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EDITORIAL

Tough at the top: must end-expiratory lung volume make way for end-inspiratory lung volume?

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A reduced exercise capacity, which limits the performance of activities of daily living and social participation, is a cardinal feature of chronic obstructive pulmonary disease (COPD). Breathlessness is the main limiting symptom, although, depending on the task undertaken [1], leg discomfort is prominent in a substantial minority of patients. Dyspnoea arises through the interplay of pulmonary manifestations of COPD (airflow obstruction, emphysema and destruction of the pulmonary vascular bed) [2], systemic effects of the disease [3] and neural mechanisms [4, 5]. These complex relationships remain incompletely understood. Traditionally, both the severity of COPD and the efficacy of treatment interventions have been assessed using resting lung function measures, particularly forced expiratory volume in 1 s (FEV_1). However, health status is more closely associated with lung volume measurements [6] than FEV_1, and bronchodilator-based therapies can improve lung volumes at rest [7] and during exercise [8] without change in FEV_1, prompting interest in the study of dynamic lung volumes and dyspnoea arising during exercise.

The metabolic demands of exercise at a given intensity require a corresponding minute ventilation in order to sustain them. Indeed, the levels of ventilation achievable during exercise in relation to oxygen consumption or carbon dioxide production are used as measures of cardiopulmonary fitness (*e.g.* before surgery). An increase in ventilation can occur through an increase in tidal volume or respiratory rate. Healthy individuals can increase their tidal volume during exercise by breathing out further to a lower end-expiratory lung volume (EELV) by contracting their abdominal muscles [9]. This manoeuvre serves both to lengthen the diaphragm, increasing the contractile power of the inspiratory muscles [10], and also to cause cranial movement of the abdominal contents. Since exercise is usually conducted in an upright position, subsequent inspiration is facilitated by their descent.

In COPD, the likelihood of EELV increasing with increased minute ventilation is suggested by data presented in 1934 by Ronald Christie who presciently noted ''The chest is already in the inspiratory position, with a consequent diminution of complemental air and inability to produce any significant increase in inspiratory depth. Expiratory depth also cannot be increased owing to diminution, or even obliteration, of the reserve air'' [11]. By 1971, POTTER *et al.* [12] were able to measure flow–volume loops during treadmill exercise. They showed that both EELV and end-inspiratory lung volume (EILV) were shifted substantially upwards in a small group of patients with COPD.

Recently, several studies have suggested that dynamic hyperinflation is the most important mechanism causing exercise limitation due to dyspnoea in patients with COPD. For example, O'DONNELL *et al.* [13] showed that decline in inspiratory capacity during exercise, an index of hyperinflation, is closely related to the magnitude of dyspnoea, and several data suggest that interventions that improve symptoms in COPD also reduce dynamic hyperinflation [14–16]. Moreover, dynamic hyperinflation is closely linked with limitation of the activities of daily living [17].

The technique for assessing dynamic hyperinflation by inspiratory capacity (IC) measurements during exercise is not entirely straightforward; the individual breathes in to total lung capacity (TLC), which has been shown to remain constant during exercise, at intervals throughout the test, and as the EELV rises, the IC falls. However, it requires the subject to make a maximal IC manoeuvre while they exercise; how satisfactorily patients do this has not been assessed. Conversely, if patients have not achieved a true TLC before exercise, but generate a maximal IC during exercise, then dynamic hyperinflation would be underestimated. Moreover, to accurately measure dynamic hyperinflation with the IC technique, it is important to ensure that the manoeuvre is started from functional residual capacity, and this ''static'' concept can be hard to evaluate during the tachypnoea that accompanies exercise. These and other technical reservations can be overcome (albeit at a cost) by the use of alternative technologies that make continuous measures of lung volume, such as optoelectronic plethysmography [18]. However, the greater scientific problem is that exercise, through flow limitation, drives both dynamic hyperinflation (*i.e.* increased EELV) and tidal volume increases, which cause increased EILV. Thus, dissecting the relative contribution of the two as aetiological factors of dyspnoea or exercise limitation through other mechanisms [19] present serious difficulties but could have rewards, since their mechanisms are potentially different.

The assessment of dynamic lung volumes has developed from a research technique employed by investigators focussing on physiological mechanisms to an outcome measure with

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acceptable responsiveness and repeatability, which has been employed in large-scale multicentre trials of newer inhaled bronchodilators. In this issue of the *European Respiratory Journal*, GUENETTE *et al.* [20] report how they exploited existing large trial databases to further refine our understanding of the role of lung volume changes during exercise and, in particular, to address the outstanding question of whether exercise limitation in COPD occurs because of true dynamic hyperinflation (*i.e.* the increase in EELV occurring during exercise) or whether it is in fact changes in end-inspiratory lung volumes, expressed either as EILV or as inspiratory reserve volume (IRV), that are the main contributors to breathlessness. To compare the role of these two parameters, from where the breath starts and where it ends, they examined patients prospectively studied in two multicentre, double-blind clinical studies designed to evaluate the clinical benefit of tiotropium, a long-acting antimuscarinic bronchodilator. As expected, a minority, some 15%, of patients were identified as nonhyperinflators (for this purpose, strictly defined as no rise in EELV, as manifested by no fall in IC). These patients were then matched in a case–control fashion to subjects from the remaining participants. The hyperinflators demonstrated an early fall in IC (achieving >70% of their hyperinflation in this time); however, the exercise performance of both groups remained identical until tidal volume plateaued (and, thus, decreased as a function of increasing minute ventilation). Based on these data, the authors concluded that it is EILV, rather than EELV, that represents the constraining factor in COPD. This is plausible, since the pressure–volume characteristics of the respiratory system are most disadvantageous at this point, requiring high levels of neural drive [21], and it is likely that this drive also causes dyspnoea [4].

From a treatment perspective, the present data would suggest significant benefit is achievable either if the system can be allowed to work more comfortably at very high lung volumes or if it can be prevented from reaching them by reducing EELV or tidal volume (thus reducing EILV). Some interventions that reduce both EELV and EILV have already been noted, but beneficial results also occur where metabolic demand is reduced through training and improved muscle metabolism [22, 23]. Further experimental data supporting the specific relevance of EILV is provided by the observation that augmenting inspiratory muscle action at high lung volumes, for example by the use of noninvasive inspiratory pressure support, can extend exercise duration [24] and increase peak work load [25]. Conceptually, interventions that increase respiratory system compliance at high lung volumes might also be effective; how this can be achieved is more difficult, although we have previously reported an increase in chest wall compliance in COPD patients receiving nocturnal noninvasive inspiratory pressure support directly supervised as an in-patient [26], and this therapy is recently reported to be an effective adjunct to rehabilitation [27].

In conclusion, going forward, it seems that when evaluating lung volumes during exercise, a focus on IRV may be most appropriate. Although further work will be required to address this, this finding is to be welcomed not least because the measurements are easier. Looking back, Christie may well have summed the case neatly by his observation that patients with COPD have an ''inability to produce any significant increase in inspiratory depth'' and that this limits their capacity [11].

STATEMENT OF INTEREST

None declared.

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