Clinical utility of work-of-breathing measurements in COPD

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The measurement of the mechanical work of breathing (WOB) has been used in clinical research for over four decades and has provided valuable insights into the pathophysiological derangements that exist in patients with chronic obstructive pulmonary disease (COPD). These WOB calculations are based on the principle that work is performed when pressure changes the volume of the respiratory system. In 1958, E.J.M. Campbell introduced a graphic analysis of the oesophageal pressure ($P_{oes}$)/tidal volume ($V_T$) plots over the respiratory cycle, which allowed work to be separated into several components [1]. These components include: inspiratory, expiratory and total resistive work rates in joules (J·min$^{-1}$); inspiratory elastic work rates (J·min$^{-1}$); and total inspiratory work (J·I$^{-1}$). A detailed discussion of the technical aspects of WOB measurement is beyond the scope of this abstract and excellent reviews are available elsewhere [2]. WOB is increased in flow-limited COPD patients at rest, mainly because of the increased flow resistive and elastic loads on the inspiratory muscles. During exercise, flow resistive work increases as ventilation increases, elastic/threshold loads increase because of the effects of dynamic hyperinflation, and dynamic lung compliance is reduced below resting levels because of the effects of exercise tachypnoea. For these reasons, WOB at any given ventilation is often markedly increased in COPD, as compared with controls, particularly during exercise.

Limitations of work-of-breathing measurement

Accurate measurement of WOB in COPD is complex and difficult to perform, and several limitations preclude its routine clinical use except in specialised research laboratories. These limitations are summarised as follows. 1) The measurement of chest wall relaxation curves and its placement on the Campbell diagram is very difficult, therefore, accurate measurements of the elastic inspiratory work is problematic. 2) In WOB calculations, the work performed in overcoming flow resistance of the chest wall is omitted, leading to underestimation. 3) In hyperinflated COPD patients, measurements of volume changes at the mouth may underestimate thoracic volume changes because of gas compression effects. 4) Mechanical work measurements are based on the assumption that the respiratory system follows its relaxation pressure/volume relationship. However, in COPD, concomitant rib cage-abdominal distortion effects occur at higher ventilation levels, increasing the elastic work, which is not accounted for in the usual $P_{oes}/V_T$ loop analysis. 5) Tonic inspiratory muscle activity may persist throughout the respiratory cycle and is not accounted for in mechanical work calculations. 6) Reliable population data on mechanical work measurements are not available in COPD. In the published literature there is considerable variation of measurement values both during rest and exercise, reflecting interstudy differences in the method of measurement and calculation. 7) There are anecdotal reports that intra-individual comparisons of overall WOB before and after therapeutic interventions in COPD are relatively insensitive. 8) WOB correlates poorly with dyspnoea intensity; healthy subjects can voluntarily increase WOB to a similar level to that of COPD patients without experiencing dyspnoea.

Important work-of-breathing components in ventilated COPD patients

Notwithstanding the aforementioned limitations, mechanical assessment continues to serve as an important research tool. In ventilated patients with COPD, measurement of dynamic ventilatory mechanics (especially elastic work components) has provided important new insights into the interface between the patient and ventilator, and has resulted in the optimisation of mechanical ventilation and weaning strategies in such patients. The presence of a “hidden” inspiratory threshold load (ITL) as a consequence of lung hyperinflation has been shown to have important clinical implications [3]. The ITL (auto-positive end-expiratory pressure effect) occurs because of progressive air trapping in the setting of expiratory flow limitation, when the breathing pattern is altered for a given ventilation or when ventilation is increased. Thus, inspiration begins before lung emptying is complete and the inspiratory muscles must first overcome the combined inward recoil of the lung and chest wall before any inspiratory flow is initiated. The threshold is measured on the Campbell diagrams as the

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horizontal distance between the static chest wall relaxation curve and the onset of inspiratory flow at isovolume. Alternatively, it can be determined from simultaneous Poes and volume tracings as the measure of reduction in tidal Poes at the point of onset of inspiratory flow. This threshold load has been shown to be associated with decreased triggering sensitivity of the ventilator and can substantially increase elastic loading of the inspiratory muscles throughout inspiration [3]. The administration of continuous positive airway pressure (CPAP) at a level just before the threshold load effectively counterbalances the load, enhances the triggering sensitivity of the ventilator, improves patient comfort and helps to unload the overburdened inspiratory muscles [3].

**Clinical importance of the inspiratory threshold load in spontaneously breathing patients with COPD**

There is increasing realisation that lung hyperinflation and the consequent threshold/elastic load on the inspiratory muscles has important clinical implications in nonventilated patients with obstructive airway disease. For example, in asthmatic patients during bronchoconstriction, respiratory discomfort has been shown to correlate better with measures of dynamic hyperinflation (such as reduced inspiratory capacity) than expiratory flow rate measurements such as the forced expiratory volume in one second [4]. Moreover, the fact that CPAP, and not inspiratory pressure support of equal magnitude, effectively relieved dyspnoea in hyperinflated asthmatic subjects, attests to the important negative sensory consequences of the ITL. In that study, inspiratory pressure support alone provided modest resistive and elastic unloading only, but did not address the ITL; therefore, it provided only minimal symptomatic relief compared with CPAP [4]. The related observation that optimised low-level CPAP can relieve dyspnoea and improve exercise endurance in some patients with COPD suggests that dynamic hyperinflation and the ITL also contribute importantly to symptom intensity and exercise intolerance in this population [5]. The clinical implication of this finding is that interventions that reduce hyperinflation or counterbalance its negative effects (i.e. CPAP) should lead to relief of dyspnoea and increased activity levels in COPD [5].

**Surrogate measurements of the elastic/threshold load in COPD during exercise**

Given that Poes measurements are cumbersome and somewhat invasive, there is increasing interest in alternative noninvasive methods of assessment of dynamic ventilatory mechanics. Quantitative flow/volume loop analysis, based on serial dynamic inspiratory capacity (IC) measurement, is one such noninvasive approach that is currently being studied. Progressive reductions of dynamic IC during exercise reflect dynamic increases in end-expiratory lung volume, since total lung capacity (TLC) has been shown not to change from rest to peak exercise in COPD. Changes in IC during exercise correlate strongly with Poes-derived measurements of respiratory elastic work and indices of neuromechanical uncoupling, such as the ratio of tidal Poes (relative to maximal inspiratory pressure) to VT (standardised as a percentage of vital capacity) [6]. The smaller dynamic IC becomes during exercise, the closer VT is positioned to TLC and the upper alinear extreme of the respiratory system’s pressure-volume relationship and the greater the ITL.

Quantitative flow/volume loop analyses, which compare exercise tidal flow/volume loops to the maximal envelope, permit an assessment of the mechanical constraints of VT expansion and the reserves of inspiratory and expiratory flow generation that exist at any point in time. Thus, reduced dynamic inspiratory reserve volume (IRV):

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\text{IRV} = \text{IC}_{\text{dyn}} - V_T
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where IC_{dyn} represents dynamic IC, and increased VT/IC_{dyn} ratios represent significant ventilatory constraints and contribute to earlier exercise termination in COPD. Changes in IC_{dyn} (and IRV) correlate strongly with dyspnoea intensity during exercise in COPD. The corollary of this is that increases in dynamic IC, following either pharmacological or surgical volume reduction correlate well with dyspnoea relief achieved as a result of these interventions [7]. Serial IC_{dyn} measurements during exercise have been shown to be both highly reproducible and responsive in clinically stable, advanced COPD, provided appropriate care is taken with the technique [7].

In summary, despite its well-recognised limitations, the assessment of the mechanical work of breathing remains a valuable research tool. In chronic obstructive pulmonary disease, mechanical assessment is used to evaluate pathophysiological impairment and to determine the therapeutic impact of interventions such as ventilatory assistance, bronchodilator therapy and surgical volume reduction. Currently, the study of the interrelationships between specific mechanical derangements (i.e. dynamic hyperinflation), symptom intensity, disability and diminished health status in chronic obstructive pulmonary disease is the focus of much attention. Noninvasive assessment of dynamic lung mechanics, based on serial dynamic inspiratory capacity measurements, may serve as a reliable surrogate for oesophageal pressure-derived measurements of elastic mechanical work. Preliminary studies have shown that this approach is reliable and has potential clinical utility, particularly in the area of therapeutic evaluation.

**References**


