66. Altered mechanisms during exercise in disease

Late-breaking abstract: Impaired carbon monoxide diffusion capacity is the strongest predictor of exercise intolerance, even in moderate COPD
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Background: Exercise intolerance is the hallmark of COPD and FEV1 is the traditional method used to define the severity of COPD. However there is a disassociation between FEV1 and exercise capacity in a large proportion of subjects with COPD. Therefore it is of interest to investigate if other lung function parameters are having an additive, predictive value of exercise capacity (EC) and if this differs according to the COPD stages.

Methods: Spirometry, measurements of lung volumes and diffusing capacity for carbon monoxide (DLCO) were performed in 88 patients with COPD GOLD stages II-IV. EC was determined by symptom-limited incremental cycle ergometer test.

Results: DLCO, FEV1 and inspiratory capacity (IC) were found to be the best predictors of EC in a stepwise regression analysis and explain 72% of EC. These lung function parameters explained 71% of EC in GOLD II, 69% in GOLD III and 32% in GOLD IV. DLCO alone was the best predictor of exercise capacity in GOLD II and IV (Table).

Predictive values of FEV1, IC and DLCO for exercise capacity in different GOLD classes

<table>
<thead>
<tr>
<th>GOLD II</th>
<th>GOLD III</th>
<th>GOLD IV</th>
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<tbody>
<tr>
<td>FEV1 0.27*</td>
<td>0.53*</td>
<td>0.13*</td>
</tr>
<tr>
<td>IC 0.42*</td>
<td>0.41*</td>
<td>0.17*</td>
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<tr>
<td>DLCO 0.29*</td>
<td>0.51*</td>
<td>0.29*</td>
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Numbers are presented as R² values from a simple regression model. *Indicates significant relation.

Discussion: Additive information regarding COPD patients’ exercise capacity is obtained by measuring diffusing capacity and inspiratory capacity. DLCO was the strongest predictor of exercise capacity in all subjects and the best individual predictor in patients with GOLD stage II. This suggests that clinically monitoring with measurements of diffusing capacity may be beneficial even in patients with moderate disease severity.

377 ACE gene polymorphisms, COPD exercise tolerance and response to acute oxygen
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Introduction: Recent studies have shown that polymorphisms of the angiotensin-converting enzyme (ACE) gene are closely associated with pulmonary disorders. The aim of this study was 1) to investigate the impact of ACE gene polymorphism on exercise tolerance and 2) to determine whether a relationship exists between oxygen responses and differential genotype (DD, DI or II). 

Methodology: Twenty-four COPD patients (FEV1=51±2.4%pred) exhibiting exercise-induced desaturation performed endurance exercise at 60% of their maximal workload in two randomised conditions: normoxia and hyperoxia. ACE genotype was determined for each patient. Endurance time (Tlim), dyspnoea, cardiac output (CO) and arterio-venous difference in oxygen (AVD) were compared.

Results: In normoxia, Tlim was greater for DI than DD (1168 vs 541s; p<0.05). Oxygen supply improved performance in both groups, but DI again exhibited better endurance than DD (1313 vs 1132s; p=0.01). This better exercise capacity in DI was associated with a greater AVD and decreased CO for comparable oxygen uptake. Although O2 significantly increased Tlim in two-thirds of patients (R+) and significantly decreased it in about one-third (R-), R+ and R- proportion was comparable in the two genotype groups (chi²=0.52, p=0.46).

Conclusion: This study showed that I-allele was associated with better endurance performance. Although DD and DI increased performance with oxygen, responses were associated with differential consequences on cardiovascular and peripheral muscle adaptations. However, ACE polymorphism could not be related to positive or negative oxygen responses.

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Influence of abdominal volume regulation on chest wall hyperinflation during constant work rate exercise in patients with COPD
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It has been recently reported that some patients with chronic obstructive pulmonary disease (COPD) may actively recruit the expiratory abdominal (AB) muscles in order to compensate for flow-related dynamic hyperinflation. However, whether this strategy is universally efficacious in counterbalancing the potential increases in rib cage (RC) volumes thereby promoting a net deflating effect on chest wall (CW) is still unclear. Thirty males with COPD (FEV1 = 43.8 ± 9.5%) performed a constant work rate cardiopulmonary exercise test (75% max) to the limit of tolerance (Tlim) on a cycle ergometer. Breath-by-breath ventilatory kinematics was continuously monitored by optoelectro plethysmography (BTS, Italy). End-expiratory volume of the RC (VE/RC) and VE/CV were significantly increased from rest to Tlim in 17 patients. VE/AB remained stable in 9 of them ("non-recruiters/hyperinflator") and in contrast, it decreased slightly in 7 "recruiters/hyperinflator" thereby lessening CW hyperinflation. VE/RC significantly increased from 1.48 ± 0.14 to 1.93 ± 0.15 l/min and non-hyperinflators (from 1.68 ± 0.12 to 1.93 ± 0.15 l/min); however, the mechanism of improvement was different as heliox improved cardiac output 0.12 to 1.93 times significantly improved in both hyperinflators (from 1.48 ± 0.14 to 1.93 ± 0.15 l/min) and non-hyperinflators [FEV1=48 ± 4.4% pred] performed a constant-load exercise tests to the limit of tolerance in air and whilst breathing heliox.

Results: The improvement in exercise tolerance by heliox was not different between hyperinflators and non-hyperinflators (by 3.8 ± 1.9 and 4.2 ± 2.0 min, respectively). This is probably due to the finding that systemic oxygen delivery significantly improved in both hyperinflators (from 1.48 ± 0.10 to 1.70 ± 0.11 l/min) and non-hyperinflators (from 1.68 ± 0.12 to 1.93 ± 0.15 l/min); however, the mechanism of improvement was different as heliox improved cardiac output in non-hyperinflators (from 3.9 ± 0.5 to 10.4 ± 0.5 l/min) whilst arterial oxygen content increased only in hyperinflators (from 160 ± 3 to 177 ± 4 mmO2/L). Nonetheless, quadriiceps and intercostal muscle oxygen delivery (measured by NIR=ICG method with arterial sampling) improved significantly and by the same magnitude in both hyperinflators (by 16.6 ± 7.4 and 4.0 ± 1.1 mmO2/min/100g, respectively) and non-hyperinflators (by 17.6 ± 8.2 and 4.5 ± 1.2 mmO2/min/100g, respectively). Conclusion: Heliox improves peripheral and respiratory muscle oxygen delivery in all COPD patients regardless of the occurrence of exercise-induced dynamic hyperinflation.

Effects of oxygen supplementation on cerebral oxygenation during progressive exercise in patients with COPD and healthy controls
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The rate of change (Δ) in cerebral oxygenation (OCO₂) during exercise is modulated by cerebral blood flow and arterial O₂ content (CaO₂). It is currently unclear whether ΔOCO₂ would be impaired in exercise during patients with chronic obstructive pulmonary disease (COPD) who are not overtly hyperoxic and (ii) improve with hyperoxia (HIOX, FIO₂ = 0.4) in these patients. Twenty non-hypercapnic males with COPD (FEV1 = 47.2 ± 11.5% predicted) and 9 age- and gender-matched controls (participants with COPD and controls underwent incremental exercise tests under HIOX and normoxia (NOX). ΔOCO₂ was determined by near infrared spectroscopy (fold-changes in HbO₂ and cardiac output (QT) by impedance cardiography. A significant drop in SpO₂ was found in 8/20 patients (peak SpO₂ = 86.2 ± 2% vs. 96.2 ± 2% for “desaturators” (DESAT) and “non-desaturators” (NONDESAT), respectively. In NOX, ΔOCO₂ was lower in DESAT versus NONDESAT and, in contrast, mean arterial pressure (MAP) was higher in the former group (p < 0.05). Increases in SpO₂ with HIOX were particularly pronounced in DESAT (86.2 ± 2% vs. 99.1 ± 4%; interestingly, a significant improvement in COPD was only found in this group (53.2 ± 20.0 vs. 2.09 ± 0.42; p < 0.01). There was no significant effect of HIOX on QT in control and COPD groups; MAP, however, decreased in DESAT (p < 0.05). ΔOCO₂ is impaired in patients with COPD who desaturate during progressive exercise even if they are not entitled to long-term O₂ therapy. O₂ supplementation (FI0₂ = 0.4) is able to correct for these abnormalities, an effect that was related to enhanced CaO₂ rather than improved cerebral haemodynamics. Supported by: CNPq and FAPESP, Brazil.
We examined the impact of changes in ventilatory profile and dynamic operating lung volumes during symptom-limited incremental cardiopulmonary cycle exercise testing (CPET) on the intensity of dyspnoea in patients with pulmonary hypertension (PH). Twenty non-smokers PH patients (n=13 idiopathic, n=7 chronic thromboembolic disease) with no evidence of spirometric obstruction (FEV1/FVC = 85±7% pred) and 10 age-matched healthy subjects performed a CPET to the limit of tolerance. Ventilatory profile, operating lung volumes [derived from inspiratory capacity (IC) measurements], and dyspnoea intensity (by Borg scale) were assessed throughout CPET. In 70% of PH patients (n=14), IC decreased progressively throughout CPET by 0.35L on average (dynamic hyperinflation), whereas in all healthy subjects IC increased by 0.2L. Dyspnoea intensity and minute ventilation (V'E) were greater in PH patients at any stage of CPET compared with healthy controls: at standardized work rate of 60watts, dyspnoea rating and V'E were 5 Borg units and 45L/min respectively in PH patients compared with 1 Borg unit and 33L/min respectively in healthy subjects. At standardized V'E of 60L/min, PH patients presented with greater dyspnoea (by 4 Borg units) and dynamic hyperinflation and the excessive ventilatory response to CPET seem to be potential contributors to increased exertional dyspnoea intensity in patients with PH.