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**Title:** Pulmonary rehabilitation affects lung hyperinflation and cardiovascular response to exercise in COPD

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**Body:** Background: Pulmonary rehabilitation (PR) including exercise training has emerged as a recommended standard of care in COPD patients. The aim of this study was to assess whether PR may influence ventilatory and cardiovascular response to training. Methods: Twenty-three COPD patients (9F; age 70 yrs  $\pm$  8; BMI 28 kg/m<sup>2</sup>  $\pm$  5) with moderate to severe airflow obstruction (FEV<sub>1</sub>/VC range: 65-36%) admitted to a 6-week PR course performed a pre-to-post evaluation of lung function test and symptom-limited cardiopulmonary exercise test (CPET). Inspiratory capacity (IC) manoeuvres, VAS dyspnoea (D) and leg fatigue (F) were assessed during the CPET. Cardiovascular response was also assessed by means of oxygen pulse (VO<sub>2</sub>/HR), product of systolic blood pressure and heart rate normalized for the maximum workload (DP/W), and heart rate recovery at the 1<sup>st</sup> min (HRR). Results: Workload (W) and Maximum oxygen uptake (VO<sub>2max</sub>) increased (from 61.2 W  $\pm$  23.7 to 74.5 W  $\pm$  33.4, p= 0.002, and from 12.9 L/kg/min  $\pm$  2 to 14.5 L/kg/min  $\pm$  4, p=0.002, respectively) following PR. The IC for a given W significantly changed from 0.03 L/W  $\pm$  0.01 to 0.02 L/W  $\pm$  0.01 (p=0.01). VO<sub>2</sub>/HR increased from 9 L/min/bpm  $\pm$  2 to 9.8 L/min/bpm  $\pm$  2.7 (p=0.006), DP/W decreased from 352.2  $\pm$  130.3 to 288.7  $\pm$  113.2 (p=0.002), and HRR changed from 8.6 bpm  $\pm$  6.7 to 13.3 bpm  $\pm$  8.8 (p=0.007) at peak of exercise. Moreover, D (from 1.5  $\pm$  0.5 to 1.3  $\pm$  0.6, p=0.005) and F (from 1.3  $\pm$  0.6 to 0.98  $\pm$  0.5, p=0.005) reduced at peak/W. Conclusions: Our study shows that training effect during rehabilitation course in COPD is associated with significant reduction of lung hyperinflation and improved cardiovascular response to exercise.