The 2018 Diagnosis of Idiopathic Pulmonary Fibrosis Guidelines: Surgical Lung Biopsy for Radiological Pattern of Probable Usual Interstitial Pneumonia Is Not Mandatory

Clinical practice guidelines advise clinicians on the management of patients based on evidence and evolving knowledge. Questions that are important to patients and clinicians are posed by an expert panel, and a full systematic review of the evidence is performed by methodologists who include acinar dysplasia of the lungs. [Am J Med Genet A. 2016;170: 2440-2444.]

In 2018, the American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JRS), and Latin American Thoracic Society (ALAT) published a clinical practice guideline on the diagnosis of idiopathic pulmonary fibrosis (IPF), updating guidelines from 2011 (1, 2). The new guidelines 1) used systematic reviews to inform each recommendation in strict accordance with the Institute of Medicine Standards for Trustworthy Guidelines (3, 2) eliminated the radiological categories of “possible UIP pattern” and “inconsistent for UIP pattern” and the pathological categories of “possible UIP” and “nonclassifiable fibrosis,” and 3) refined the radiological and pathological patterns of “UIP” and defined “probable UIP” and “indeterminate for UIP.” The overriding goal of the guidelines was to help clinicians diagnose IPF more accurately, thereby facilitating appropriate treatment, as described in the 2015 guidelines for the treatment of IPF (4).

The radiological patterns of usual interstitial pneumonia (UIP) described in the ATS/ERS/JRS/ALAT guidelines are like those described in a statement from the Fleischner Society (5); however, the two documents make seemingly different recommendations about whether to perform surgical lung biopsy (SLB) in patients with the radiological probable UIP pattern by high-resolution computed tomography (HRCT) (6). Specifically, the ATS/ERS/JRS/ALAT guidelines make a conditional recommendation for SLB after multidisciplinary discussions (MDDs), whereas the Fleischner Society statement indicates that a confident diagnosis of IPF can be made without SLB in the right clinical context. This reflects differences in methodology and terminology rather than any substantive difference in principles and recommended practices.

It is apparent that the recommendations in the ATS/ERS/JRS/ALAT guidelines are subject to misinterpretation as a mandate for SLB in patients with probable UIP. Avoiding this misinterpretation is precisely why the ATS/ERS/JRS/ALAT recommendation was assigned a strength

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Table 1. Strengths of Recommendations

| From the GRADE Working Group | From the ATS/ERS/JRS/ALAT Diagnosis of Idiopathic Pulmonary Fibrosis Guidelines panel discussion |
|-----------------------------|--------------------------------------------------------------------------------------------------|
| **For patients**            | The overwhelming majority of individuals in this situation would want the recommended course of action, and only a small minority would not. |
| **For clinicians**          | The overwhelming majority of individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences. |
| **For policy makers**       | The recommendation can be adapted as policy in most situations, including for use as a performance indicator. |

**Strong Recommendation (“We recommend . . .”)**

- It is the right course of action for >95% of patients.
- "Just do it."
- You would be willing to tell a colleague who did not follow the recommendation that he/she did the wrong thing.
- The recommended course of action may be an appropriate performance measure.

**Conditional Recommendation (“We suggest . . .”)**

- The majority of individuals in this situation would want the suggested course of action, but a sizeable minority would not.
- Different choices will be appropriate for different patients and you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may be useful to help individuals make decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision.
- Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.
- It is the right course of action for >50% of patients but may not be right for a sizeable minority.
- "Slow down, think about it, discuss it."
- You would not be willing to tell a colleague who did not follow the recommendation that he/she did the wrong thing; it is a matter of "style" or "equipoise."
- The recommended course of action is not appropriate for a performance measure.

*Definition of abbreviations:* ALAT = Latin American Thoracic Society; ATS = American Thoracic Society; ERS = European Respiratory Society; GRADE = Grading of Recommendations, Assessment, and Evaluation; JRS = Japanese Respiratory Society.

The ATS/ERS/JRS/ALAT proposal suggests that MDDs among experts in interstitial lung diseases may play a pivotal role in navigating this key inflection point.

The ATS/ERS/JRS/ALAT guideline panel formulated its recommendations by weighing the diagnostic characteristics of SLB (100% adequate samples, 90% diagnostic yield) versus the risks of SLB (1.7% surgical mortality) in patients with newly detected interstitial lung disease, along with patient preferences, cost, and feasibility. The panel voted 17 to 4 to suggest SLB (i.e., make a conditional recommendation for SLB), while acknowledging the very low quality of the evidence. The panel emphasized the need for an MDD to decide whether to proceed to SLB, as well as the conclusion that SLB should not be performed in patients at high risk for intra-, peri-, and/or postoperative complications, such as those with severe hypoxemia at rest and/or severe pulmonary hypertension with $D_{lCO_2} < 25\%$ after correction for the hematocrit (7). The panel also stated that SLB may be unnecessary in some familial cases.

The suggestion to perform SLB in patients with probable UIP was supported by a prospective study (8). In that study, IPF experts who were not on the ATS/ERS/JRS/ALAT guideline panel and had no
knowledge of the guideline’s systematic reviews or recommendations answered the same questions as the ATS/ERS/JRS/ALAT panel using the modified Convergence of Opinion on Recommendations and Evidence (CORE) approach, an electronic consensus-building process (8). The recommendations developed using the modified CORE process were highly concordant with those developed by the guideline panel, including the suggestion for SLB.

In summary, it is apparent that the ATS/ERS/JRS/ALAT guideline’s recommendation for SLB in patients with probable UIP has been interpreted as a mandate for SLB. This was never the intent. We emphasize that the recommendation was assigned a strength of “conditional” for the primary purpose of avoiding this interpretation, and we reiterate that there is equipoise in deciding which patients with a probable UIP pattern on HRCT warrant an SLB. Specifically, patients with probable UIP for whom the clinical context is suggestive of IPF may forgo SLB, whereas patients with probable UIP for whom the clinical context is uncertain may undergo SLB. The clinician and patient need to discuss SLB within the individual clinical context, including potential desirable and undesirable consequences, and then make the decision to either pursue or forgo SLB.

Author disclosures are available with the text of this article at www.atsjournals.org.

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