Diagnosing idiopathic pulmonary fibrosis in 2018: bridging recommendations made by experts serving different societies

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Two new documents on the diagnosis of IPF have been published in 2018: their similarities and differences are described and discussed http://ow.ly/856P30lnB2O

Cite this article as: Richeldi L, Wilson KC, Raghu G. Diagnosing idiopathic pulmonary fibrosis in 2018: bridging recommendations made by experts serving different societies. *Eur Respir J* 2018; 52: 1801485 [https://doi.org/10.1183/13993003.01485-2018].

Two guidance documents for the diagnosis of idiopathic pulmonary fibrosis (IPF) have been recently published by international experts representing major respiratory and radiological societies [1, 2]. Similar documents from other societies are anticipated. This is clearly a positive sign of the increasing attention being paid by the scientific community to a group of fibrotic lung diseases of which IPF is the prototype.

Clinical practice guidelines (CPGs) guide clinicians in the management of patients with a specific disease, based upon evolving knowledge and evidence. They are expected to adhere to Institute of Medicine standards [3] which include, for every recommendation, a full systematic review of the evidence performed by methodologists who have neither financial nor intellectual conflicts, a discussion of the synthesised evidence by content experts whose potential conflicts of interest are carefully managed, and the formulation of recommendations based upon consideration of the balance of benefits *versus* harms and burdens, quality of evidence, patient values and preferences, cost, and feasibility.

CPGs impact at least three important domains. First, they inform clinical practice, where the diagnostic approach needs to be standardised based on the most up-to-date evidence generated by clinical research. Second, they harmonise the population of patients enrolled in different multicentre randomised trials. This helps regulatory agencies accurately assess the safety and the efficacy of new treatments in a defined spectrum of patients. Last, but not least, they support single patients and patient advocacy groups/associations to better understand the nature of diseases like IPF, a rare condition for which a large portion of the information available on the internet is inaccurate [4].

Consensus statements similarly guide clinical management; however, recommendations are based on the consensus of content experts whose opinions reflect their knowledge and experience. Consensus statements do not adhere to the same robust methodology as CPGs and, therefore, usually do not have the same impact as CPGs in terms of acceptance and implementation by policy makers, regulating agencies, and stakeholders. Despite their different methods, CPGs and consensus statements have many similarities. Both involve a large number of multidisciplinary experts in the field; both are sponsored, developed, endorsed and published by scientific societies; and both answer specific clinical questions with

Received: Aug 04 2018 | Accepted: Aug 06 2018

recommendations (table 1). Given such similarities, it is not surprising that the guidance provided by CPGs and consensus statements are often similar and overlapping.

This is highlighted by two recent publications on the diagnosis of IPF: the American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin American Thoracic Society (ALAT) guidelines on the diagnosis of IPF [1] and the Fleischner Society consensus statement on diagnostic criteria for IPF [2].

The ATS/ERS/JRS/ALAT guidelines and Fleischner Society statement reach similar conclusions and recommendations (table 2), with only minimal semantic differences. In particular, three components are nearly identical. First, both documents acknowledge the critical role of the clinician in evaluating patients suspected to have IPF. To make an accurate diagnosis, clinicians must consider the clinical context at presentation (*e.g.* the age of the patient), eliminate the possibility of significant environmental or medication exposures, and exclude the presence of connective tissue disease. Second, both documents emphasise the critical importance of high-quality, high-resolution computed tomography (HRCT) images in the evaluation of patients suspected to have IPF. This is illustrated by the documents' detailed descriptions of the technical aspects needed to generate adequate images of the lungs from volumetric scanning of the chest. Third, both documents conclude that discussions among experienced experts from multiple disciplines (*i.e.* "multidisciplinary discussions") are necessary to make an accurate diagnosis of IPF. Multidisciplinary discussions should include the clinician, a radiologist and, when histopathology is available, a pathologist. A rheumatologist should also be included on a case-by-case basis.

Additional similarities exist. Both documents acknowledge surgical biopsy as the gold standard for obtaining a tissue sample. The ATS/ERS/JRS/ALAT guidelines do not make a recommendation for or against transbronchial cryobiopsy due to a paucity of evidence and insufficient agreement among the expert panel, while the Fleischner Society statement describes transbronchial cryobiopsy as a procedure with an unclear role in clinical practice. Both documents have eliminated the previous category of "possible usual interstitial pneumonia (UIP)" pattern and provide refined features for the UIP pattern, probable UIP pattern, indeterminate for UIP pattern, and patterns that sway away from the diagnosis of UIP and are indicative of an alternative diagnosis. Finally, both documents conclude that, for many individual patients, a definite diagnosis cannot be made, but a highly probable working diagnosis can be achieved with the multidisciplinary discussion.

The only apparent substantial dissimilarity between the two documents is related to the need for a surgical lung biopsy in patients with a probable UIP pattern on HRCT. While the ATS/ERS/JRS/ALAT guidelines recommend surgical lung biopsy in patients with a probable UIP pattern on HRCT, the Fleischner Society statement indicates that a confident diagnosis of IPF can be made without surgical lung biopsy in patients with a consistent clinical context and a probable UIP pattern on HRCT. It is important to note, however, that the ATS/ERS/JRS/ALAT recommendation is a conditional recommendation. This indicates that the guideline panel concluded that biopsy is appropriate for a

TABLE 1 Diagnosis of idiopathic pulmonary fibrosis (IPF): similarities and differences between the 2018 ATS/ERS/JRS/ALAT clinical practice guideline and the 2018 Fleischner white paper

	ATS/ERS/JRS/ALAT clinical practice guideline [1]	Fleischner white paper consensus statement [2]
Number of authors	34	17
Overlapping authors	8	
Endorsing scientific societies	Multiple	Single
Multidisciplinary nature	Yes	Yes
Question-based structure	Yes	Yes
Systematic search of the literature	Yes	Yes
Evidence-based approach (Institute of Medicine standards)	Yes	No
PICO questions/format	Yes	No
Expert opinion-based approach	No	Yes
Grading of recommendations	Yes	No
Published in a peer-reviewed journal	Yes	Yes
Implementation and interest to all stakeholders (policy makers, regulating agencies, IPF community-at-large)	Yes	?

ATS: American Thoracic Society; ERS: European Respiratory Society; JRS: Japanese Respiratory Society; ALAT: Latin American Thoracic Society; PICO: population, intervention, comparison, outcome.

TABLE 2 Diagnostic components for idiopathic pulmonary fibrosis (IPF)

	ATS/ERS/JRS/ALAT clinical practice guideline [1]	Fleischner white paper consensus statement [2]
Age limit for increased diagnostic confidence	60 years	
HRCT pattern	**UIP**	**Typical UIP**
	Subpleural and basal predominance Presence of honeycombing with or without peripheral traction bronchiectasis Biopsy not recommended	
	Probable UIP	
	Subpleural and basal predominance Presence of peripheral traction bronchiectasis	
	Biopsy recommended (conditional)	*Biopsy **not** recommended*
	Indeterminate for UIP	
	Subpleural and basal predominant May have mild GGO or distortion	Variable or diffuse Features suggestive of non-UIP pattern
	Biopsy recommended	
	Alternative diagnosis	**Most consistent with non-IPF diagnosis**
	Findings suggestive of another diagnosis *Biopsy recommended*	
Histopathology pattern	**UIP**	**Definite UIP**
	Dense fibrosis with architecture remodelling Predominant subpleural or paraseptal distribution of fibrosis Patchy lung involvement by fibrosis Presence of fibroblastic foci	
	Probable UIP	
	Honeycomb fibrosis only Fibroblastic foci may or may not be present	
	Indeterminate for UIP	
	Fibrosis with or without architecture distortion Some histological features from the UIP pattern	Occasional foci of centrilobular injury or scarring Rare granulomas or giant cells Minor degree of lymphoid hyperplasia or diffuse inflammation Diffuse homogenous fibrosis favouring fibrotic nonspecific interstitial pneumonia
	Alternative diagnosis	**Features most consistent with an alternative diagnosis**
	Histological findings indicative of other diseases	A UIP pattern with ancillary features strongly suggesting an alternative diagnosis A non-UIP pattern

Criteria have been summarised for purposes of comparison. ATS: American Thoracic Society; ERS: European Respiratory Society; JRS: Japanese Respiratory Society; ALAT: Latin American Thoracic Society; HRCT: high-resolution computed tomography; UIP: usual interstitial pneumonia; GGO: ground-glass opacities.

majority of patients (⩾50%), but may not be appropriate for a sizeable minority (up to 49%) of patients; in other words, the guidelines indicate that there is clinical equipoise when deciding whether or not to biopsy a patient with a probable UIP pattern on HRCT. When the clinical context is strongly suggestive of IPF, patients are likely fall into the sizeable minority for whom a biopsy is unnecessary and the recommendation becomes essentially identical to the Fleischner Society recommendation. In other words, the ATS/ERS/JRS/ALAT guidelines and the Fleischner Society Statement recommend the same course of action for patients with both a high clinical likelihood of IPF and a probable UIP pattern on HRCT, but the ATS/ERS/JRS/ALAT recommendation can also be applied to patients for whom the clinical likelihood of IPF is uncertain, providing greater flexibility. Among the 21 expert members of the ATS/ERS/JRS/ALAT guidelines panel, 17 supported a conditional recommendation for biopsy, while only four members supported a conditional recommendation against biopsy.

Given the similarities in the recommendations made by these two official documents on the diagnosis of IPF, it is likely that following the algorithm provided in the ATS/ERS/JRS/ALAT guidelines will yield the same diagnosis as following the guidance provided by the Fleischner Society statement for

any given patient suspected of having IPF. Nevertheless, the CPGs for clinical management of IPF have advanced from a consensus-based statement in 2000 to become evidence-based from 2011 onwards [5, 6].

It is hoped that implementation of the new diagnostic criteria and approach by all stakeholders and the IPF community-at-large worldwide will yield accurate diagnoses for patients and, thus, appropriate therapeutic interventions can be initiated promptly to improve outcomes that are clinically meaningful for the patient with IPF.

Conflict of interest: L. Richeldi reports personal fees from Sanofi-Aventis (consultancy), Roche (member of advisory board), Celgene (consultancy), Nitto (consultancy), Fibrogen (member of advisory board), Promedior (member of advisory board), Bristol Myers Squibb (consultancy), DynaMed (editorial activity), Pliant Therapeutics (consultancy), Prometic (consultancy), Asahi Kasei (consultancy) and Biogen (consultancy), and grants and personal fees from Boehringer Ingelheim (member of Steering Committee), all outside the submitted work. K.C. Wilson reports being the American Thoracic Society Chief of Documents and Patient Education; therefore, he may have an intellectual bias in favour of ATS-sponsored documents. G. Raghu reports other (consultant for IPF studies) from BI, BMS, Biogen, Bellerophan, Fibrogen, Gilead, Nitto, Promedior, Sanofi and Veracyte, and grants from NIH (for IPF studies), all outside the submitted work.

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