Inspiratory capacity and exercise tolerance in chronic obstructive pulmonary disease

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During the past half-century, many studies have investigated the correlation of exercise tolerance to routine lung function in patients with obstructive pulmonary disease. In virtually all of these studies, the degree of airway obstruction was assessed in terms of forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC). Because in most studies only a weak correlation was found between exercise tolerance and degree of airway obstruction, it has been concluded that factors other than lung function impairment (eg, deconditioning and peripheral muscle dysfunction) play a predominant role in limiting exercise capacity in patients with chronic airway obstruction. Recent work, however, suggests that in patients with chronic obstructive pulmonary disease, the inspiratory capacity is a more powerful predictor of exercise tolerance than FEV_1 and FVC.

Key Words: *Chronic obstructive pulmonary disease; Exercise; Inspiratory capacity; Total expiratory flow limitation*

Capacité inspiratoire et tolérance à l'exercice dans la maladie pulmonaire obstructive chronique

Pendant la moitié du siècle dernier, de nombreuses études ont recherché une corrélation entre la tolérance à l'exercice et les épreuves courantes de fonction pulmonaire chez des patients atteints d'une maladie pulmonaire obstructive. Dans presque toutes ces études, le degré d'obstruction bronchique a été évalué en utilisant le volume expiratoire maximal par seconde (VEMS) et la capacité vitale forcée (CVF). Parce que la plupart des études n'ont démontré qu'une faible corrélation entre la tolérance à l'exercice et le degré d'obstruction bronchique, il a été conclu que des facteurs autres qu'une altération de la fonction pulmonaire (par exemple, le déconditionnement et le dysfonctionnement des muscles périphériques) jouent un rôle prédominant dans la limitation de la tolérance à l'exercice chez les patients accusant une obstruction bronchique. Cependant, des travaux récents laissent penser que chez les patients atteints d'une maladie pulmonaire obstructive chronique, la capacité inspiratoire est un prédicteur plus puissant de la tolérance à l'exercice que ne le sont le VEMS ou la CVF.

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In the late 1960s I went specifically to London, England, to meet professor Ronald V Christie, whose research inspired me to study respiratory mechanics. To my great disappointment, I did not meet Ronald in London because he had already left for his post at McGill University, Montreal, Quebec. Nevertheless, I was destined to join him later in Montreal, and worked happily under him when he was the Chief of Medicine and Dean of Medicine. I was inspired not only by his scientific work but also by his distinct personality. He had class, style and wit. Furthermore, he was a clear and concise speaker, and I tried my best to copy him. In fact, it is largely through his example that I learned to formulate concisely in research, which served me well in my career.

I am grateful to Ronald for his friendship, and I am proud that I have led the Meakins-Christie Laboratories for many years (1979 to 1995).

Dyspnea and exercise limitation are the predominant complaints of patients with chronic obstructive pulmonary disease (COPD), and are commonly the reason for seeking medical attention. Yet, the routine assessment of lung function is generally focused almost entirely on forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC), although there is ample evidence that in COPD patients these tests correlate poorly with both dyspnea and exercise tolerance (1). Accordingly, it is axiomatic that in COPD the response to any treatment assessed in terms of FEV_1 and FVC should differ from that based on exercise tolerance or on subjective measures of dyspnea and quality of life. In fact, in COPD it is hyperinflation that plays a central role in eliciting dyspnea, decreased exercise tolerance and ventilatory failure (1-4). Hyperinflation is commonly assessed by measuring the functional residual capacity (FRC) with body plethysmography, which is complex, expensive and in patients with severe airway obstruction may lead to overestimation of the actual FRC because the transmission of alveolar pressure to the mouth during the panting manoeuvre is delayed by increased airway resistance (5). However, the increase of FRC in patients with obstructive pulmonary disease is necessarily accompanied by a reduction in inspiratory capacity (IC) (Figure 1). In contrast to FRC, the measurement of IC is simple, cheap and reliable. Thus, IC testing provides a useful tool for the indirect assessment of pulmonary hyperinflation in COPD patients. Indeed, in such patients a reduction of IC implies hyperinflation with concomitant dyspnea and decreased exercise tolerance (3,4,6).

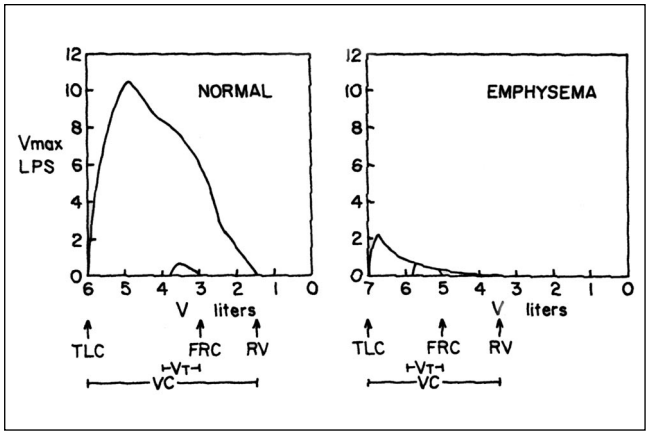

Figure 1) *Flow-volume curves during forced and quiet expiration in a normal subject (***left***) and in a patient with severe emphysema (***right***). While in the normal subject there is considerable flow reserve over the resting tidal volume range, in the patient the tidal expiratory flow rates are maximal, ie, expiratory flow limitation is present. The latter causes increased functional residual capacity (FRC) with concomitant reduction of inspiratory capacity (IC=TLC-FRC). LPS Litres/s; RV Residual value; TLC Total lung capacity;VC Vital capacity; VT Tidal volume during quiet breathing. Data from reference 18*

IC AND EXERCISE TOLERANCE

The maximal ventilation that a patient can achieve plays a dominant role in determining exercise capacity and may be limited by the highest flow rates that can be generated. Most normal patients and endurance athletes do not exhibit tidal expiratory flow limitation (FL), even during maximal exercise (7). In contrast, in COPD patients, tidal expiratory FL is frequently present already at rest (1,2,6), as first suggested by Hyatt (8). Tidal FL promotes dynamic hyperinflation (DH) with a concomitant decrease in IC (Figure 1). In fact, Diaz and coworkers (6) have recently shown that, in most COPD patients who are FL at rest, the IC is lower than normal, while in patients who are non-FL, IC at rest is within normal limits (Figure 2).

In normal patients there is a substantial expiratory flow reserve both above and below the FRC, as shown by the fact that the maximal expiratory flow rates available are much higher than the flow rates used during resting breathing (Figure 1). As a result, in normal patients, the tidal volume during exercise can increase at the expense of both the inspiratory and expiratory reserve volumes (2). In contrast, in COPD patients who exhibit FL at rest, the flows available below FRC are insufficient to sustain even resting ventilation, as shown in Figure 1. Consequently, in such patients the maximal tidal

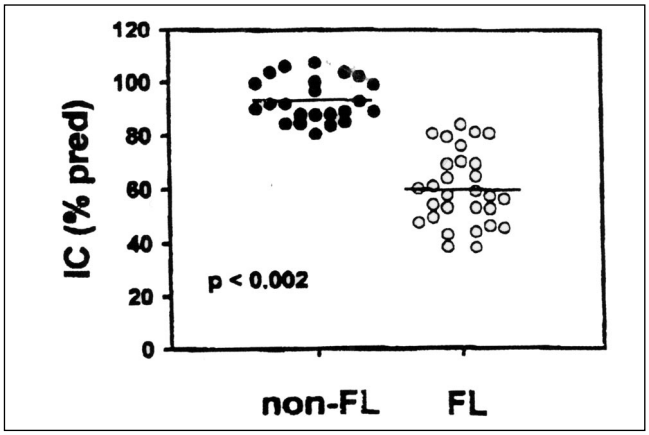

Figure 2) *Inspiratory capacity (IC), expressed as percentage predicted (% pred), in 23 patients with chronic obstructive pulmonary disease (COPD) without, and 29 COPD patients with, tidal expiratory flow limitation (FL) at rest. In most FL patients, IC was decreased while in the non-FL patients, IC was within normal limits. Data from reference 6*

volume during exercise (VTmax), and hence the exercise tolerance, should be limited by their reduced IC. In fact, recent studies have shown that in COPD patients there is a much stronger correlation of maximal oxygen uptake ($\dot{V}O_2max$) to IC than to FEV_1 and FVC (3,6) (Figure 3). Although the correlation of $\dot{V}O_2max$ to IC is relatively high (Figure 3), the coefficient of determination (r^2) is only 0.56, indicating that IC explained only 56% of the variance in $\dot{V}O_2max$. Diaz et al (7), however, showed that FEV_1/FVC also plays a significant role in predicting $\dot{V}O_2max$. In fact, using multiple regression analysis, they showed, that, taken together, IC and FEV_1/FVC account for 72% of the variance of $\dot{V}O_2max$. The remainder (28%) is probably because of other factors such as reduced cardiac output as a result of intrinsic positive end expiratory pressure, deconditioning and peripheral muscle dysfunction (9). Because reduced exercise capacity in COPD patients shows only a weak link to lung function impairment measured in terms of FEV_1 and FVC (1,3,10), it has been argued that factors other than lung function impairment (eg, deconditioning and peripheral muscle dysfunction) are the predominant contributors to reduced exercise tolerance (11,12). The recent studies based on assessment of IC, however, have shown that lung function impairment is probably the major contributor to reduced exercise tolerance, at least in COPD patients who are FL at rest (6).

Assessment of IC provides useful information in terms of bronchodilator treatment. The effect of bronchodilators in patients with obstructive lung disease is commonly assessed in terms of the change in FEV_1 seen after bronchodilator administration relative to the control values. According to the American Thoracic Society's recommended criteria, a change in FEV_1 of more than 12% is a significant response (13). Although some COPD patients may not exhibit a significant change in FEV_1 after bronchodilator administration, they nevertheless claim improvement in symptoms (14). Because pulmonary hyperinflation plays a paramount role in determining the intensity of dyspnea (1), it is likely that in such patients there is a decrease in the degree of DH (decreased FRC and increased IC) after bronchodilator administration. In fact, Tantucci et al (4) have recently shown that, in many COPD patients with little or no change in FEV_1, there was an increase in IC of more than 12% after salbutamol administration, reflecting significantly decreased DH. In the present study, a negative correlation was found between the degree of chronic dyspnea and IC. An increase in IC after bronchodilator administration in COPD patients has also been reported by Pellegrino and Brusasco (15). Thus, in obstructive lung disease patients, the benefit of bronchodilator therapy should be assessed not only in terms of change of FEV_1, but also, most importantly, in terms of change in IC as well. Because performance of IC precedes the FVC manoeuvre, FEV_1 and IC are, in fact, commonly recorded together during bronchodilator testing. Though in the past bronchodilator testing focused on assessment of changes in FEV_1, the scrutiny of changes in IC should be mandatory because it provides useful information pertaining to both dyspnea and exercise tolerance. Indeed, it has also been recently shown that in COPD patients the increase in IC after anticholinergic therapy best reflected the improvements in exercise endurance (16).

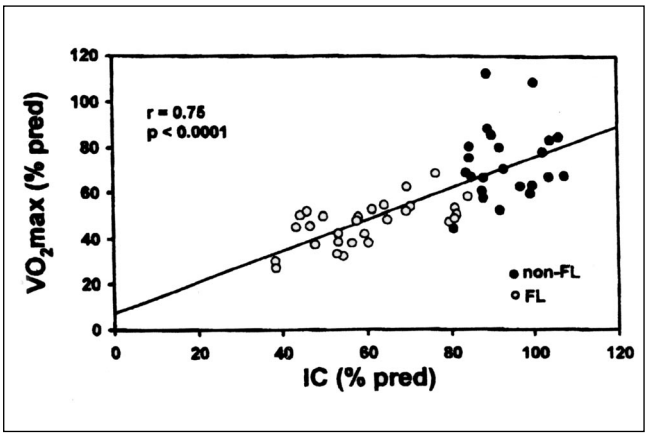

Figure 3) *The relationship of maximal oxygen uptake during exercise ($\dot{V}O_2max$) to resting inspiratory capacity (IC) in 52 patients with chronic obstructive pulmonary disease with and without tidal expiratory flow limitation (FL) at rest. These data involve the same patients as in Figure 2. % Pred Percentage predicted. Data from reference 6*

The assessment of IC has also provided useful information on the effects of surgical treatment in COPD patients (16).

CONCLUSIONS

Measuring the IC is useful for monitoring the status and progress of COPD patients, and for assessing the efficacy of their treatment. It is time for inspiratory capacity, the Cinderella of lung function testing, to take pride of place with her two stepsisters, FEV_1 and FVC.

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