Med. 2020 Jun;14(8):665-674

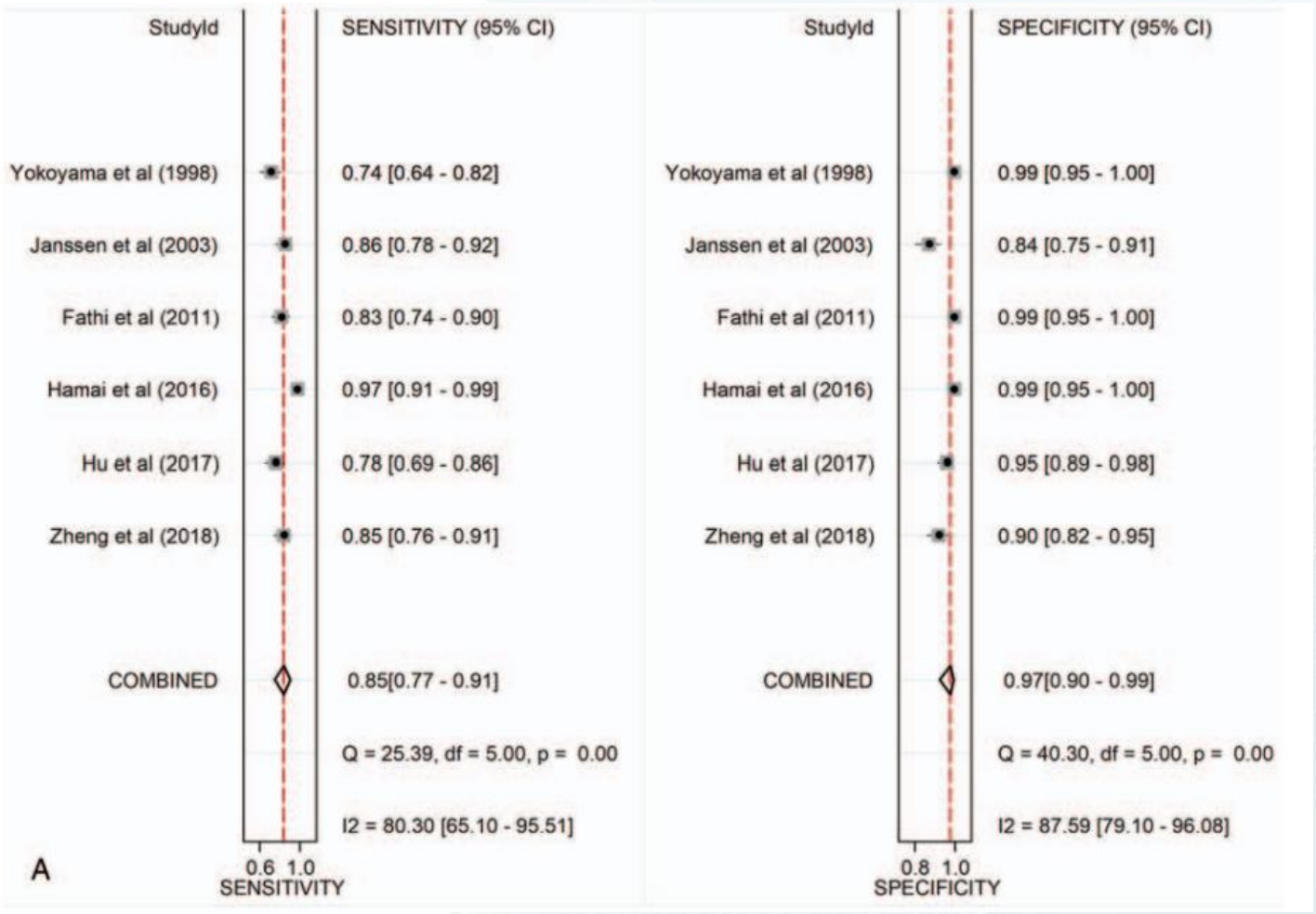
Biomarker: Krebs von den Lungen-6 (KL-6)

- **The meta-analysis (n=23 studies)**

- For ILD diagnosis:

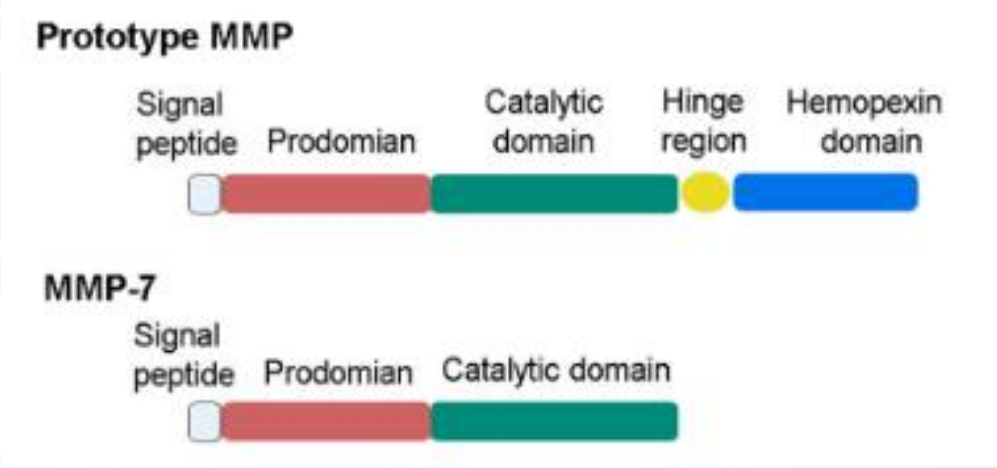
✓Sensitivity: 0.85 (95% CI: 0.77–0.91)

✓Specificity: 0.97 (95% CI: 0.90–0.99)



Medicine (Baltimore). 2020 Apr; 99(16): e19493.

Biomarker: MMP-7



- **Matrix Metalloproteinase-7 (MMP-7)**
- A member of the matrix metalloproteinase family, which consists of enzymes involved in the breakdown of extracellular matrix components.

- **Mechanism of fibrosis**

✓ Extracellular matrix degradation: facilitates tissue remodeling and fibrosis.

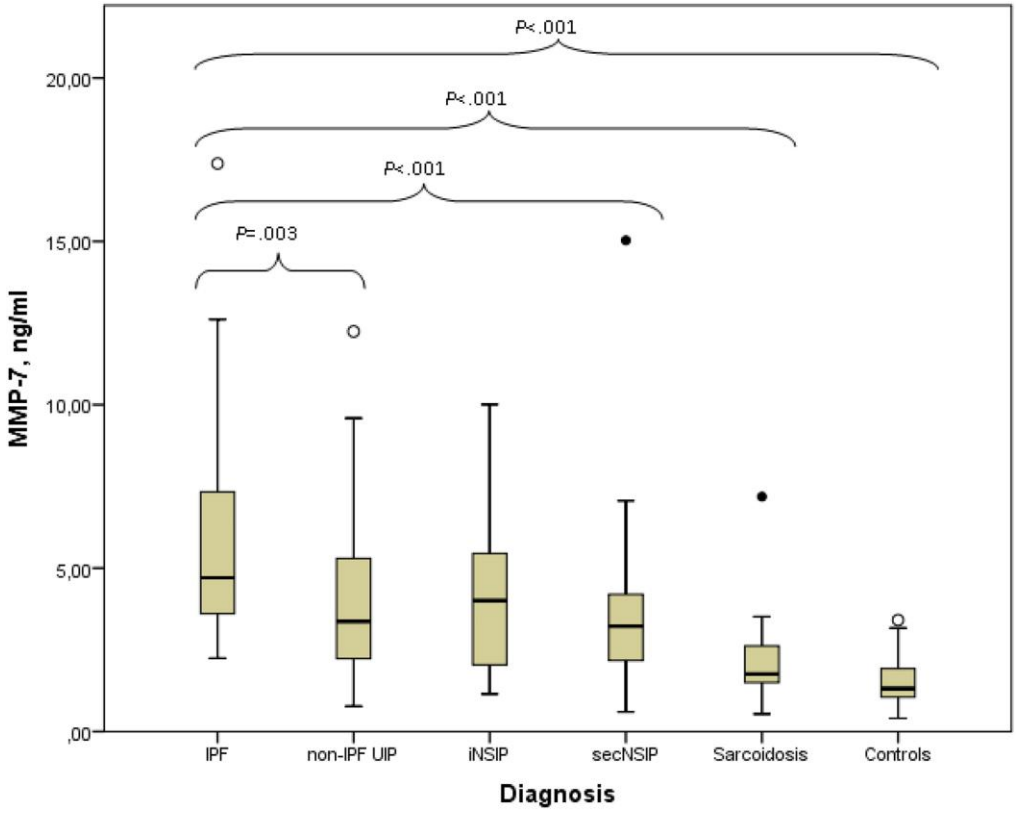
✓ Epithelial-mesenchymal transition (EMT): Epithelial cells acquire mesenchymal characteristics, contributing to fibrosis.

✓ Inflammatory response: Modulates the activity of various cytokines and growth factors, influencing inflammatory responses and tissue repair processes.

Biomolecules. 2020 Jun 25;10(6):960

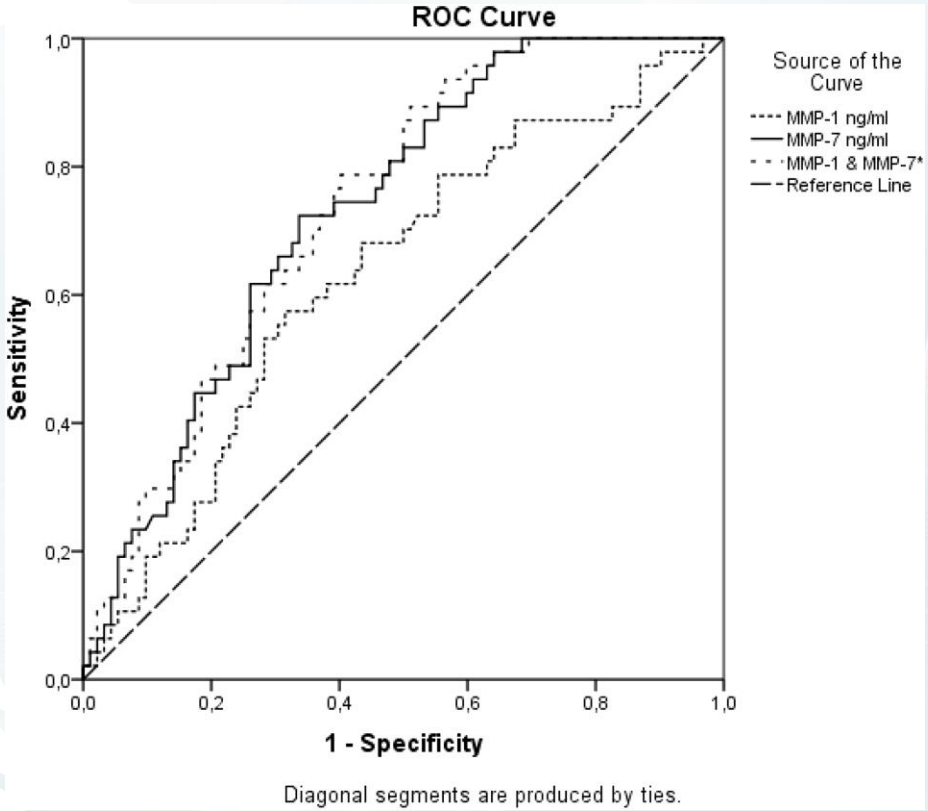
Biomarker: MMP-7

- 139 patients with ILD



- IPF diagnosis

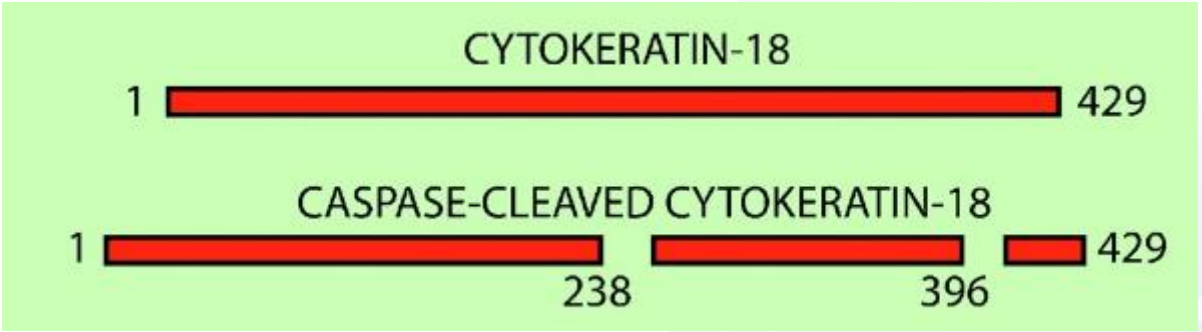
	AUC (95% CI)
MMP-1	0.63 (0.53-0.73)
MMP-7	0.73 (0.65-0.81)
MMP-1 and MMP-7 combined	0.74 (0.66-0.82)



Respir Med. 2015 Aug;109(8):1063-8. doi

Biomarker: cCK-18

- **CK-18:** An intermediate filament protein in epithelial cells that maintains cell structure and integrity.

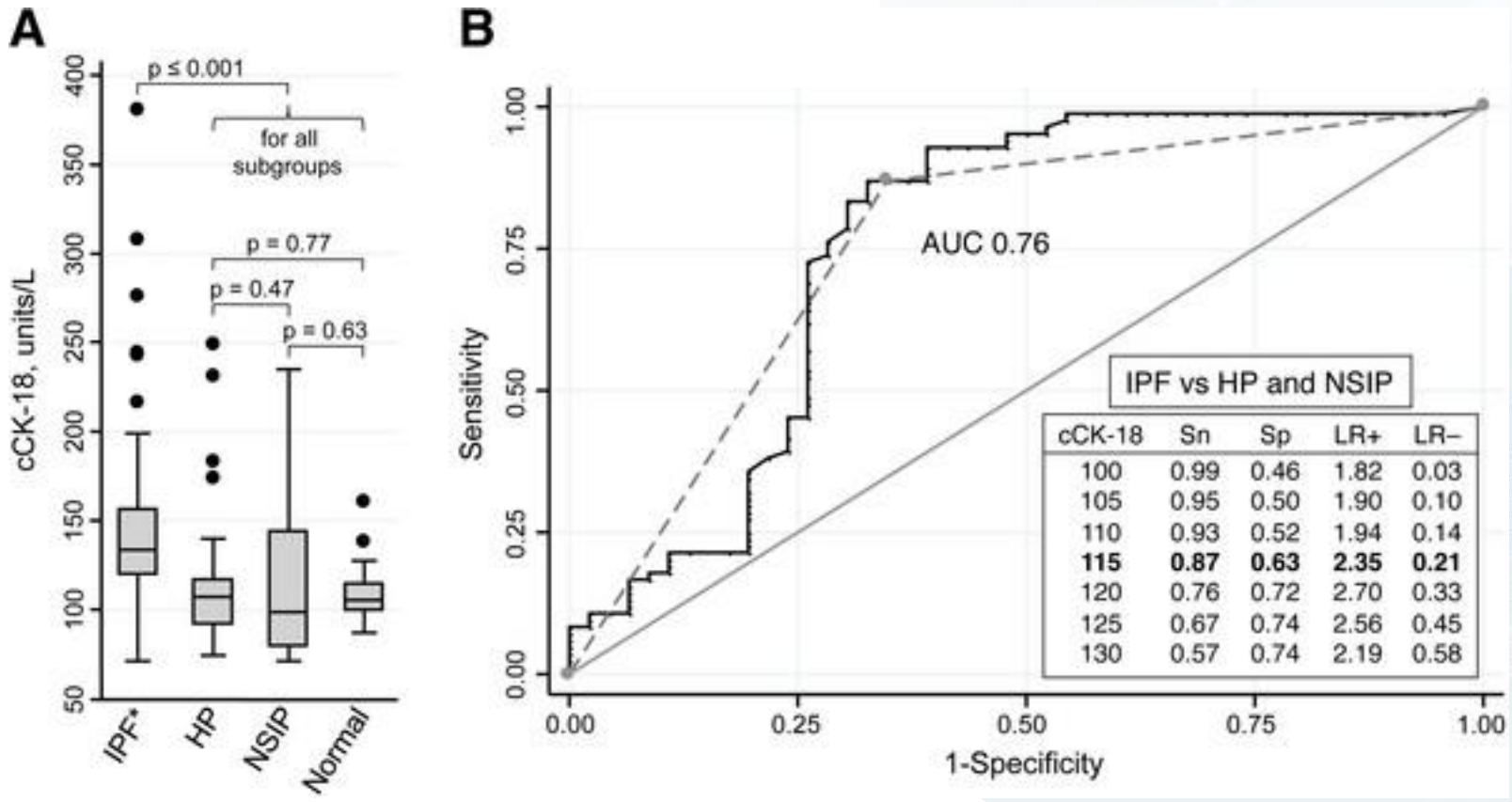


- **cCK-18:** Formed when CK-18 is cleaved by caspases during **apoptosis.**
- **A marker of apoptosis.**

Respir Res. 2012 Nov 20;13(1):105.

Biomarker: cCK-18

- 169 patients ILD



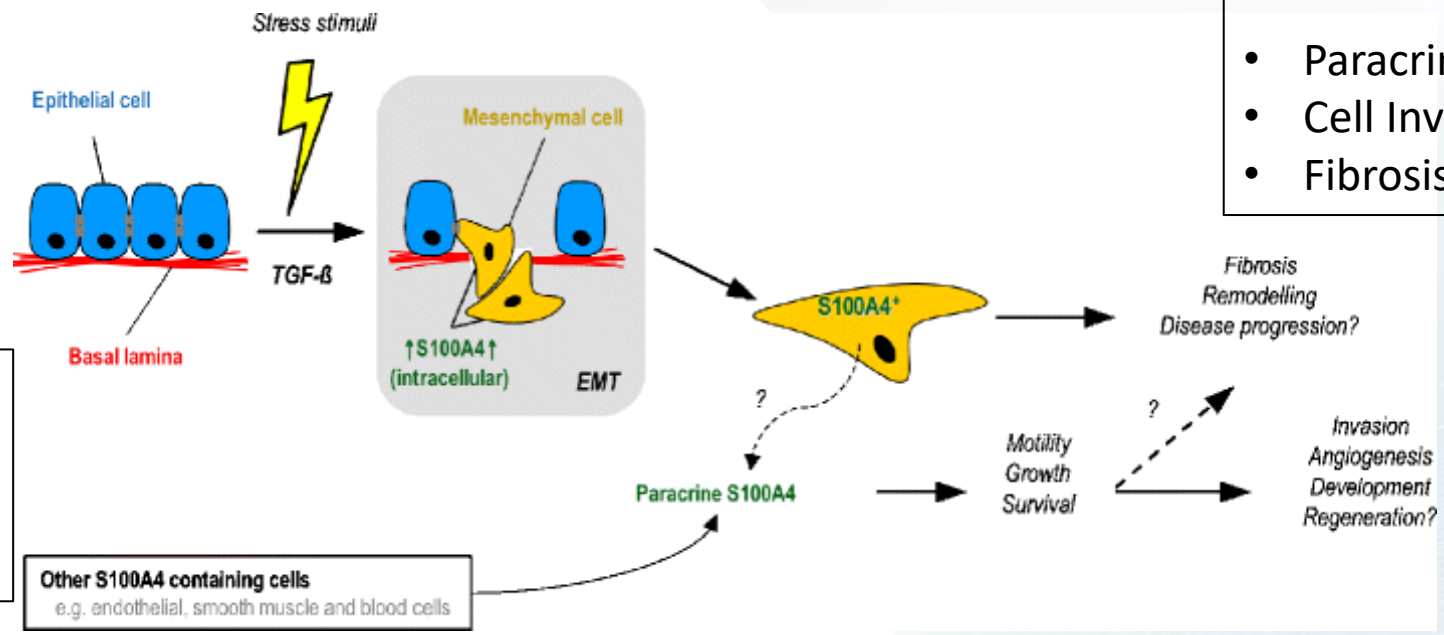
Respir Res. 2012 Nov 20;13(1):105.

Biomarker: S1004

- **S100 Calcium-Binding Protein A4 (S100A4)**
- Known as fibroblast-specific protein 1 (FSP1), is a member of the S100 family of proteins containing two EF-hand calcium-binding motifs.

- Extracellular Roles

- Paracrine effects
- Cell Invasion and angiogenesis
- Fibrosis and remodeling



- Intracellular Roles

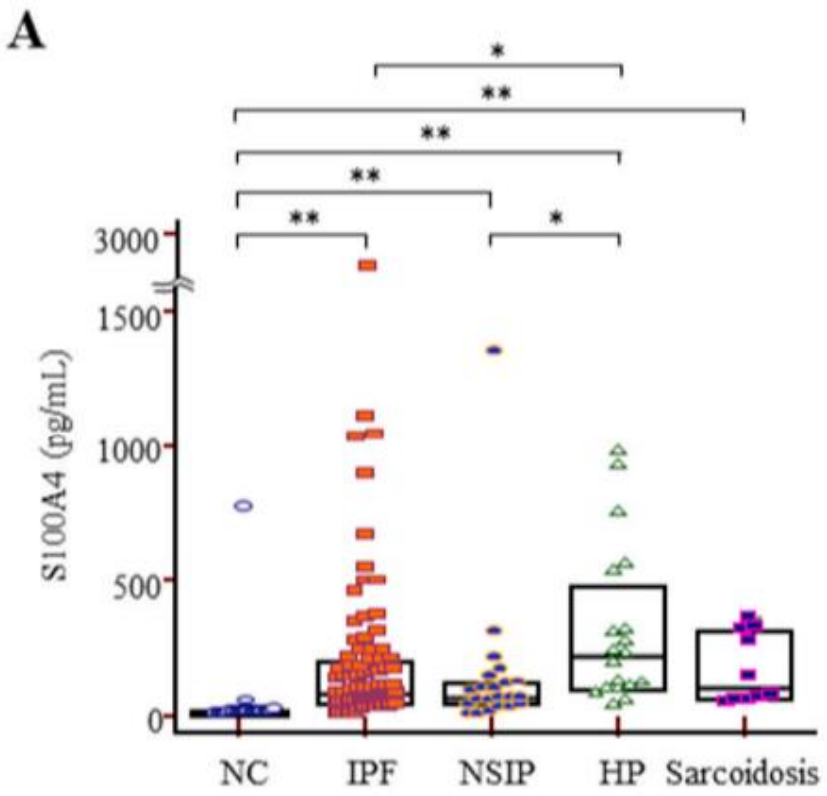
- EMT Induction
- Fibrosis and remodeling

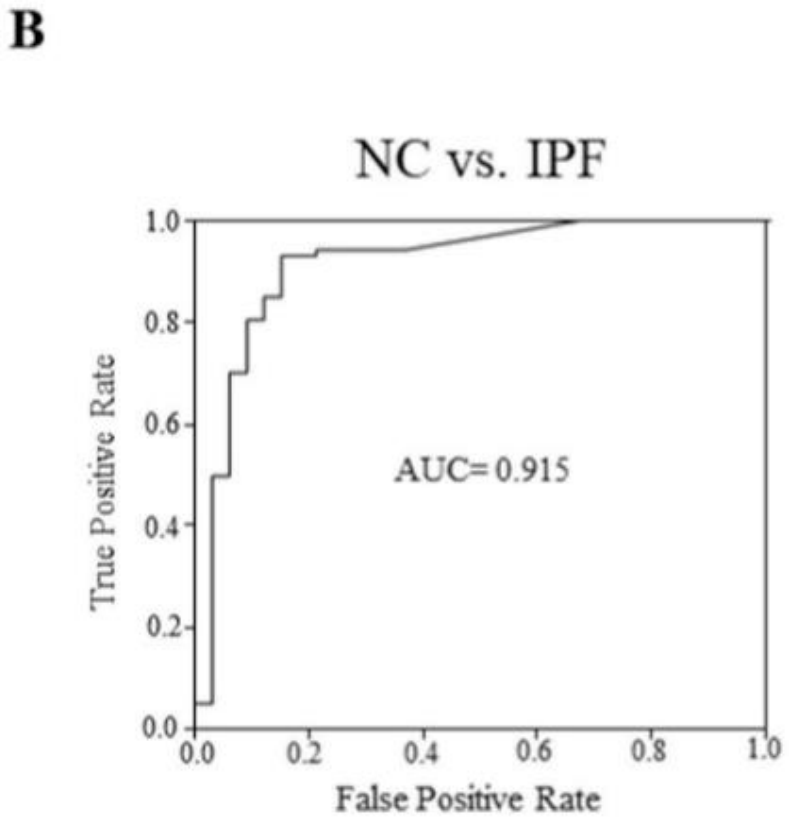
J Mol Med (Berl) . 2008 May;86(5):507-22

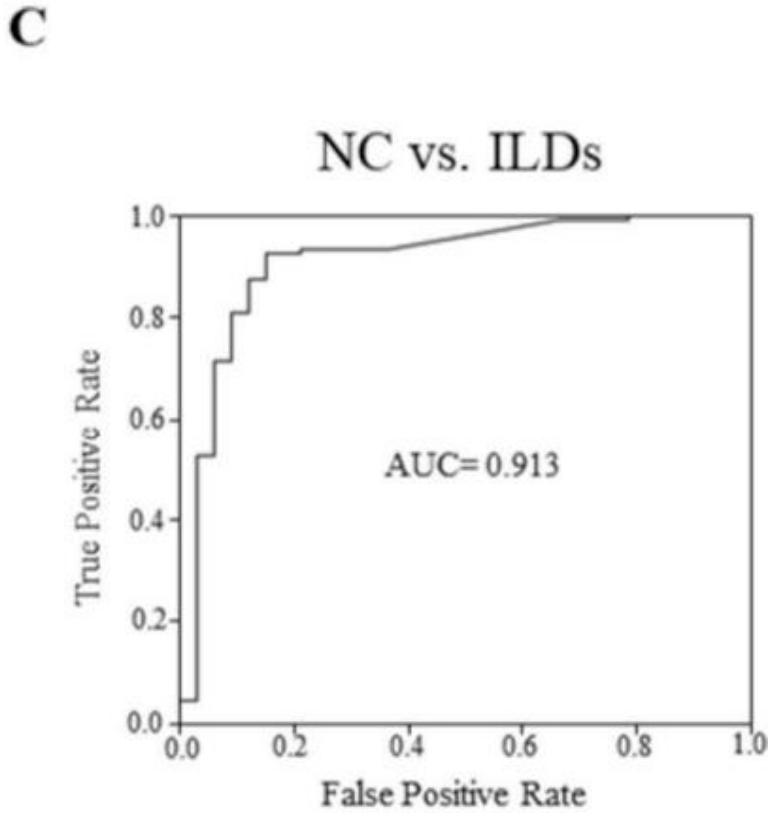
Biomarker: S1004

- 138 patients with ILD

	Cutoff Value (pg/mL)	Accuracy (%)	Specificity (%)	Sensitivity (%)
IPF vs NC	18.85	87.4	81.8	93.1
ILD vs NC	28.88	87.8	87.9	87.8



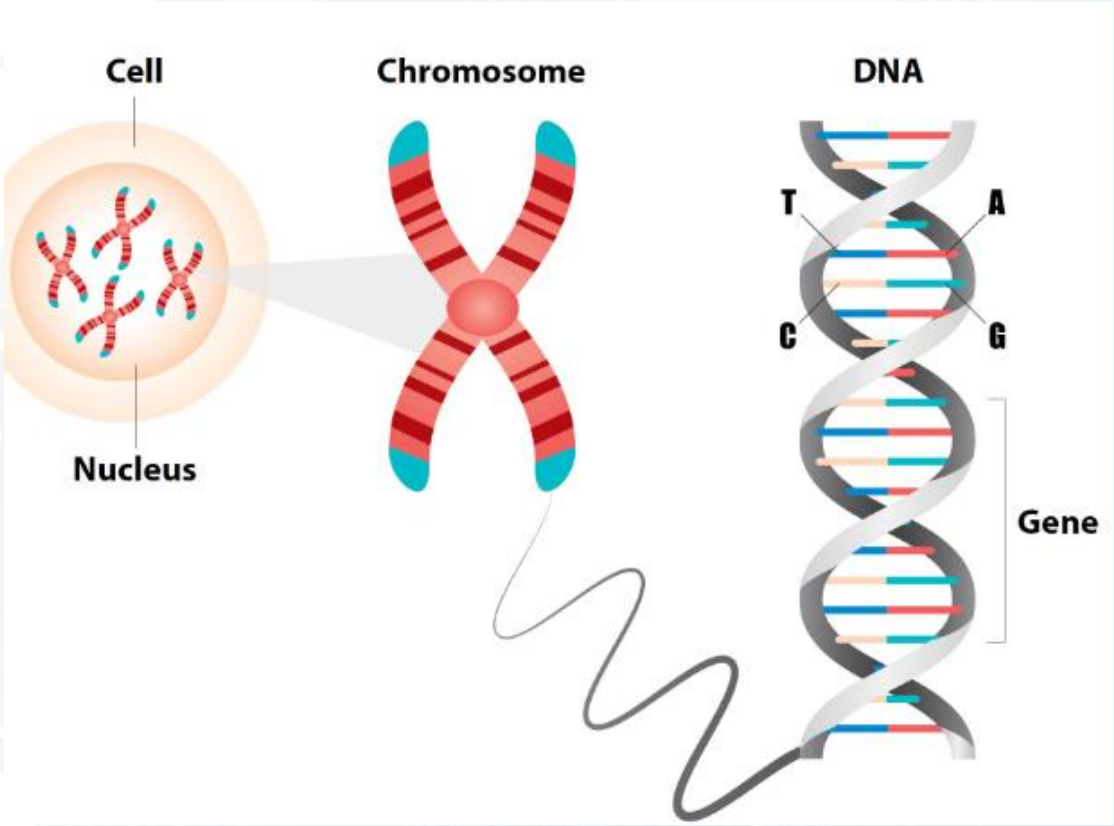




Respir Med. 2020 Sep:171:105945.

Genetics: Types of genetic tests

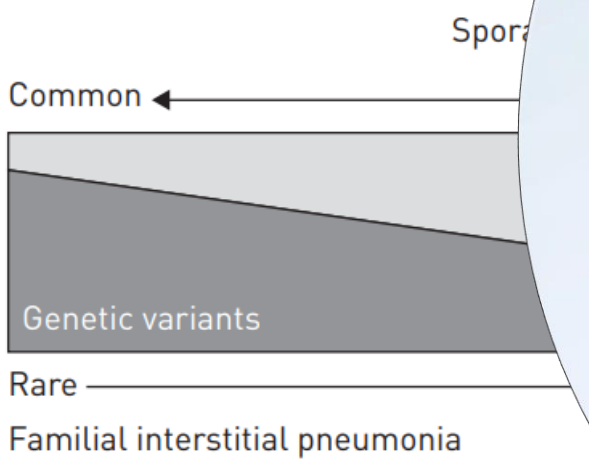
- **Molecular tests:** DNA Sequencing
  - Targeted single variant
  - Single gene
  - Gene panel
  - Whole exome/Genome sequencing
- **Chromosomal tests:** analyzes whole chromosomes/large DNA segments.
- **Gene expression tests:** analyses mRNA to determine active genes.
- **Biochemical tests:** protein/enzyme levels or activity.

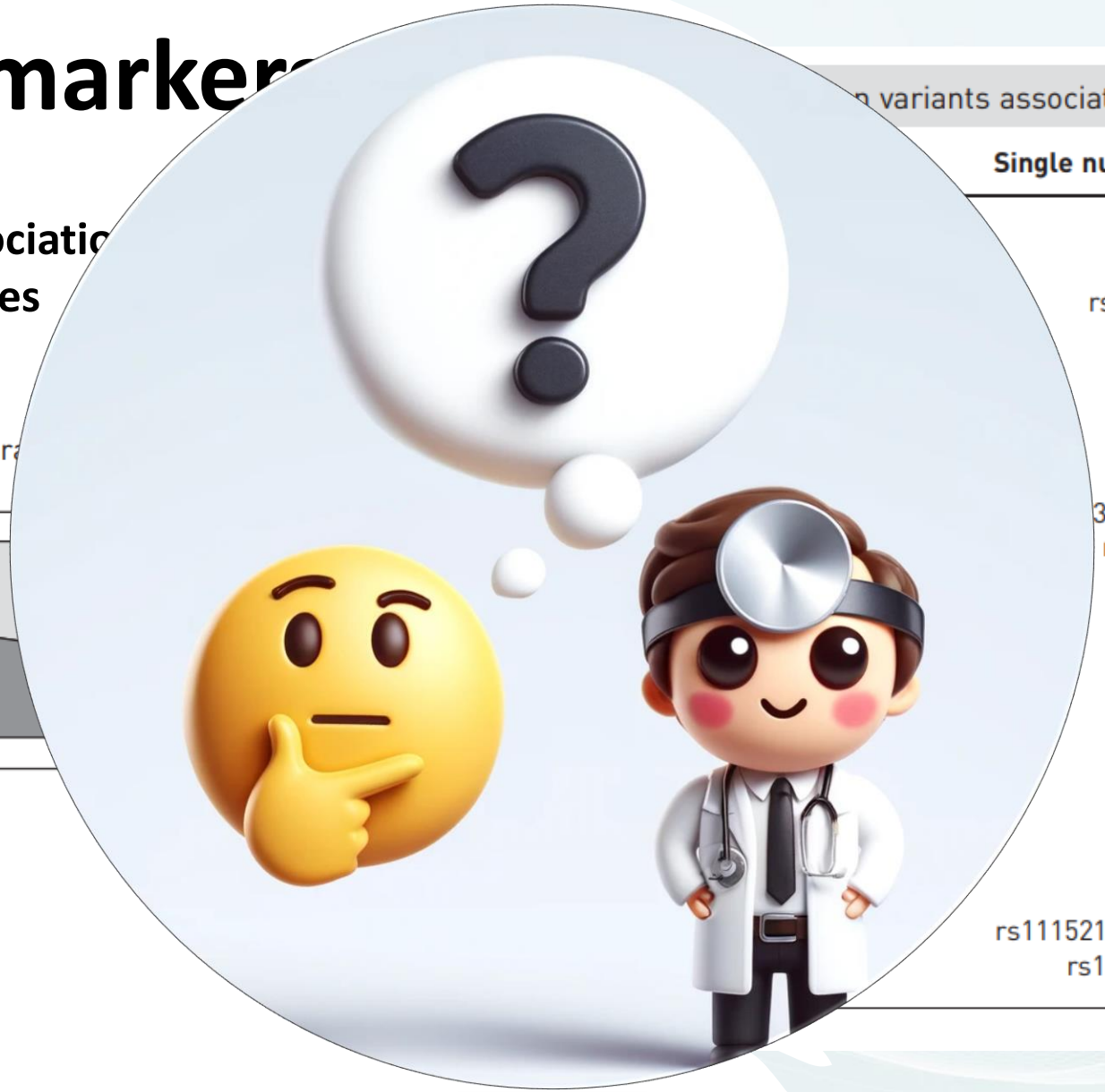


Chest. 2022 Aug;162(2):394-405.

Genetic marker

- **Genome-wide associatio**
- **Family-based studies**





n variants associated with idiopathic pulmonary fibrosis

Single nucleotide polymorphism(s)
rs62025270
rs1278769
rs2395655, rs733590
rs12610495
rs2076295
Unknown
rs2609255
rs2395655
392, rs419598, rs2637988
rs4073, rs2227307
rs1981997
rs7144383
rs7934606
rs35705950
rs11191865
rs17690703
rs6793295
rs2736100
rs1800470
rs3775291
rs111521887, rs5743894, rs5743890
rs12951053, rs12602273

Eur Respir Rev. 2019 Sep 25;28(153):190053
Eur Respir J . 2015 Jun;45(6):1717-2

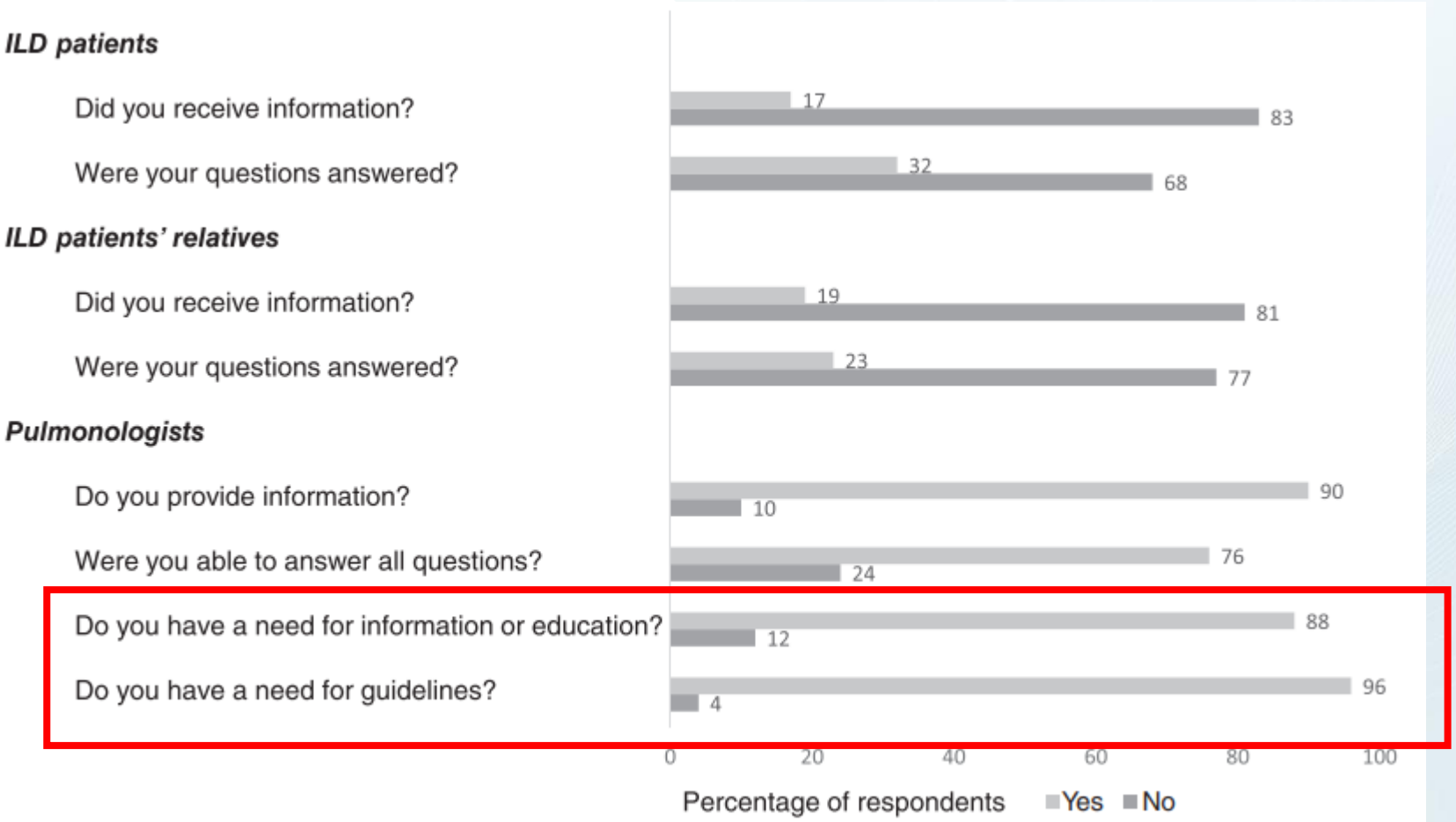
Received: 12 January 2022 | Accepted: 5 May 2022
DOI: 10.1111/resp.14303

ORIGINAL ARTICLE

Respirology
WILEY

Genetic testing in interstitial lung disease: An international survey

- 458 patients with ILD
- 181 patients' relatives
- 352 pulmonologists



Respirology. 2022 Sep;27(9):747-757.

Received: 12 January 2022 | Accepted: 5 May 2022

DOI: 10.1111/resp.14303

ORIGINAL ARTICLE

Respirology

WILEY

Genetic testing in interstitial lung disease: An international survey

TABLE 3 Modification of clinical work-up by the pulmonologist ($n = 240$)

Do you modify your diagnostic work-up according to the results of the genetic analysis? *n* (%)	**Yes 76 (32)**	**Sometimes 95 (40)**	**No 69 (29)**
Reported modifications in diagnostic work-up	If yes or sometimes		
Postponement or exclusion of surgical lung biopsy	123 (78)		
Exclusion of BAL	36 (23)		
Use of haematological parameters	46 (29)		
Performing telomere length measurement	62 (39)		
Change of diagnosis	85 (54)		
Do you modify your therapeutic proposal according to the results of genetic analysis in a mutation carrier?	**Yes 43 (18)**	**Sometimes 94 (39)**	**No 103 (43)**
Reported changes of therapeutic proposal	If yes or sometimes		
Propose antifibrotic treatment	91 (74)		
Exclude lung transplantation	18 (15)		

Respirology. 2022 Sep;27(9):747-757./

The Role of Genetic Testing in Pulmonary Fibrosis

A Perspective From the Pulmonary Fibrosis Foundation Genetic Testing Work Group

TABLE 2] Clinical Scenarios in Which Clinicians May Consider Genetic Testing and the Potential Yield for Identifying a Variant

Clinical Scenario	Consider Testing and Potential Yield for Variant
Patient with pulmonary fibrosis with family history of pulmonary fibrosis	Yes, high yield
Patient with pulmonary fibrosis (sporadic or familial) with personal or family history of telomeropathy manifestations	Yes, high yield
Syndromic presentations (short telomere syndrome, Hermansky-Pudlak syndrome)	Yes, high yield
Targeted testing in unaffected family members (> 18 y of age) of proband with known pathogenic variant in disease-causing gene	Yes, high yield
Young age at PF onset (< 50 y)	Yes, low yield
Personal or family history of coexistent pulmonary fibrosis with lung adenocarcinoma	Consider, low yield
Sporadic pulmonary fibrosis with no suggestive extrapulmonary manifestations	Not currently recommended
Unaffected relative if proband has not undergone genetic testing, or recent comprehensive testing showed negative results for disease-causing variant	Not currently recommended
Common variants in sporadic pulmonary fibrosis (eg, *MUC5B*)	Not currently recommended
Evaluation before lung transplantation	Not currently recommended

Chest. 2022 Aug;162(2):394-405.

The Genomic Classifier

- **Identify UIP pattern using TBBx**
  (Transbronchial Forceps Biopsies)

- **Development**

✓ Machine learning algorithm

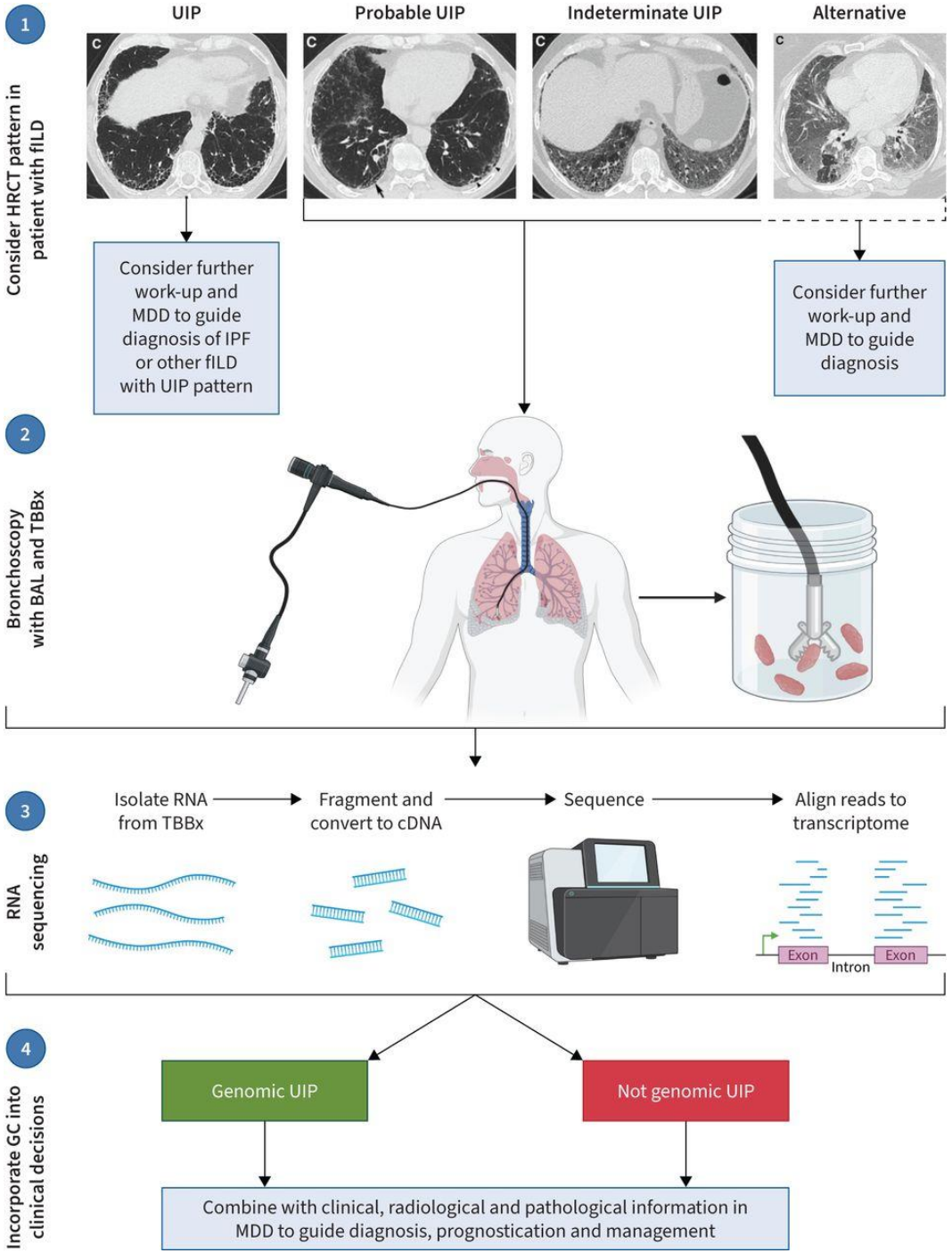
✓ Based on genomic data from SLBs

- **Benefits**

✓ Minimally invasive

✓ Accurate and efficient diagnosis

Ann Am Thorac Soc. 2022 May; 19(5): 725–727.



1. HRCT Patterns

- Assess HRCT for UIP, Probable UIP, Indeterminate UIP, or Alternative.
- Guide diagnosis based on pattern.

2. Sample Collection

- Use bronchoscopy with BAL and TBBx to collect lung tissue samples.

3. RNA Sequencing

- Isolate RNA from TBBx.
- Convert RNA to cDNA and sequence.
- Align sequences to the transcriptome.

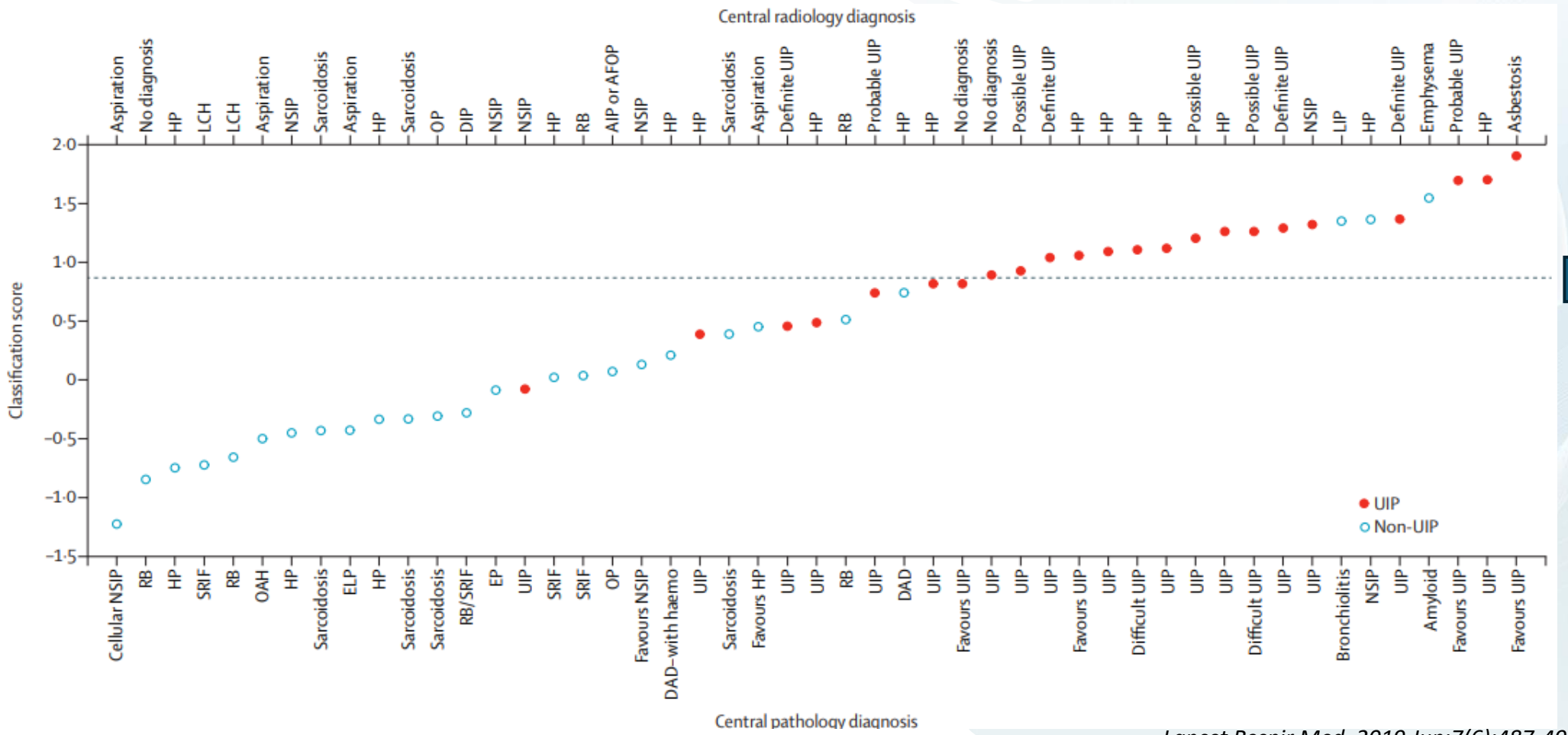
4. Clinical Decision

- Genomic UIP: Integrate with clinical and radiological data in MDD for diagnosis and management.
- Not Genomic UIP: Continue diagnostic evaluation.

Eur Respir J. 2023 Apr 1;61(4):2300033

The Genomic Classifier

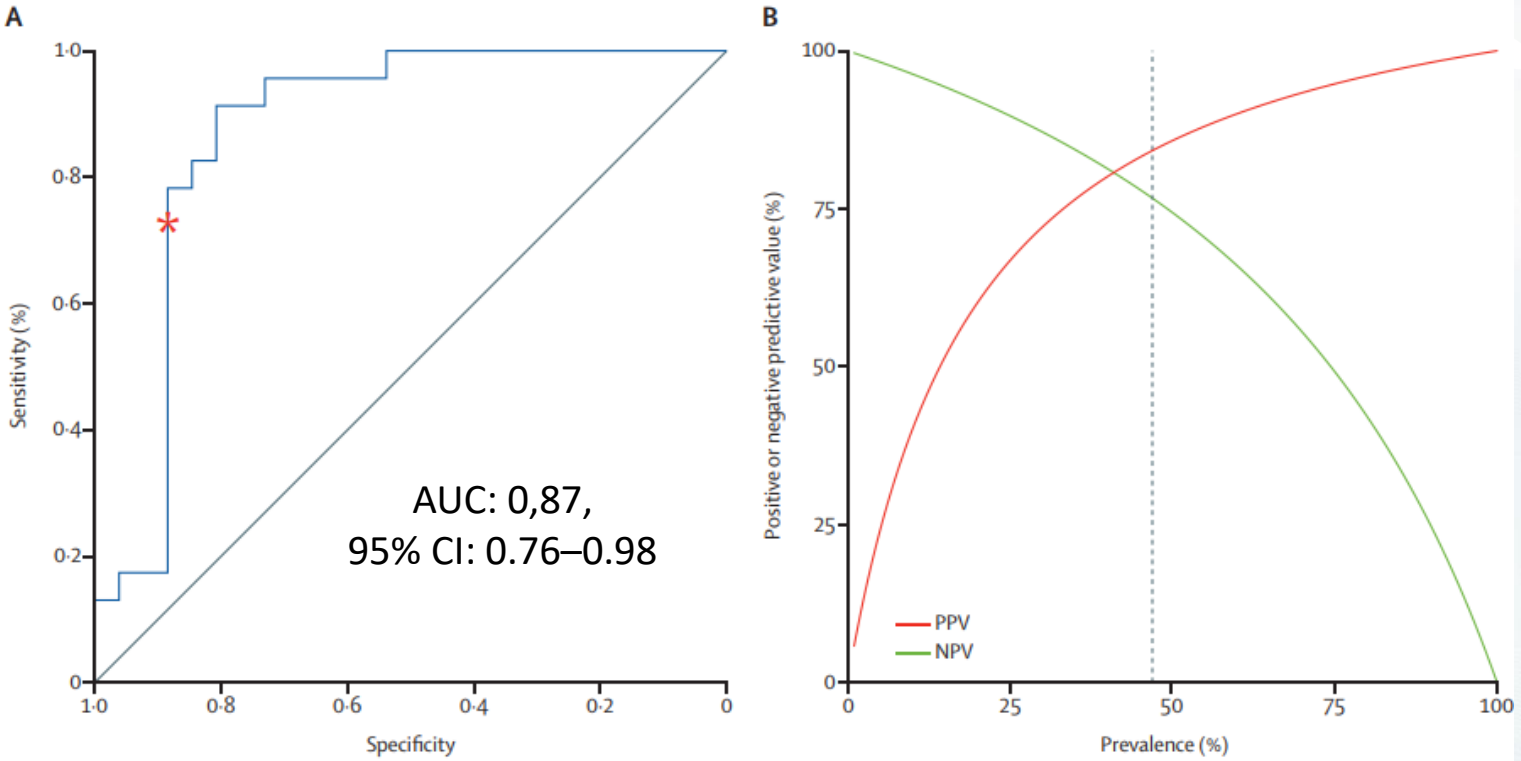
- Bronchial Sample Collection for a Novel Genomic Test (BRAVE) study in 29 US and European sites.
- N=49



0.87

Lancet Respir Med. 2019 Jun;7(6):487-496

The Genomic Classifier



Classifier results	UIP Reference Standard (n=23)	Non-UIP Reference Standard (n=26)
UIP	16	3
Non-UIP	7	23
Sensitivity	**70% (95% CI 47-87)**	
Specificity	**88% (95% CI 70-98)**	
NPV	**77% (95% CI 58-90)**	
PPV	**84% (95% CI 60-97)**	
UIP frequency in study	0.47	

Lancet Respir Med. 2019 Jun;7(6):487-496

Genomic Classifier

- Meta-analysis (n=4)

Check for updates
SYSTEMATIC REVIEWS

Use of a Genomic Classifier in Patients with Interstitial Lung Disease
A Systematic Review and Meta-Analysis

Fayez Kheir[1], Juan Pablo Uribe Becerra[2], Brittany Bissell[3,4], Marya Ghazipura[5,6], Derrick Herman[7], Stephanie M. Hon[8], Tanzib Hossain[9], Yet H. Khor[10,11], Shandra L. Knight[12], Michael Kreuter[13], Madalina Macrea[14], Manoj J. Mammen[15], Fernando J. Martinez[16], Venerino Poletti[17,18], Lauren Troy[19], Ganesh Raghu[20], and Kevin C. Wilson[21]

Table 2. Evidence profile: use of a genomic classifier versus not using a genomic classifier

Quality Assessment							Summary of Findings			
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other	No. of Patients	Effect (95% CI)	Quality	Importance
Accuracy (sensitivity and specificity)										
4*	Accuracy	None	None	None	Serious†	Serious‡	200	Sensitivity = 68% (55–73%) Specificity = 92% (81–95%)	⊕⊕◯◯; Low	Critical
Agreement (kappa coefficient)										
2§	Observational	None	None	None	Serious†	Serious‡	73	Cohort 1 = 0.64 (0.46–0.82)‖¶ Cohort 2 = 0.75 (0.48–1.00)¶**	⊕◯◯◯; Very low	Important
Diagnostic confidence (%)										
2§	Observational	None	None	None	Serious†	Serious‡	73	Cohort 1 = 56% vs. 89%‖ Cohort 2 = 43–93%**	⊕◯◯◯; Very low	Important

Ann Am Thorac Soc. 2022 May;19(5):827-832

Genomic Classifier

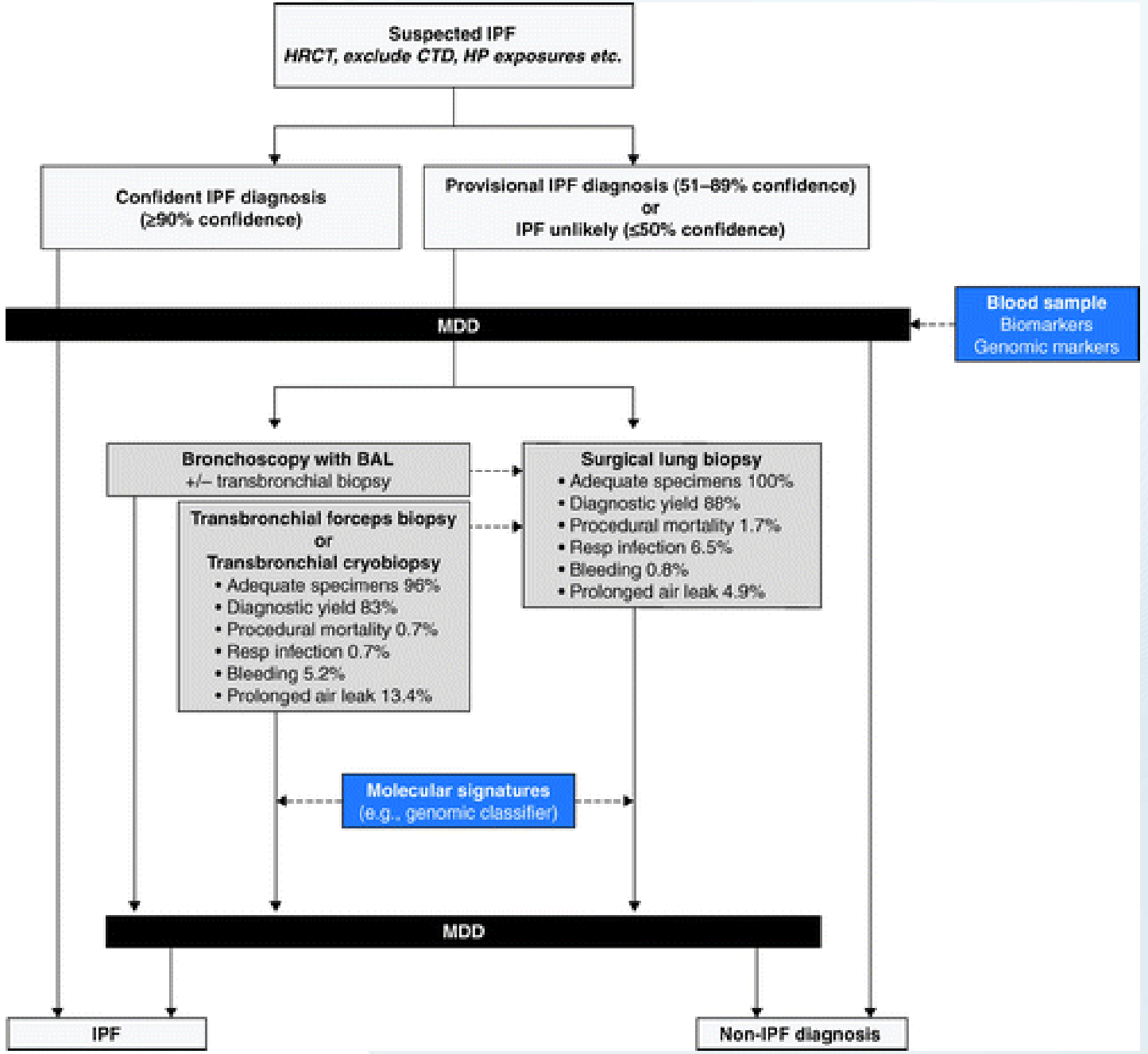
- *Should genomic classifier testing be used for diagnosing UIP in ILD of unknown type undergoing transbronchial forceps biopsy?*

➔ **We make no recommendation for or against the addition of genomic classifier testing** for the purpose of diagnosing UIP in patients with ILD of undetermined type who are undergoing transbronchial forceps biopsy, because of insufficient agreement among the committee members.

- No Recommendation: Due to insufficient agreement among committee members.
- Proponents: **High specificity** adds diagnostic value, may reduce need for additional sampling.
- Opponents: **Concerns about sensitivity**, consequences of false negatives, need for more precise data, limited incremental value over current data, not widely available, and does not provide granular histopathology details.

Ann Am Thorac Soc. 2022 May;19(5):827-832

Future IPF diagnosis?

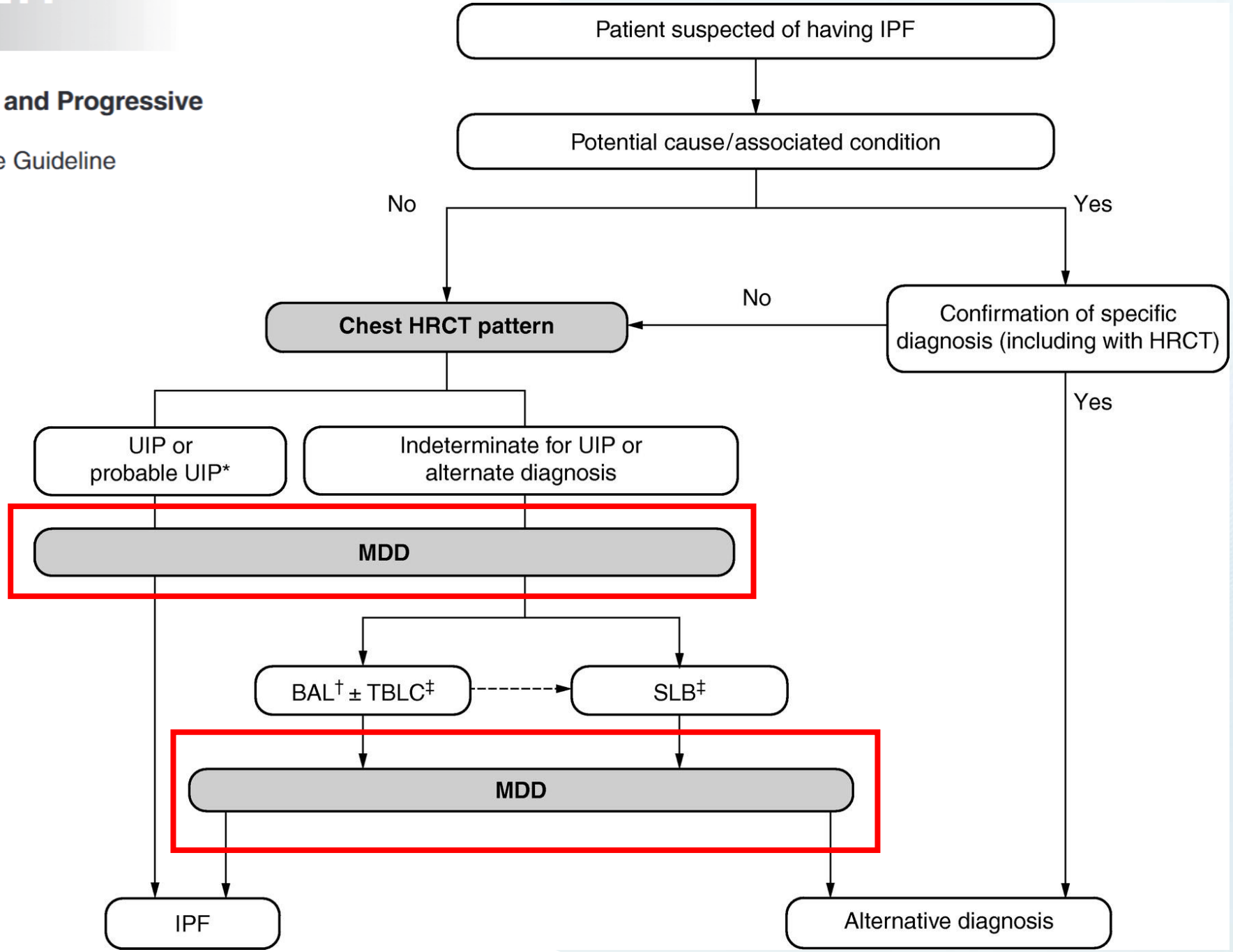


Ann Am Thorac Soc. 2022 May; 19(5): 725–727.

Contents

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline



Am J Respir Crit Care Med. 2022 May 1;205(9):e18-e47.

Multidisciplinary Discussion (MDD)

- A Multidisciplinary Discussion (MDD) is a collaborative meeting where healthcare professionals from various specialties come together to discuss and manage patient care.

- Holistic patient care
- Improved diagnostic accuracy
- Enhanced treatment planning
- Better management of comorbidities
- Shared decision-making
- Case study or example demonstrating benefits

Multidisciplinary Discussion (MDD)

- **Roles of Different Specialties**
- **Pulmonology:** Leads the discussion, provides clinical insights
- **Radiology:** Interprets imaging studies, identifies disease patterns
- **Pathology:** Analyzes tissue samples, provides definitive diagnosis
- Rheumatology: Manages autoimmune aspects in connective tissue diseases
- Cardiology: Assesses cardiovascular complications
- Thoracic surgery: Performs biopsies, surgical interventions
- Nursing and allied health professionals: Provides patient education, support, rehabilitation
- Pharmacy: Manages medications, educates on adherence and side effects

MDD: process

The primary physician presents the patient's case, including medical history, current symptoms, and previous treatments.

Comprehensive review of the patient's clinical data, including imaging studies, biopsy results, and laboratory tests.

Open discussion where each specialist contributes their expertise, sharing insights and recommendations.

The team works together to reach a consensus on the diagnosis and develop a coordinated treatment plan.

Regular follow-up meetings to monitor the patient's progress, adjust the treatment plan as needed, and address any new issues.

MDD : process

- **Core data to be presented for each case:**
- Comprehensive clinical history and physical examination findings, including:
  - ✓Smoking history
  - ✓Occupational, environmental, drug or other exposures known to be associated with hypersensitivity pneumonitis or occupational lung disease
  - ✓Family history of pulmonary fibrosis or autoimmune disease
  - ✓Symptoms and signs suggestive of underlying CTD
- **Investigations, including:**
  - ✓Autoimmune serology – including at least ANA, anti-CCP, RF.
  - ✓Detailed pulmonary function testing results
  - ✓High-resolution CT scan

Front Med (Lausanne). 2022; 9: 1017501.

MDD : process

- **Core outputs to be documented for each case:**

1. Consensus ILD diagnosis
2. Degree of diagnostic confidence
3. Any differential diagnoses
4. Expected disease behavior
5. Suggested management plan, including whether there is a need for additional testing with BAL, TBLC, SLB.

Front Med (Lausanne). 2022; 9: 1017501.

Contents

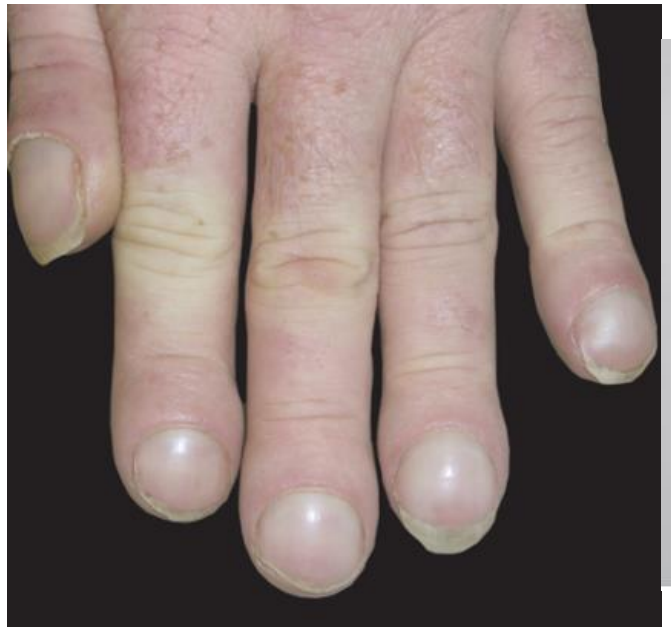
Case 1

- 나이: 65세
- 성별: 남성
- 주요 증상: 1년전부터 시작된 기침, 호흡곤란, 피로감
- 주요진료 기록
  - ✓1년 전: 간헐적인 기침과 피로감
  - ✓6개월 전: 호흡곤란이 점차 심해짐
  - ✓3개월 전: 가슴 X-ray에서 간질성 폐질환 의심

- 직업: 은퇴, 과거 교사
- 병력: 고혈압, 당뇨병
- 약물력: 베타블로커, 스타틴, GLP-1
- 흡연력: 1x20 pyrs, 10년전 중단/Social drinker

Case 1

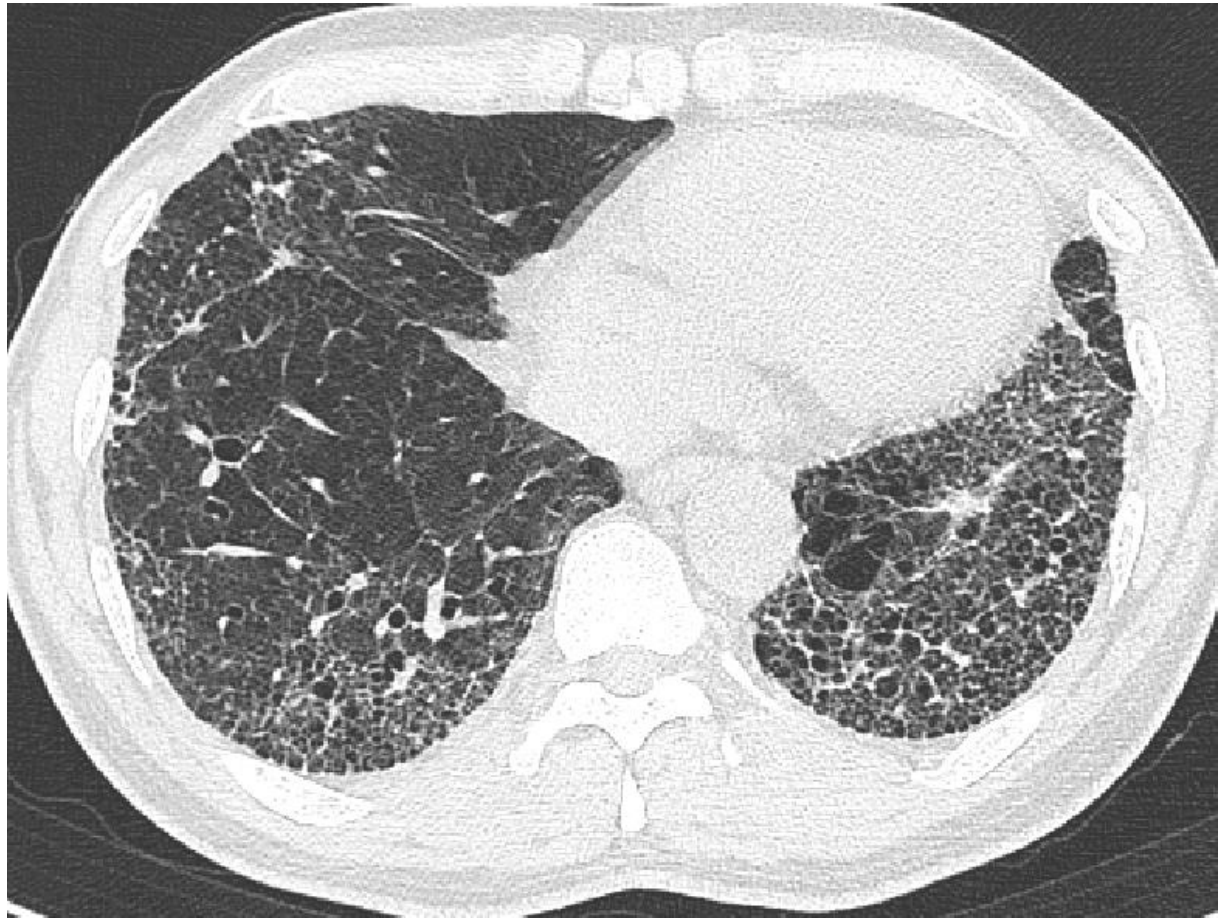
- **신체진찰**



수포음

- **Blood Tests:** anti-nuclear antibodies (ANA) 양성.

Case 1



Spirometry

		Ref	Pre Meas	Pre % Ref
FVC	Liters	4.56	2.77	61
FEV1	Liters	3.50	2.42	69
FEV6	Liters		2.76	
FEV1/FVC	%	75	87	
FEF25-75%	L/sec	3.00	3.65	122
FEF50%	L/sec	3.93	5.44	139
FEF75%	L/sec	1.43	1.52	106
PEF	L/sec	7.91	6.25	79
PIF	L/sec		4.37	
FIVC	Liters	4.19	1.96	47

Lung Volume (Body Plethysmography)

		Ref	Pre Meas	Pre % Ref
VC	Liters	4.19	2.84	68
TLC	Liters	6.51	3.96	61
RV	Liters	2.29	1.13	49
RV/TLC	%	37	28	
FRC PL	Liters	3.43	2.79	81
IC	Liters	2.83	1.17	41

DLCO

		Ref	Pre Meas	Pre % Ref
DLCO	mL/mmHg/min	23.7	6.1	26
DL Adj	mL/mmHg/min	23.7	6.3	27
DLCO/VA	mL/mHg/min/L	3.94	1.89	48
DL/VA Adj	mL/mHg/min/L		1.94	
VA	Liters		3.24	
IVC	Liters		2.43	

Hb: 13.7 gm/dL

Case 1: MDD

- 호흡기내과
- 영상의학과
- 류마티스내과
- 병리과
- 호흡기치료사
- 간호사

Case 1: MDD

- **호흡기내과**
  - 환자의 전반적인 병력 및 현재 증상에 대해 설명
  - 의견: HRCT 결과를 바탕으로 UIP 패턴이 의심되며, 환자 임상 경과 고려시 특발성 폐섬유증(IPF)을 강하게 고려함
- **영상의학과**
  - HRCT소견에 대한 상세한 설명
  - 의견: 양측 폐 하엽에 확인된 Honecombing과 traction BE는 UIP와 일치함. 추가적인 급성 변화 인 GGO 및 consolidation이 관찰되지 않아 급성 악화 가능성은 낮은것으로 보임.
- **류마티스내과**
  - 환자의 자가 면역 질환 가능성에 대한 평가
  - 의견: ANA가 양성이지만 다른 자가면역 질환의 증거는 부족함. 현재로는 특발성 폐섬유증의 가능성이 높음

Case 1: MDD

- **병리과**
  - 조직학적 진단 필요성에 대해서 상의
  - 의견: 진을 위해 SLB나 TBLC를 고려할 수 있으나 현 상황에서 영상 소견과 임상증상으로 진단을 뒷받침 할 수 있다고 생각
- **호흡기치료사**
  - 환자의 현재 호흡 상태 및 재활 계획
  - 의견: 현재 환자의 FVC와 DLCO 수치가 낮아 산소 치료가 필요할 수 있으며, 호흡 재활 프로그램이 권장됨
- **간호사**
  - 환자의 일상 생활 및 환자 교육 필요성
  - 의견: 환자와 가족에게 질병에 대한 교육이 필요하며, 호흡 재활 및 생활 습관 개선 방법을 안내할 예정

Case 1: 종합결론 및 치료계획

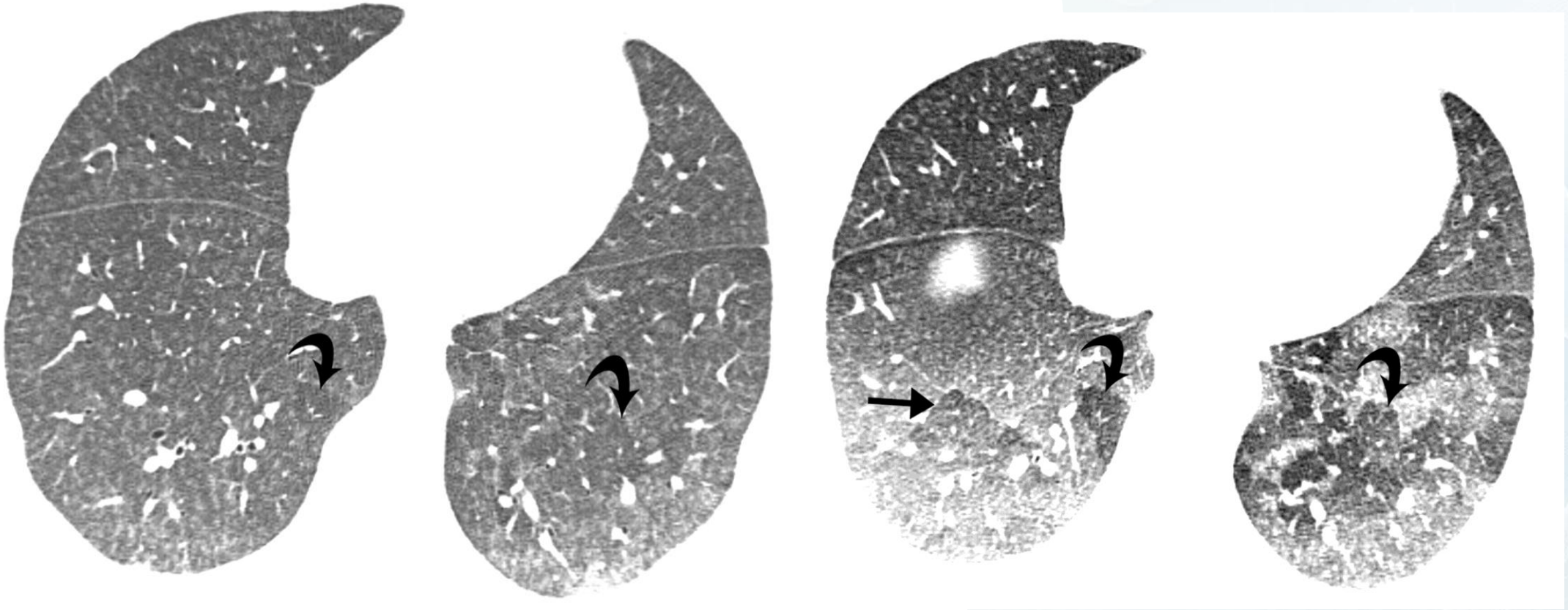
- 환자는 UIP 패턴에 부합하는 **특발성 폐섬유증(IPF)**으로 진단
- **치료 계획**
  - ✓항섬유화제 처방 (Pirfenidone 또는 Nintedanib)
  - ✓산소 치료폐 재활 프로그램 참여
  - ✓정기적인 모니터링과 추적 검사
  - ✓환자 및 가족 대상 교육 프로그램 실시
- **추가 논의 사항**
  - ✓임상 시험 참여 가능성 검토.
  - ✓환자의 삶의 질 개선을 위한 추가 지원 방안 논의

Case 2

- 나이: 45세
- 성별: 여성
- 주요 증상: 6개월 전부터 시작된 호흡곤란 및 발열
- 주요진료 기록
  - ✓6개월 전: 지속적인 기침 과 호흡곤란
  - ✓3개월 전: 발열 및 체중감소
- 직업: 비둘기 사육사
- 병력: 없음
- 약물력: 없음
- 비흡연자

Case 2

Expiration view



bilateral poorly defined centrilobular nodules and ground-glass opacities.

Air trapping

Case 2

- BAL fluid analysis

전체 세포수 : 5.2×10^5 /ml
생존율 : 84.6%
검체 육안 소견 : mucoid

세포구성(전체500개의 Cell)

세포 구성	개	%
Lymphocyte	: 2	: 0.4
Macrophage	: 28	: 5.6
Neutrophil	: 382	: 76.4
Eosinophil	: 19	: 3.8
Columnar epithelial cell	: 69	: 13.8
Squamous epithelial cell	: 0	: 0

세포수 합산 : 500

- 혈액검사
- ANA(-), RF(-)

- PFT

Spirometry

		Ref	Pre Meas	Pre % Ref
FVC	Liters	3.98	2.69	68
FEV1	Liters	2.81	2.37	84
FEV6	Liters		2.69	
FEV1/FVC	%	73	88	
FEF25-75%	L/sec	2.43	3.91	161
FEF50%	L/sec	2.98	7.01	235
FEF75%	L/sec	0.94	1.43	152
PEF	L/sec	6.76	7.89	117
PIF	L/sec		3.98	
FIVC	Liters	3.44	2.47	72

Lung Volume (Body Plethysmography)

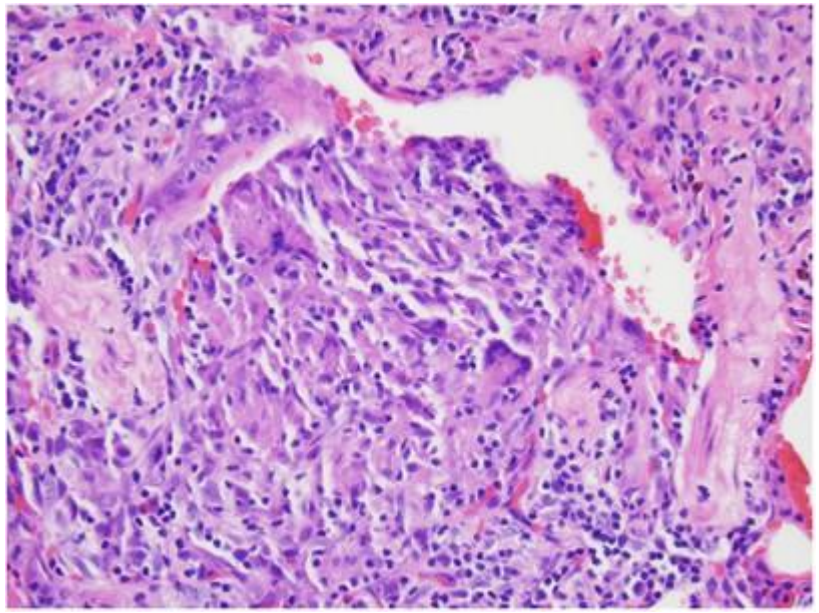
		Ref	Pre Meas	Pre % Ref
VC	Liters	3.44	2.92	85
TLC	Liters	5.79	4.33	75
RV	Liters	2.37	1.41	60
RV/TLC	%	40	33	
FRC PL	Liters	3.30	2.50	76
IC	Liters	2.35	1.83	78

DLCO

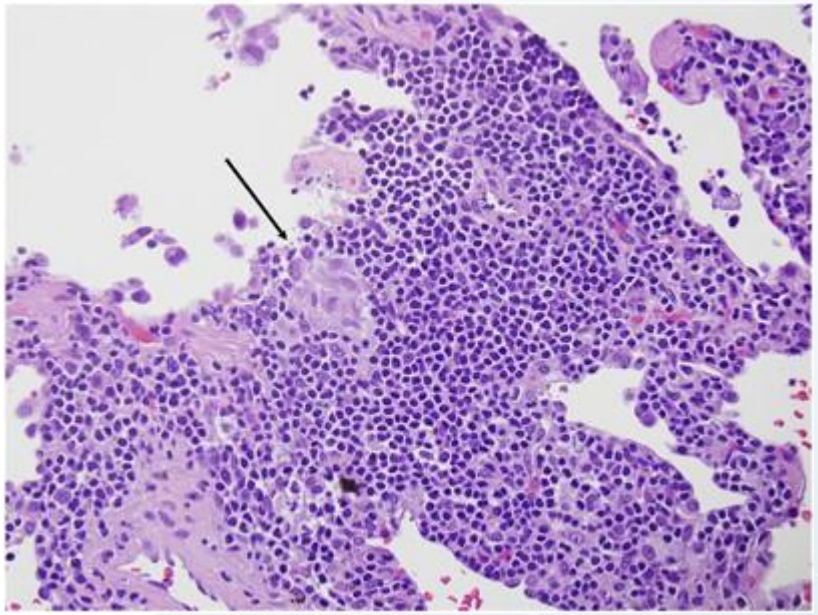
		Ref	Pre Meas	Pre % Ref
DLCO	mL/mmHg/min	18.6	11.0	59
DL Adj	mL/mmHg/min	18.6	11.4	61
DLCO/VA	mL/mHg/min/L	3.87	3.10	80
DL/VA Adj	mL/mHg/min/L		3.22	
VA	Liters		3.55	
IVC	Liters		2.55	

Hb: 13.3 gm/dL

Case 2



granuloma



(arrow) cluster of loosely organized epithelioid histiocytes

Case 2: MDD

- **호흡기내과**
  - 환자의 전반적인 병력, 환경 노출 평가 및 현재 증상에 대해 설명.
  - 의견: 환자가 비둘기 사육사로서 새 깃털과 배설물에 지속적으로 노출된 점을 고려할 때, 새 관련 과민성 폐렴(Bird Fancier's Lung) 가능성이 큼. HRCT 결과와 폐생검 소견도 뒷받침함.
- **영상의학과**
  - HRCT소견에 대한 상세한 설명
  - 의견: 양측 폐에 나타난 diffuse ground-glass opacity, centrilobular nodules, mosaic attenuation은 과민성 폐렴과 일치함.
- **병리과**
  - 생검 샘플의 병리 소견.
  - 의견: 다핵 대식세포 및 림프구 침윤 소견은 과민성 폐렴과 일치함.

Case 2: 종합결론 및 치료계획

- 환자는 **새 관련 과민성 폐렴(Bird Fancier's Lung)**으로 진단
- **치료 계획**
  - ✓새 깃털과 배설물에 대한 노출 회피 및 직업 변경 권장
  - ✓스테로이드 치료
  - ✓산소 치료
  - ✓폐 재활 프로그램 참여
  - ✓정기적인 모니터링과 추적 검사
  - ✓환자 및 가족 대상 교육 프로그램 실시
- **추가 논의 사항**
  - ✓환자의 환경적 요인 개선 방안 논의.
  - ✓환자의 법적 권리 및 보상에 대한 정보 제공

Take home messages

- Diagnosing ILD is complex due to its diverse presentations and overlapping features with other lung diseases.
- **High-resolution CT (HRCT)** is essential for detailed imaging, helping in diagnosing ILD and monitoring disease progression.
- **Selecting the right biopsy method**, such as BAL, TBLC, or SLB, is crucial and depends on the patient's condition and available expertise.
- **Biomarkers** and **genetic testing** are useful for early diagnosis, monitoring, and guiding treatment decisions in ILD.
- **MDD** and collaborative care involving specialists from different fields can improve diagnostic accuracy and treatment outcomes by integrating diverse expertise, ensuring accurate diagnosis and effective treatment planning for ILD patients.

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경청해 주셔서 감사합니다.

Q & A

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