EDITORIAL

Should We Be Paying Attention to Inspiratory Capacity?

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The measurement of inspiratory capacity (IC) has traditionally been used in research that mainly assessed the relation between dyspnea and airway obstruction in patients with asthma or chronic obstructive pulmonary disease (COPD).[1] Important changes in our concept of COPD in recent years[2,3] have been accompanied by new views of the possible role of IC, which we will discuss in this editorial.

The main pathophysiological finding in COPD is airway obstruction, traditionally expressed through forced expiratory volume in 1 second (FEV_1). However, this parameter is not closely correlated with dyspnea, the main symptom of this disease.[4,5] This mismatch is better understood today through the current concept of COPD as a multidimensional disease in which factors other than FEV_1 can better express phenotypic heterogeneity.[3] Notable among these dimensions is pulmonary hyperinflation, defined as an abnormal increase in the volume of air trapped in the lungs at spontaneous end expiration.[6] Air trapping is associated with a loss of elastic support in the pulmonary parenchyma and, though its development in the natural course of COPD is unknown, its prevalence increases while FEV_1 decreases.[6] Hyperinflation initially passes through a silent phase during which patients are unaware of it, since their respiratory system compensates for the mechanical disadvantage it causes. Nevertheless, these mechanisms may be compromised in situations that require increased ventilatory demand. As the disease advances, air trapping increases and provokes a neuromechanical respiratory dissociation, which is the main reason for exertional dyspnea in patients.[7] During exercise, increased ventilatory demand leads to increased respiratory frequency and tidal volume. Because of resistance that is mainly expiratory plus the patient's inability to shorten inspiratory time or lengthen expiratory time, air becomes trapped and dynamic hyperinflation is added proportionally to the static hyperinflation already present at rest.[8]

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Altered inspiratory mechanics that condition pulmonary hyperinflation are appropriately expressed through IC. In recent years, various studies have shown how diminished IC is related to reduced peak oxygen uptake during a maximal exercise test on a cycle ergometer[9] and to increased dyspnea (Borg scale) during a 6-minute walk test.[10]

In addition to providing insight into limited exercise capacity in patients with COPD, IC is a parameter that can change with the various therapeutic options for COPD and that is even more sensitive than FEV_1 to such changes. These findings have helped bring about a less fatalistic attitude to this disease.[11] Significant increases have been described in controlled clinical trials of anticholinergics, theophyllines and β_2-agonists, either alone or combined with inhaled corticosteroids.[12-16] Several of these studies revealed how increased IC correlated with a reduction in dyspnea at the same work load and with an increase in exercise duration at a constant level of effort. Furthermore, IC has demonstrated its sensitivity to changes in circadian rhythms and to capturing the added benefits of combining bronchodilators.[13,15] IC has also improved after exercise with respiratory rehabilitation programs that targeted lower[17] or upper[18] extremities, with oxygen therapy (fractions of inspired oxygen close to 50%) either alone or combined with helium,[19] with noninvasive ventilation,[20] and after surgical removal of giant bullae from the lung parenchyma.[21] Although all these recently published studies reinforce the role of IC in monitoring patients with COPD, we should bear in mind that studies with bronchodilators are carried out over the short and medium term and that the effect on IC of several nonpharmacological treatments has been assessed in uncontrolled trials and small samples of patients.

Aside from the important effect that improved IC can have on dyspnea, exercise tolerance and therefore quality of life in COPD patients, our group has recently shown that pulmonary hyperinflation expressed by IC corrected by total lung capacity (IC/TLC) significantly influences survival in this disease, independently of the degree of airway obstruction.[5] Furthermore, IC/TCL was more closely related to body mass index than FEV_1 was, possibly indicating that the first parameter better reflects the overall impact of the disease. We described the IC/TLC ratio conceptually as an "inspiratory fraction," since it represents

the volume of air inhaled after maximal inhalation in relation to total capacity. To a certain extent, this parameter is similar to the familiar cardiac ejection fraction, which is extremely useful and often serves diagnostic and prognostic purposes in patients with heart disease. A practical IC/TCL cutoff point of 25% proved to be an important predictor, since mortality in patients tripled when their inspiratory fractions were below this threshold. These findings could explain the beneficial effect on survival and quality of life observed in a subgroup of patients who underwent lung volume reduction surgery in the National Emphysema Treatment Trial.[22] The research team that conducted that trial also corroborated the importance of inspiratory fraction in the course of COPD, although the threshold they applied was somewhat lower (17%) for the subgroup of patients with very severe COPD and an emphysematous phenotype.[23] In reality, the influence of IC/TLC on the prognosis of patients with COPD was to be expected, given the good correlation of pulmonary hypertension with other fairly strong predictors of mortality that are independent of FEV_1, such as dyspnea[4] and exercise capacity.[24,25]

Until now, IC alone has demonstrated no prognostic value, but it may yet be shown to have such ability and establish itself as a more simplified version of the inspiratory fraction in settings where no plethysmographic equipment is available. However, clinical practice requires appropriate reference values, which have currently only been validated in very small population samples.[26] Furthermore, inspiratory fraction after bronchodilation has recently been described as a better predictor of exercise capacity than IC at a slightly higher cutoff value than that used to predict survival (28%).[27]

In the past year, 3 studies have supported the importance of IC as a useful tool for assessing COPD exacerbations,[28-30] which is usually accomplished through clinical parameters and arterial blood gas analysis. Objective, quantitative measures of airway obstruction (FEV_1 and/or peak flow) and of the repercussions on ventilatory mechanics (through IC) could lead to improved evaluation and grading of exacerbations as well as to better assessment of response to treatment. Moreover, improved portability of measurement devices has made their use more feasible. The 3 studies mentioned showed that, as in stable patients, IC was more sensitive than FEV_1 for evaluation of an early response to bronchodilator treatment in exacerbated patients. Both parameters correlated with the development of symptoms over the short and medium terms. These findings in patients with moderate exacerbations might be transferable to more severe cases, which require noninvasive ventilation and in which IC may also assist in assessing the initial response to therapy and later to weaning. However, there is currently a lack of studies designed for this group of patients, in whom the short-term mortality rate after discharge is high and in whom hyperinflation and ventilatory instability may play an important role.[31]

According to the studies reviewed, there should be no doubt that IC estimation is useful for evaluating COPD. However, we should bear in mind that IC does not replace the main parameter in COPD, which continues to be FEV_1, since this factor currently determines the diagnosis and classification of disease severity. As with IC, FEV_1 has been shown to be a good predictor of mortality. Despite its previously mentioned weaknesses, it is determined by a highly standardized method and is therefore highly reliable and reproducible. FEV_1 is also the only available marker for which longitudinal data show its correlation with the natural course of COPD. Furthermore, although advances have been made in the method for determining IC, there is still a need for international prediction equations and for determining how IC evolves over the course of the disease.

Moreover, that this highly prevalent disease is underdiagnosed is well known, as is the need to encourage greater use of spirometry in the smoking population.[32] Adding IC measurement to FEV_1 assessment might therefore be difficult to accomplish in all patients with COPD. However, we believe that greater use of diagnostic spirometry does not exclude an additional and more complete assessment of the disease through IC measurement in severe COPD (FEV_1 <50%) or when pulmonary hyperinflation is suspected. Although it seems logical to monitor this parameter when treatment is applied, it is unclear how IC checks should be timed in a stable patient, and further data are required to know its long-term response to bronchodilator treatment.

In summary, although expiratory airflow limitation is the fundamental pathophysiologic finding in COPD, its main consequence is hyperinflation and its expression comes through IC. Although this parameter appears to be highly sensitive and reliable for assessing therapeutic response and predicting morbidity and mortality in patients with COPD, its use in ordinary clinical practice is not clearly defined. However, inclusion of IC in future consensus guidelines is likely, perhaps for advanced forms of the disease where hyperinflation is more prevalent and the multidimensional nature of COPD is more evident.

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