Ventilatory inefficiency predicts abnormal hemodynamic response to exercise in chronic thromboembolic disease


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Background: Chronic thromboembolic disease (CTED) refers to the presence of chronic thrombotic pulmonary vascular occlusion in the absence of pulmonary hypertension (PH) at rest. Nevertheless, their exercise tolerance may be decreased. We hypothesized that exercise intolerance may be explained by an abnormal haemodynamic response to exercise and that this may correlate to the functional and ventilatory parameters exhibited at the cardiopulmonary exercise test (CPET).

Objective: To evaluate the values reached in the CPET according to the hemodynamic response to exercise at the exercise right heart catheterization (RHC) in patients with CTED.

Methods: We selected symptomatic patients with confirmed perfusion defects in lung scintigraphy despite optimal anticoagulant therapy for a minimum of 6 months after a pulmonary embolism with normal lung function tests. Thrombotic burden was assessed with computed tomography (CT). Left heart disease (LHD) and PH were ruled out with RHC (inclusion criteria implied mean pulmonary arterial pressure (mPAP) <25 mmHg and pulmonary vascular resistance (PVR) <3 uW and pulmonary arterial wedge pressure (PAWP) <15 mmHg). All patients underwent a cardiopulmonary exercise test (CPET). Exercise RHC was performed within 24 hours after CPET. The exercise protocol was the same for both tests. Pulmonary pressures and cardiac output (CO) were collected at each exercise level. Abnormal hemodynamic exercise response was considered following the proposal of the 2020 CTED consensus (mPAP/CO slope >3 mmHg/L/min).

Results: 22 patients (median age 54.5±14.8 years, 32% females) were included, of whom 13 (59%) showed an abnormal hemodynamic response (mPAP/CO slope 4.5 vs 2.3 mmHg/L/min, Figure 1A). Baseline characteristics and time from the embolic event were similar in both groups (3.4 vs 2.5 years, p=0.815) (Table 1). Patients with abnormal exercise response showed worse ventilatory efficiency at the CPET: 1) a flattened end-tidal carbon dioxide pressure pattern (PetCO2) (Figure 1B, 2) a steeper VE/CO2 slope, and 3) a higher ventilatory equivalent for CO2 at the anaerobic threshold (EqCO2_AT); compared to the group with normal hemodynamic behavior. Oxygen consumption at the anaerobic threshold (VO2_AT) and peak oxygen consumption (VO2) were slightly decreased without statistically significant differences between groups. VE/CO2 slope, EqCO2_AT and PetCO2_AT showed a moderate mPAP/CO slope correlation (r=0.66, p<0.001; r=0.63, p=0.003; r=-0.51, p=0.017 respectively). PetCO2_AT and EqCO2_AT accurately discriminated between both groups with an area under the receiver operating characteristic curve of 0.752 and 0.710 respectively.

Conclusion: In patients with CTED and normal/near normal pulmonary pressures at rest, ventilatory inefficiency parameters in CPET correlate with an abnormal hemodynamic exercise response. PETCO2 pattern and EqCO2_AT accurately discriminated the subgroup with abnormal hemodynamic behaviour.

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