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Title: Recovery from dynamic exercise dissociates ventilatory from pulmonary gas exchange responses in patients with chronic thromboembolic pulmonary hypertension

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Body: Background: Exercise is characterized by an excessive ventilatory (V'E) response to metabolic demand (i.e., CO₂ output, V'CO₂) in chronic thromboembolic pulmonary hypertension (CTEPH). We investigated whether this would also be the case when the neural ventilatory drive (by "feed-forward" mechanisms) is likely to be reduced, e.g, immediately after exercise. Methods: Forty-three patients with CTEPH (50 ± 13 yrs, cardiac index= 2.0 ± 0.5 L/kg/min⁻¹; PVR= 1034 ± 402 dynes.s.cm⁻²) and 21 sedentary controls performed a ramp-incremental exercise test followed by unloaded recovery. Results: In patients, V'CO₂ (and O₂ uptake) kinetics were significantly delayed compared to V'E (1st min decrease in % peak values= 13 ± 7 vs 19 ± 1%; 2nd min= 26 ± 13 vs 33 ± 12%; 3rd min= 46 ± 12 vs 53 ± 10 %; 4th min= 54 ± 13 vs 59 ± 13%; 5th min= 61 ± 11 vs 65 ± 4%, p<0.05). This sharply contrasted with results found in the controls in whom V'E kinetics were consistently slower than V'CO₂ throughout the recovery (p<0.05). Consequently, V'E/V'CO₂ ratio decreased (and end-tidal CO₂ (P_{ET}CO₂) increased) as exercise ceased in 41/43 (95%) patients with opposite patterns (i.e, V'E/V'CO₂ increase and P_{ET}CO₂ decrease) been found in all controls. Conclusion: Exercise recovery dissociates ventilatory to pulmonary gas exchange responses in patients with CTEPH. Although this might be related to lower post-exercise metabolic drive due to less lactacidosis in patients than controls, it might also indicate that enhanced neural drive - which was suddenly reduced at exercise cessation- contributes to patients' excessive exercise V'E.