In previous studies, the presence of reticulation and traction bronchiectasis without GGO (previous possible IPF) usually yielded a UIP pathological diagnosis and a final diagnosis of IPF (5). Would it not be easier to remove GGO from probable UIP and keep this feature in the indeterminate UIP category? This will assist the clinician in opting not to do invasive procedures in UIP or probable UIP on high-resolution computed tomography imaging. The various presentations of indeterminate UIP can then be better characterized in future studies.

Finally, although beyond the scope of this discourse, the role of antifibrotics will need future clarification. From this article, subjects with inflammatory change (GGO) and fibrosis will potentially have the diagnosis of IPF. Antifibrotics may need to be combined with other modalities, such as antiinflammatory agents, in the new diagnosis of IPF.

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

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New Idiopathic Pulmonary Fibrosis Guidelines: Are Cryobiopsy and Surgery Competitive in Clinical Practice?

To the Editor:

Recently, new updated guidelines for diagnosis of idiopathic pulmonary fibrosis (IPF) have been published (1), which Repropose a well-established and key questions–based approach. One of the questions analyzed by the panel of experts was if transbronchial lung cryobiopsy could be considered a reasonable alternative to surgical lung biopsy to ascertain the histopathological diagnosis of usual interstitial pneumonia (UIP) pattern. To avoid any incorrect interpretation by nonexpert readers, it may be emphasized that in clinical practice the two procedures may be considered not really competitive; this means that cryobiopsy should not be used automatically as an alternative to surgical biopsy but rather as a complementary investigation in the complex diagnostic approach of interstitial lung diseases. In fact, a patient might undergo cryobiopsy (associated with a not-negligible diagnostic yield and a 0.3% mortality rate, lower compared with surgery) as first approach and subsequently might undergo video-assisted thoracoscopic surgery if cryobiopsy proves to be nondiagnostic (2–4). In this scenario, the total rate of complications would not be the sum of the two; the 1.7% mortality associated with surgical lung biopsy (which becomes much higher with increasing age, higher comorbidity score, open rather than thoracoscopic surgery, provisional diagnosis of “IPF-clinical syndrome” or connective tissue disease–related interstitial lung disease, and lower DLCO, and which can even reach 16% for nonelective procedures) (5, 6) should not be applied to all patients (100%) but only to the minority of patients in whom cryobiopsy is not diagnostic and who may be potential candidates for surgery. Pathologists identify a pattern in 80% of patients undergoing the procedure for interstitial lung diseases of unknown cause (including those with a probable UIP or indeterminate UIP radiological pattern) (1, 2); therefore, nondiagnostic procedures may be around 20% of all patients undergoing cryobiopsy. However, data confirming that this value represents the diagnostic accuracy of transbronchial lung cryobiopsy (data provided by a head-to-head comparison between cryobiopsy and surgical lung biopsy) are not yet available. Furthermore, we have to take into account that the calculus of risks may be biased, as the 0.3% mortality rate associated with cryobiopsy reflects selected cases at expert centers, but there may well be unpublished cases with life-threatening complications in nonexpert centers or when adequate precautions are not taken. In contrast, the 1.7% to 16% mortality rate associated with surgical biopsy reflects a wide range of practice patterns, with both expert and nonexpert centers.

In conclusion, this diagnostic approach to patients with interstitial lung disease and suspected IPF could be successful and associated with a final risk of mortality (considering cryobiopsy and surgery together) lower than the overall mortality with video-assisted thoracoscopic surgery alone. Finally, older patients (age >70 yr) and/or those with reduced lung function (DLCO <45%), who may frequently be excluded from surgery, could still have a diagnostic opportunity with cryobiopsy (2).
We introduced the subcategory of early usual interstitial pneumonia (UIP) to alert the individual clinical scenario of IPF relatively early in the disease course. This interest is triggered by the possibility of detection of subclinical interstitial lung disease in smokers that can evolve toward obvious fibrosis on CT follow-up (2–6). Although uncertainty still remains regarding the long-term prognostic implications of subclinical interstitial lung disease (3), it may be relevant to investigate these situations in select populations, with the ultimate goal of recognizing and treating IPF earlier.

The degree of lung attenuation is influenced by numerous variables on HRCT examinations, varying from the degree of inspiration to the kernels of reconstruction. Therefore, there is no recommendation for defining GGO with quantitative variables. Although they can be proposed in clinical research programs, they are not applicable to routine clinical practice.

Contrary to Moodley’s statement, the presence of traction bronchiectasis was not clearly stated in the previous “possible UIP” category. The only difference was the absence of honeycombing. Removing GGO from the probable category would not make great differences in the categorization of patients. The indeterminate pattern (“truly indeterminate”) corresponds to HRCT features that do not correspond to an HRCT pattern of UIP, nor do they suggest any specific etiology for lung fibrosis. Among the HRCT features reported as indeterminate for UIP on CT sections, one can describe GGO of high attenuation; this HRCT feature has no further diagnostic value.

Moodley also raises an important issue, acknowledging that in circumstances of uncertainty regarding the histopathologic features conveyed by terms like “probable” or “indeterminate,” the uncertainty often centers on the difficulty of consistently separating the fibrotic variant of nonspecific interstitial pneumonia (NSIP) from UIP/IPF. The histologic features that define fibrotic NSIP are nonspecific, as the term implies, precisely because this same histology can occur focally (“NSIP-like changes”) in other conditions, including UIP/IPF. For that reason, deciding that a biopsy diagnosis of a fibrotic NSIP pattern is representative of a patient’s underlying condition is necessarily a matter of exclusion. In that sense, patients with biopsy diagnoses of fibrotic NSIP may indeed have UIP/IPF, depending on other information.

Because HRCT is imperfect in separating patients with fibrotic NSIP from patients with UIP/IPF who lack diagnostic radiological findings, it remains true that some patients considered to have fibrotic NSIP at diagnosis will ultimately prove to have UIP/IPF over time. This reflects the imperfect state of the art and the vulnerabilities that persist even in the context of multidisciplinary discussion. We agree that different groups of pulmonologists, radiologists, and pathologists may resolve these levels of uncertainty differently, meaning that patients assigned to a category of fibrotic NSIP in one institution may legitimately be assigned to other categories, including UIP/IPF, by others. This remains a key area for further investigation, with the hope of greater diagnostic reproducibility and precision.

Finally, Moodley raises the consideration of using combinations of antiinflammatory agents besides antifibrotic treatment strategy for patients with a new diagnosis of IPF, because subjects with subtle inflammation (suggested by allowance of some GGO in the appropriate clinical setting and meeting other criteria of the UIP pattern in the new guideline for the diagnosis of IPF) will be diagnosed with IPF from now on. Because the guideline focused on the diagnosis of IPF, the discussion regarding the therapeutic role of antifibrotics...