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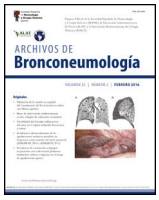

Editorial

Lung Cryobiopsy and the KISS Principle☆

Criobiopsia pulmonar y el principio KISS

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Recent years have seen a paradigm shift in the management of fibrosing interstitial lung diseases (FILD). It is now accepted that idiopathic pulmonary fibrosis (IPF) can be diagnosed by high-resolution computed tomography (HRCT) when a typical pattern of usual interstitial pneumonia (UIP) is observed, and the clinical context is correct.[1] In the absence of this pattern, as occurs in 50% of cases of IPF, surgical lung biopsy (SLB) is indicated.[2] After IPF is diagnosed, drugs to delay disease progression (pirfenidone, nintedanib) can be given, contraindicated drugs can be avoided, patients can be included in clinical trials, and strategies for early inclusion in transplant programs can be implemented.[3] Despite the importance of a specific histological diagnosis, the number of SBLs performed has steadily declined in recent years.[4] Mortality associated with SBL is 1.7%, a rate that is far from imperceptible; morbidity is 30%, and includes pneumonia, persistent air leak, and respiratory failure. Morbidity and mortality increase significantly in older patients, and in individuals with functional respiratory decline and associated comorbidities.[4] The introduction of lung cryobiopsy (LC), a semi-invasive endoscopic technique with significantly less morbidity and mortality than SBL and lower health costs, represents a great opportunity for increasing the number of cases of FILD with histological confirmation. Results obtained with LC are highly promising, as this technique offers the possibility of obtaining lung parenchyma specimens with a diagnostic yield of 70–85%.[5] Indeed, some authors propose that SLB should only be considered in cases in which LC does not provide a specific diagnosis.[6] However, before LC can be considered an alternative to SLB, prospective studies are needed to clarify a series of diagnostic and methodological issues.

Diagnostic accuracy. The diagnostic accuracy of LC is unknown, and this information will be essential if we are to evaluate its real utility.[7] This is of particular importance, since most published series include highly heterogeneous populations in which the diagnostic yield of LC may vary. Prospective studies must be performed in a single population of patients with suspected IPF to compare the results of LC with those of the gold standard SLB.[7] Although some authors claim that this comparative study would be difficult to conduct for ethical reasons, it may be wrong to assume that LC offers the same histopathological information as SLB in these patients. The histological study of the different FILDs is a complicated task due to the heterogeneity in the grade and characteristics of the histopathological changes in different areas of the lung. In fact, the degree of concordance among pathologists is far from ideal, and varies according to the specific type FILD under consideration.[8] Indirect evidence suggests that LC has certain diagnostic limitations. Concordance among pathologists regarding a UIP pattern is lower when LC samples are analyzed than when SBL samples are analyzed (50% vs 39%).[7] Moreover, the diagnosis of IPF was more frequent with LC than with SLB, all of which suggests that the greater amount of tissue from the SLB facilitates alternative diagnoses other than IPF.[7,8] Understanding the diagnostic accuracy of LC in different types of FILD, and in particular IPF, will help define better which patients are candidates for LC and which are candidates for SLB.

Lack of standardization of the technique. There are gaps in our knowledge of certain important methodological factors. One of the most important factors to be determined is the number of samples that must be taken to optimize the diagnostic efficiency of LC, and especially from which sites the samples should be obtained. A recent study demonstrated the importance of obtaining biopsies from at least 2 different segments of the same lobe, although these results need to be confirmed in larger series.[9]

Safety measures. There are also methodological variations associated with safety that probably have no influence on diagnostic accuracy, but that might considerably complicate the performance of a seemingly simple technique. The vast majority of published series justify tracheal intubation or the use of a rigid bronchoscope for optimal airway control in the event of massive bleeding. A review of the literature including over 1000 patients informs us that the incidence of massive bleeding with LC is exceptional, around 0.3%, a rate similar to conventional transbronchial biopsy (TBB).[3,5,10] The second reason for justifying tracheal intubation derives from the alleged need to extract the fiberoptic bronchoscope repeatedly *en bloc* together with the cryoprobe, in order to avoid "losing" the sample, as its diameter is greater than that of the working channel. In our experience, when a working channel of 2.8 mm is used, and the cryoprobe is 1.9 mm, the sample attaches to the cryoprobe sufficiently firmly to safely extract perfectly preserved samples, as occurs with TBB. The fiberoptic bronchoscope can therefore be held in position and aspiration can be initiated

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immediately, without the need for a second operator. Furthermore, a sheath has been recently designed through which the cryoprobe can be passed, in such a way that the probe can be withdrawn when each sample is obtained, while the fiberoptic bronchoscope remains in position.[11] Several groups have reported successful LC using the TBB method, with conscious sedation and airway intubation.[12,13] This simplified technique has been used in specialized centers, and larger safety studies are needed before it can be definitively endorsed. However, it may become a very promising option (perhaps with the systematic use of an occlusion balloon) that would facilitate the generalized use of LC, thus providing considerable savings in time, costs, and personnel, with airway intubation being used only in the most complicated cases. Simplification of the technique would expand its potential applications to include repeated LC throughout the course of the disease to evaluate biological makers of treatment response, for example.

In summary, although prospective, multicenter studies are needed to confirm the clinical usefulness and safety of LC, it seems clear that this endoscopic technique is here to stay. Its potential applications are wide-ranging, and not only limited to interstitial disease, as it could be extended to other fields of respiratory medicine, such as malignant disease, follow-up of the lung transplant patient, or critical patients with persistent pulmonary infiltrates.[14] The progressive simplification of the technique would help expand its use as a diagnostic technique, in the sentiment of the acronym KISS (Keep it simple, stupid).

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