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Respiratory muscles in interstitial lung disease: poorly explored and poorly understood

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Interstitial lung diseases (ILDs) are a heterogeneous group of parenchymal lung disorders characterized by permanent structural changes that result in mechanical modifications, notably a significant reduction in the elasticity of the lung parenchyma.[1] Among individuals with ILDs, dyspnea and lower exercise tolerance are quite common complaints, varying in severity and having psychosocial repercussions, as well as a negative impact on quality of life, affecting the patients and their families. [2] Many factors, alone or in combination, can contribute to those symptoms, including altered gas exchange, airflow limitation, pulmonary vascular involvement (usually by pulmonary capillary destruction and hypoxemia-induced vasoconstriction) and left ventricular dysfunction, as well as impairment of the respiratory musculature and accessory muscles,[1-8] together with possible mechanisms specifically related to the etiology of the ILD in question.

Due to the typical predominance of parenchymal changes in ILDs, the contribution of extrapulmonary factors to the pathophysiology of exercise intolerance is often overlooked. Despite its potential importance, the respiratory musculature has rarely been evaluated in studies addressing the mechanisms of dyspnea in ILDs in particular or in those investigating exercise intolerance in general.[9] In individuals with ILDs, the increased elastic recoil overloads the respiratory musculature, increasing its activity and the work of breathing.[4] Often, inspiratory pressure is preserved in the early stages of ILD,[10] largely due to the fact that ILD has a minimal impact on the position of the diaphragm—as compared with that of COPD, for example—the muscle fiber length-tension ratio therefore being maintained, with no mechanical disadvantage for generating inspiratory force. However, in the more advanced stages of the disease, with the progression of volume loss, there is a breakdown of this positioning, promoting the occurrence of neuromuscular dissociation (i.e., reduced ability to activate the respiratory musculature in response to increased demand from the respiratory center), which often exacerbates during exercise.[3,6,10]

In an article published in the current issue of the JBP, Santana et al.[11] show that a change in diaphragmatic mobility during deep breathing, as assessed by ultrasound, is quite prevalent (60%) in patients with ILDs of various etiologies and levels of functional severity. Theirs was the first study to assess diaphragm thickness during tidal breathing in patients with ILDs. The authors established a cut-off point derived from a simple spirometric measure (FVC < 60% of the predicted value) as a risk factor for reduced diaphragmatic mobility.[11]

There have been few studies evaluating the function of the respiratory muscles, including the diaphragm, by invasive or noninvasive measures, in patients with ILD, and those that have been conducted have produced discrepant results. He et al.[12] demonstrated that the mobility of the diaphragm during deep breathing, as assessed by ultrasound, was reduced only in patients with pulmonary fibrosis accompanied by emphysema and not in patients with idiopathic pulmonary fibrosis (IPF) alone. Therefore, the authors were unable to establish a correlation between ILD and a reduction in diaphragmatic mobility. However, in that study, a limiting factor in the interpretation of the results was the fact that patients with IPF had mild functional limitation.[12] In the study conducted by Elia et al.,[13] who evaluated the diaphragms of 16 patients with ILD, using catheters to measure pressures in the stomach and esophagus, there was no diaphragmatic fatigue at rest or after exercise. In the study conducted by Walterspacher et al.,[6] involving 25 patients with ILD, there was a reduction in diaphragmatic strength, as assessed with non-volitional measures.[6] In the study conducted by Faisal et al.,[10] diaphragmatic activity at rest and during exercise, as assessed by electromyography, was found to be greater in patients with ILD than in control and COPD patients.

As noted in the article published in this issue of the JBP,[11] ultrasound has several advantages for the evaluation of the diaphragm, especially because it is noninvasive, is easily performed and does not use ionizing radiation, as well as allowing the mobility and thickness of the diaphragm to be evaluated.[11] However, there is still a need for the development of reference values and the dissemination of clinical experience before ultrasound markers can be fully incorporated into medical practice for the clinical management of patients. In addition, this technique does not apply to the observation of the respiratory musculature during exercise, which would be a highly desirable attribute in the search for correlations between changes in the musculature and reduced exercise capacity.[13]

Although muscle involvement is common in patients with ILD, as evidenced in the study conducted by Santana et al.[11] and in previous studies, there are many aspects of the topic that have yet to be explored. From a pathophysiological point of view, the question is related to the significance of the observed changes in muscle function, whether they in fact attributable to a muscular mechanism primarily associated with the genesis of dyspnea or are only adaptive changes secondary to a reduction in lung volume, as observed during the progression of an ILD. In this context, it does not seem to be fully established whether the severity of the underlying disease acts as a

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confounding factor in the interpretation of data from the assessment of the respiratory musculature. Regarding clinical implications, it is essential that future studies of the respiratory musculature evaluate specific subgroups of ILD separately, because the peculiarities of each disease could alter the results, as well as because the systemic inflammatory process associated with diseases such as inflammatory myopathies and sarcoidosis can have a direct effect on the respiratory musculature.[3,4,6,8] In addition, the true impact of the use of ultrasound in the longitudinal evaluation of patients, its prognostic implications, and its value in monitoring the progress of ILDs have yet to be explored, as has been done for other indicators, such as the degree of dyspnea, FVC, DLCO, and SpO_2.[1,14]

It is obvious that there are still many gaps in our knowledge of the role that the respiratory musculature plays in the pathophysiology of functional limitation and its monitoring in the clinical management of ILDs. We also emphasize that measures derived from ultrasound alone are not able to describe all aspects of respiratory muscle function. Ideally, functional assessments of the respiratory musculature would involve the use of ultrasound in combination with complementary methods, such as (invasive or noninvasive) measurements of force or electromyography. It is undeniable, however, that the study conducted by Santana et al.[11] represents a relevant and robust step in that direction, encouraging further research to supplement our knowledge in this area.

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