2026.07.04

ILD School 2026

Management of Inflammatory ILDs:

Focus on COP and Idiopathic NSIP

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CONTENTS

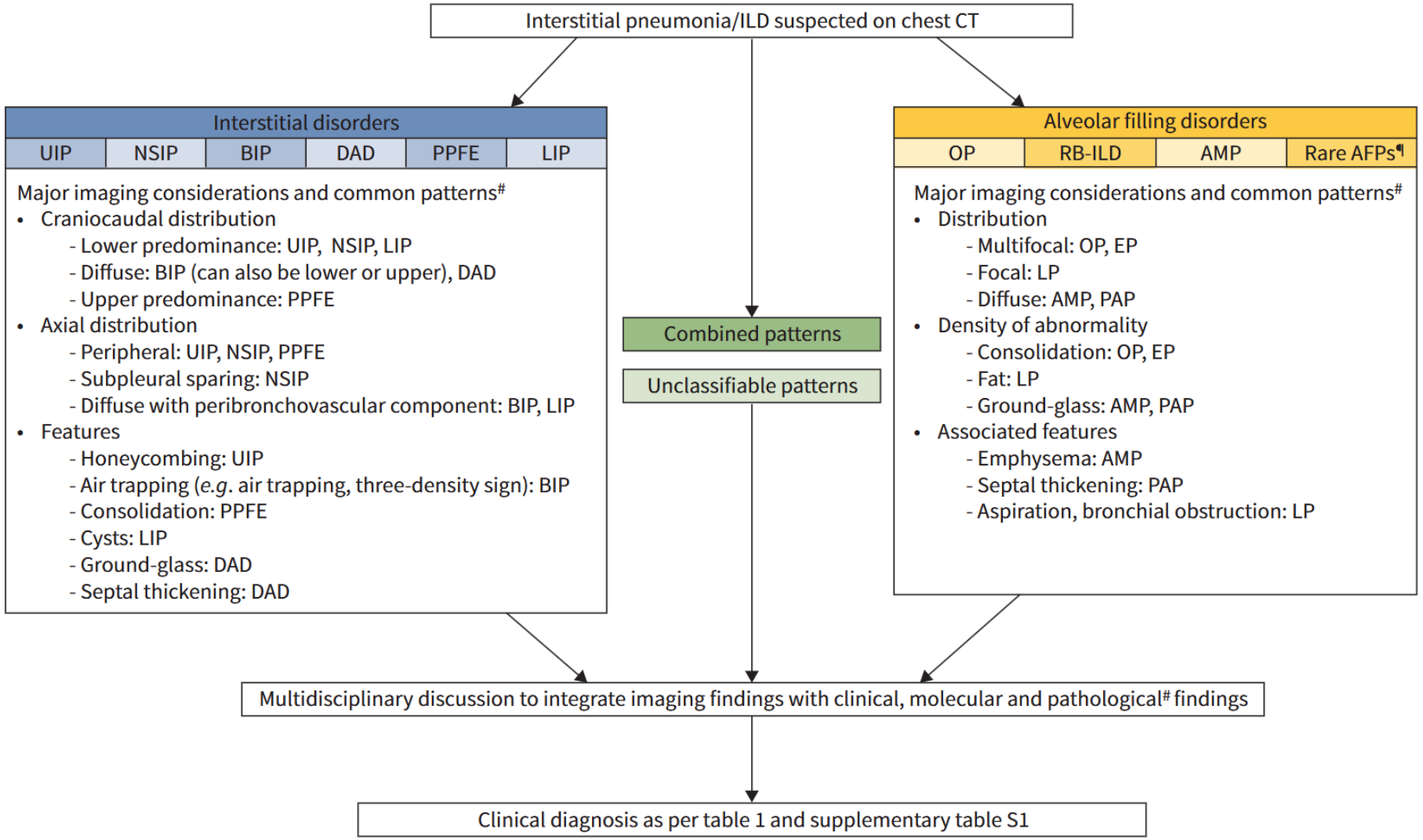
Interstitial Lung Disease (ILD)

- **Heterogenous group of disorders**
  - Refers to heterogenous group of diffuse parenchymal infiltrative disorders (Not a single disease entity)
  - Impairment of gas exchange function by disruption of the alveolar walls

- **Characteristics of ILD**
  - Acute or chronic inflammatory and/or fibrotic disease of the lung parenchyma, mainly involving interstitium, caused by non-infectious, non-malignant etiologies

Broaddus V et al. *Murray and Nadel's Textbook of Respiratory Medicine*. 7th ed. 2022
Longo DL *et al*. *Harrison's Principles of Internal Medicine*. 22nd ed. 2025

Classification of ILDs



Ryerson CJ *et al*. *Eur Respir J*. 2025;66

Classification of ILDs

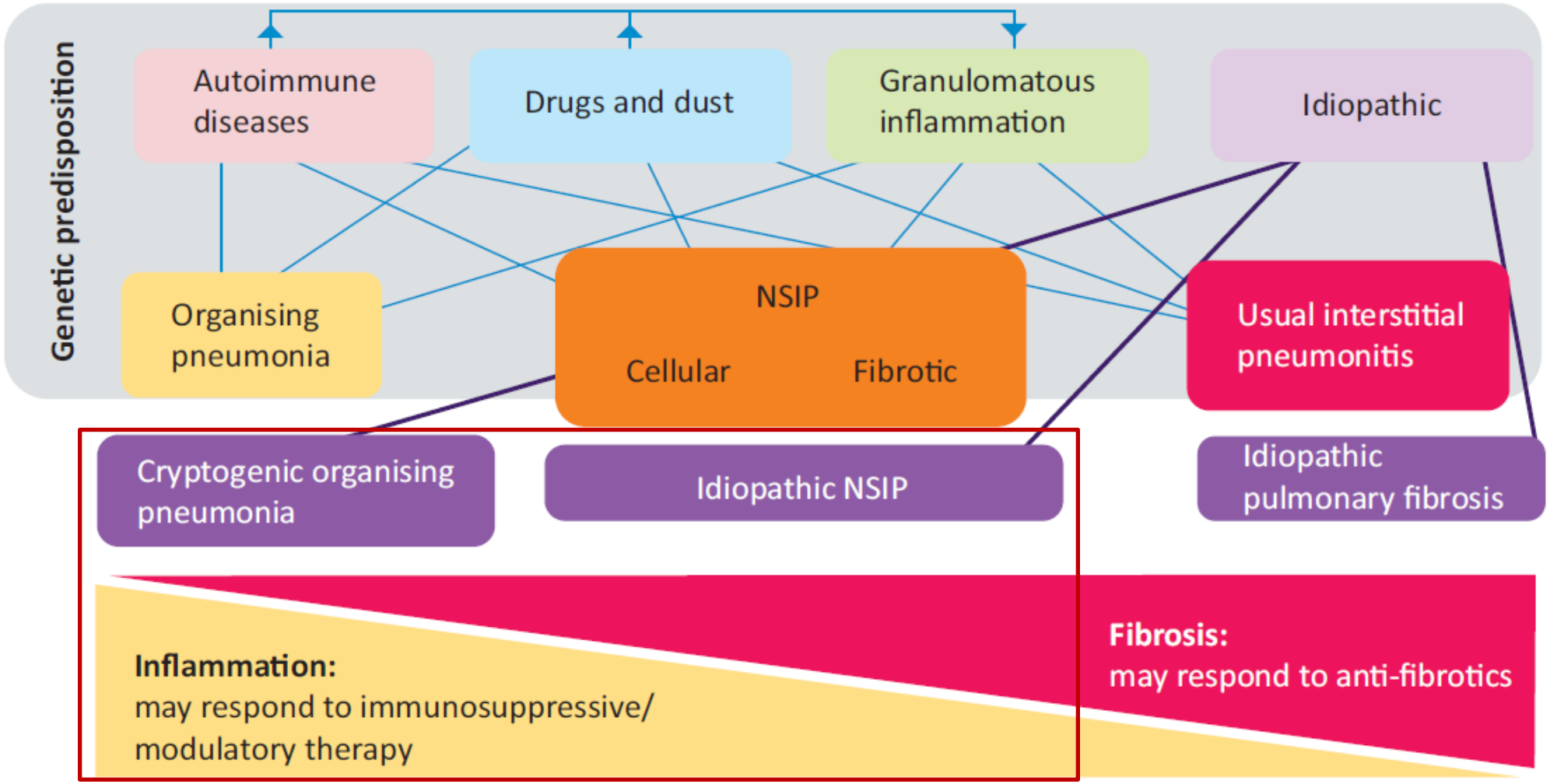
TABLE 1 Morphological patterns of interstitial and alveolar filling disorders and associated clinical-radiological-pathological diagnoses. Secondary aetiologies are listed before primary/idiopathic aetiologies to emphasise the importance of excluding an underlying cause before considering a diagnosis to be primary/idiopathic

Morphological patterns by pathology and imaging	Major clinical-radiological-pathological diagnoses	
	Secondary	Primary/idiopathic
Interstitial patterns		
UIP	Secondary UIP (*e.g.* CTD, HP, medications)	IPF (idiopathic UIP)
NSIP	Secondary NSIP (*e.g.* CTD >>> HP, medications)	Idiopathic NSIP
BIP[#]	Secondary BIP (*e.g.* HP >>> CTD, aspiration, inhalational exposures, medications)	Idiopathic BIP (provisional diagnosis[#])
DAD	Secondary DAD (multiple causes)	Idiopathic DAD (acute interstitial pneumonia)
PPFE	Secondary PPFE (*e.g.* IPF, CTD, HP, medications, radiation, transplant (restrictive allograft syndrome, pulmonary infection (post-tuberculosis), occupational)	Idiopathic PPFE
LIP	Secondary LIP (*e.g.* CTD, immune deficiency)	Idiopathic LIP
Alveolar filling patterns		
Organising pneumonia	Secondary organising pneumonia (*e.g.* CTD, post-infectious, medications, aspiration)	Cryptogenic organising pneumonia (idiopathic organising pneumonia)
RB-ILD	Secondary RB-ILD (*e.g.* smoking >>> CTD, medications, aspiration, hereditary)	Idiopathic RB-ILD
AMP[¶]	Secondary AMP (*e.g.* smoking >>> CTD, medications, aspiration, hereditary	Idiopathic AMP
Rare alveolar filling disorders	*e.g.* Acute and chronic eosinophilic pneumonia, pulmonary alveolar proteinosis, lipoid pneumonia (supplementary table S1)	
Other		
Combined pattern	Multiple combinations (*e.g.* NSIP + organising pneumonia, UIP + PPFE)	
Unclassifiable pattern	Unclassifiable ILD (multiple undefined patterns)	

UIP: usual interstitial pneumonia; NSIP: nonspecific interstitial pneumonia; BIP: bronchiolocentric interstitial pneumonia; DAD: diffuse alveolar damage; PPFE: pleuroparenchymal fibroelastosis; LIP: lymphoid interstitial pneumonia; RB-ILD: respiratory bronchiolitis-interstitial lung disease; AMP: alveolar macrophage pneumonia; CTD: connective tissue disease; HP: hypersensitivity pneumonitis; IPF: idiopathic pulmonary fibrosis. [#]: the committee voted 29 to four (88% to 12%) in favour of including BIP as a pattern and 27 to six (82% to 18%) in favour of introducing idiopathic BIP as a provisional multidisciplinary diagnosis; [¶]: formerly referred to as desquamative interstitial pneumonia.

Ryerson CJ *et al*. *Eur Respir J*. 2025;66

Spectrum of ILD (Inflammation vs. Fibrosis)



Mikolasch TA *et al. Clin Med*. 2016;16(6)

CONTENTS

Nonspecific Interstitial Pneumonia/Fibrosis

The American Journal of Surgical Pathology *18(2): 136–147, 1994*

Nonspecific Interstitial Pneumonia/Fibrosis

Histologic Features and Clinical Significance

Anna-Luise A. Katzenstein, M.D., and Robert F. Fiorelli, B.S.

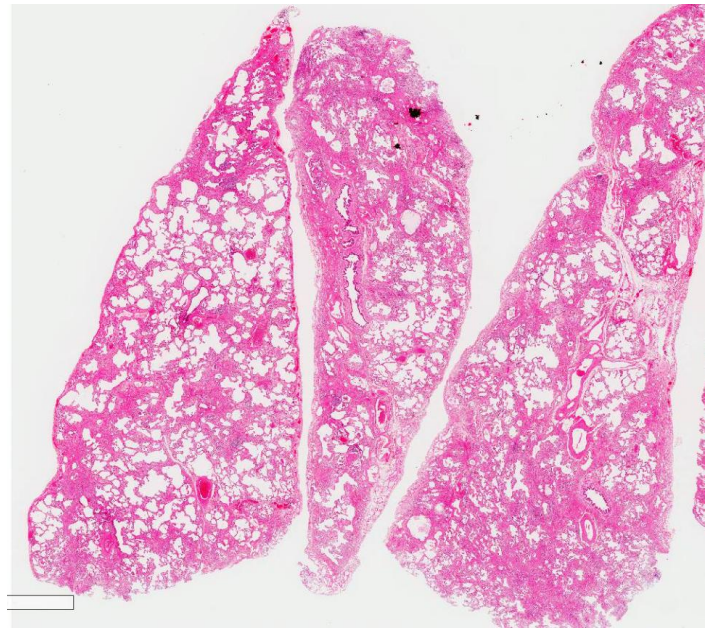
drome) (8). It has been our impression that in addition to these entities, a fairly sizeable group of idiopathic interstitial pneumonias cannot be pigeonholed into one of the three main groups, and we have termed these lesions nonspecific interstitial pneumonia or fibrosis. This study was undertaken

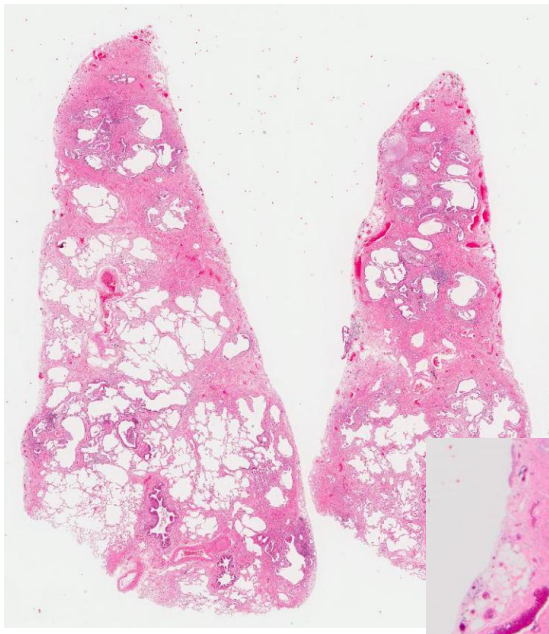
showed pure inflammation and no fibrosis. Nonspecific interstitial pneumonia must be separated from the three main forms of idiopathic interstitial pneumonia because of better prognosis and different treatment options. It should not be considered a specific disease, however, because it may have varying etiologies including underlying connective tissue diseases, organic dust or other exposures, and prior acute lung injury; less often, it may reflect a nonrepresentative biopsy of another process.

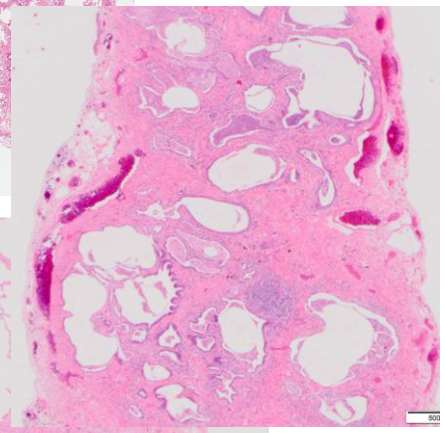
Katzenstein ALA and Fiorelli RF. *Am J Surg Pathol*. 1994;18(2)

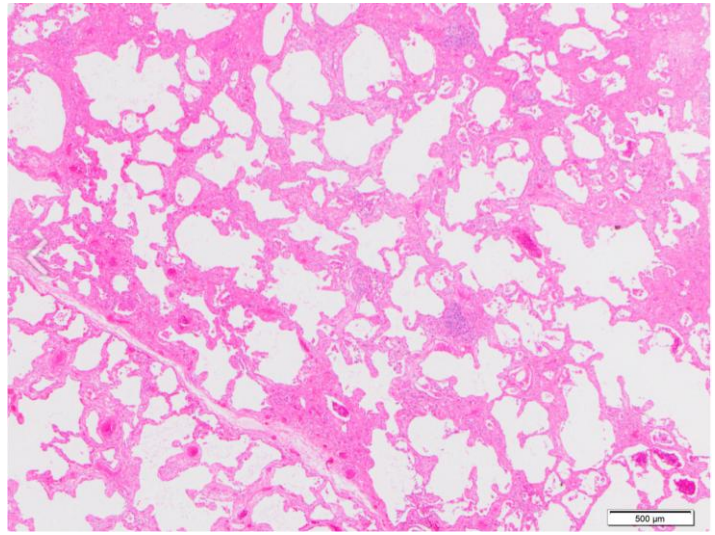
NSIP vs. UIP (Pathologic Features)

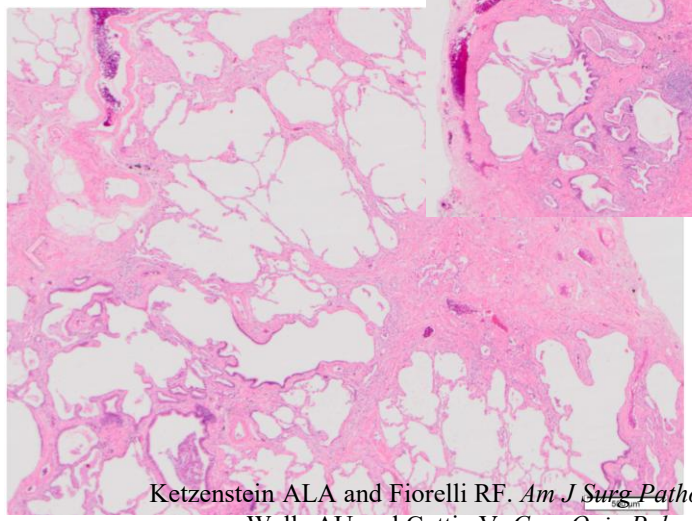
- **Pathologic term**
  - Characterized by an interstitial inflammatory or fibrosing process or both .. [that] appeared temporally uniform within each case (Katzenstein et al.)
  - Contrary to temporally heterogenous process of UIP pattern
  - First viewed as "waste basket pattern"











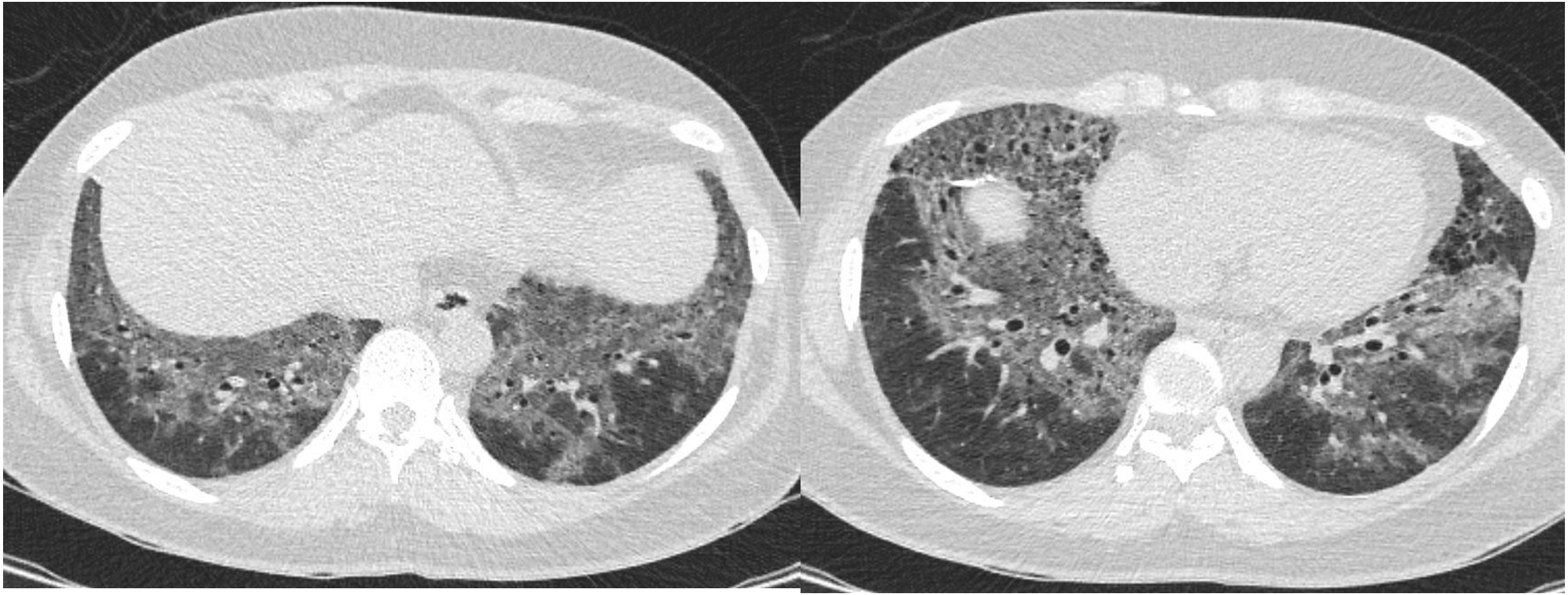
Ketzenstein ALA and Fiorelli RF. *Am J Surg Pathol*. 1994;18(2)
Wells AU and Cottin V. *Curr Opin Pulm Med*. 2016;22

Radiologic Features of NSIP

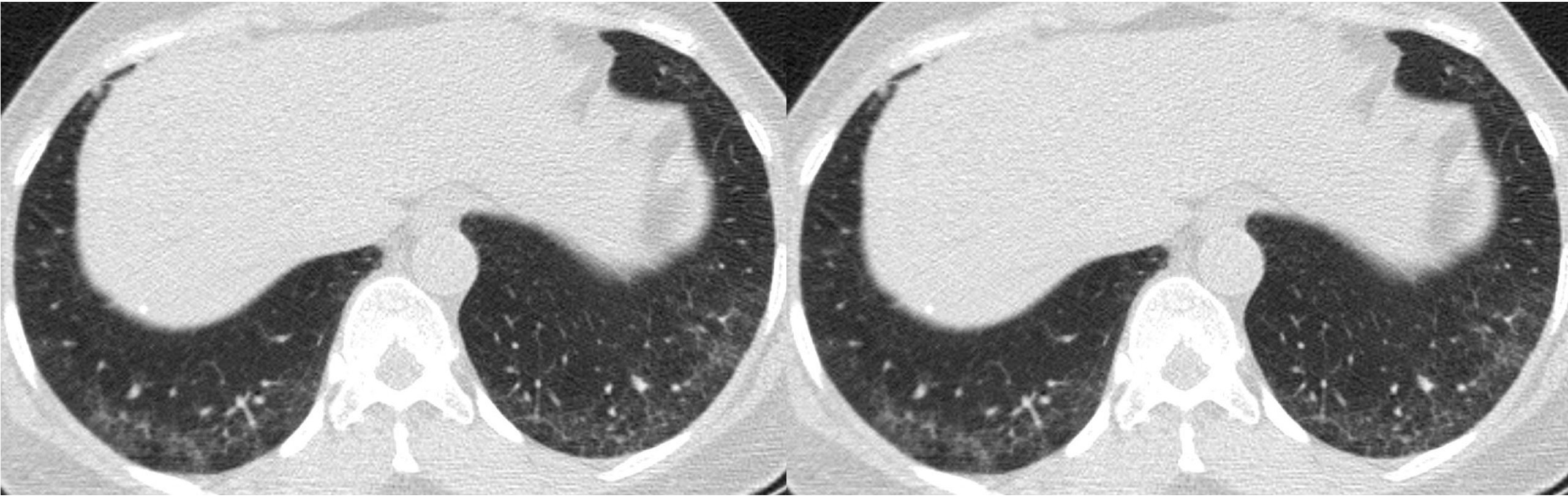
- **Bibasilar predominance**
- **Subpleural sparing (40~60%)**
- **Ground-glass opacities**
- **Fine reticulation and traction bronchiectasis**
- **Lobar volume loss**
- **Little or no honeycombing**

Broaddus V et al. *Murray and Nadel's Textbook of Respiratory Medicine*. 6th ed. 2016

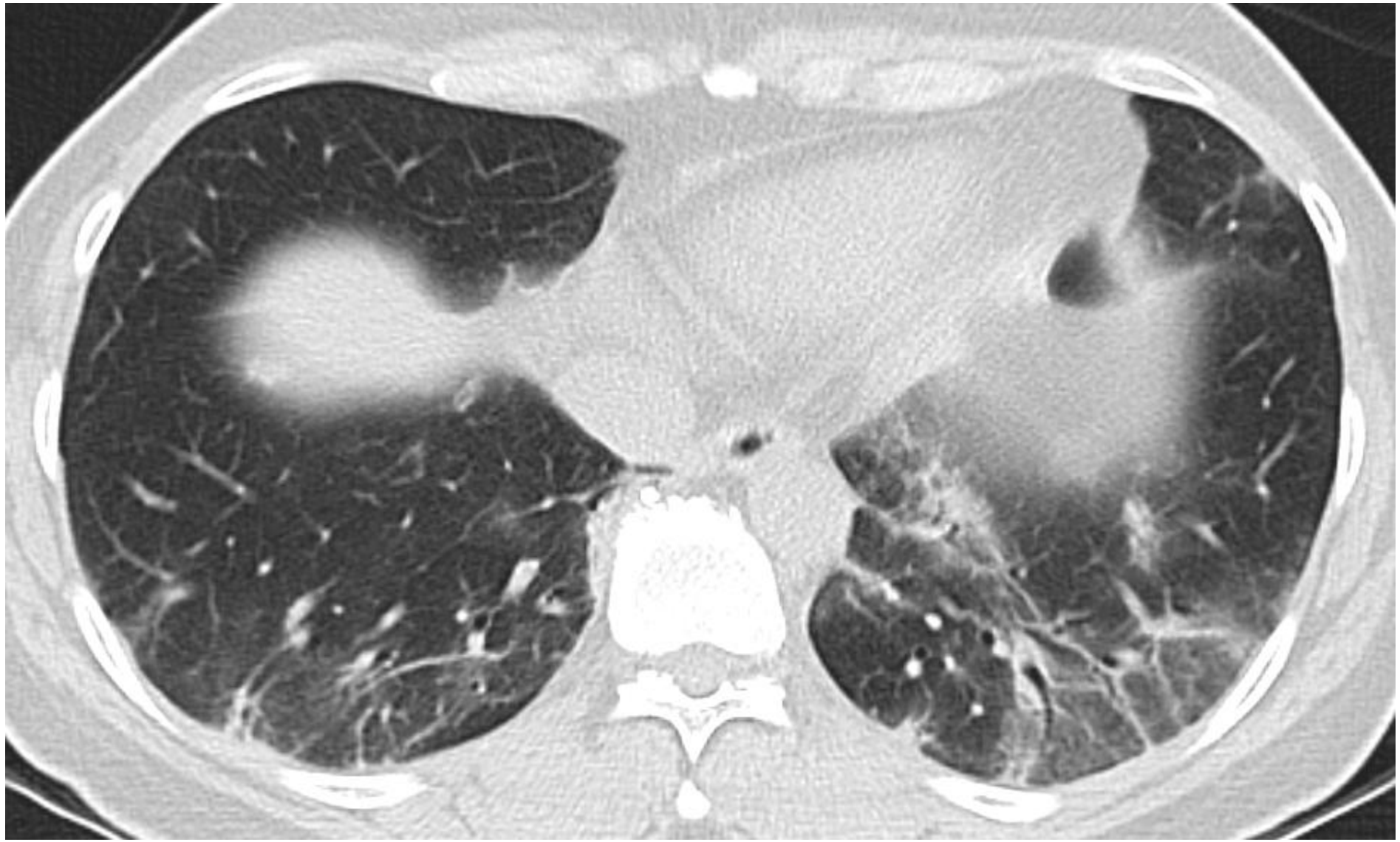
Radiologic Features of NSIP



Radiologic Features of NSIP



Radiologic Features of NSIP



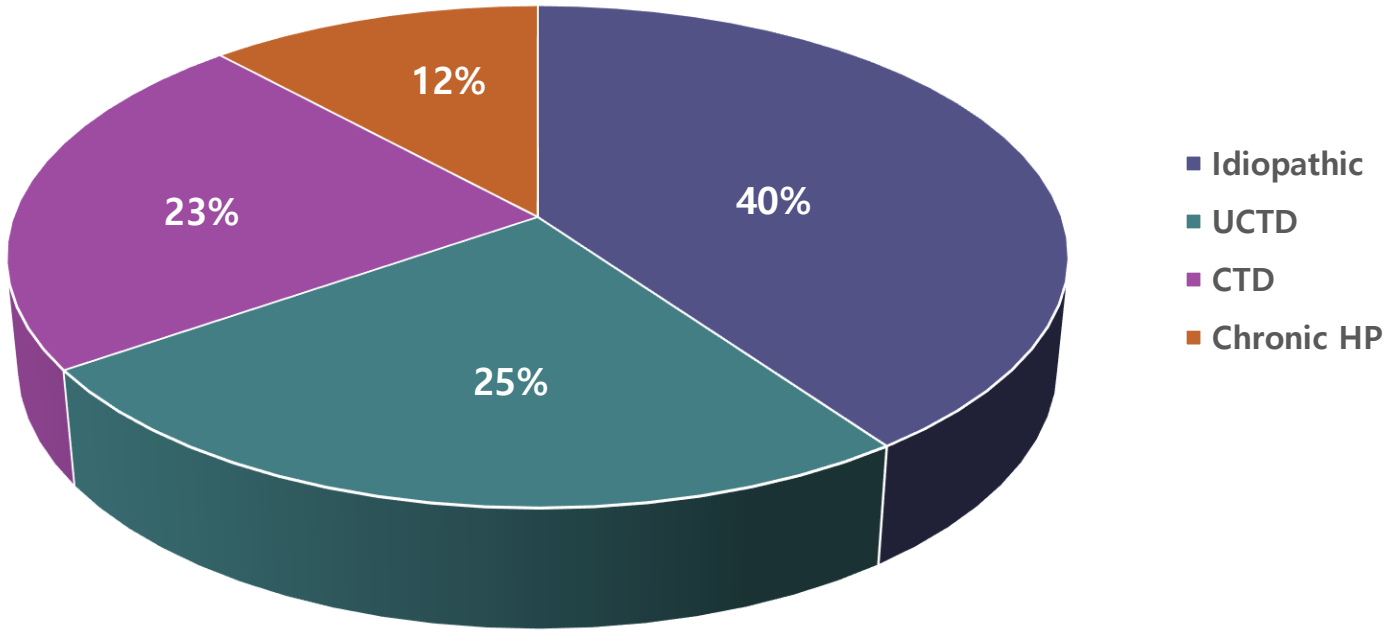
Differential Diagnosis of Idiopathic NSIP

폐침범으로 발현한 결체조직질환
과민성폐렴
다른 특발성간질성폐질환(특히 기질화폐렴, 특발성폐섬유증, 흡연관련 간질성폐렴)
약제 반응
유육종증
감염(폐포자충, HIV 등)
만성호산구폐렴
림프구증식폐질환

간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)

Etiologies of Bx-proven NSIP (France)

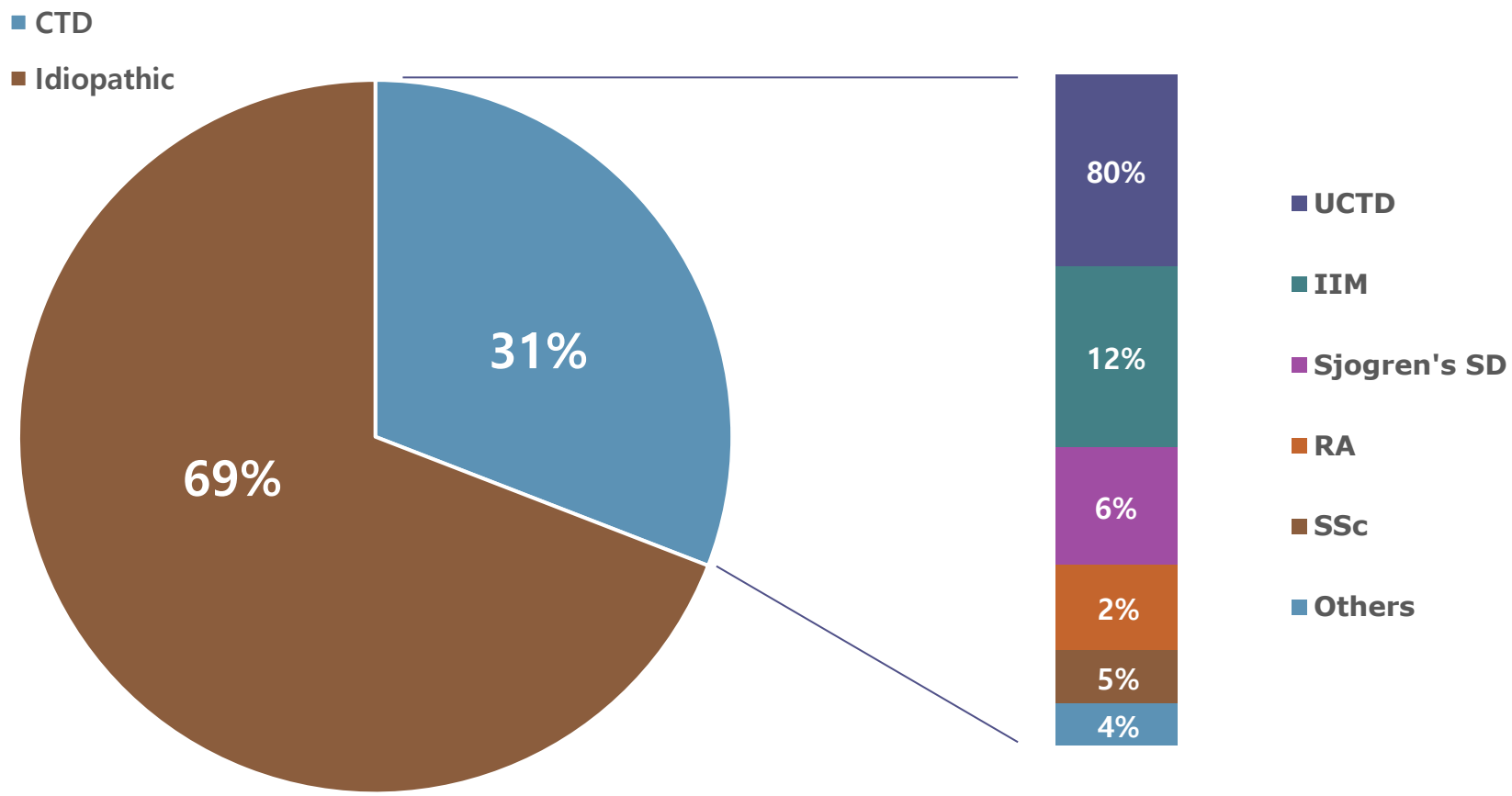
- 127 pathologically proven NSIP cases from single center (France)



Nunes H *et al*. *Eur Respir J*. 2015; 45(3)

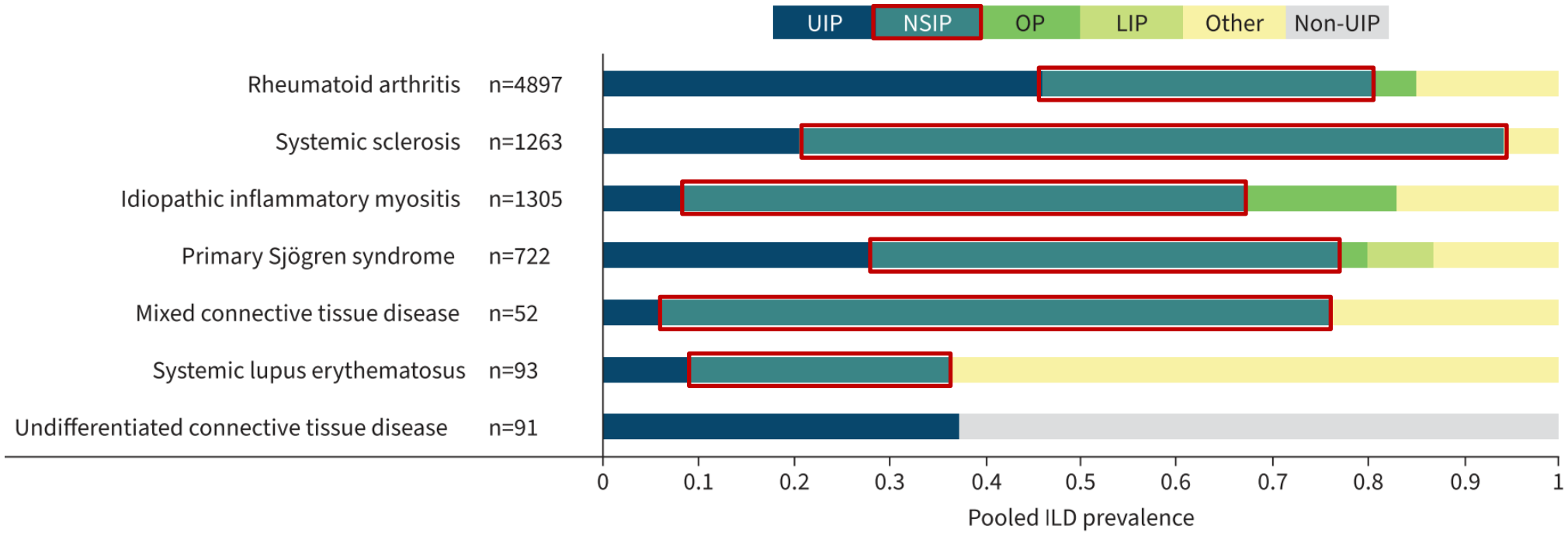
Etiologies of Bx-proven NSIP (SMC)

- 204 pathologically proven NSIP cases from single center (SMC)



Cho HK, Chung MP et al. *Ther Adv Respir Dis*. 2022;16

HRCR Patterns of CTD-ILD



Joy GM *et al*. *Eur Respir Rev*. 2023;32

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Ryerson CJ *et al*. *Eur Respir J*. 2025;66

Etiologies of NSIP (ATS/ERS Guidelines)

Nonspecific interstitial pneumonia

NSIP encompasses a spectrum of non-fibrotic (*i.e.* cellular) and fibrotic patterns. NSIP most often presents with underlying causes such as CTD or drug toxicity, is sometimes seen in fibrotic HP, AMP (formerly referred to as DIP), or following cryptogenic or secondary organising pneumonia, and is rarely idiopathic [8, 31]. Based on a recent systematic review of 122 publications that included 8266 patients, fibrotic NSIP is the most common ILD pattern in CTD-ILD (range 27–76% of all CTD-ILD), excluding rheumatoid arthritis associated ILD where UIP is slightly more common at 46% of all cases [31, 32]. A study of 109 patients who had lung biopsy of multiple lobes showed that a histological pattern of NSIP can also coexist with UIP, in which case the histological pattern is considered to be UIP [24]. Autoimmune serologies for CTD-ILD are the only laboratory tests typically used to screen for an underlying cause of an NSIP pattern, while serum precipitins for HP rarely have clinical utility in this setting [25, 33, 34].

Ryerson CJ *et al*. *Eur Respir J*. 2025;66

Diagnosis of Idiopathic NSIP (Guidelines)

3) 수술적 폐생검

확진을 위해서는 폐생검이 필수적이며 조직학적으로는 미만성으로 나타나는 간질의 염증과 섬유화를 볼 수 있는데 이는 전체적으로 보아 균일한 형태로 나타나고 보통 폐포의 기본 구조는 보존되어 있는 점이 UIP 양상, 즉 IPF 와는 다르다[2,3] (그림 2). 이를 NSIP양상이라고 하며 조직학적으로 세포성(cellular) NSIP와 섬유성

Lung biopsy is not indicated in typical cases of fibrotic NSIP that are linked to an underlying cause such as a CTD or high-risk medication exposure temporally associated with disease onset, given the high confidence in the diagnosis of CTD-ILD in this setting. However, NSIP can be radiologically indistinguishable from UIP [43, 52, 57], BIP (including fibrotic HP) [25, 33], or AMP, and thus may warrant lung biopsy for histological interstitial pneumonia pattern diagnosis in patients without an identified underlying cause [58]. The previous recommendation that adequate histopathology and review by multidiscipliniary discussion is needed to establish a confident diagnosis of idiopathic NSIP was informed by its rarity, lack of clearly distinguishing clinical, radiological, and laboratory features, and apparent better survival and different treatment approaches compared to IPF [2, 35]; however, additional data are needed to confirm the appropriateness of this approach. The wide range in prevalence of idiopathic NSIP in various cohorts probably relates in large part to whether histopathology was required to support this diagnosis, with more stringent diagnostic criteria resulting in a larger proportion of patients being considered to have unclassifiable ILD (box 2).

간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)
Ryerson CJ *et al*. *Eur Respir J*. 2025;66

Treatment of Idiopathic NSIP

- **권고사항**
  - 특발성비특이간질성폐렴(iNSIP)에서 질병 완화를 위해 일차 치료로 스테로이드를 사용할 수 있다. (근거수준: 전문가 합의, 권고등급: 조건부 권고)

    투표결과 조건부 권고 6/6

  - 특발성비특이간질성폐렴(iNSIP)에서 스테로이드 단독 치료로 효과가 적거나 스테로이드 의존적일 경우 스테로이드와 면역억제제 병합요법을 사용할 수 있다 .(근거수준: 전문가 합의, 권고등급: 조건부 권고)

    투표결과 조건부 권고 6/6

  - 폐 섬유화가 진행하는 경우(progressive pulmonary fibrosis, PPF) 항섬유화제를 사용을 권고한다. (근거수준: 전문가 합의, 권고등급: 강하게 권고)

    투표결과 강하게 권고 6/6

간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)

Treatment of Idiopathic NSIP

- **Corticosteroid**
  - ✓ Optimal dose and duration: Not known (retrospective observational studies)
  - ✓ Initial: prednisone 0.5-1.0 mg/kg (40-60 mg) for 1 month → slow tapering
  - ✓ Fulminant: methylprednisolone pulse (750-1000mg/day IV for 3 days → 1mg/kg oral)

- **Immunosuppressants**
  - ✓ Azathioprine, cyclophosphamide, cyclosporin, mycophenolate mofetil (MMF)
  - ✓ Role: Dose of steroid ↓, adverse events of steroid ↓, stabilization of lung function
  - ✓ Usually added when refractory to or dependent on steroid

간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)
Belloli E et al. *Respirology*. 2016;21(2)

Treatment of Idiopathic NSIP

- Single-center retrospective observational study (AMC)
- 83 patients with idiopathic NSIP (Fibrotic 72 / Cellular 12)

Characteristics	Total	Fibrotic NSIP	Cellular NSIP	p-value
Subjects	83	72	11	
Age yrs	54.4±10.1	54.3±10.1	55.4±10.8	0.739
Males/females	27/56	23/49	4/7	0.743
Follow-up period months	56.1±39.0	58.0±40.9	43.4±20.1	0.071
Smoking never/ex/current	57/13/13	51/10/11	6/3/2	0.470
Duration of dyspnoea months	5.7±6.7	5.9±7.0	4.9±4.5	0.666
Antinuclear antibody	46/81 (57)	38/70 (54)	8/11 (73)	0.335
Rheumatoid factor	14/81 (17)	13/70 (19)	1/11 (9)	0.679
Resting P_{a,O_2} mmHg	82.5±14.4	83.4±14.3	77.2±15.0	0.187
Initial PFTs				
FVC % pred	63.6±14.6	63.3±14.9	66.8±13.1	0.594
FEV_1 % pred	71.3±17.1	71.1±17.4	72.5±16.1	0.792
$D_{L,CO}$ % pred	58.9±19.1	58.4±19.9	62.3±13.2	0.532
TLC % pred	72.9±19.1	73.2±20.3	71.1±9.5	0.752
Initial BAL finding %				
Macrophage	51.5±19.6	55.5±17.9	26.6±7.7	<0.001
Lymphocyte	35.3±21.0	30.7±18.0	63.8±15.8	<0.001
Neutrophil	10.3±11.4	10.5±10.7	8.9±16.2	0.714
Eosinophil	2.5±3.8	2.6±4.0	1.7±2.2	0.520
T4/T8 ratio	0.91±0.81	1.00±0.84	0.45±0.37	0.077
Initial treatment				
Initial dose of PD mg	51.5±11.9	51.5±12.0	51.4±12.1	0.980
Combination with CX	62/79 (78)	56/68 (82)	6/11 (54)	0.052
Time to 15 mg of PD months	6.8±7.2	5.7±3.7	12.8±15.5	0.187
Total duration months	17.2±12.1	17.4±12.1	15.8±12.4	0.706

Park IN *et al*. *Eur Respir J*. 2009; 33

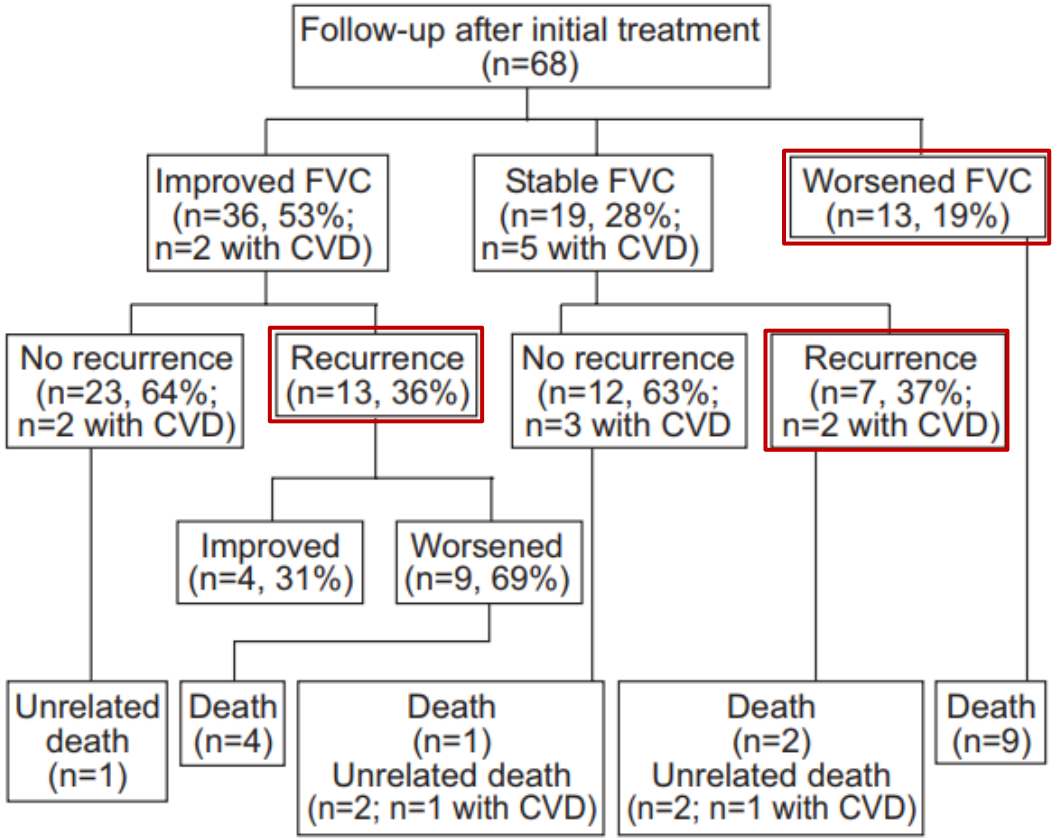
Treatment of NSIP Pattern

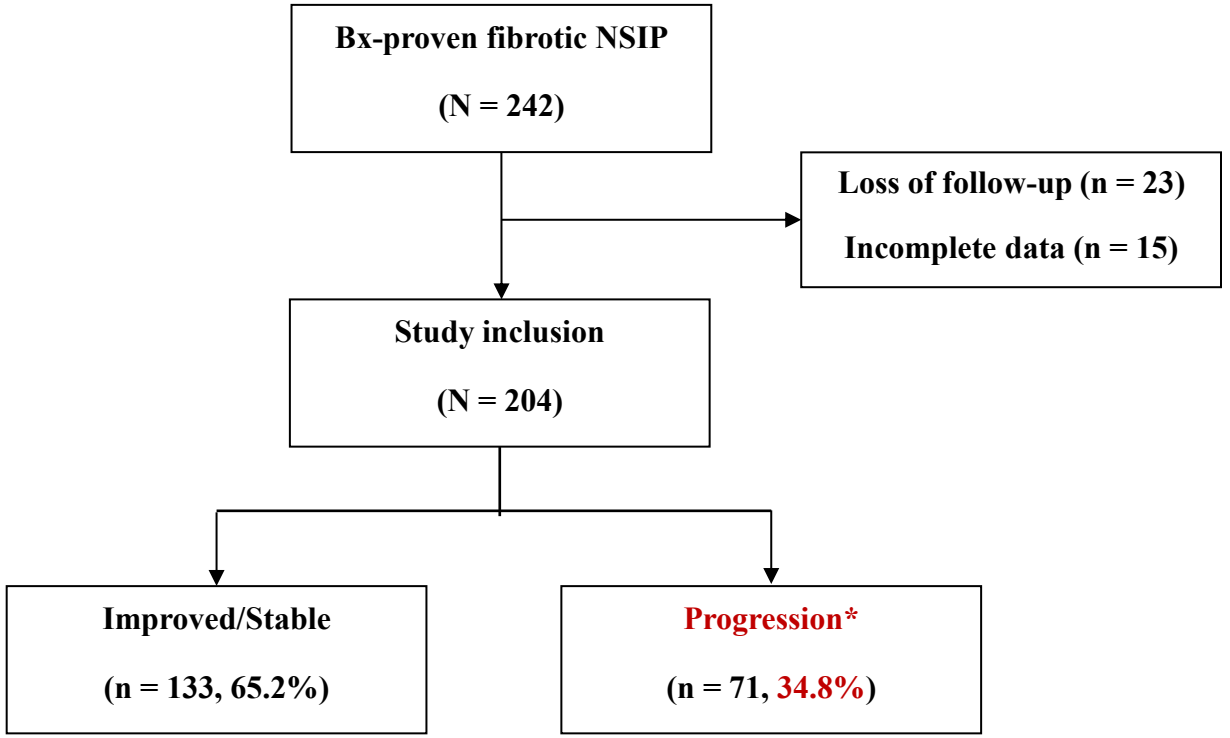
- Single-center retrospective observational study (SMC)
- 204 patients with Bx-proven NSIP [Idiopathic 141 (69%) vs. CTD 63 (31%)]

	No. (%) or median (IQR)
Initial treatment	
Corticosteroid + azathioprine	94 (46)
Corticosteroids only	52 (25)
Corticosteroid + cyclophosphamide	23 (11)
Azathioprine only	20 (10)
Cyclophosphamide only	6 (3)
No treatment	7 (3)
Other treatments[a]	2 (1)
Duration of treatment, months	17.8 (12.5–19.9)
Treatment outcome (n = 197)	
Progression[b]	71 (36)
Relapse[c,d]	47 (24)
Progression or relapse[e]	100 (51)
Mortality	18 (9)

Cho HK *et al. Ther Adv Respir Dis*. 2022; 16

Treatment Outcomes of NSIP



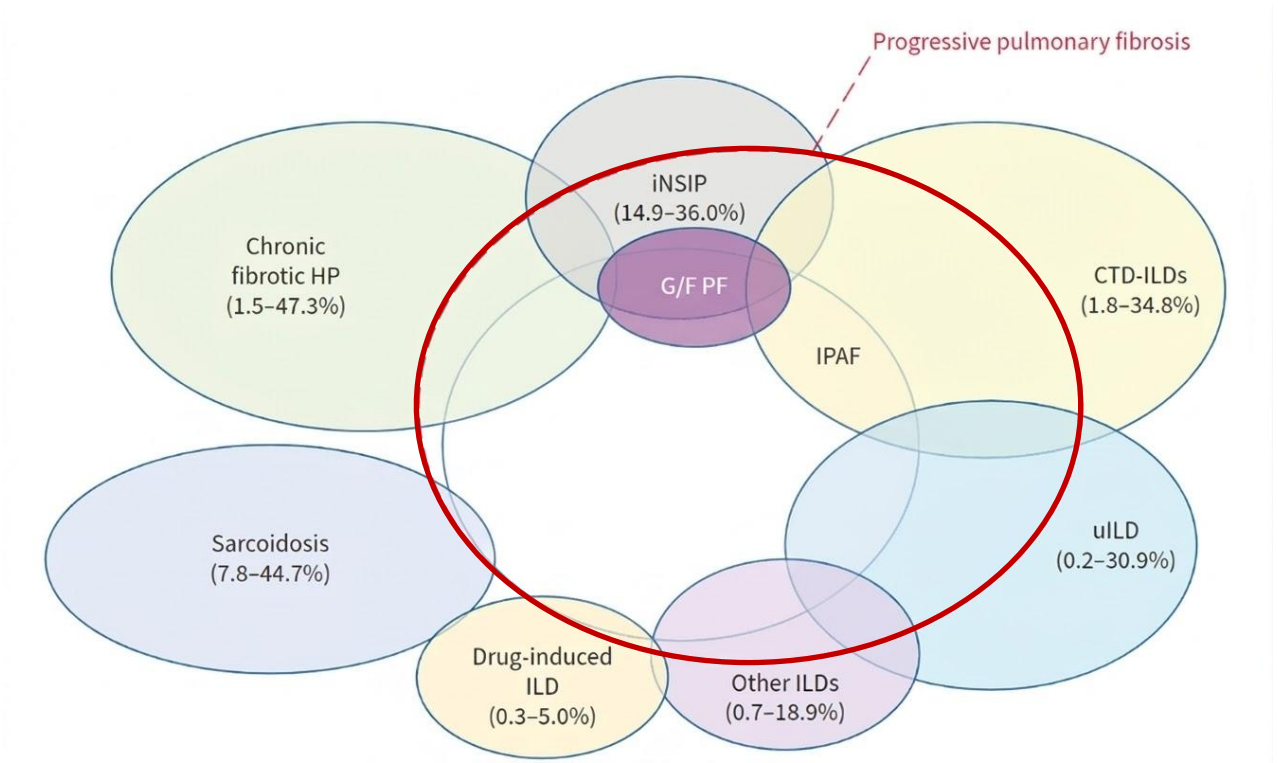


*** Progression defined according to INBUILD criteria**

Park IN *et al*. *Eur Respir J*. 2009; 33
Cho HK *et al*. *Ther Adv Respir Dis*. 2022; 16

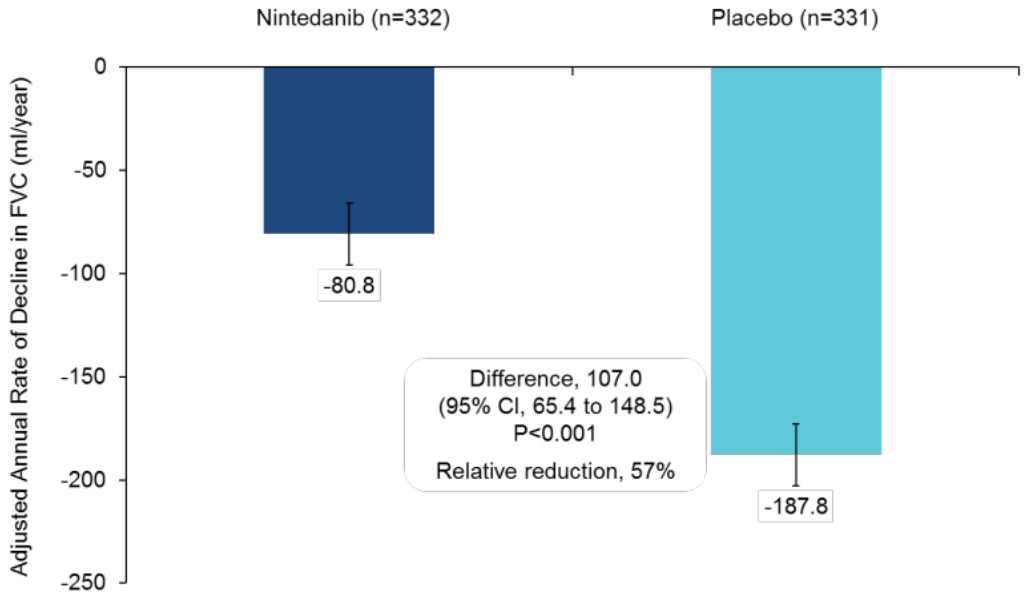
Progressive Pulmonary Fibrosis (PPF)

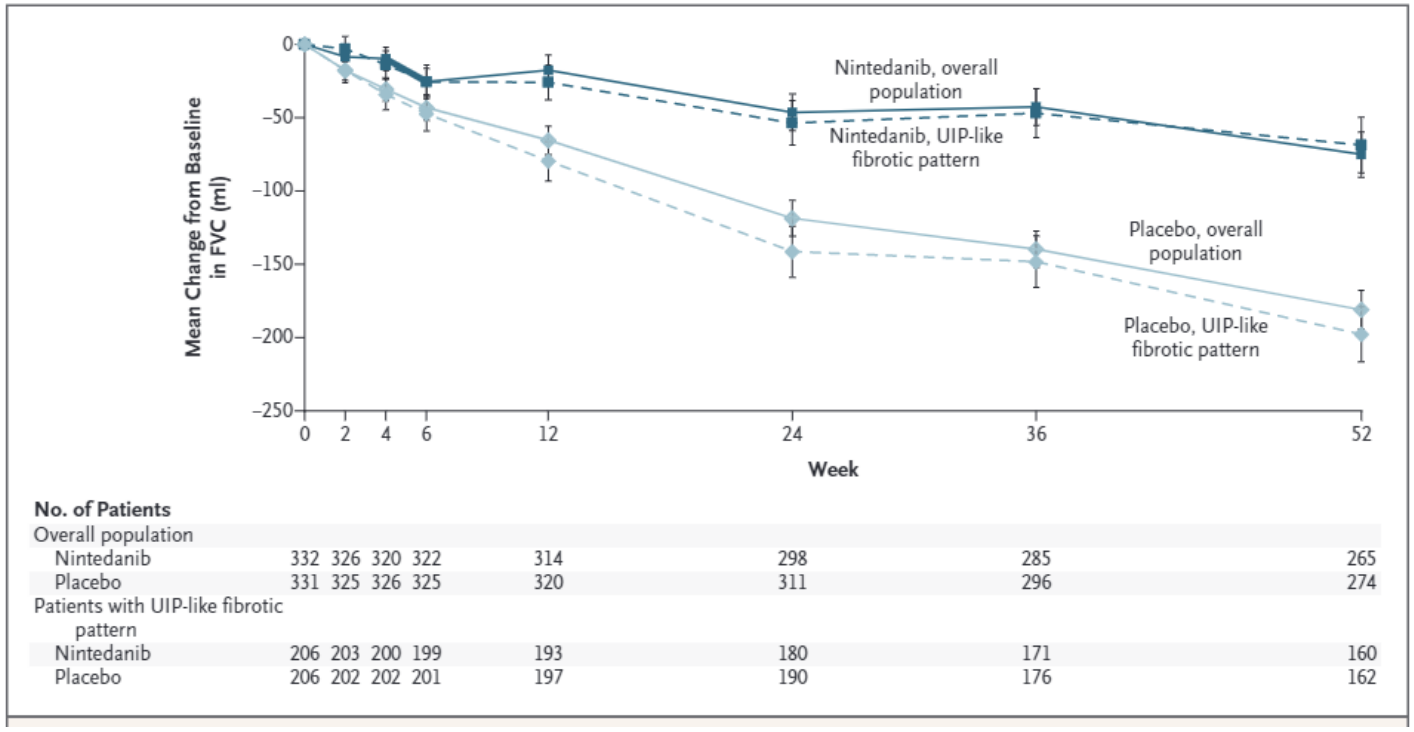
- Newly suggested classification concept of ILD
- Chronic fibrosing ILD with progressive course (despite treatment)
- Examples of PF-ILD
  - ✓ Idiopathic fibrotic NSIP, CTD-ILD (eg. RA-ILD, SSc-ILD), fibrotic HP (chronic HP), unclassifiable ILD, sarcoidosis etc.



Cottin V. Eur *Respir Rev*. 2019; 28
George PM *et al*. *Lancet Respir Med*. 2020; 8
Raghu G *et al*. *Am J Respir Crit Care Med*. 2022;205(9)
Rajan SK. *Eur Respir Rev*. 2023;61

Nintedanib for PF-ILD (INBUILD trial)

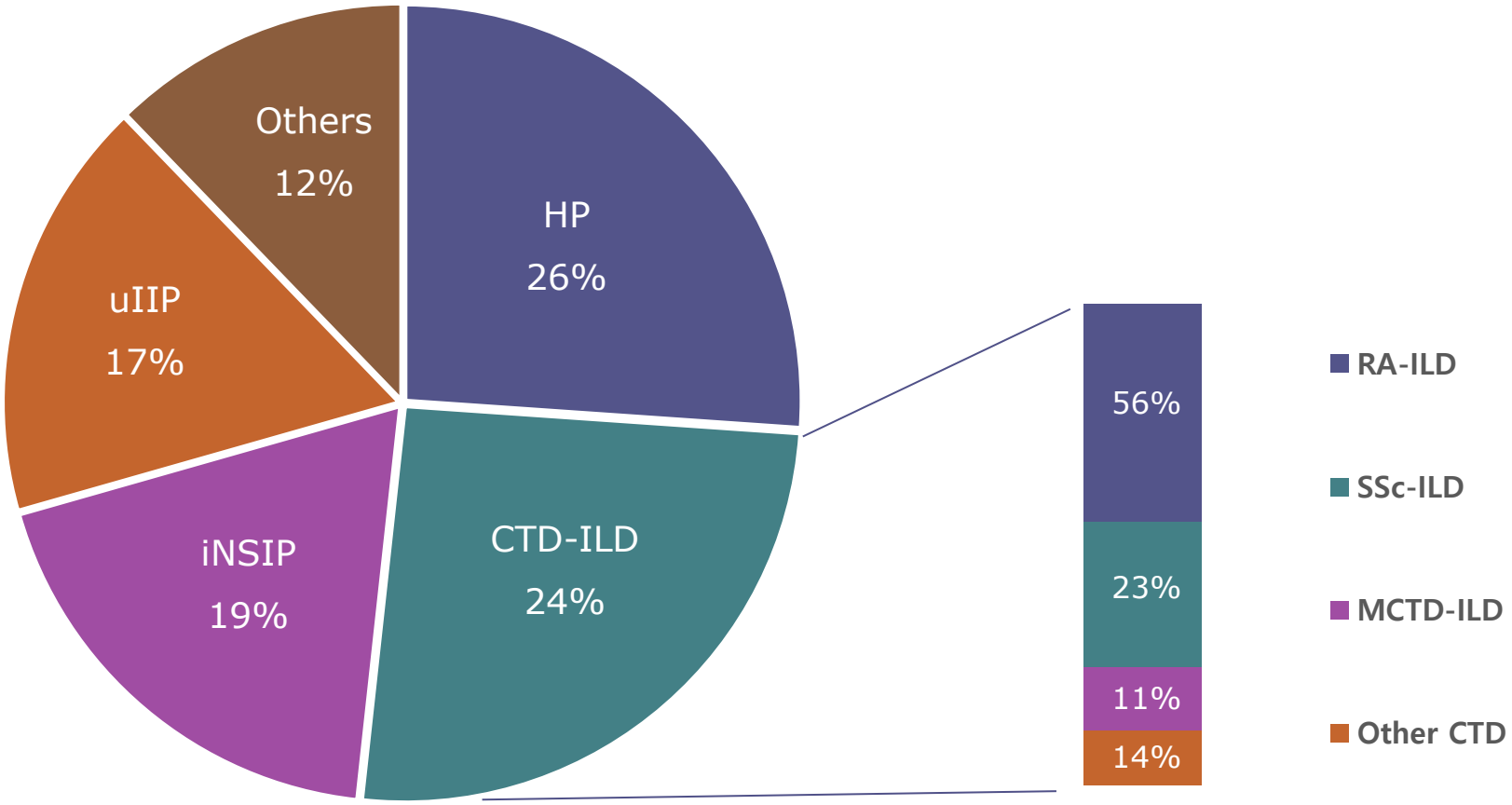




No. of Patients								
Overall population								
Nintedanib	332	326	320	322	314	298	285	265
Placebo	331	325	326	325	320	311	296	274
Patients with UIP-like fibrotic pattern								
Nintedanib	206	203	200	199	193	180	171	160
Placebo	206	202	202	201	197	190	176	162

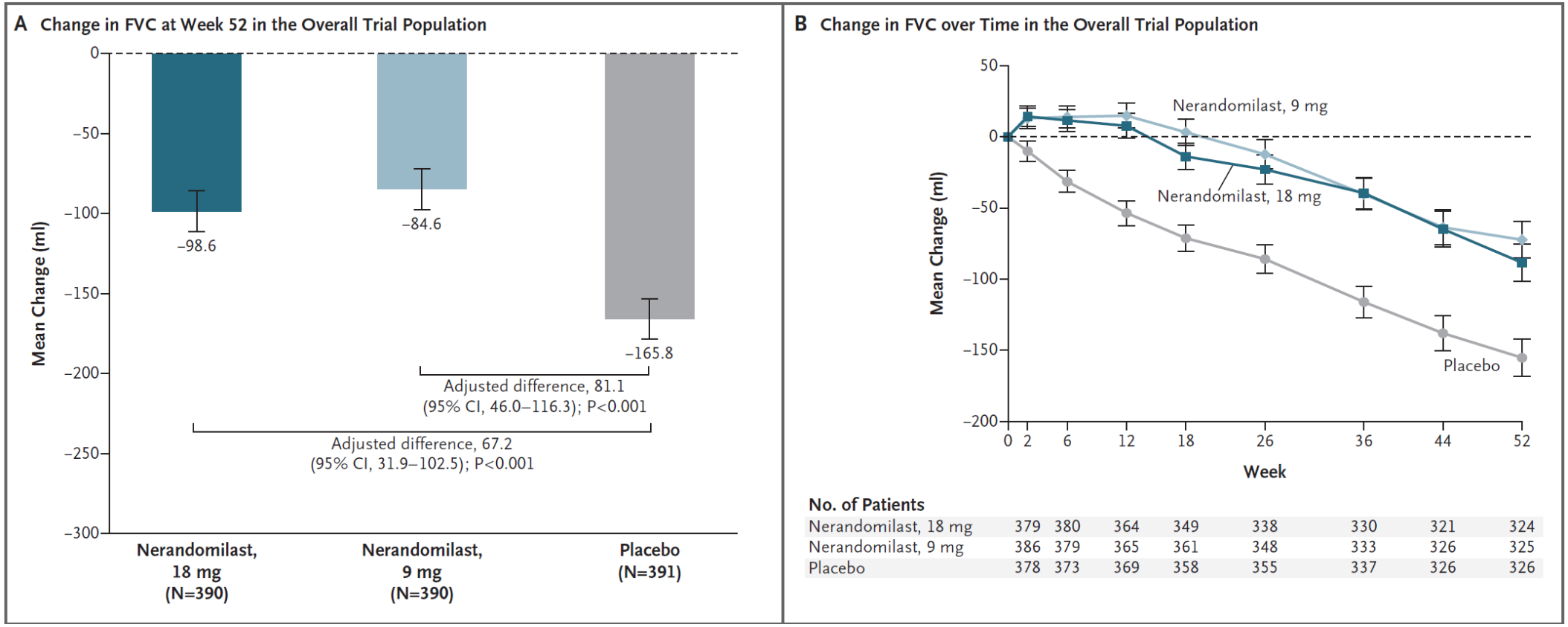
Flaherty KR *et al*. *N Engl J Med*. 2019; 381(18)

Nintedanib for PF-ILD (INBUILD trial)



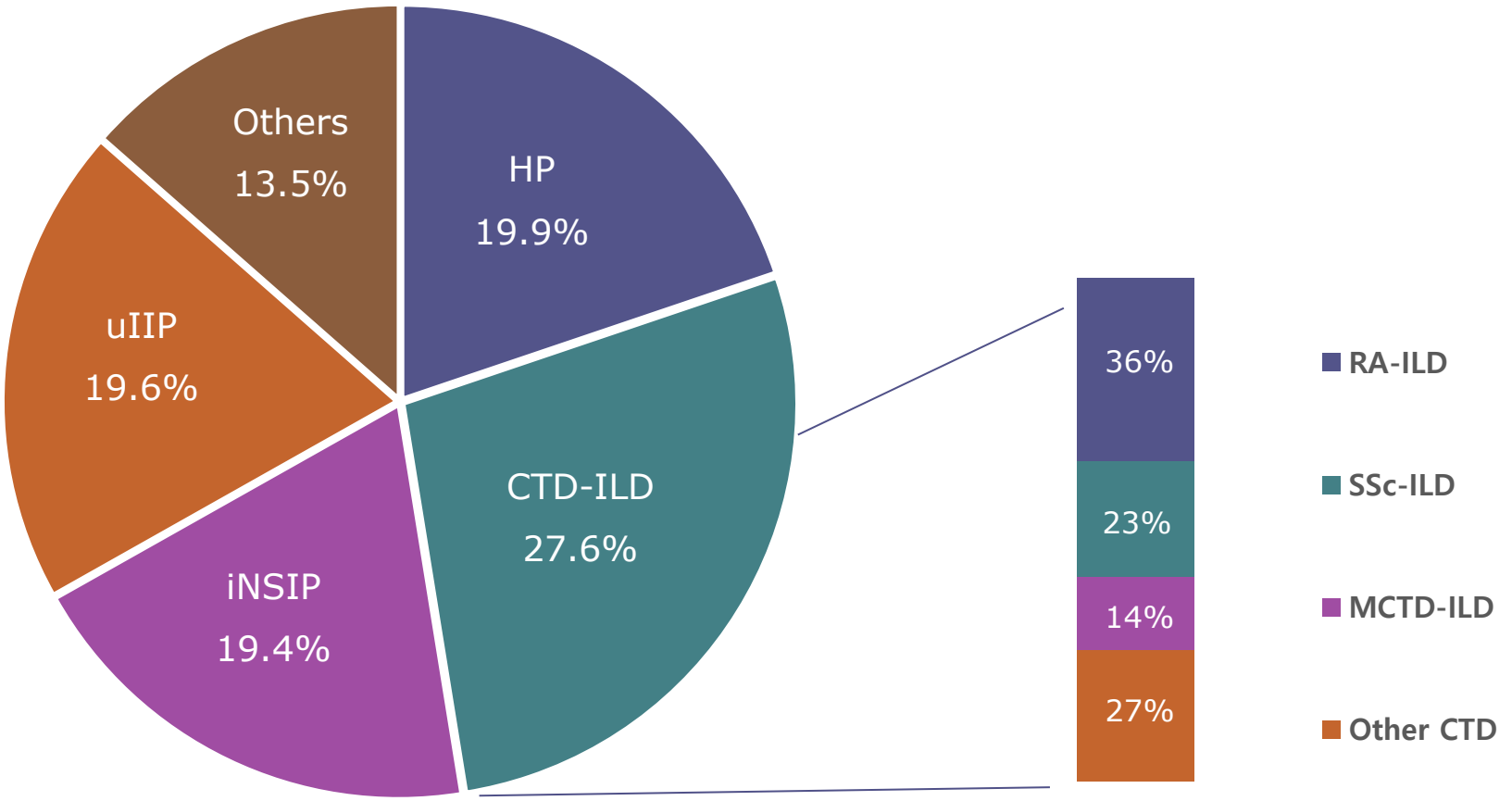
Flaherty KR *et al*. *N Engl J Med*. 2019; 381(18)

Nerandomilast for PPF (FIBRONEER-ILD trial)



Maher TM *et al*. *N Engl J Med*. 2025; 392(22)

Nerandomilast for PPF (FIBRONEER-ILD trial)

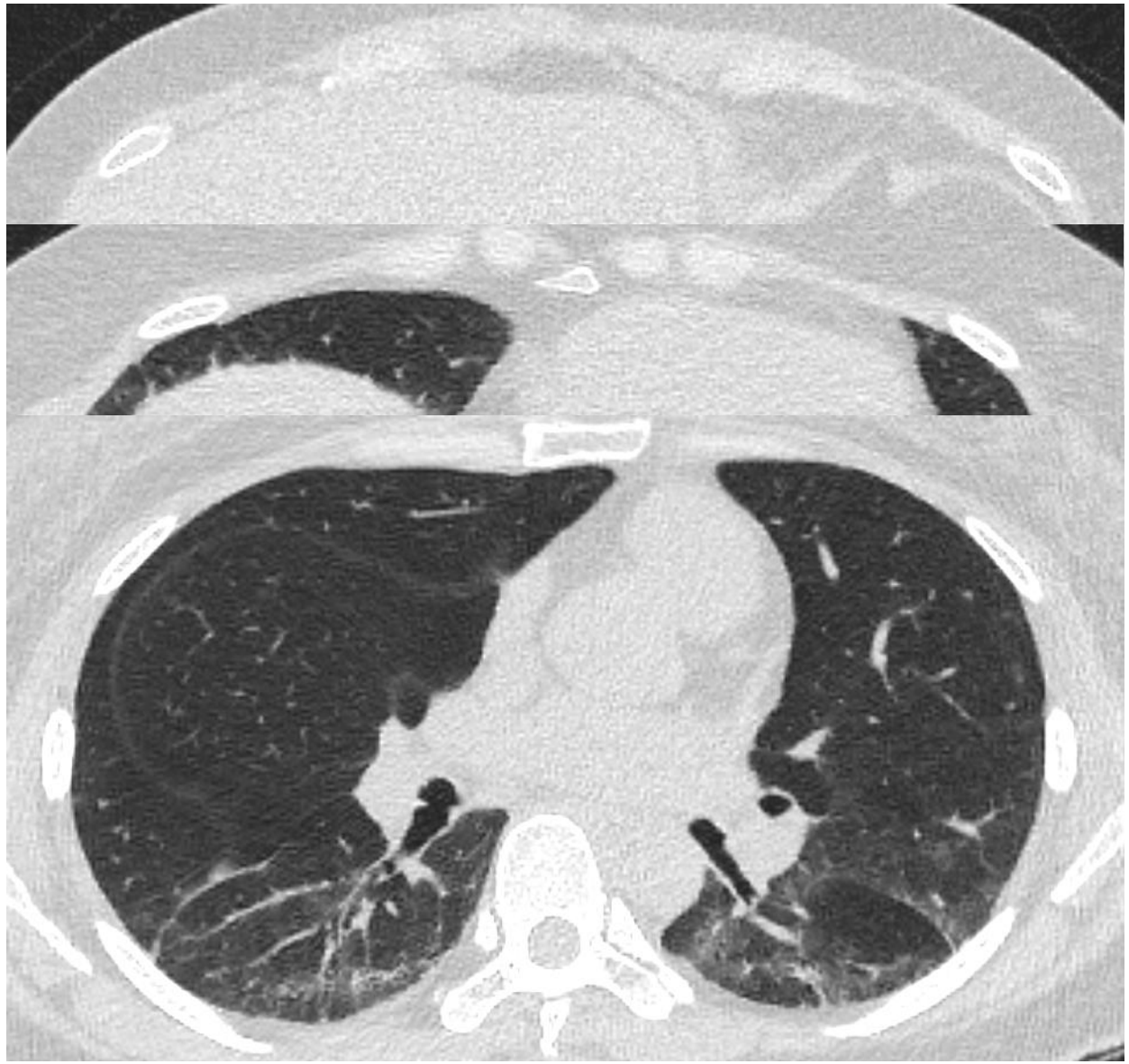


Maher TM *et al*. *N Engl J Med*. 2025; 392(22)

Case (I)

- F/45
- CC: Dyspnea (1.5 years)
- Sx: Cough (3 years)
- Suspected ILD (from another university hospital)

- Previously healthy
- Never smoker



Case (I)

- No medication
- No environmental exposure
- Occupation: 가정 주부
- Pet: None

- Cough/sputum (+/-)
  Rhinorrhea (-)
  Dyspnea (+) mMRC Gr II
  Orthopnea (-)
  Reflux symptoms (-)

- Arthralgia (-) / Morning stiffness (-)
  Dry eye/mouth (-/-)
  Proximal muscle weakness (-)
  Raynaud's ph (-)

- **Serology tests for CTD**
  FANA: 1:40
  Rheumatoid Factor (-) / Anti-CCP Ab (-)
  Anti-SS-A / SS-B Ab (-/-)
  Anti-Scl-70 / centromere Ab (-/-)

Case (I)

- **Surgical lung biopsy**

1. Lung, R) lower lobe, wedge resection
   - Uniform subpleural, interlobular septal fibrosis
2. Lung, R) upper lobe, wedge resection
   - Subpleural, interlobular septal fibrosis with lymphocytic infiltration, ample of normal lungs

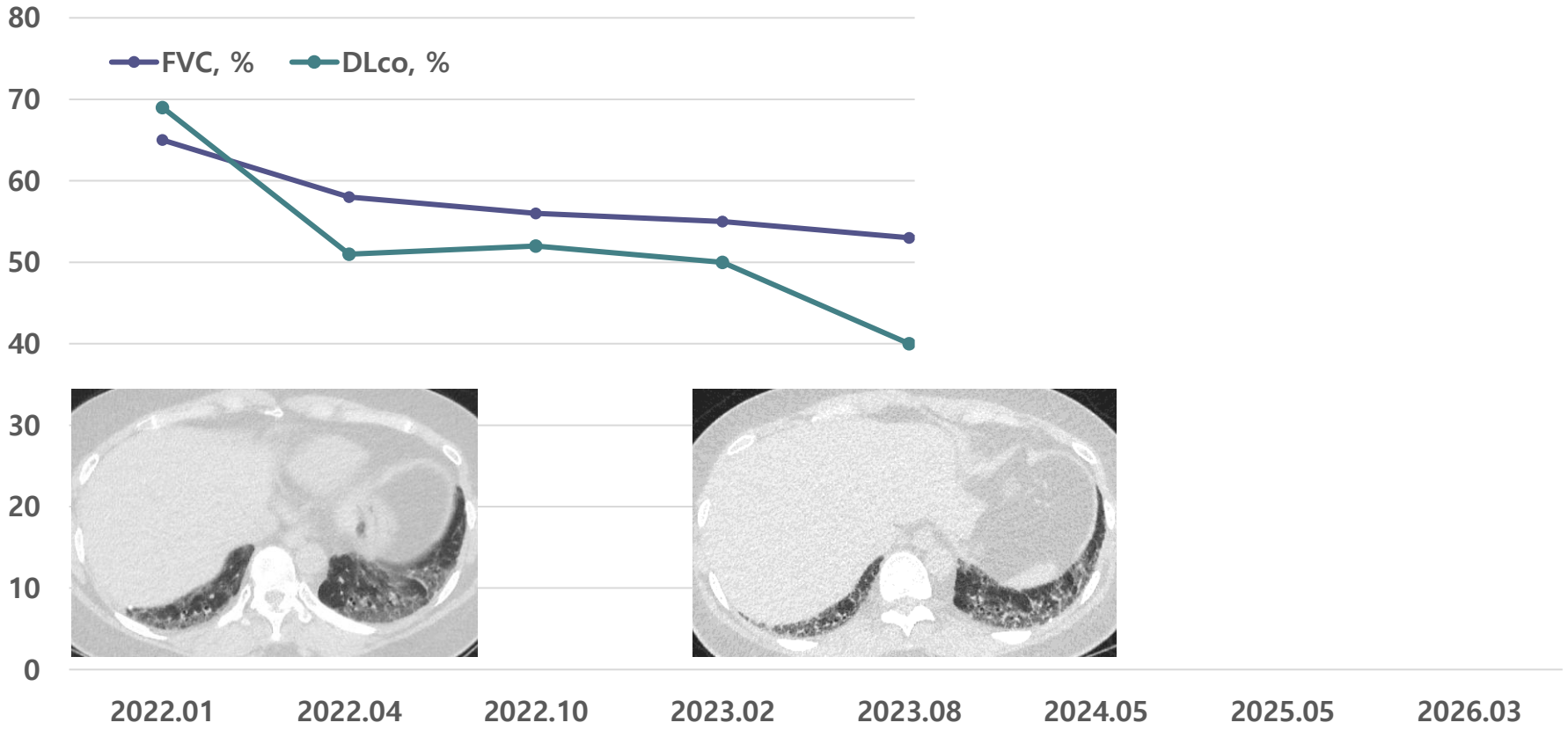
* Temporally uniform fibrosis consistent with fibrotic NSIP

→ Idiopathic fibrotic NSIP

Case (I)

Prednisone (20mg→ tapering)

Azathioprine (25mg)



CONTENTS

Cryptogenic Organizing Pneumonia (COP)

- **Cryptogenic organizing pneumonitis**
  - Patients with histologic intra-alveolar organization without evidence of infective or other etiological agents
  - A short history of severe dyspnea, cough, malaise, weight loss, bilateral radiographic shadowing
  - Dramatic response to prednisolone but relapse occurred
  - Term: cryptogenic organizing pneumonitis (to avoid confusion with post-infective organizing pneumonia)

- **Bronchiolitis obliterans organizing pneumonia (BOOP)**
  - Bronchiolitis obliterans associated with patchy organizing pneumonia without apparent cause or associated disease
  - Polypoid masses of granulation tissue in lumens of small airways, alveolar ducts, and some alveoli
  - Patch densities with a ground-glass appearances
  - Cough or flu-like illness for 4-10 weeks
  - Complete recovery with corticosteroids in 65% (two died from progressive disease)

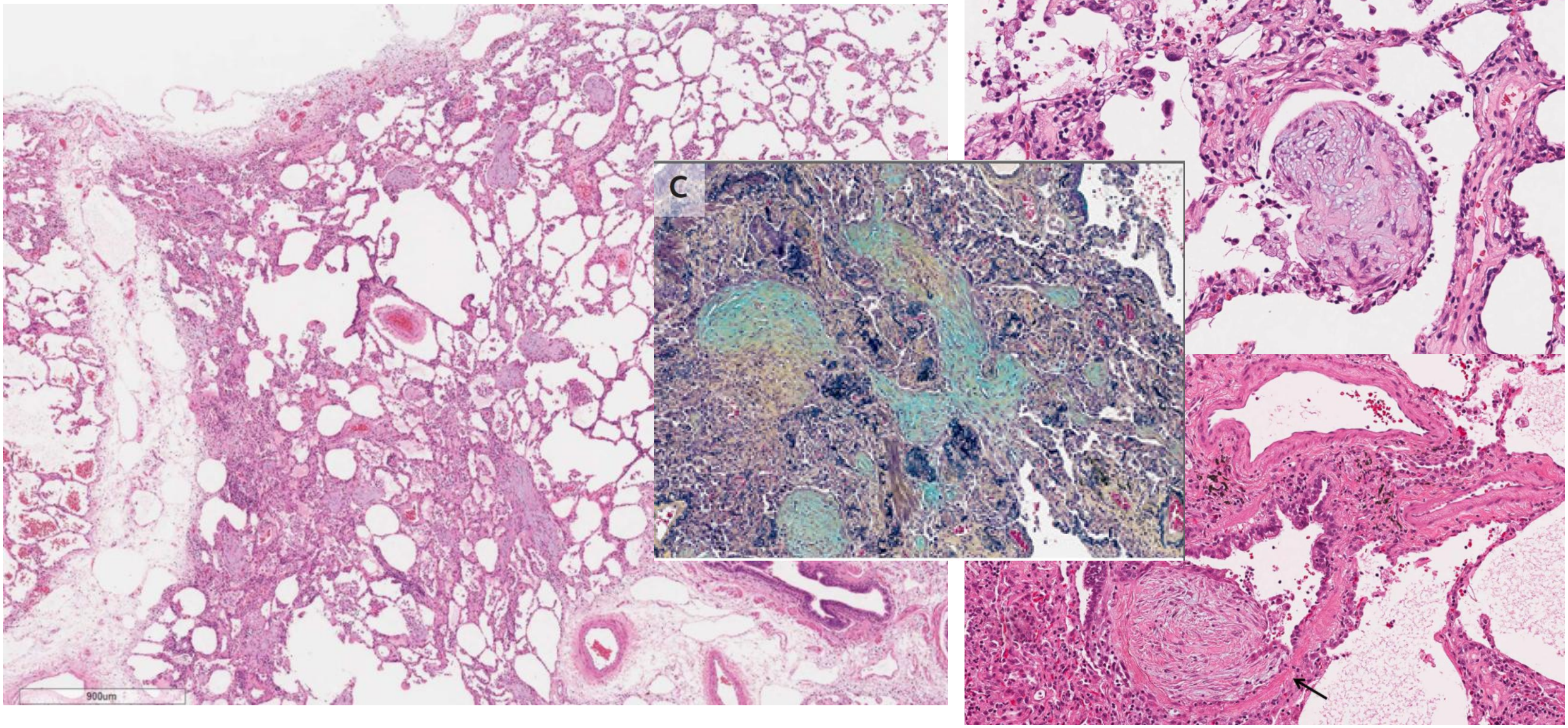
Davidson AG et al. *Q J Med*. 1983;52(207)
Epler GR *et al*. *N Engl J Med*. 1985;312(3)

Pathologic Features of OP

- **Polypoid plugs of loose fibroblastic connective tissue within alveoli and alveolar ducts (Masson's body)**
- **Connection of intraluminal plugs to alveolar walls by narrow stalks and extension from one alveolus to another (through pores of Kohn)**
- **Patchy distribution**
- **Preserved lung architecture (some cases progress to fibrosis)**

Ryerson CJ *et al*. *Eur Respir J*. 2025;66
Talmadge EK *et al*. *N Engl J Med*. 2022;386

Pathologic Features of OP

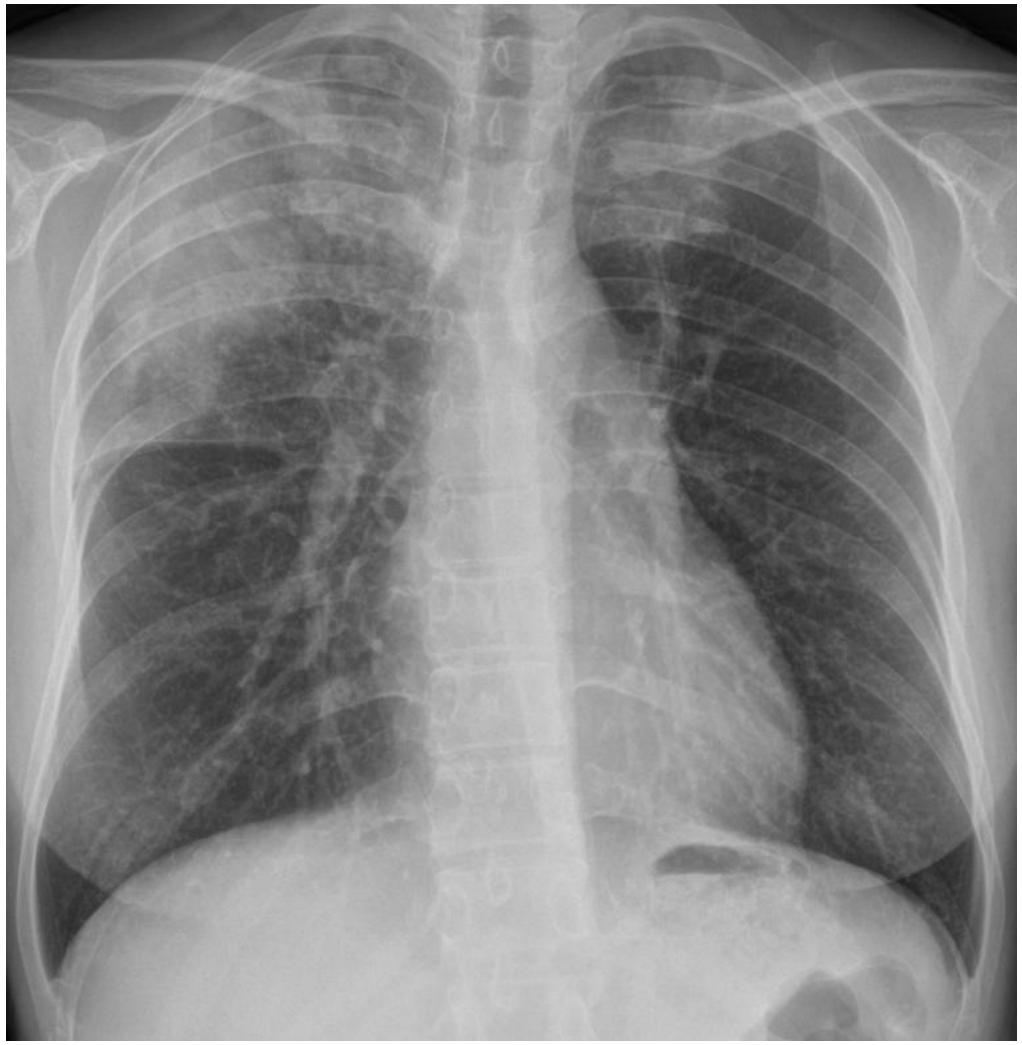


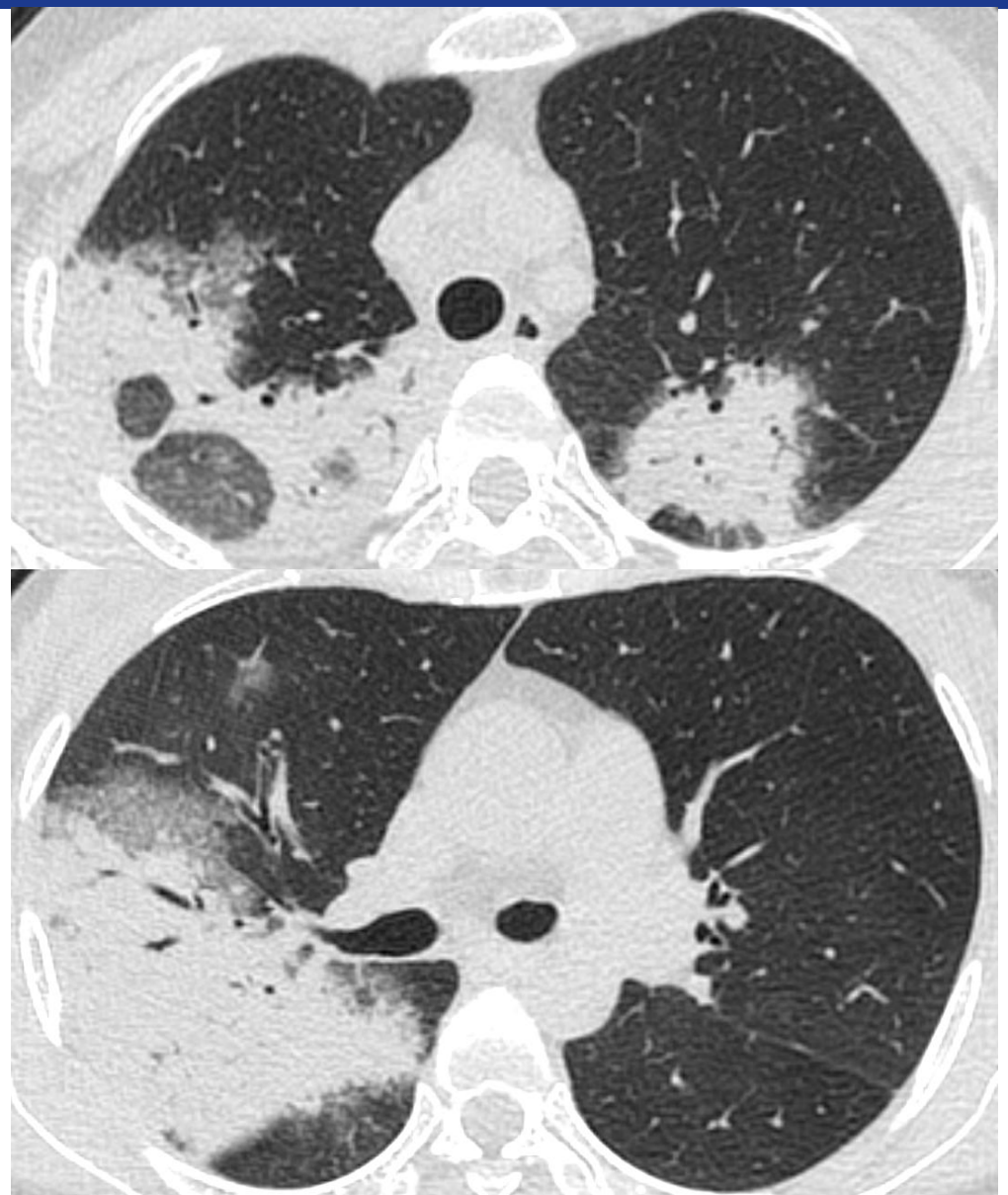
Radiologic Features of OP

- **Subpleural and/or peribronchial distribution**
- **Consolidation or ground-glass opacities**
- **Focal mass or nodules with air-space pattern (occasional)**
- **Reversed halo (Atoll sign)**
- **Can be migratory on serial imaging**
- **Ancillary features (tree-in-bud, cavitations etc.) suggesting underlying etiology (e.g. infection, vasculitis, drug)**

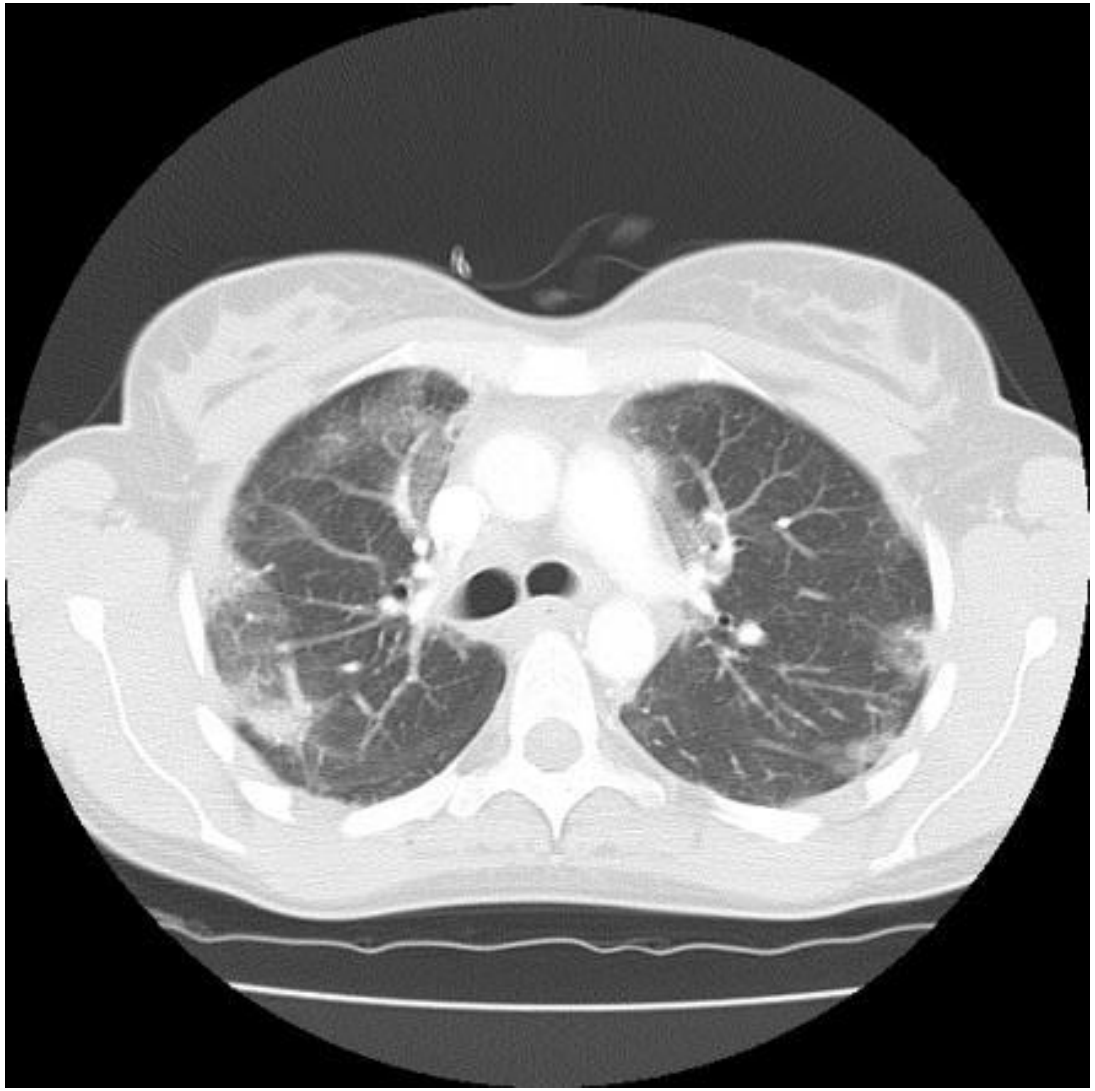
Broaddus V et al. *Murray and Nadel's Textbook of Respiratory Medicine*. 6th ed. 2016

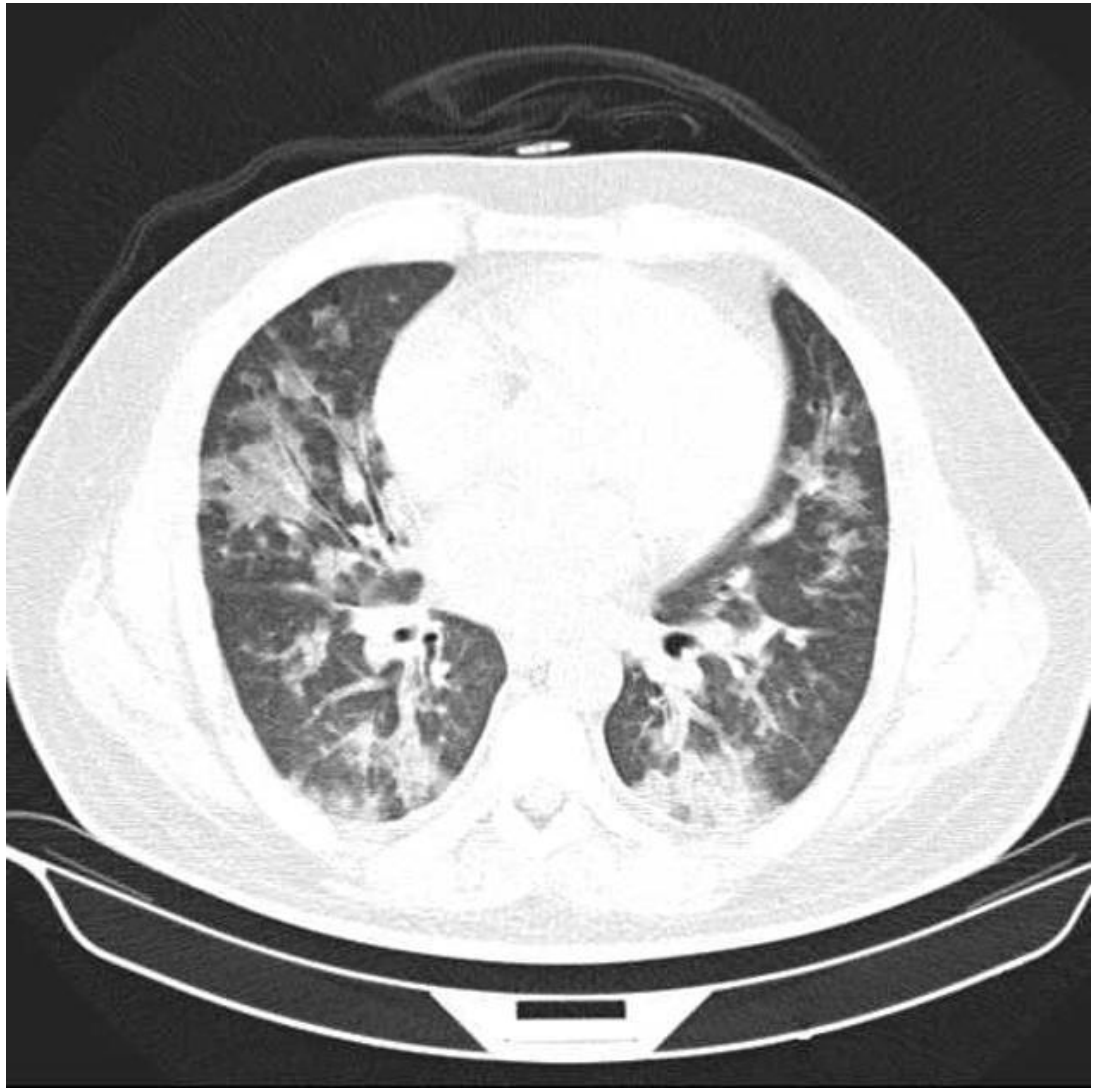
Radiologic Features of OP



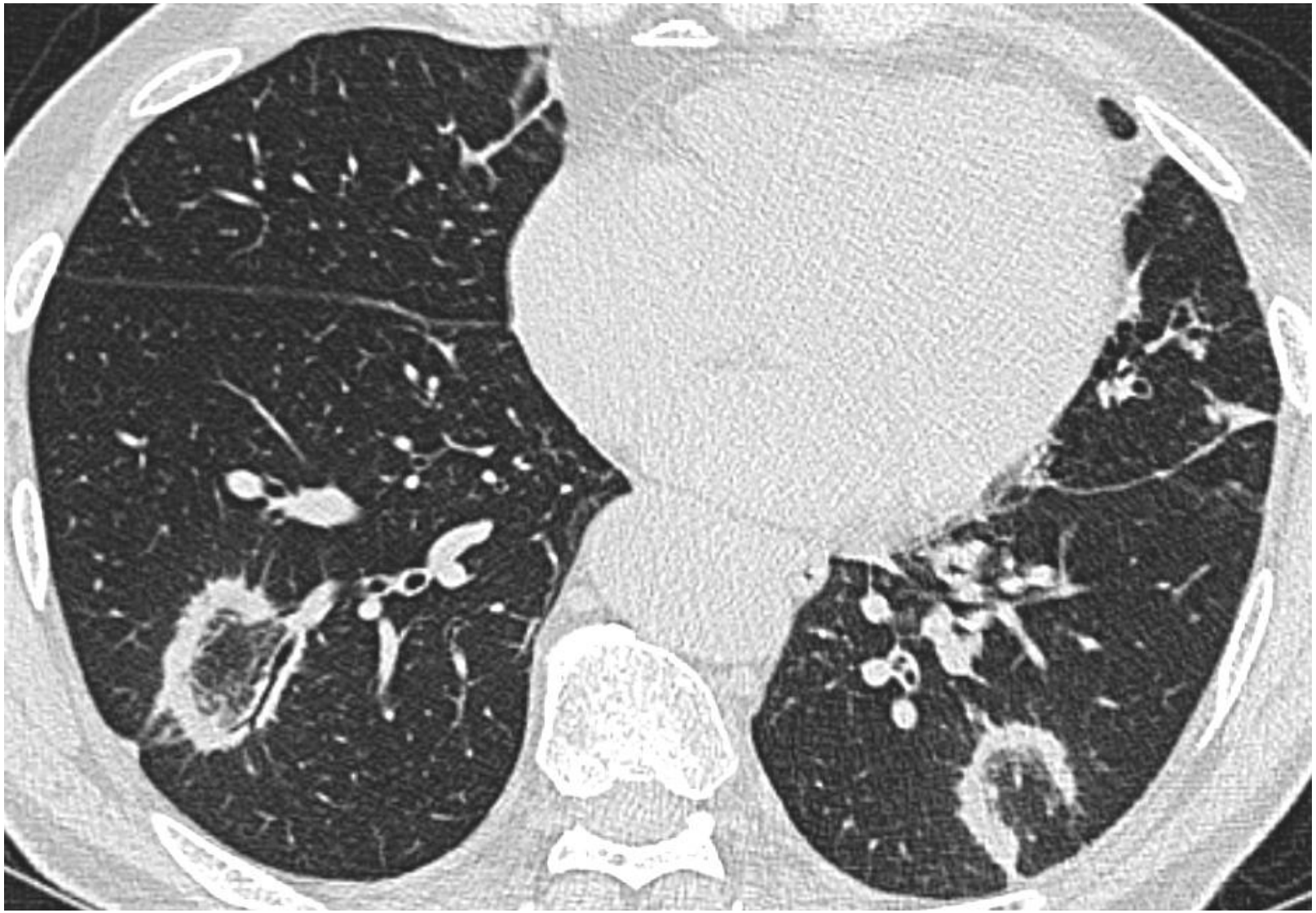


Radiologic Features of OP





Radiologic Features of OP



Etiologies of OP

Table 1. Causes of Secondary Organizing Pneumonia.*

Infection

- Bacteria: *Burkholderia cepacia*, *Chlamydia pneumoniae*, *Coxiella burnetii*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, *Nocardia asteroides*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Staphylococcus aureus*, *Streptococcus pneumoniae*
- Viruses: adenovirus, SARS-CoV-2, cytomegalovirus, herpesvirus, HIV, influenza virus, parainfluenza virus, HHV-7, RSV
- Parasites: *Plasmodium vivax*, *Dirofilaria immitis*
- Fungi: aspergillus, *Cryptococcus neoformans*, *Penicillium janthinellum*, *Pneumocystis jirovecii*

Drugs: amiodarone, nitrofurantoin, bleomycin, methotrexate, freebase cocaine

Connective-tissue disease: rheumatoid arthritis, Sjögren's syndrome, polymyositis or dermatomyositis, systemic sclerosis, antisynthetase syndrome, vasculitis

Hematologic cancer: leukemia, lymphoma

Transplantation: lung, liver, bone marrow

Radiation injury from breast cancer treatment

Common variable immunodeficiency

Association with other interstitial lung diseases: eosinophilic pneumonia, hypersensitivity pneumonitis, organizing diffuse alveolar damage, usual interstitial pneumonia

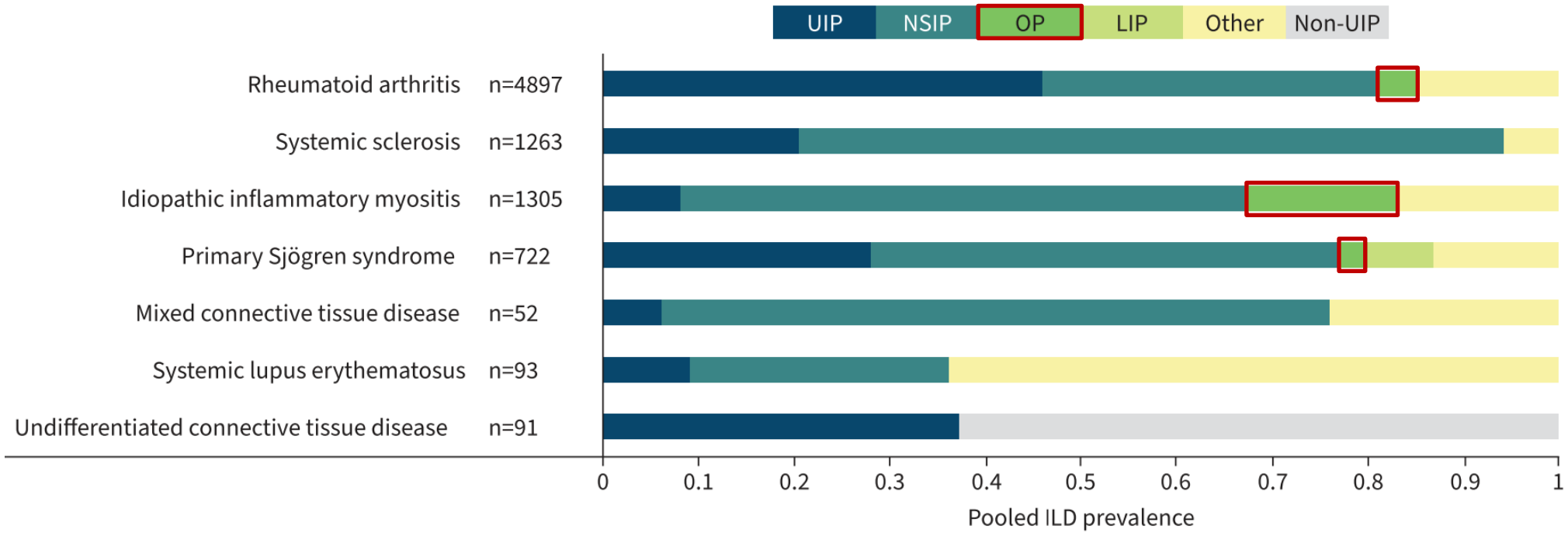
Inflammatory bowel disease: Crohn's disease, ulcerative colitis

Miscellaneous causes

- Reaction to other lung processes: abscess, diffuse alveolar hemorrhage, airway obstruction
- Inhalation injury: aspiration, aerosolized textile dye, mustard gas

Talmadge EK *et al*. *N Engl J Med*. 2022;386

HRCR Patterns of CTD-ILD



Joy GM *et al*. *Eur Respir Rev*. 2023;32

Classification of ILDs

TABLE 1 Morphological patterns of interstitial and alveolar filling disorders and associated clinical-radiological-pathological diagnoses. Secondary aetiologies are listed before primary/idiopathic aetiologies to emphasise the importance of excluding an underlying cause before considering a diagnosis to be primary/idiopathic

Morphological patterns by pathology and imaging	Major clinical-radiological-pathological diagnoses	
	Secondary	Primary/idiopathic
Interstitial patterns		
UIP	Secondary UIP (*e.g.* CTD, HP, medications)	IPF (idiopathic UIP)
NSIP	Secondary NSIP (*e.g.* CTD >>> HP, medications)	Idiopathic NSIP
BIP[#]	Secondary BIP (*e.g.* HP >>> CTD, aspiration, inhalational exposures, medications)	Idiopathic BIP (provisional diagnosis[#])
DAD	Secondary DAD (multiple causes)	Idiopathic DAD (acute interstitial pneumonia)
PPFE	Secondary PPFE (*e.g.* IPF, CTD, HP, medications, radiation, transplant (restrictive allograft syndrome, pulmonary infection (post-tuberculosis), occupational)	Idiopathic PPFE
LIP	Secondary LIP (*e.g.* CTD, immune deficiency)	Idiopathic LIP
Alveolar filling patterns		
Organising pneumonia	Secondary organising pneumonia (*e.g.* CTD, post-infectious, medications, aspiration)	Cryptogenic organising pneumonia (idiopathic organising pneumonia)
RB-ILD	Secondary RB-ILD (*e.g.* smoking >>> CTD, medications, aspiration, hereditary)	Idiopathic RB-ILD
AMP[¶]	Secondary AMP (*e.g.* smoking >>> CTD, medications, aspiration, hereditary	Idiopathic AMP
Rare alveolar filling disorders	*e.g.* Acute and chronic eosinophilic pneumonia, pulmonary alveolar proteinosis, lipoid pneumonia (supplementary table S1)	
Other		
Combined pattern	Multiple combinations (*e.g.* NSIP + organising pneumonia, UIP + PPFE)	
Unclassifiable pattern	Unclassifiable ILD (multiple undefined patterns)	

UIP: usual interstitial pneumonia; NSIP: nonspecific interstitial pneumonia; BIP: bronchiolocentric interstitial pneumonia; DAD: diffuse alveolar damage; PPFE: pleuroparenchymal fibroelastosis; LIP: lymphoid interstitial pneumonia; RB-ILD: respiratory bronchiolitis-interstitial lung disease; AMP: alveolar macrophage pneumonia; CTD: connective tissue disease; HP: hypersensitivity pneumonitis; IPF: idiopathic pulmonary fibrosis. [#]: the committee voted 29 to four (88% to 12%) in favour of including BIP as a pattern and 27 to six (82% to 18%) in favour of introducing idiopathic BIP as a provisional multidisciplinary diagnosis; [¶]: formerly referred to as desquamative interstitial pneumonia.

Ryerson CJ *et al*. *Eur Respir J*. 2025;66

Diagnosis of COP (Korean Guidelines)

4. 진단

COP를 진단하기 위해서는 비슷한 임상양상을 보이는 다른 질환과의 감별 및 기질화폐렴을 유발할 수 있는 원인을 배제하는 것이 중요하다(표 1)[15,16]. 감별 진단으로 가장 흔하고 중요한 질환은 지역사회획득성폐렴이며 항생제 치료에 대한 반응이 없을 경우 COP를 의심해볼 수 있다. 영상학적으로 변화가 있는 다발성의 폐경화 소견이 보일 경우 과민성폐렴, 호산구성폐렴, 폐포 출혈 및 혈관염을 감별해야 하고, 공기 기관지음영(air bronchogram)을 동반한 결절성 폐경화 소견이 보일 경우 폐 림프종과 침윤성 점액성선암종(invasive mucinous adenocarcinoma)의 가능성을 염두에 두어야 한다. 기질화폐렴과 비특이간질성폐렴이 동시에 발생하거나 순차적으로 발현될 경우 기저 원인(예: 결체조직질환, 항합성효소 증후군, 과민성폐렴 또는 약물 독성)에 대한 감별이 필요하며 이런 경우는 특히 쇼그렌증후군, 다발성근염/피부근염 및 기타 류마티스 질환에서 발생할 수 있다. 기질화폐렴에 비특이간질성폐렴 양상이 공존하는 경우 질병 진행 위험이 증가한다는 보고가 있다[23].

COP는 조직검사 없이 임상적으로 진단 후 치료할 수 있지만, 진단이 모호한 경우 확진을 위한 폐 조직검사가 필요하며 이러한 경우 다학제 토의를 통해 폐생검 여부를 결정해야 한다(그림 1). 폐생검의 조직학적 소견을 통해 이차성 기질화폐렴(예: 흡인, 혈관염 또는 감염)의 원인을 알 수 있는 경우도 있다. 조직검사 없이 치료하는 경우 임상 경과와 추적 관찰 소견이 COP와 일치하지 않는 경우 진단을 재평가해야 하며 이 때 조직검사가 필요할 수도 있다[15,16].

간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)

Diagnosis of COP (ATS/ERS Guidelines)

- **Pathologic confirmation of OP**
  - COP can often be managed without histopathological confirmation
  - Decision to perform a biopsy should be guided by MDD

- **Identification of OP**
  - OP can be identified on a transbronchial forceps biopsy, cryobiopsy, or transthoracic needle biopsy
  - OP can also be a nonspecific reaction adjacent to unsampled lesions such as vasculitis, neoplasm, abscess, or infarct.

    → Careful clinical and radiological correlation is critical, particularly with small biopsies to ensure the presentation is consistent with OP

Ryerson CJ *et al*. *Eur Respir J*. 2025;66

Treatment of COP

- **권고사항**
  - 특발성기질화폐렴(COP) 치료로 스테로이드 사용을 권고한다. (근거수준: 전문가 합의, 권고등급: 강하게 권고)

    투표결과 강하게 권고 5/6, 조건부 권고 1/6
  - 특발성기질화폐렴(COP) 환자에서 스테로이드 단독 치료에도 진행하거나 재발하는 경우 면역억제제를 사용할 수 있다. (근거수준: 전문가 합의, 권고등급: 조건부 권고)

    투표결과 조건부 권고 6/6

간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)

Treatment of COP

- **Watchful waiting**
  - ✓ Spontaneous improvement: Mild disease (~10%)
  - ✓ Severity (clinical, radiological, physiological) and rapidity of progression

- **Corticosteroid**
  - ✓ Optimal dose and duration: Not known (retrospective observational studies)
  - ✓ Initial: PD 0.5-1.0 mg/kg (maximum 60 mg/d qd) for 2-4 weeks → slow tapering over 4-6 months
  - ✓ Fulminant: Methylprednisolone pulse (500-1000mg/d IV for 3-5 days)
  - ✓ Good response to corticosteroid (clinical improvement within 1-3 days)
  - ✓ Pneumocystis prophylaxis (PD ≥ 20mg/d)

간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)

Treatment of COP

- **Proposed regimen for typical COP**

Step	Duration (weeks)	Doses of Prednisone
Treatment of initial episode		
1	4	0.75 mg/kg/d
2	4	0.5 mg/kg/d
3	4	20 mg/d
4	6	10 mg/d
5	6	5 mg/d

Cottin V, Cordier J. *Semin Respir Crit Care Med.* 2012;33(5)

Treatment of COP

- **Immunosuppressants**
  - ✓ Immunoglobulin, rituximab, cyclophosphamide, mycophenolic acid, azathioprine
  - ✓ No solid evidence

- **Macrolide**
  - ✓ Anti-inflammatory properties of macrolides
  - ✓ Erythromycin, azithromycin, clarithromycin
  - ✓ Usually added when refractory to or dependent on steroid
  - ✓ Adjuvant or alternative to oral corticosteroid
  - ✓ Duration: 3-6 months (longer in some cases)

Talmadge EK et al. *N Engl J Med.* 2022;386(11)
간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)
Stover DE, Mangino D. *Chest*. 2005;128(5)

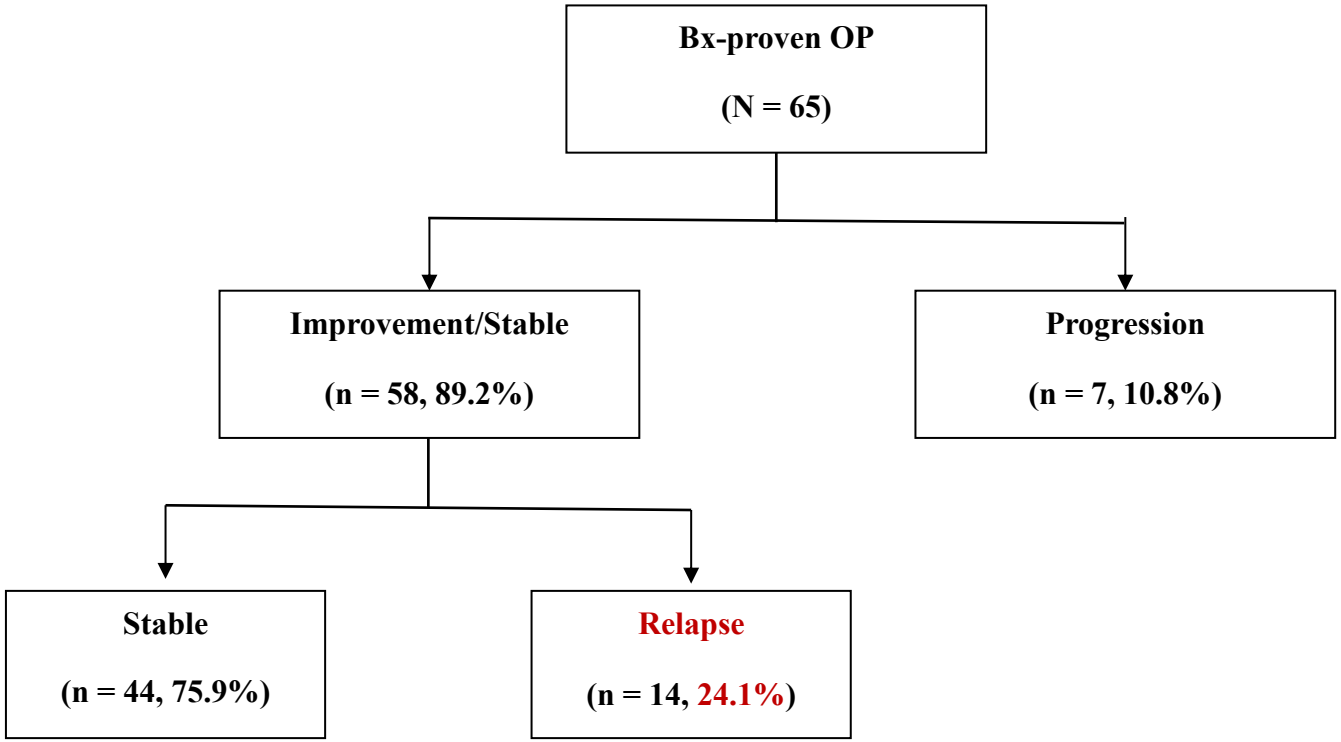
Prognosis of COP

- **Prognosis**
  - ✓ Favorable response to treatment
  - ✓ 5-yr survival rate > 90% (most death not related to COP)
- **Relapse**
  - ✓ Relapse: 13%~58% (more than one relapse in 20%)
  - ✓ Risk factors: Severity (at presentation), hypoxemia, radiographic extent, treatment delay etc.
  - ✓ Good response to re-treatment with corticosteroid

Treatment of relapse		
1	12	20 mg/d
2	6	10 mg/d
3	6	5 mg/d

Talmadge EK et al. *N Engl J Med.* 2022;386(11)
간질성폐질환(ILD) 임상진료지침. 1차 개정판 (2023)
Stover DE, Mangino D. *Chest*. 2005;128(5)

Treatment Outcomes of Bx-proven COP (SMC)

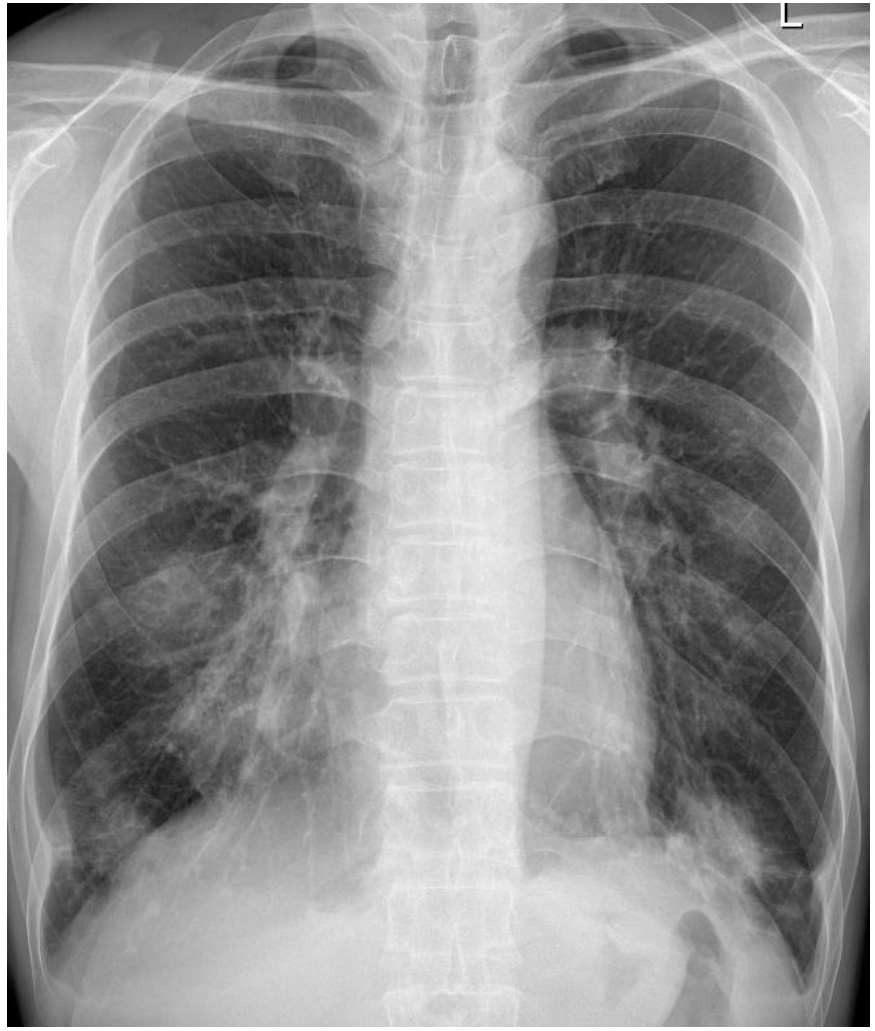


SMC Unpublished data

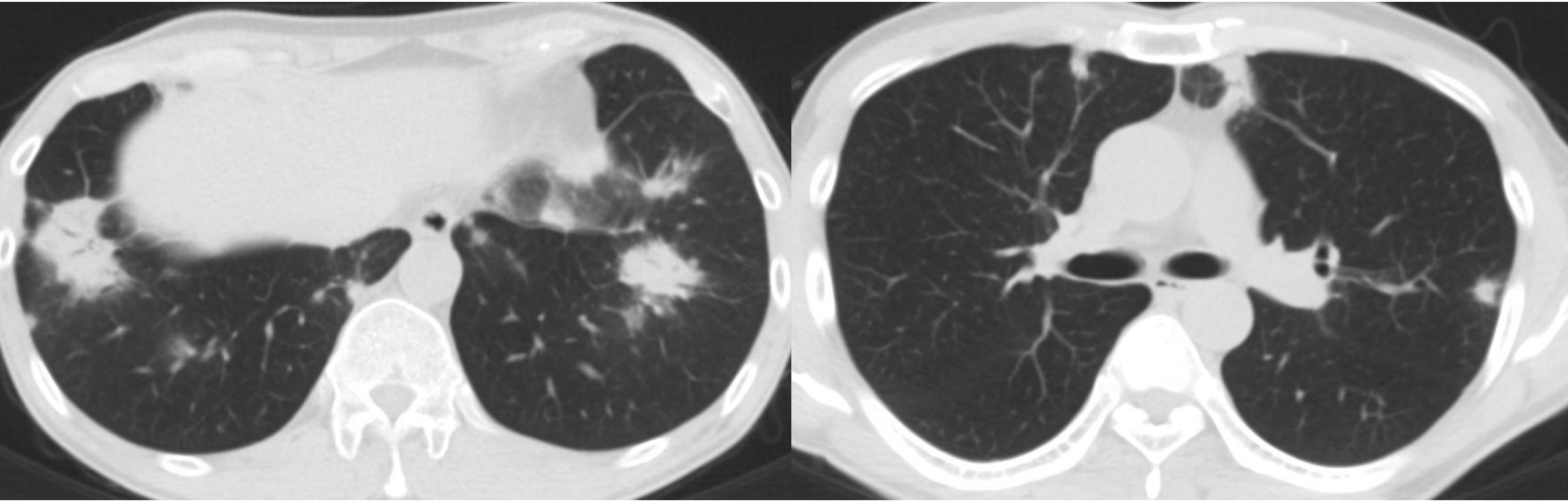
Case (II)

- M/55
- CC: Cough (3 weeks)
- Sx: Mild febrile sense, mild dyspnea
- Treated with antibiotics from a local clinic for 1 week

- Known hypertension, dyslipidemia, gout
- Ex-smoker (2 YA quit, 20 PY)



Case (II)



Case (II)

- Amlodipine, thiazide
- No environmental exposure
- Occupation: 사무직 직원
- Herbal medication (3 months ago)

- Cough/sputum/Rhinorrhea (+/-/-)

  Febrile sense (+)

  Dyspnea (+) mMRC Gr II

  Weakness/paresthesia (-/-)

  Skin lesion (-)

- Arthralgia (-) / Morning stiffness (-)

  Dry eye/mouth (-/-)

  Skin rash (-)

- **Serology tests for CTD**

  FANA: 1:40

  Rheumatoid Factor (-) / Anti-CCP Ab (-)

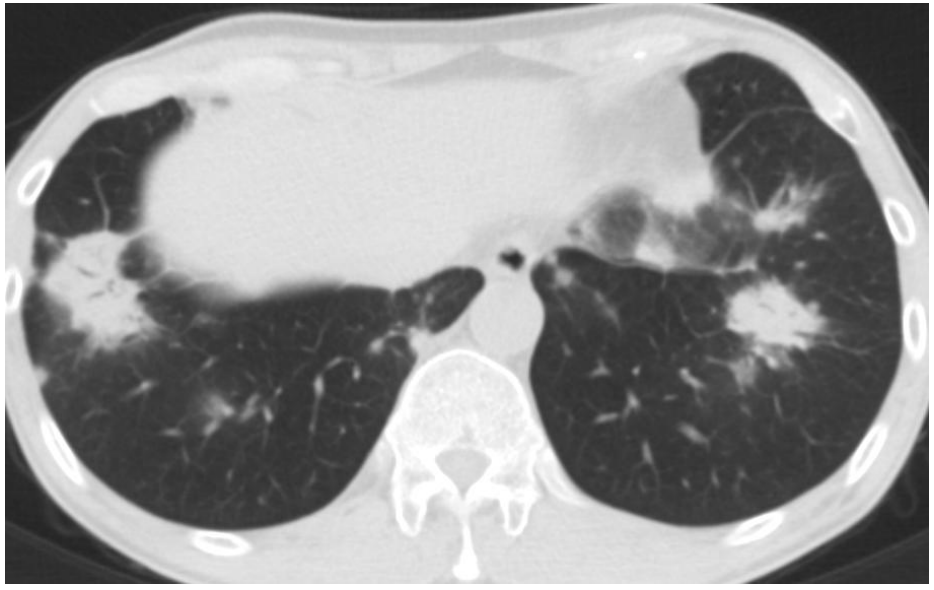
  Anti-ds-DNA (-)

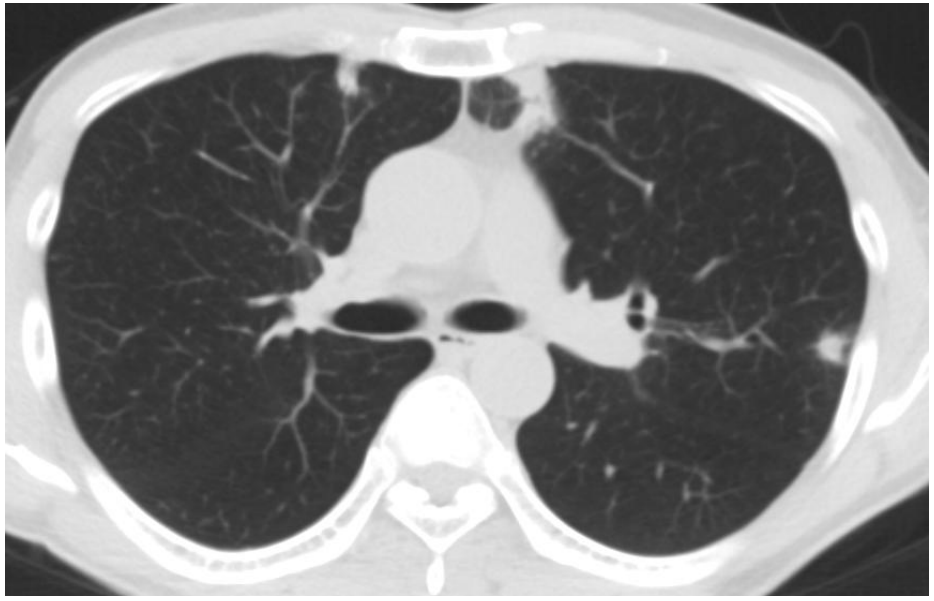
  ANCA (Atypical P, 1:40)

  Anti-Jo-1 Ab (-)

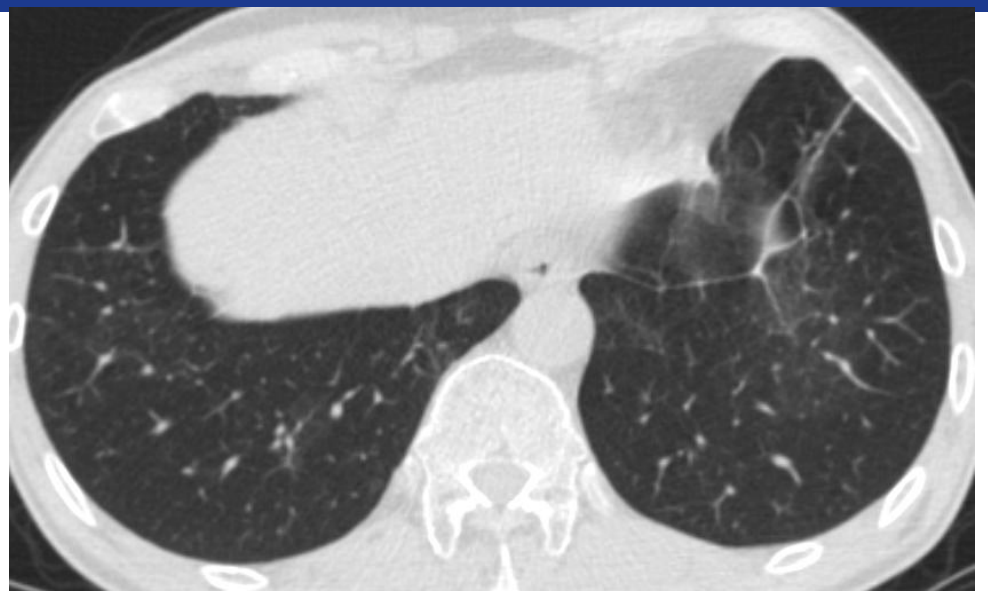
TBLB: Organizing pneumonia → Cryptogenic organizing pneumonia

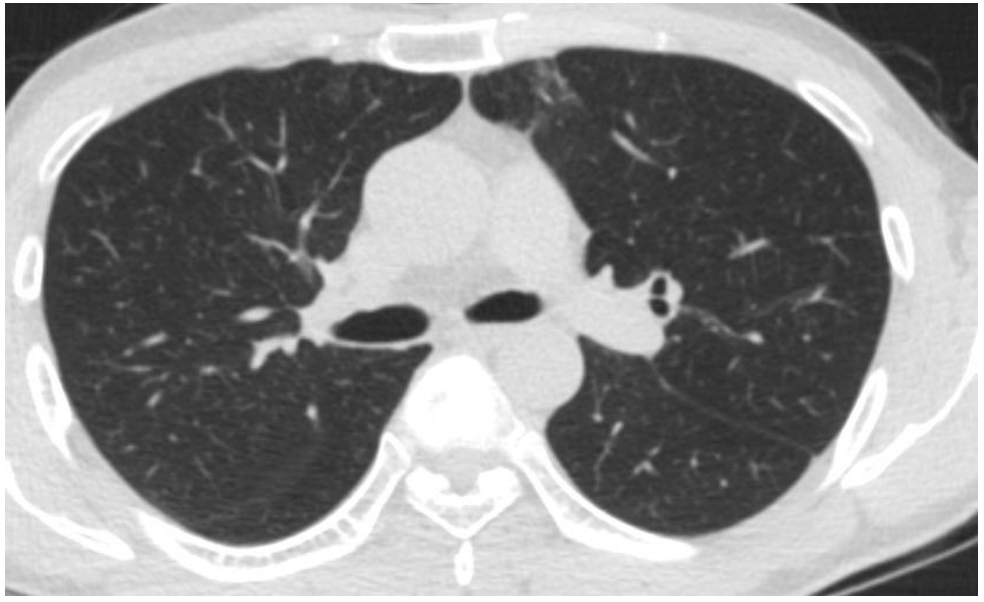
Case (II)



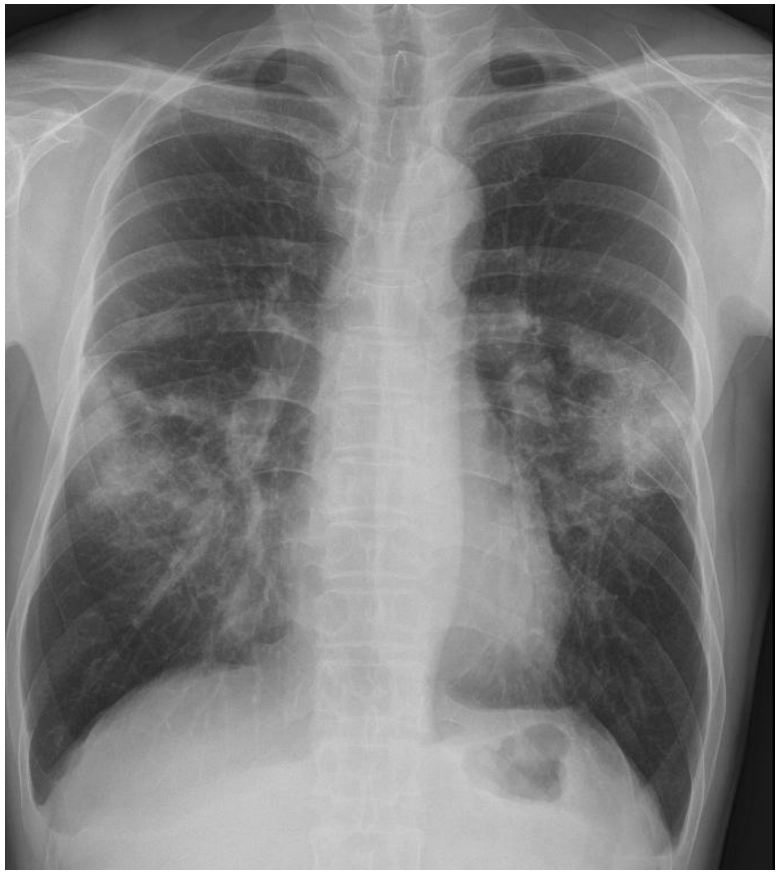


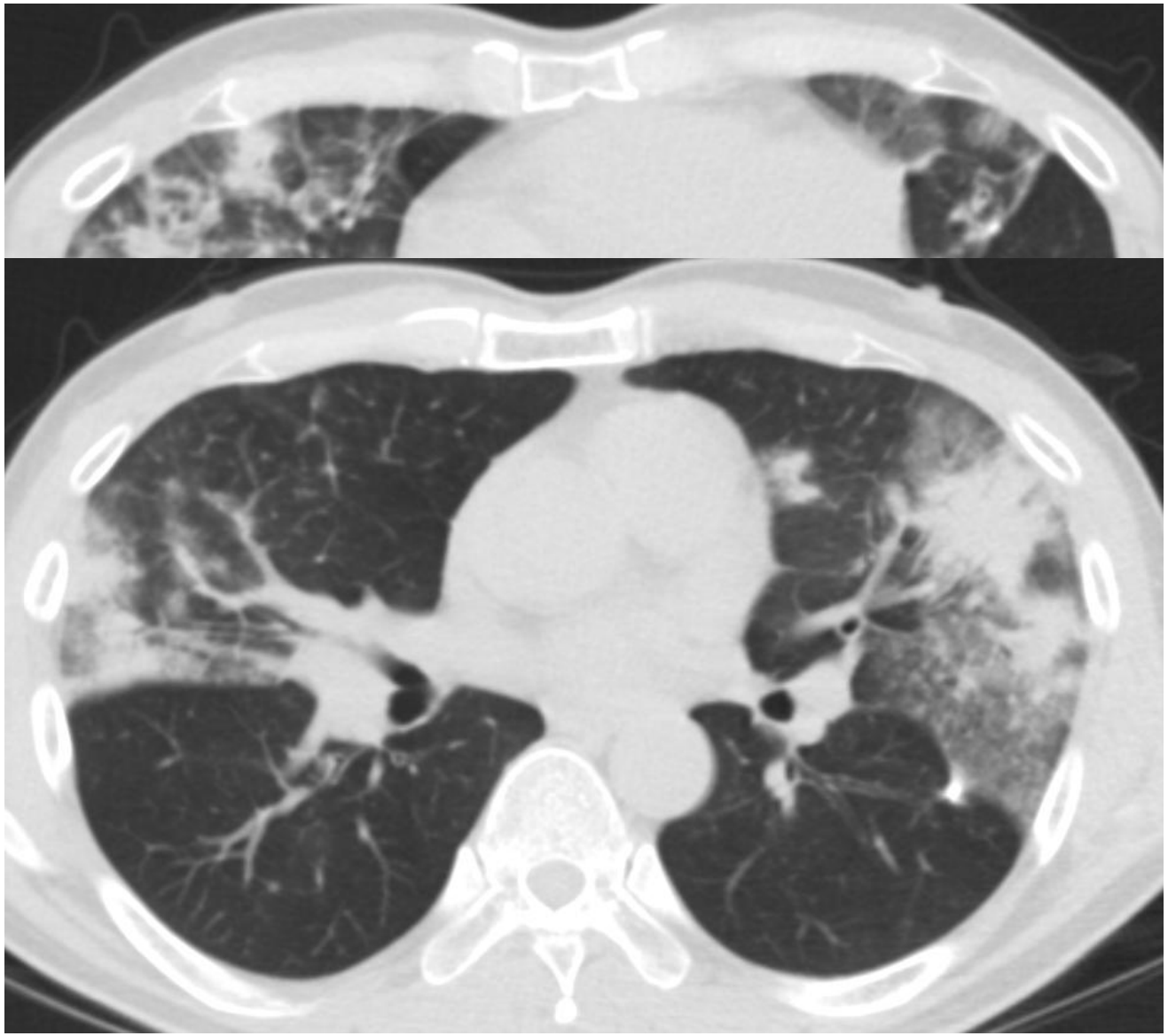
Steroid Tx for 6 mo



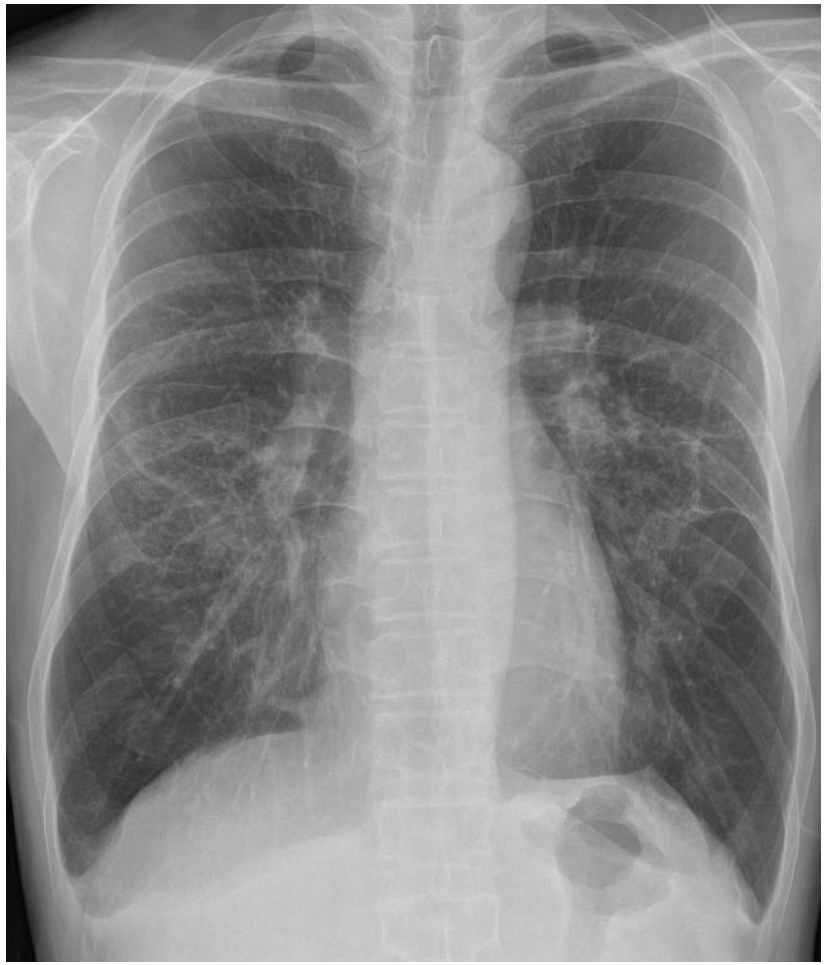


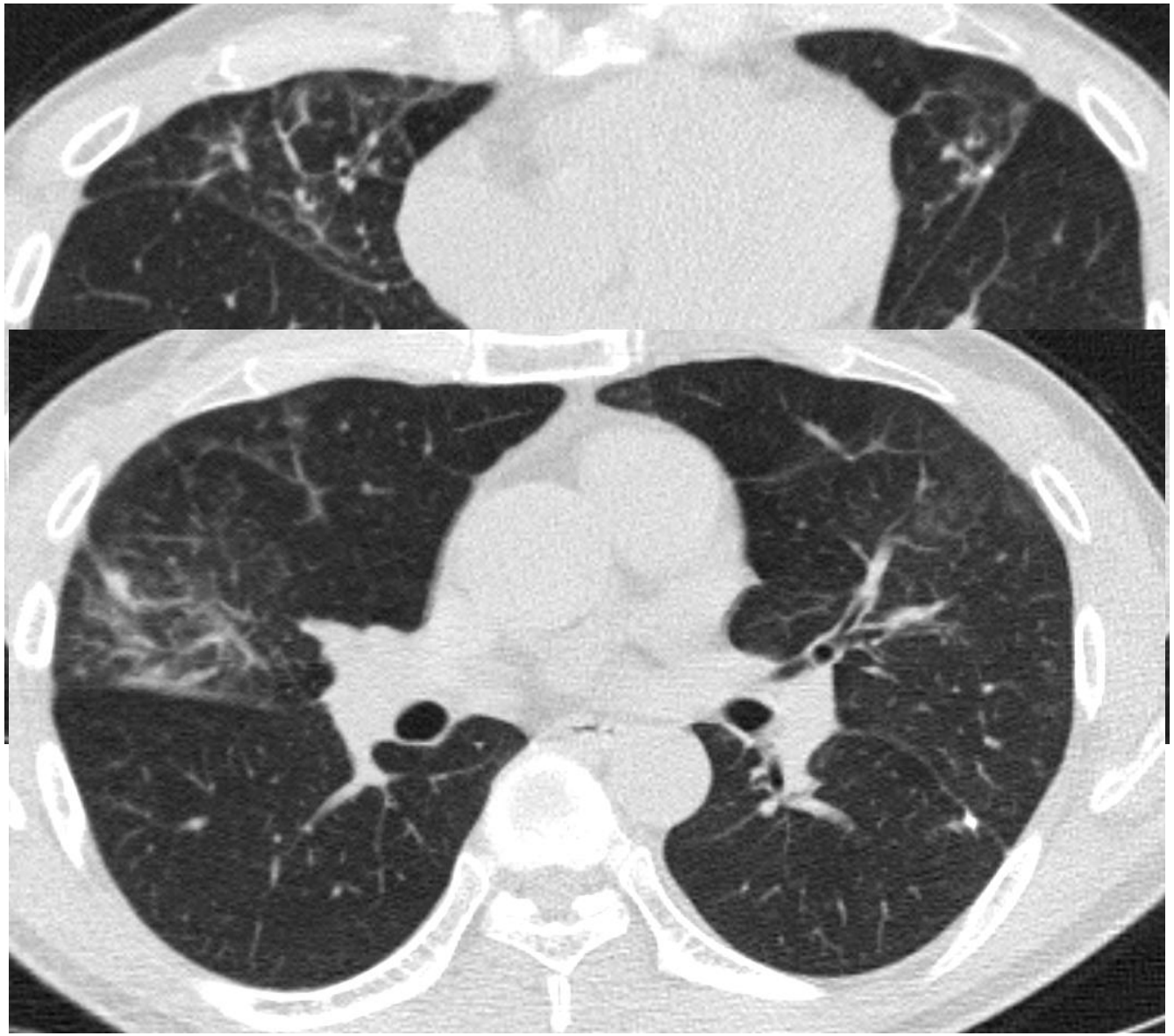
Case (II)





Case (II)





Takeaway

Nonspecific interstitial pneumonia (NSIP)

- Uniform inflammation and fibrosis of interstitium / Bibasilar GGO and reticulation, traction BE
- Various etiologies (CTD, HP, drugs etc.)
- Pathologic confirmation may be necessary (especially in idiopathic NSIP)
- Steroid ± immunosuppressants (optimal regimen or duration is not yet known)
- Antifibrotics (nintedanib or nerandomilast) in PPF

Cryptogenic organizing pneumonia (COP)

- Connective tissue plugs in alveolus and ducts / patchy consolidation and GGOs
- Various etiologies (post-infectious, CTDs, drugs, radiation etc.) / Exclusion of infection
- Treatment with corticosteroid (good response)
- Relapse may occur (severe disease, hypoxemia, large extent)