Online supplement – Methods section

Dynamic lung volumes. The inspiratory capacity (IC) manoeuvre was demonstrated to the subject before each exercise test. Subjects were required to practice the manoeuvre to ensure that satisfactory and repeatable measurements could be obtained. Indeed, there was no significant decline in the degree of inspiratory effort during IC manoeuvres throughout graded exercise – P_{OES} swings were similar in magnitude to those observed at rest. To compensate for signal-drift, we corrected the volume trace using the IC ratio method detailed by Dolmage and Goldstein [1]. Based on previous data from our laboratory [2], we assumed that residual volume was not different between control subjects and patients with HF. IC values were then used to calculate end-inspiratory lung volume (EILV = VC – [IC – V_T]) and end-expiratory lung volume (EELV = VC – IC), where VC represents the largest vital capacity obtained during multiple vital capacity manoeuvres performed at varying degrees of expiratory effort (i.e., 20% through 100% of maximal effort). A significantly higher dynamic EELV compared to resting values represented an end-expiratory lung volume *above* functional residual capacity (i.e., dynamic hyperinflation), whereas a dynamic EELV significantly lower than resting values denoted an end-expiratory lung volume *below* functional residual capacity [3]. All pulmonary function tests were performed while seated on the cycle ergometer.

Ventilatory constraint. The methods used to estimate maximal ventilatory capacity (MVC) were modified from those described by others [4-6]. In brief, MVC was calculated from the maximal achievable inspiratory and expiratory flow-rates for a given EILV and EELV. The tidal-breath was sub-divided into 0.01 L increments, for $n = V_T/0.01$ number of segments. Each segment was then divided by the corresponding mean expiratory flow-rate to yield an expiratory-time. The expiratory times of all segments were summed to provide a minimal expiratory-time for the breath (T_{Emin}). Similarly, minimal inspiratory-time (T_{Imin}) was determined by applying the same procedure to the individual's maximal inspiratory flow-volume envelope. The summation of T_{Emin} and T_{Imin} were used to derive a maximal achievable f_R (i.e., $f_{Rmax} = (1/(T_{Emin} + T_{Imin}) \times 60)$). Consequently, f_{Rmax} was multiplied by V_T to calculate MVC. This method of estimating MVC assumes an individual can generate maximal flow-rates instantaneously at the start of each breath [7]. Therefore, as suggested by Babb and Rodarte [4], the computed T_{Emin} and T_{Imin} values were arbitrarily increased by ~11% to compensate for inertia of the respiratory system.

The degree of expiratory flow-limitation during exercise was assessed in two ways. First, expiratory flow-limitation was quantified as the percentage of tidal volume where expiratory flow rates met or exceeded the boundary of the maximal expiratory flow-volume envelope. Secondly, P_{OES}, flow and volume data were recorded during the graded vital capacity manoeuvres. These data were used to construct isovolume pressure-flow relationships at lung volumes corresponding to 15, 30, 50 and 70% of vital capacity. From these data, a range of maximum effective expiratory pressures were identified as a function of lung volume [8-9]. Using this method, expiratory flow-limitation was considered present when expiratory pressures exceeded those required to produce maximal flow (Figure 1).

Static chest wall compliance. Static chest wall compliance was measured before graded exercise using the quasi-static relaxation technique [10]. The subjects were provided with clear instructions on how to perform the manoeuvre, and were given sufficient time (~ 30–40 mins) to become familiar with relaxing against an occluded airway with the glottis held open at various lung volumes. A pneumatic respiratory valve was used to impose the external occlusion (Series 4260A, Hans Rudolph, Kansas City, MO, USA). When subjects were well-practiced, they were instructed to perform three consecutive inhalations to TLC, followed by complete occlusion on the final breath. The subject’s inhaled volume was released in stepwise fashion via rapid actuation of the pneumatic valve. This procedure was repeated 3–5 times. In this manner, P_{OES} values were obtained over a range of lung volumes between TLC and functional residual capacity. The static recoil pressure of the chest wall ($P_{cw,st}$) was taken as the mean value of P_{OES} after a steady plateau (1–2 s) at each volume decrement during the relaxation manoeuvre. The slope of the $P_{cw,st}$–volume relationship above resting functional residual capacity described the static compliance of the chest wall. All subjects performed the relaxation technique while seated on the cycle ergometer. The age-predicted values for chest wall compliance in the upright position were estimated from data published by Estenne *et al.*[11].

The work of breathing. The components of the work of breathing were quantified using modified Campbell diagrams constructed from flow, pressure and volume data obtained during graded exercise (Figure 1). These diagrams were obtained from 10-20 breaths corresponding to minute ventilations of 20, 40, 60, and 80 $L \cdot min^{-1}$, and 25%, 50%, 75% and 100% of $\dot{V}_{Epeak}$. All subjects were able to achieve these levels of $\dot{V}_E$. Figure 1 illustrates a representative P_{OES}-volume loop for a control subject at an absolute $\dot{V}_E$ of 108 $L \cdot min^{-1}$ (~75% $\dot{V}_{Epeak}$) during graded exercise. A linear segment was fit through points of zero-flow representing the dynamic compliance of the lung tissue (i.e., $C_{L,dyn}$). The $P_{cw,st}$–volume relationship was then positioned according to the subjects resting end-expiratory P_{OES} at EELV [12-13]. The intersection between the lines drawn for $C_{L,dyn}$ and chest wall compliance represents the lung volume at which 'inward' elastic forces of the lung tissue are in equal, and opposite magnitude to the 'outward' recoil of the chest wall; i.e., functional residual capacity (FRC). The area inside the P_{OES}-volume loop to the left of both the lung and chest wall compliance segments (coarse stippling) represents the work performed by the respiratory muscles to overcome the resistance of the lung during inspiration (inspiratory resistive Wb). Conversely, the area bound by the P_{OES}-volume loop to the right of both $C_{L,dyn}$ and chest wall compliance segments (light stippling) represents the work performed by the respiratory muscles to overcome the resistive properties of lung during expiration (expiratory resistive Wb). The area between $C_{L,dyn}$ and chest wall compliance segments above FRC (horizontal hatching) represents the magnitude of work required to inflate the lungs during inspiration in opposition to the elastic properties of the total respiratory system (inspiratory elastic Wb). The area between $C_{L,dyn}$ and chest wall compliance segments below FRC (vertical hatching) represents the magnitude of respiratory work required to oppose the recoil of the chest wall below relaxation volume during expiration (expiratory elastic Wb). Importantly, when an individual presents with static or dynamic hyperinflation (EELV above FRC), no expiratory elastic work is performed. The above component areas (Joules) were multiplied by f_R ($J \cdot min^{-1}$). All components of respiratory muscle work were summed to yield the total Wb.

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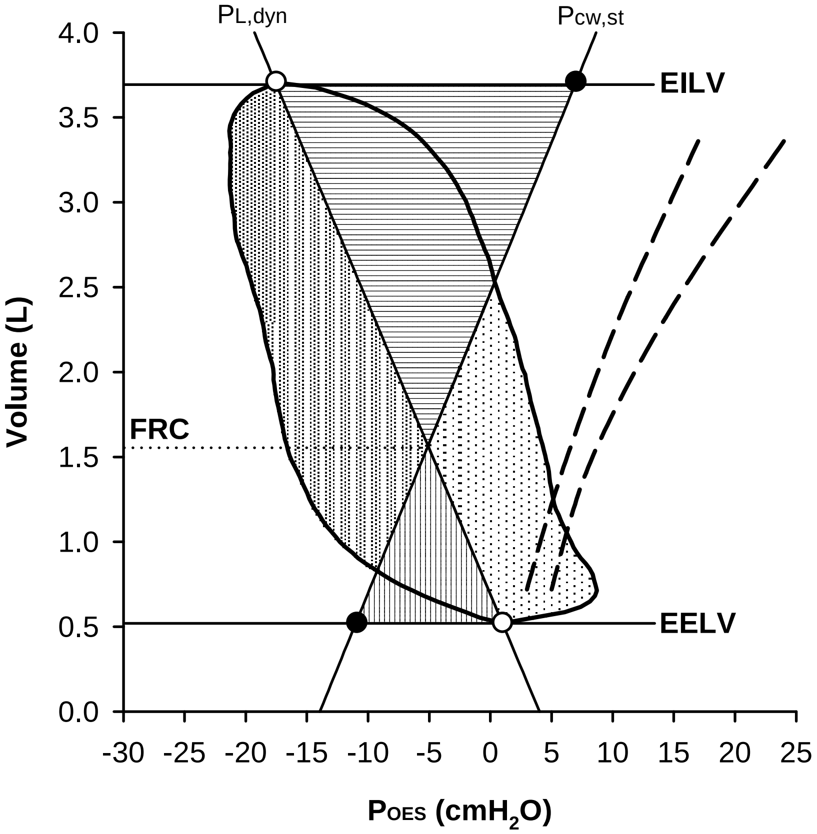

Figure 1. Schematic of the modified Campbell diagram used to quantify the elastic and resistive components of the work of breathing (Wb). FRC: functional residual capacity; EILV: end-inspiratory lung volume (EILV = VC – [IC – VT]); EELV: end-expiratory lung volume (EELV = VC – IC); POES: oesophageal pressure; PL,dyn: dynamic recoil pressure of the lung; Pcw,st: static recoil pressure of the chest wall. The continuous solid loop represents the POES-volume relationship during inspiration (upward) and expiration (downward) of a representative control subject during exercise at a minute ventilation of ~108 $L\cdot min^{-1}$, with a minor degree of expiratory flow-limitation towards the end of expiration. The open circles represent pressure points of zero-flow during the tidal breath. The slope of the intersecting line between open circles equals the dynamic lung compliance. The closed circles denote recoil pressures of the chest wall at points of zero-flow during the tidal breath. Fine stippling (▒) represents inspiratory resistive Wb. Coarse stippling (░) denotes expiratory resistive Wb. The horizontal hatching (▤) represents inspiratory elastic Wb, whereas vertical hatching (▥) denotes expiratory elastic Wb. The dashed lines demarcate the range of maximum effective expiratory pressures.