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Title: Low hypercapnic ventilatory response in long-term lung transplant recipients predicts exercise impairment

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Body: Background: Only few studies reported findings on CO₂ rebreathing in long-term bilateral lung transplant recipients. Bilateral lung transplantation causes denervation of the donor lung. This might have an impact on control of breathing as measured by the hypercapnic ventilatory response (HCVR). The influence of gender on HCVR and the relation to exercise capacity is unknown yet. Objectives: To study HCVR and the relation to exercise capacity after bilateral lung transplantation. Methods and patients: Minute ventilation, respiratory rate and HCRV were studied in 24 bilateral lung transplant recipients (12 male). HCVR was measured according to the Read protocol. Exercise testing was performed to evaluate the maximum level of workload. This was expressed as percentage of the corresponding reference value. Results: Age and body mass index (BMI) of men and women were similar (age: 56 ± 9 years vs. 54 ± 9 years (n.s.), BMI: 26 ± 3 kg/m² vs. 25 ± 6 kg/m² (n.s.)). Post-transplant period ranged from 6 months to 9 years. HCVR in lung transplant recipients was 1.71 ± 1.25 l/min/mmHg in men and 0.95 ± 0.38 l/min/mmHg in women (p<0.05). In healthy controls HCVR at our laboratory were 2.02 ± 0.77 l/min/mmHg for men and 1.51 ± 0.64 l/min/mmHg for women (p<0.05). After adjustment for FEV₁ and gender in multivariate analysis we found a statistically significant correlation between the exercise capacity and HCVR. Conclusion: There is a remarkable difference in ventilatory response to carbon dioxide between male and female bilateral lung transplant recipients, suggesting a role for denervation of the lung in the impairment of exercise capacity after bilateral lung transplantation.