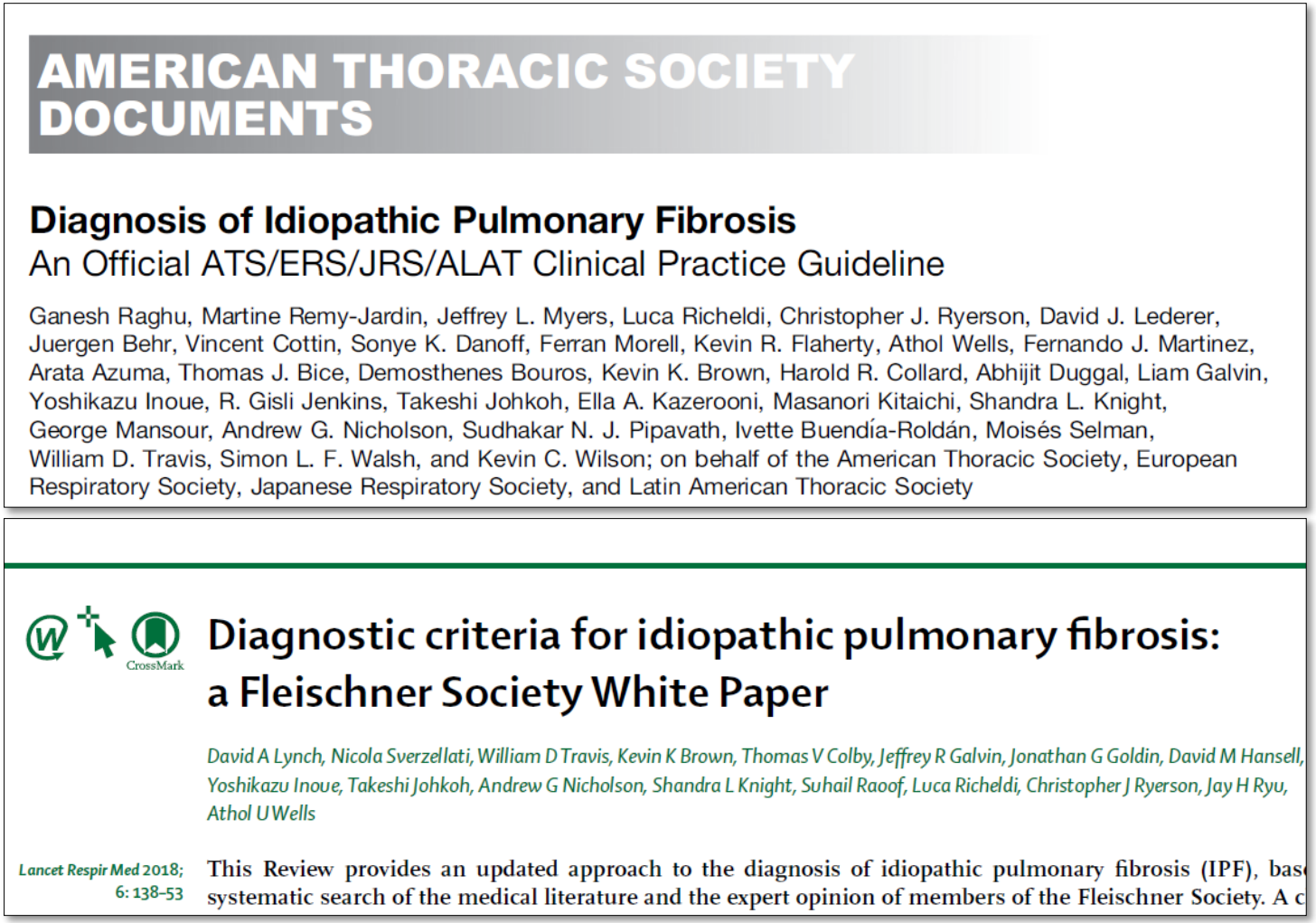
IPF의 새로운 진단지침

순천향대학교 부천병원
호흡기-알레르기내과
박 성 우

2018 ATS/ ERS/JRS/LAT guideline



AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis of Idiopathic Pulmonary Fibrosis

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

Ganesh Raghu, Martine Remy-Jardin, Jeffrey L. Myers, Luca Richeldi, Christopher J. Ryerson, David J. Lederer, Juergen Behr, Vincent Cottin, Sonye K. Danoff, Ferran Morell, Kevin R. Flaherty, Athol Wells, Fernando J. Martinez, Arata Azuma, Thomas J. Bice, Demosthenes Bouros, Kevin K. Brown, Harold R. Collard, Abhijit Duggal, Liam Galvin, Yoshikazu Inoue, R. Gisli Jenkins, Takeshi Johkoh, Ella A. Kazerooni, Masanori Kitaichi, Shandra L. Knight, George Mansour, Andrew G. Nicholson, Sudhakar N. J. Pipavath, Ivette Buendía-Roldán, Moisés Selman, William D. Travis, Simon L. F. Walsh, and Kevin C. Wilson; on behalf of the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Society

Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper

David A Lynch, Nicola Sverzellati, William D Travis, Kevin K Brown, Thomas V Colby, Jeffrey R Galvin, Jonathan G Goldin, David M Hansell, Yoshikazu Inoue, Takeshi Johkoh, Andrew G Nicholson, Shandra L Knight, Suhail Raoof, Luca Richeldi, Christopher J Ryerson, Jay H Ryu, Athol U Wells

Lancet Respir Med 2018; 6: 138–53

This Review provides an updated approach to the diagnosis of idiopathic pulmonary fibrosis (IPF), bas systematic search of the medical literature and the expert opinion of members of the Fleischner Society. A c

Am J Respir Crit Care Med 2018; 198, e44–e68

Lancet Respir Med 2018; 6: 138–53

2011 VS 2018 guideline

HRCT				
2011	UIP pattern	Possible UIP		Inconsistent UIP
2018	UIP pattern	Probable UIP	**Indeterminate for UIP**	Alternative diagnosis

Histopathology				
2011	UIP	Probable UIP	Possible UIP	Not UIP
2018	UIP	Probable UIP	**Indeterminate for UIP**	Alternative diagnosis

2018 guideline

HRCT scanning patterns

UIP	Probable UIP	Indeterminate for UIP
Subpleural and basal predominant; distribution is often heterogeneous	Subpleural and basal predominant; distribution is often heterogeneous	Subpleural and basal predominant Subtle reticulation; may have mild GGO or distortion ("early UIP pattern")
Honeycombing with or without peripheral traction bronchiectasis or bronchiolectasis	Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis	CT features and/or distribution of lung fibrosis that do not suggest any specific etiology ("truly indeterminate for UIP")

31% of Inconsistent with UIP are histopathologically UIP

-Radiologic–pathologic discordance in biopsy-proven usual interstitial pneumonia

ERJ 2016 ;47(4):1189-97

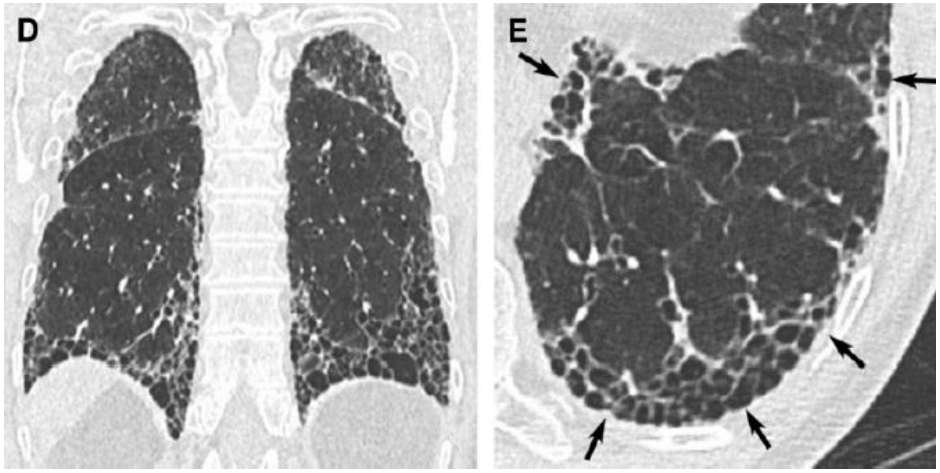
2018 guideline

HRCT scanning patterns

Alternative Diagnosis		
CT features : • Cysts • Marked mosaic attenuation • Predominant GGO • Profuse micronodules • Centrilobular nodules • Nodules • Consolidation	Predominant distribution : • Peribronchovascular • Perilymphatic • Upper or mid-lung	Other: • Pleural plaques (consider asbestosis) • Dilated esophagus (consider CTD) • Distal clavicular erosions(consider RA) • Extensive lymph node enlargement • Pleural effusions, pleural thickening (consider CTD/drugs)

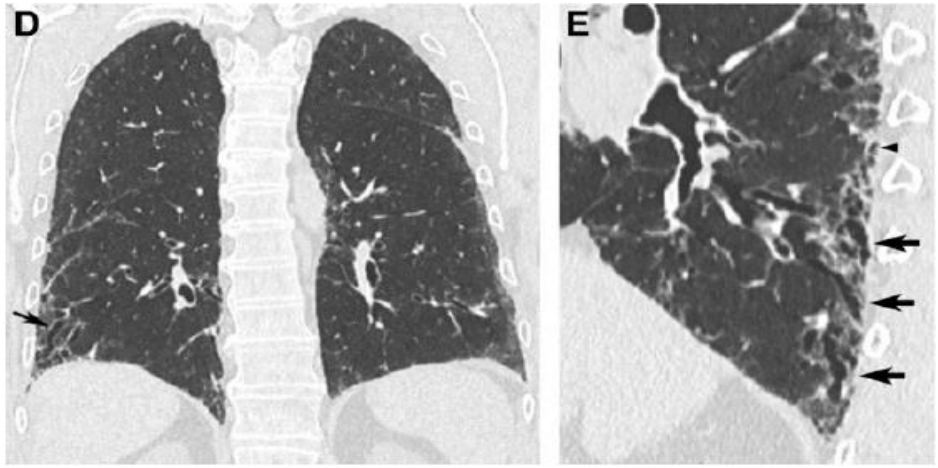
HRCT findings

UIP pattern



- Honeycombing,
- Subpleural and basal predominance

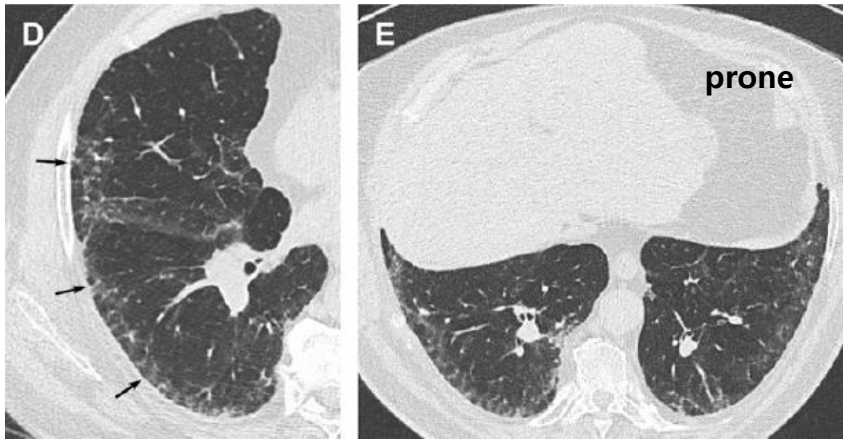
Probable UIP



- Reticular pattern
- peripheral bronchiolectasis
- Subpleural and basal predominance

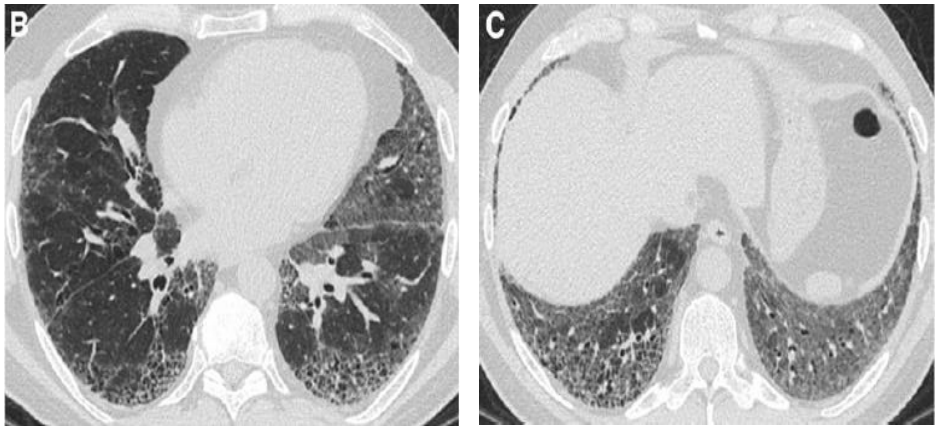
HRCT findings

Indeterminate for UIP



- **GGO with subtle reticulation**

“ Early UIP ”



Extensive lung infiltration combining honeycombing, mild to marked GGO, asymmetrical distribution no subpleural predominance

“ True Indeterminate UIP ”

2018 guideline

Histopathology patterns

Definite UIP	Probable UIP	Indeterminate UIP	Alternative diagnosis
Dense fibrosis with architectural distortion (i.e., destructive scar and/or honeycombing)	Some feature from UIP but to an extent that precludes definite Dx. of UIP and absence of alternative Dx. or honeycombing only	Fibrosis with or without architectural distortion, with features favoring either a other than UIP or favoring UIP secondary to another cause. Some histologic features from UIP, but with other features suggesting an alternative DX.	Feature of other histologic patterns of IIPs -No fibroblastic foci or loose fibrosis
Predominant subpleural and/or paraseptal distribution of fibrosis			Indicative of other diseases -Hyaline membrane -organizing pneumonia -granulomas -marked interstitial inflammation lacking fibrosis -Predominant airway centered changes -marked fibrous pleuritis
Patchy involvement of lung parenchyma by fibrosis			
Fibroblastic foci No alternative Dx.			Histologic findings indicative of other diseases (e.g. HP, LCH, LAM, sarcoidosis)

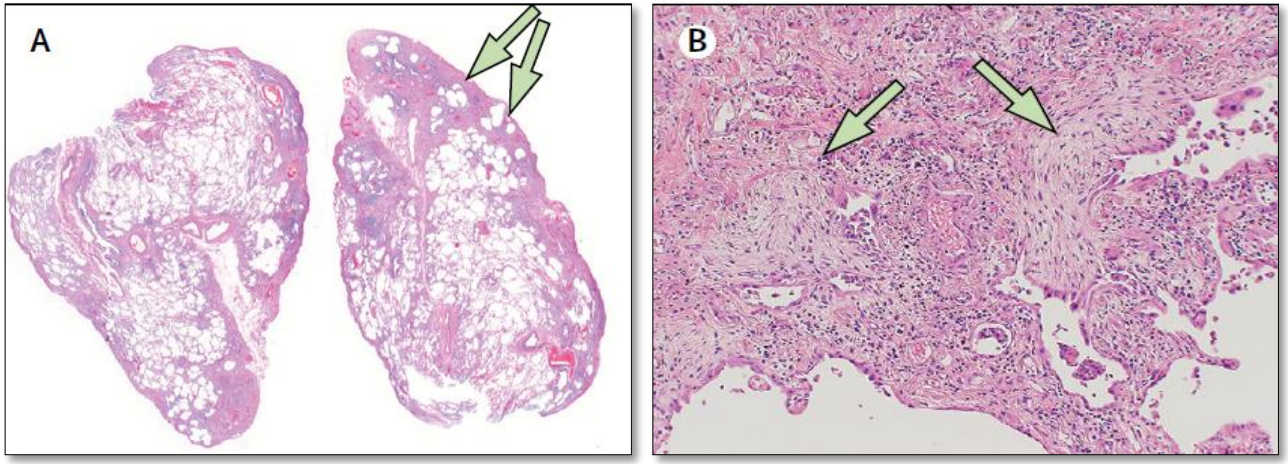
Histopathology

UIP -Definite

patchy subpleural/
paraseptal scarring

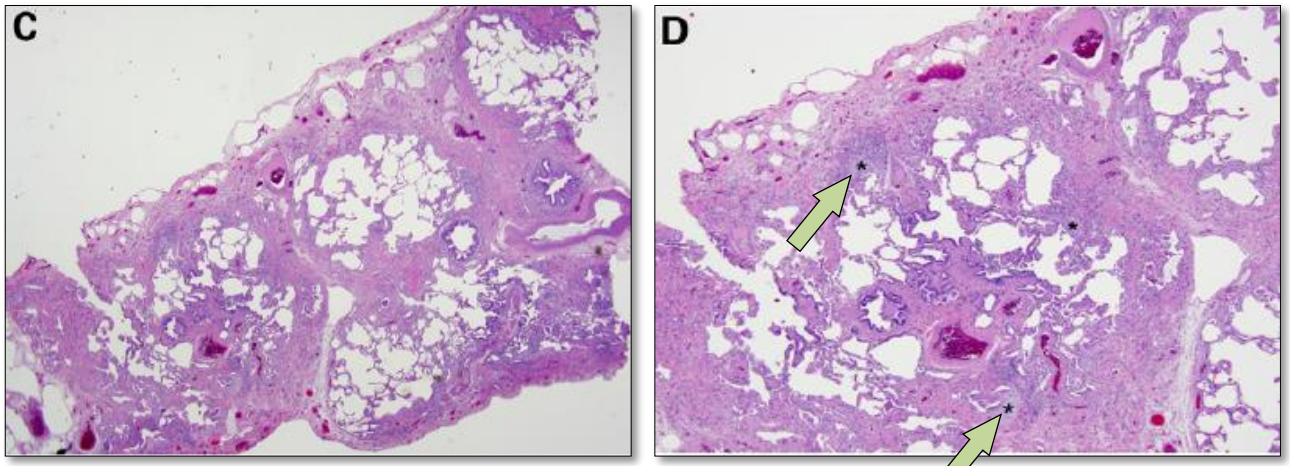
microscopic honeycombing

Fibroblastic foci



UIP -Probable

-Less architectural distortion
-No honeycombing



Fibroblastic foci

Histopathology

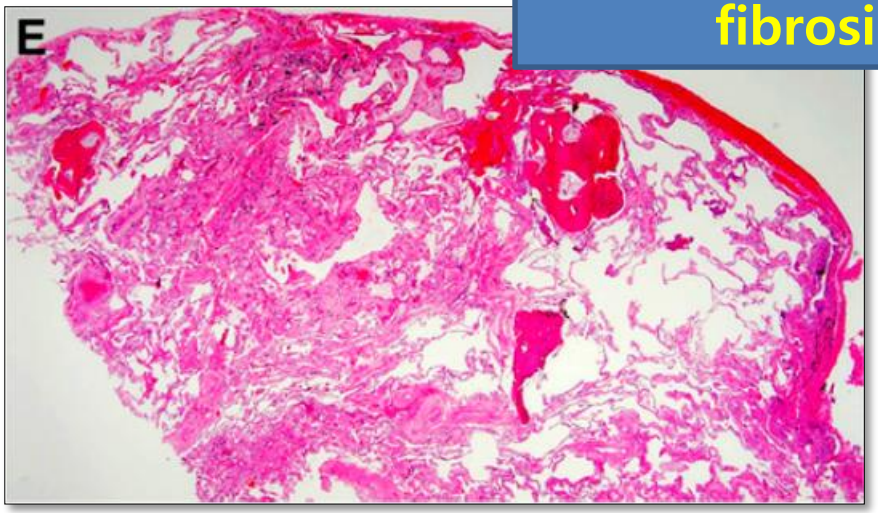
UIP – Indeterminate

- mild nonspecific fibrosis

- No patch and subpleural/ paraseptal distribution

- No architectural distortion
- No fibroblastic foci

Un(non)classifiable fibrosis



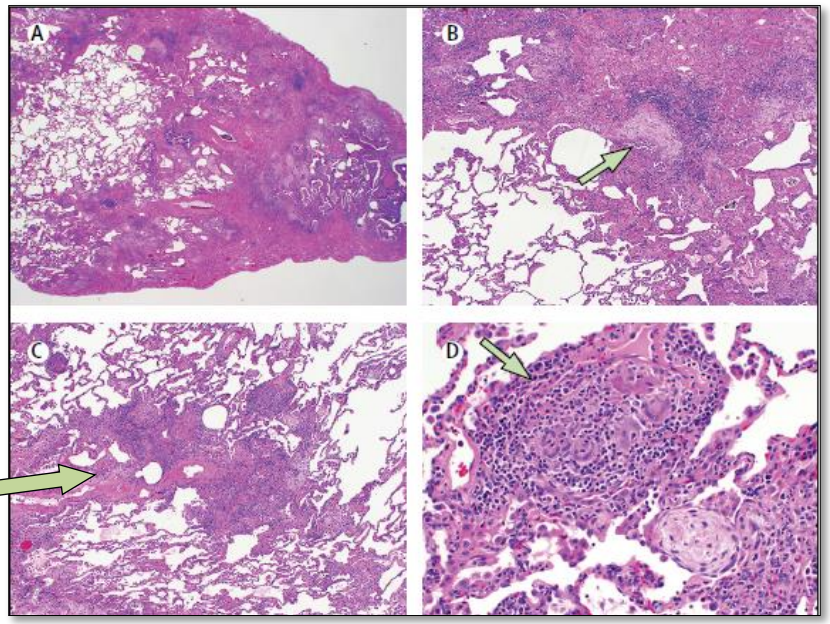
Alternative diagnosis ex) chronic HP

Subpleural scarring

Fibroblastic foci

Centrilobular injury

Granuloma



IPF (likely)-any of one

- Moderate-to-severe traction bronchiectasis /bronchiolectasis in age 50>man or 60>woman
- Extensive (>30%) reticulation on HRCT and an age >70 years
- Increased neutrophils and/or absence of lymphocyto
- Multidiscip confident

Indeterminate for IPF

- Without an adequate biopsy is unlikely to be IPF
- With an adequate biopsy may be reclassified to a more specific diagnosis after multidisciplinary discussion and/or additional consult

		pattern			
					Alternative diagnosis
HRCT pattern					Non-IPF dx
	Probable UIP	IPF	IPF	IPF (Likely)	Non-IPF dx
	Indeterminate for UIP	IPF	IPF (Likely)**	Indeterminate for IPF***	Non-IPF dx
	Alternative diagnosis	IPF (Likely)** /non-IPF dx	Non-IPF dx	Non-IPF dx	Non-IPF dx

Diagnostic Interventions
– newly detected ILD clinically suspected of having IPF

Q 1. Should do taking a detailed history of both medication use and environmental exposures at home, work, and other places the patient frequently visits to exclude potential causes of the ILD ?

- Hypersensitivity pneumonitis : 47% from new- on set ILD of unknown cause
- Pneumoconiosis , drug toxicity, radiation

- Questionales : environmental exposure at home, work, frequently visited places
  -mold, birds, animals, metal dusts, wood dust, stone polishing, medication
  -occupation, hobby : current, recent,

Diagnostic Interventions
– newly detected ILD clinically suspected of having IPF

Q2. Should Patients Undergo Serological Testing to exclude CTDs as Potential Causes of the ILD?

Yes, we do

- Routine test : CRP, ESR, ANA, RA factor, anti-CCP Ab.

- case by case : muscle Ez. Antisynthetase ab (Jo-1)
  anti-Scl-70, anti-centromere,
  anti-SSA/Ro, anti-SSB/La
  anti-cytoplasmic Ab

- Refer to rheumatologist when,
  (+) clinical manifestation, (+) serology, other atypical IPF (Female, age< 60)

- Interstitial pneumonia with autoimmune features (IPAF)

Diagnostic Interventions
– newly detected ILD clinically suspected of having IPF

Q3. Should do cellular analysis of their BAL fluid ?

1. HRCT pattern of UIP
   - **NOT** performing cellular analysis from BAL fluid
     (conditional recommendation, very low quality of evidence)

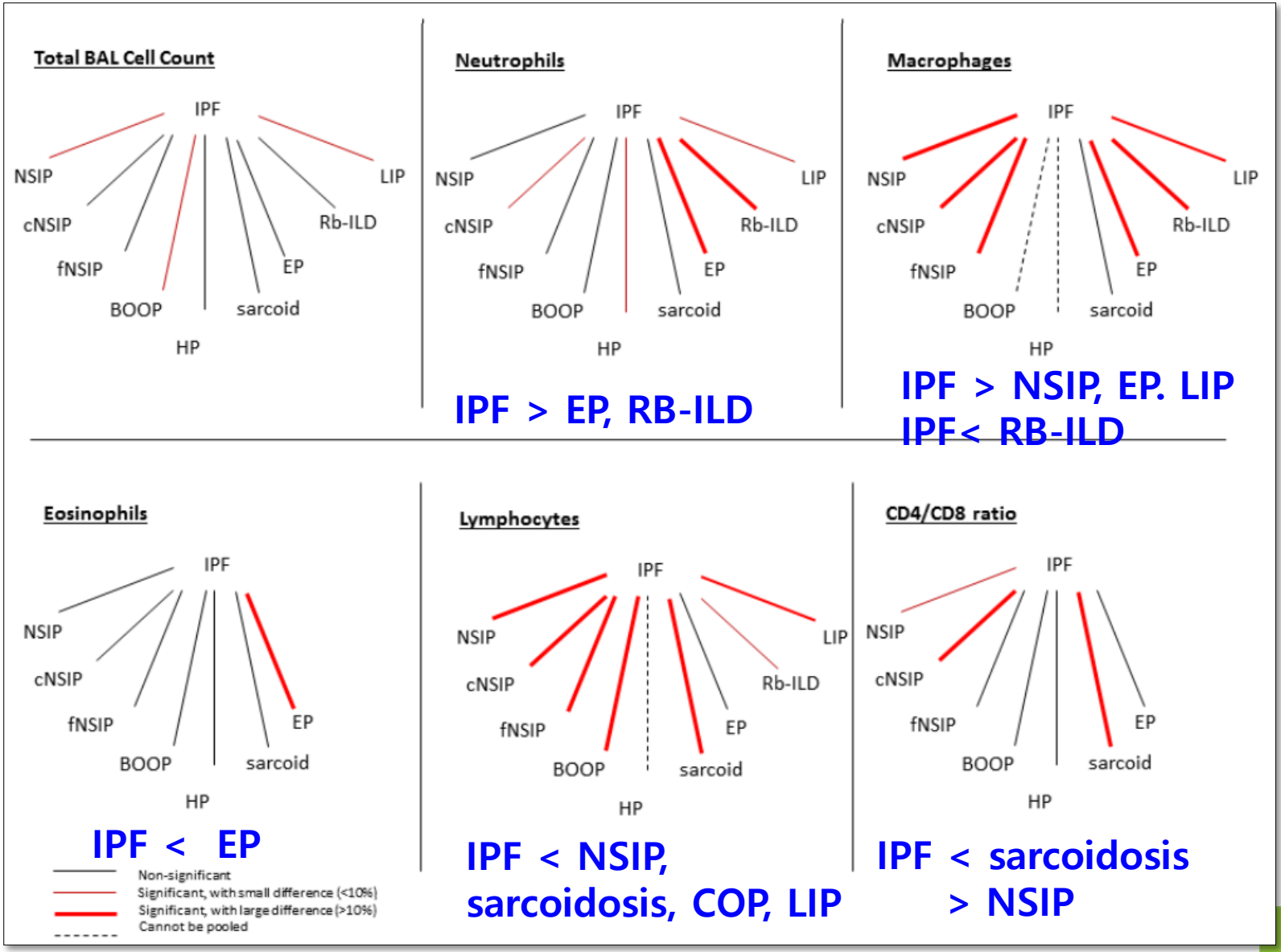
2. HRCT pattern of probable or indeterminate or alternative Dx.
   - **YES,** suggest cellular analysis of BAL fluid
     (conditional recommendation, very low quality of evidence)

BAL is useful for radiologic DDx. from

Eosinophilic pneumonia, COP,

Sarcoidosis, infection, malignancy

BAL cell type differences among IPF vs. other types of ILD



Diagnostic Interventions
– newly detected ILD clinically suspected of having IPF

Q4. Should surgical lung biopsy (SLB) be performed to ascertain the histopathology diagnosis of UIP pattern ?

1. HRCT pattern of UIP
   - **NOT** performing SLB
     (strong recommendation, very low quality of evidence)

2. HRCT pattern of probable or indeterminate or alternative diagnosis
   - **YES,** performing SLB by context of an MDD by expert clinicians
     (conditional recommendation, very low quality of evidence)

- Definitive diagnosis 89%
- mortality : 3.5 % ,
- exacerbation 6.1%, infection 6.5%, prolonged air leak 5.9%,

Diagnostic Interventions
– newly detected ILD clinically suspected of having IPF

Q5-6. Transbronchial lung biopsy or cryobiopsy(TBBx/CryoBx.) can be alternative to SLB to ascertain the histopathology diagnosis of UIP pattern ?

1. HRCT pattern of UIP
   - **NOT** performing TBBx/cryoBx.
     (strong recommendation, very low quality of evidence)

2. HRCT pattern of probable or indeterminate or alternative diagnosis
   - **No recommendation for or against**
     (strong recommendation, very low quality of evidence)

- Undiagnosis rate 20- 64%
- bleeding or prolonged air leakage than SLB

Diagnostic Interventions
– newly detected ILD clinically suspected of having IPF

Q7. Should do measurement of serum biomarkers for the purpose of diagnosis ?

biomarker	Sensitivity/ specificity	Accuracy	Diagnostic odds ratio	reference
MMP-7	71.1/64.4 (%)	68.4 (%)	4.7 (4.2-5.1)	12
SPD	70.0/65.0(%)	68.5 (%)	3.1	16
CCL-18	none	none	none	6
KL-6	none	none	none	55

More than one-third of results will be incorrect.

recommend NOT measuring biomarkers for diagnosis of IPF

Diagnostic Interventions
– newly detected ILD clinically suspected of having IPF

Q8. Should Multi discipline decision (MDD) be performed for decision making ? Suggest, YES

Comparison between SDD and MDD - analysis of 5 article

- Median agreement between SDD and MDD 70% (47- 87%)
  Kappa score (k= 0.331; 95% CI, 0.269-0.392) moderate

- SDD is more efficient for decision making (less time and effort)

- If MDD is accepted as reference, SDD in sub-optimal agreement
  : incorrect therapy , delayed therapy, unnecessary additional procedure.

MDD : greatest when the HRCT pattern is probable ,indeterminate for UIP, or an alternative diagnosis, or when there exist discordant clinical, radiologic, and/or histologic data.

MDD : pulmonologist, radiologist, pathologist and/or rheumatologist

Pathways to a confident working multidisciplinary diagnosis of IPF

- Clinical context of IPF includes all of the following
  - older than 60 years, absence of clinically significant environmental or medication exposure, no evidence of connective tissue disease

- Clinical context indeterminate for IPF includes any of the following
  - aged <60 years, potentially significant environmental or medication exposure, or evidence of connective tissue disease

1. **When can one make a confident diagnosis of IPF without biopsy?**
   - Clinical context of IPF, with CT pattern of typical or probable UIP

2. **When is a diagnostic biopsy necessary to make a confident diagnosis of IPF?**
   - Clinical context of IPF with CT pattern either indeterminate or suggestive of an alternative diagnosis
   - Clinical context indeterminate for IPF with any CT pattern

Lancet Respir Med 2018; 6: 138–53

Pathways to a confident working multidisciplinary diagnosis of IPF

3. When is MDD necessary in the context of suspected IPF ?

- When the clinical context or the CT pattern, or both, are indeterminate; the outcome of MDD will be a decision whether to perform an additional clinical evaluation, BAL or diagnostic biopsy, or some combination of these procedures
- After biopsy, to integrate the clinical, imaging, and histological features
-To re-review patients in whom the longitudinal course of disease is discordant with the previously established multidisciplinary diagnosis

- When diagnostic tissue is not available, to consider a working diagnosis of IPF

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Pathways to a confident working multidisciplinary diagnosis of IPF

4. What should be done when diagnostic tissue is not available ?

- MDD with consideration of the patient's age, sex, smoking status, findings on BAL, and longitudinal disease behaviour

- In this context, a working diagnosis of IPF can be made in the presence of a progressive fibrosing interstitial pneumonia, and absence of an alternative explanation;
  the level of diagnostic confidence of such a working diagnosis should be recorded, and the diagnosis should be reviewed at regular intervals, since it might change over time

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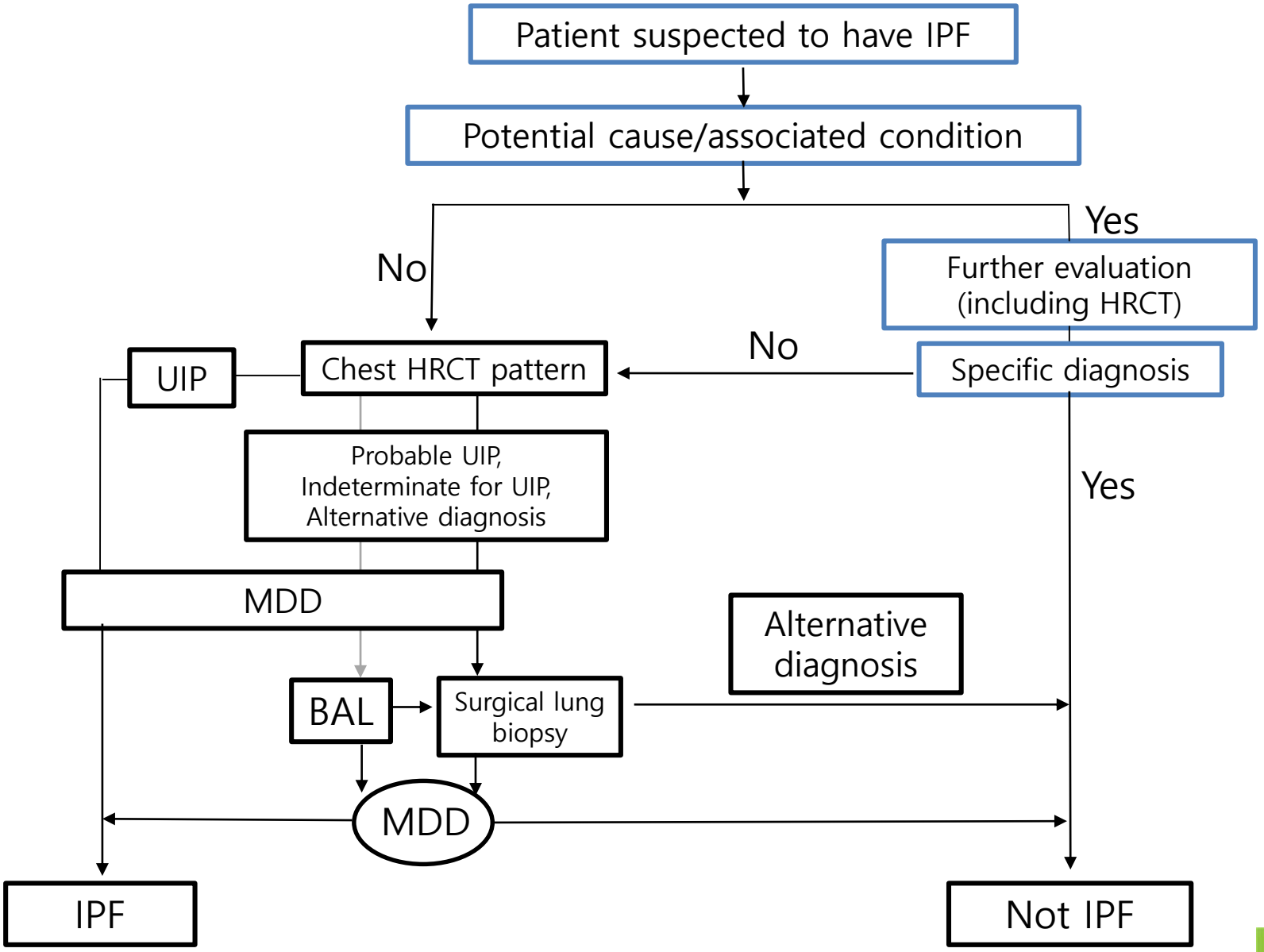
Diagnostic algorithm for IPF



Summary

- 2018 Guideline
- Indeterminate pattern : HRCT, pathology
- BAL cell analysis
- Recommendation of multidisciplinary diagnosis

Thanks for your attention !