Exertional ventilation-CO_2 output relationship in COPD: from physiological mechanisms to clinical applications

ON-LINE SUPPLEMENT

Figure S1. Modelled exertional ventilation as a function of carbon dioxide (CO_2) output and work rate (WR) (x and z axis, respectively) (*left panels*) in hypothetical COPD patients presenting with progressively higher ventilation-CO_2 output slopes. Peak WR corresponds to the point at which ventilation reached different maximal breathing capacities (MBC_1-MBC_3). "A", "B" and "C" indicate differences in peak WR between patients showing the highest and the lowest slopes at progressively higher MBCs, respectively. The right panels show peak WR as a function of the slopes at a given MBC. Data calculated assuming y-intercepts of 5 L/min and 10 L/min, respectively (upper and lower panels). Note that the steeper the slope, the higher the intercept and the lower the MBC, the quicker ventilation reached MBC; accordingly, estimated peak WR varied negatively with the ventilation-CO_2 output parameters but positively with MBC (*left panels*). At a given MBC (*right panels*), peak WR decreased non-linearly as the slope increased (regardless of the intercept). The curvature constant increased significantly from MBC_3 to MBC_1, i.e., less severe "patients" showed a larger variability on peak WR as the slope increased (*right panels*).

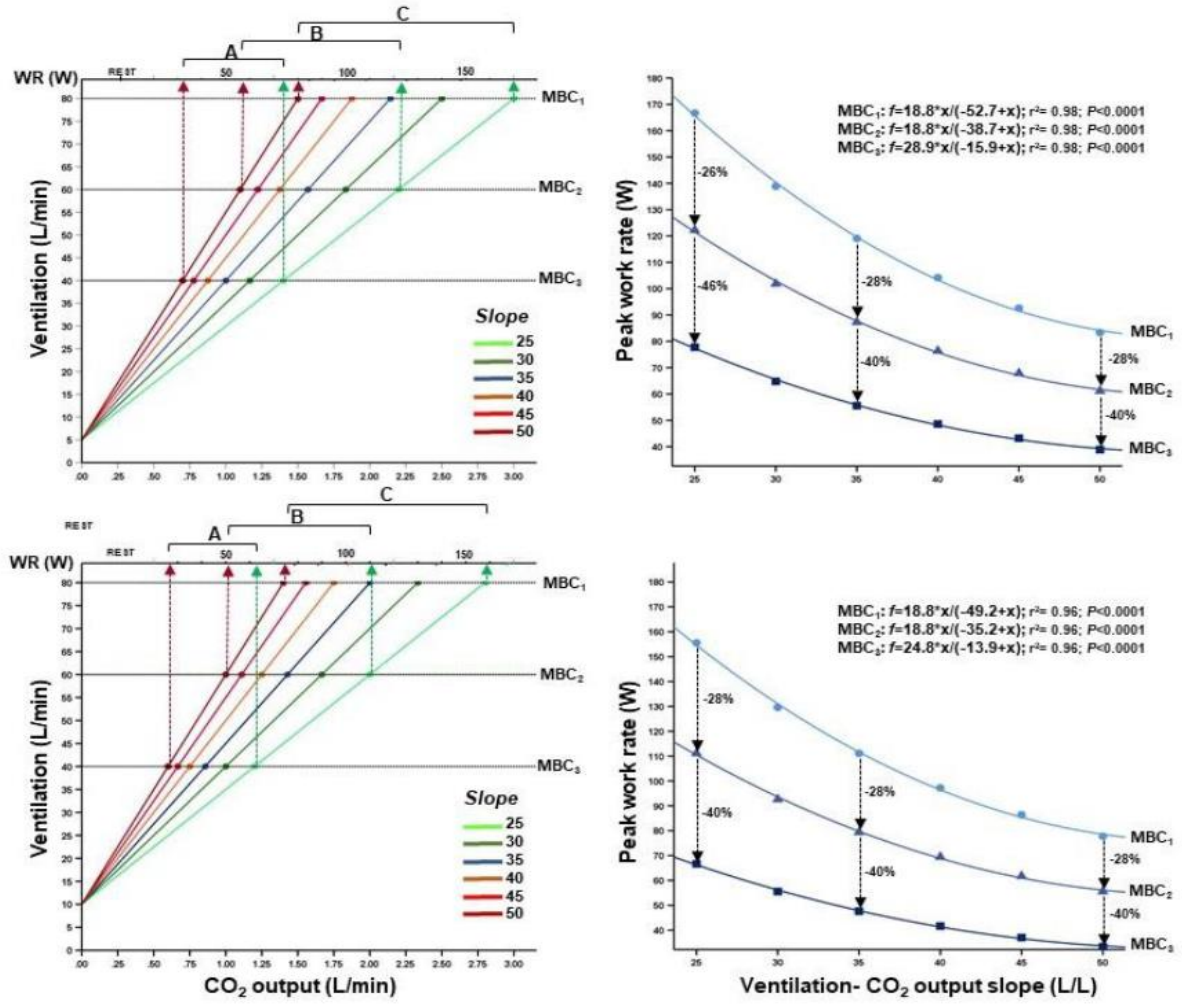

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Figure S2. Selected ventilatory and gas exchange responses to incremental CPET in a young healthy male. Proportional decreases in dead space (V_D) / tidal volume (V_T) (a) and ventilation ($\dot{V}_E$) / carbon dioxide output ($\dot{V}CO_2$) (b) ratios maintain arterial PCO_2 close to resting value during mild to moderate exercise (c). The $\dot{V}_E/\dot{V}CO_2$ response contour is established by both slope and intercept of the linear $\dot{V}_E$-$\dot{V}CO_2$ relationship (d). Thus, the lowest (nadir) $\dot{V}_E/\dot{V}CO_2$ closely approximates slope plus intercept. $\dot{V}_E$ increases out of proportion to $\dot{V}CO_2$ after the respiratory compensation point (RCP) (b-d) leading to respiratory alkalosis (C) to compensate for progressive lactacidemia. Note the increases in nadir when the lactate threshold is reached earlier (dashed line in panel b).

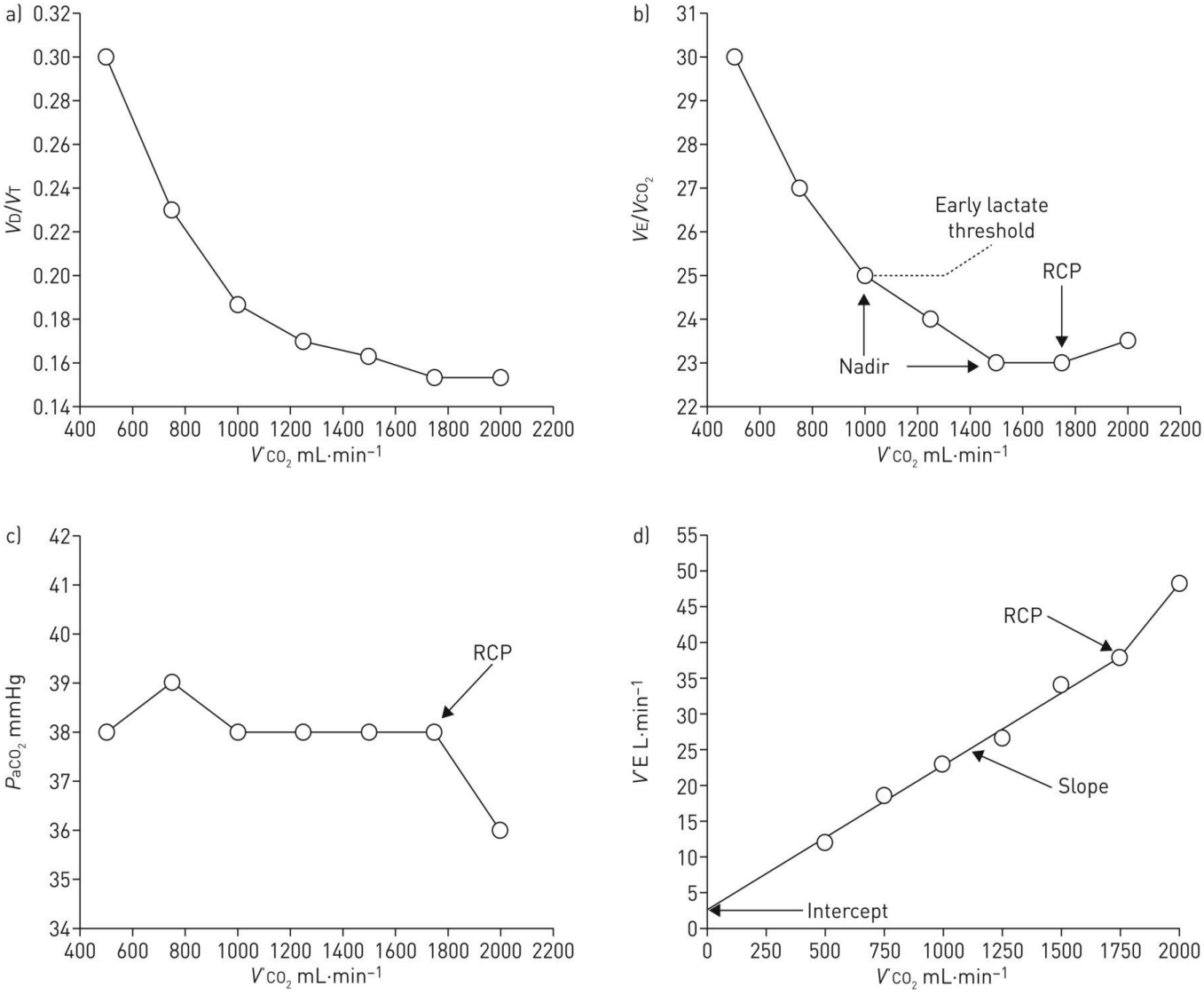

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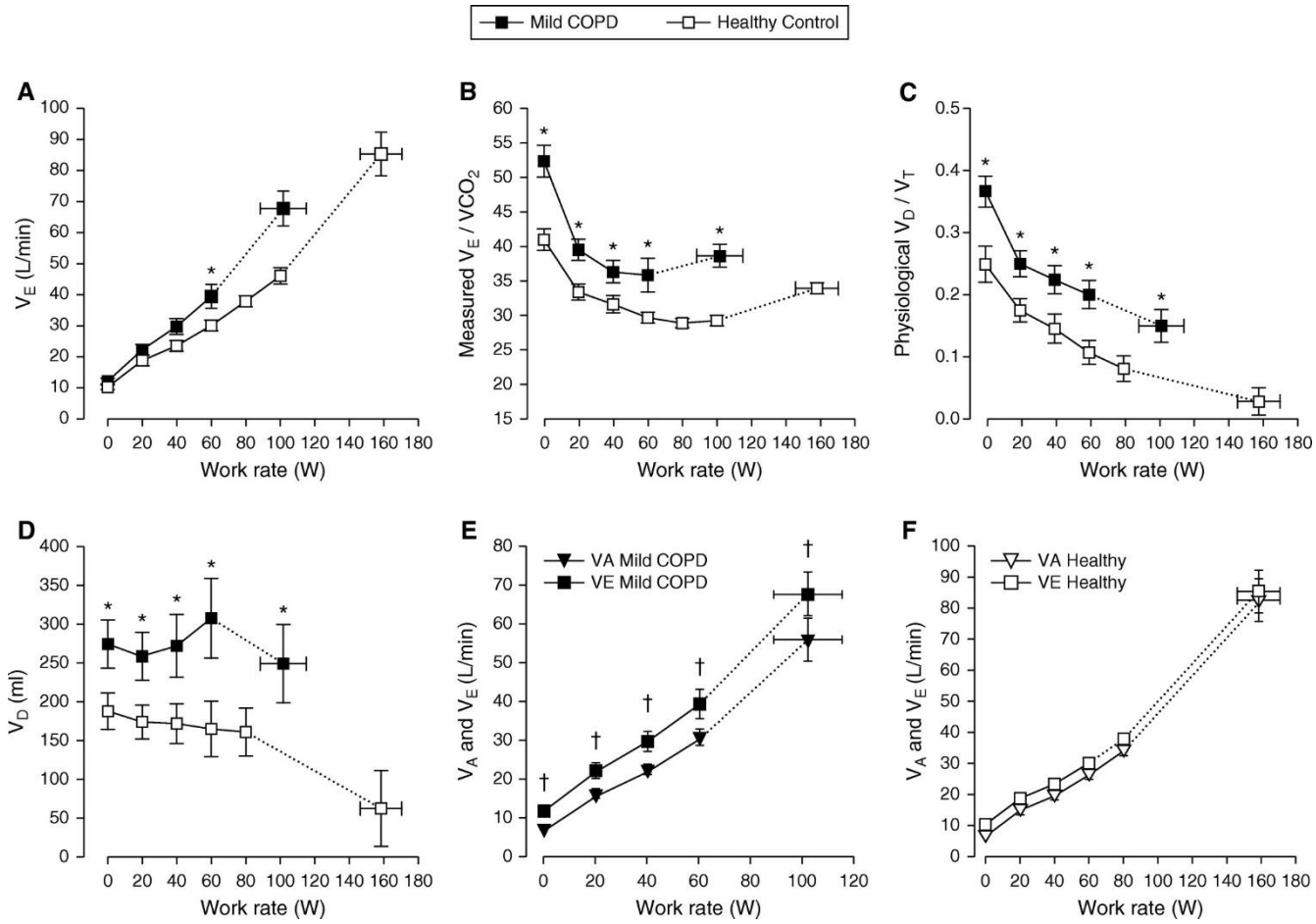
Figure S3. Ventilatory and derived gas exchange parameters during incremental cycle exercise in patients with mild chronic obstructive pulmonary disease (COPD) and age-matched healthy control subjects. Note that higher ventilation ($\dot{V}_E$) relative to metabolic demand (panel B) was associated with higher "wasted" $\dot{V}_E$ (panels C and D), leading to less alveolar ventilation ($\dot{V}_A$) at a given $\dot{V}_E$ in patients compared to controls (panels E and F, respectively).



Values represent means ± SEM. *$P < 0.05$, patients with mild COPD versus healthy control subjects at rest, at standardized work rates, or at peak exercise; †$P < 0.05$, difference between V.e and V.a in patients with COPD versus healthy control subjects at rest, at a standardized work rate, or at peak exercise. VD/VT = dead space to tidal volume ratio.

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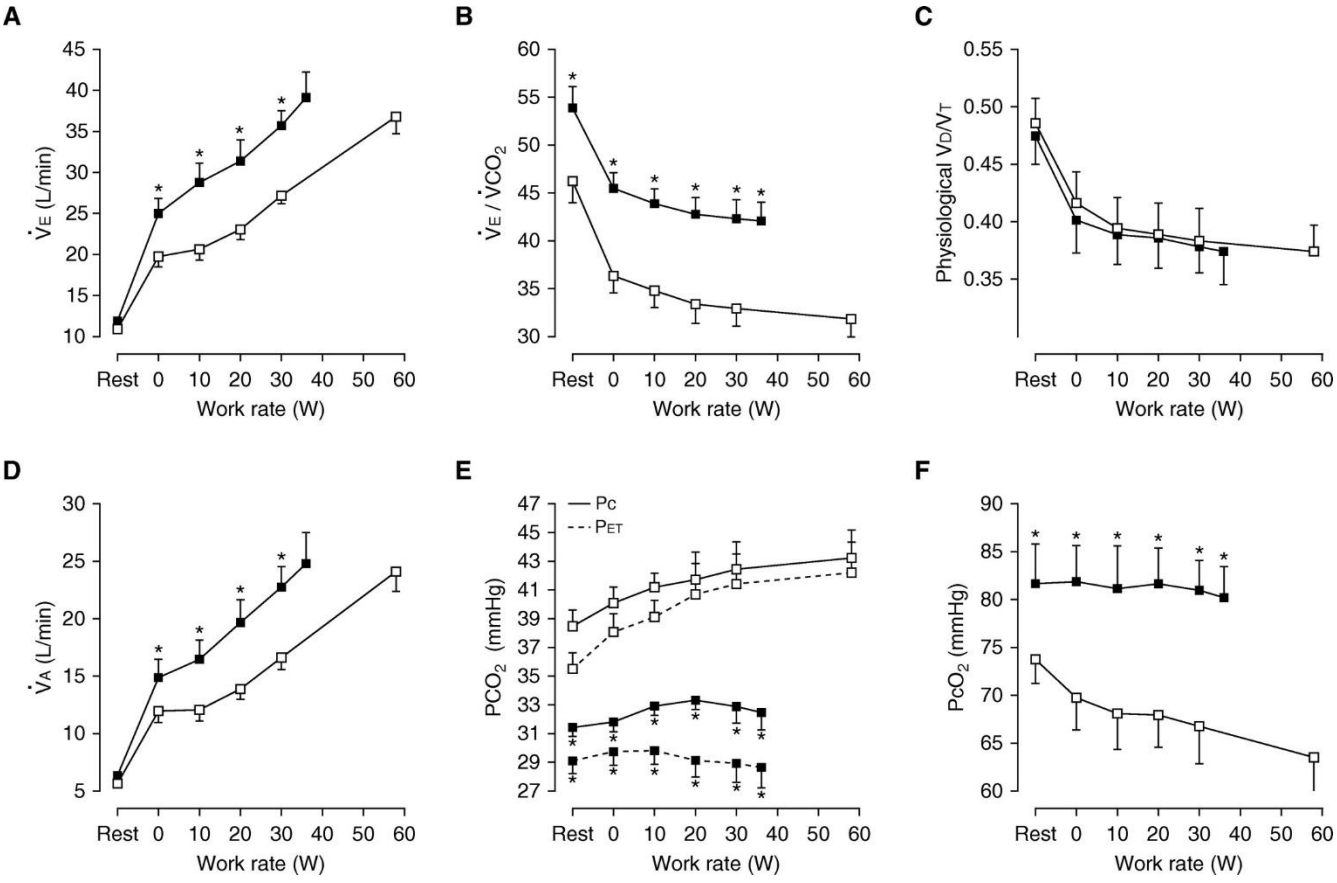
Figure S4. Ventilatory (*A–D*) and pulmonary gas exchange (*E* and *F*) responses to incremental cardiopulmonary exercise testing in chronic obstructive pulmonary disease–heart failure patients separated by presence (n = 10) or not (n = 12) of exercise hypocapnia (*solid* and *open symbols*, respectively) (*panel E*). Note that higher ventilation ($\dot{V}_E$) relative to work rate and metabolic demand in the hypocapnic group (*panels A and B*, respectively) was associated with, similarly increased physiological dead space (*panel C*) compared to the non-hypocapnic patients.



*$P < 0.05$ for between-group comparisons at rest, standardized work rates, and the highest work rate attained by all subjects in a given group. Values are means ± SEM. Pc = capillary (arterialized) partial pressure; Pet = end-tidal partial pressure.

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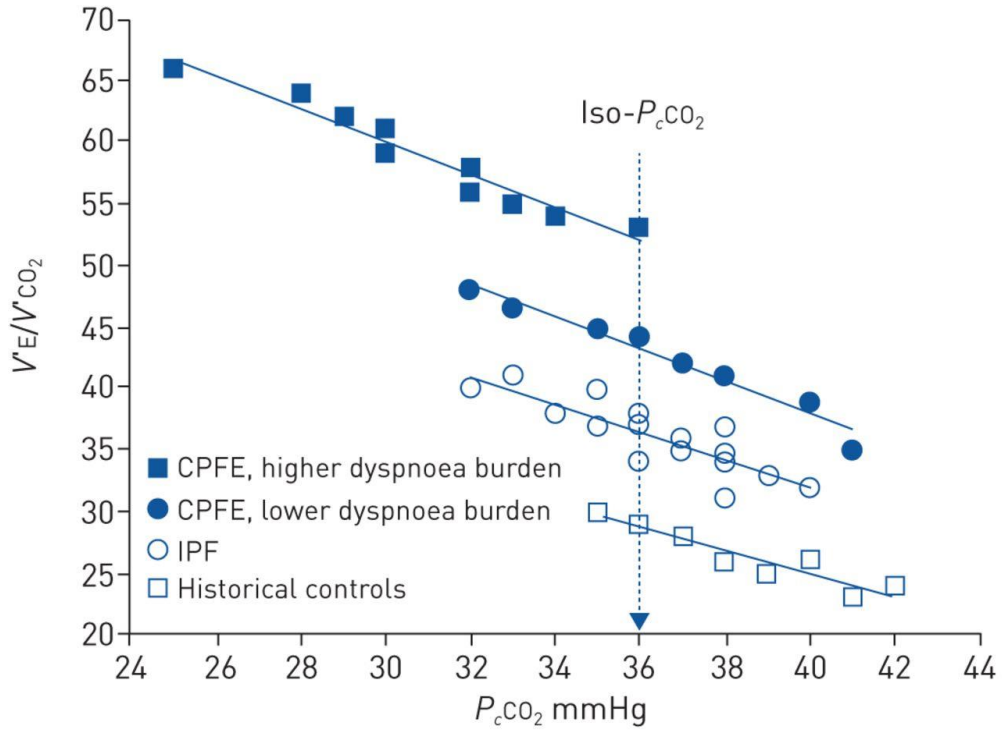
Figure S5. Minute ventilation ($\dot{V}_E$)/carbon dioxide output ($\dot{V}CO_2$) ratio as a function of capillary carbon dioxide tension (P_cCO_2) in patients with idiopathic pulmonary fibrosis (IPF) in isolation or in association with emphysema (combined pulmonary fibrosis and emphysema (CPFE)). The latter group was separated according to the burden of exertional dyspnoea. Whereas a leftward shift in $P_{c}CO2$ associated with high V'_E/V'_{CO2} indicates alveolar hyperventilation, the upward shift in V'_E/V'_{CO2} at a given $P_{c}CO2$ demonstrates increased "wasted" ventilation in the more dyspnoeic patients with CPFE.



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