### 452. Limiting factors in exercise

#### P4432

## Gas exchange abnormality during cardiopulmonary exercise test in patients with primary pulmonary hypertension

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**Background:** Decline in ventilation and oxygen uptake efficiency is found in patients with primary pulmonary hypertension. Such reduction may sustain from rest to exercise. Our primary hypothesis was that ratio of ventilation to CO2 output (VE/VCO2) and ratio of O2 uptake/ventilation (VO2/VE) would differ between normal subjects and patients during cardiopulmonary exercise testing (CPET).

**Methods:** We administered incremental cycle ergometry tests to 20 normal subjects and 20 patients. We compared ratio of ventilation to CO2 output (VE/VCO2) and ratio of O2 uptake/ventilation (VO2/VE) at rest, unloaded pedaling, anaerobic threshold, and peak exercise.

**Results:** Patients had distinguished decreased peak O2 uptake (P<0.001). The levels and patterns of change for two groups for VE/VCO2 and VO2/VE were significantly distinctive. As hypothesized, the patients group always had markedly higher VE/VCO2 and lower VO2/VE than normal subjects group (P<0.001). In addition, the fall in VE/VCO2 between rest and peak exercise was slight for patients. In the contrast, the VE/VCO2 distinguishably decreased with exercise for normal subjects (P<0.001). At the same time, patients had slightly higher VO2/VE at anaerobic threshold than rest. Comparatively, the VO2/VE greatly increased at anaerobic threshold for normal subjects (P<0.001).

**Conclusions:** The levels and changes in VE/VCO2 and VO2/VE during CPET are distinctive for patients with primary pulmonary hypertension. CPET provide valuable information for diagnosis and evaluation for primary pulmonary hypertension.

#### P4433

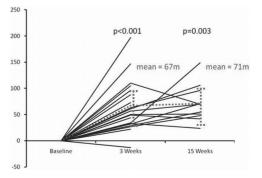
## Exercise training in pulmonary arterial hypertension associated with connective tissue diseases

 Connective Bissie discussional status
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**Background:** The objective of this prospective study was to assess short-and longterm efficacy of exercise training(ET) as add-on to medical therapy in patients with connective tissue diseases-associated pulmonary arterial hypertension(CTD-APAH).

Patients with invasively confirmed CTD-APAH received ET in-hospital for 3 weeks and continued at home for 15 weeks. Efficacy parameters have been evaluated at baseline and after 15 weeks by blinded-observers. Survival rate has been evaluated in a follow-up period of  $2.9\pm1.9$  years.

**Results:** Twenty-one consecutive patients were included and assessed at baseline, and after 3 weeks, 12 after 15 weeks. Patients significantly improved the mean distance walked in 6 minutes compared to baseline by  $67\pm52$  meters after 3 weeks(p<0.001) and by  $71\pm35$  meters after 15 weeks(p=0.003), scores of quality of life(p<0.05), heart rate at rest and maximal workload. Systolic pulmonary artery pressure and diastolic systemic blood pressure improved significantly after



3 weeks of ET. The 1- and 2-year overall-survival rates were 100%, the 3-year survival 73%. In one patient lung transplantation was performed 6 months after ET.

**Conclusion:** ET as add-on to medical therapy is effective in patients with CTD-APAH to improve work capacity, quality of life and prognostic parameters and improves the 1-, 2- and 3-year survival rate. Further randomized controlled studies are needed to confirm these results.

#### P4434

#### Respiratory muscle training (REMT) with normocapnic hyperpnoea (NH) improves respiratory muscle strength, exercise performance and ventilatory pattern in COPD patients

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Few data are available about the effect of RMET in COPD patients even if it has been shown that RMET improves endurance performance and decreases VE during exercise in healthy subjects.

Aim: To evaluate the effect of 4 weeks of RMET with NH (Spirotiger<sup>®</sup>) on respiratory function and exercise capacity in 23 moderate/severe COPD patients. **Materials and methods:** 20 M, 3 F (aged 42-80). Respiratory function tests (FEV1, FVC, MIP), QoL (St George's Questionnaire), 6MWT and endurance exercise test (75-80% of peak-work rate measured during an incremental test and performed to the limit of tolerance, tLIM).

9 of 21 patients were instrumented with a portable inductive plethysmografhy (Lifeshirt System) to evaluate breathing pattern during exercise test. After 4 supervised training sessions, the patients trained at home for 4 weeks: 10 min twice a day roughly at 55% of MVV (FEV1x0,375).

Results: Results are reported in Tables 1 and 2.

6 patients dropped out (poor compliance).

Ventilatory pattern after RMT, during tLIM, is characterized by a significantly lower trend of VE and RR with a higher TV (p<0,05, ANOVA test).

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Mean±SD	FEV1 (%)	FVC (%)	MIP (cmH2O)	QoL (total)	6MWD (m)	SpO2 (%)
pre RMET post RMET	59,1±16,5	- )- )	84±33 93+33*	29,2±18,0 21,2±12,3*	422±74 459±55*	92±3 93+2*
POST KIVIE I	<i>39,1</i> ±1 <i>3,5</i>	82,3±22,9	93±33*	21,2±12,3*	439±33*	93±2*

Table 2

Mean±SD	tLIM (sec)	Borg dyspnea tLIM
pre RMET	351±238	8/10±0,6
post RMET	523±440*	6/10±1,7*

\*p<0,05 (T test and Wilcoxon signed rank test.)

**Conclusion:** After a short RMT, COPD patients show an improvement in MIP, QoL, a higher exercise capacity and an intriguing change in ventilatory pattern during exercise, which improves SpO2.

#### P4435

#### Reduced oxygen uptake efficiency slope in patients with cardiac sarcoidosis Wilhelm Ammenwerth<sup>1</sup>, Mark A. Klemens<sup>2</sup>, Catharina Crolow<sup>1</sup>,

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**Background:** The non-invasive diagnosis of cardiac sarcoidosis (CS) is difficult. Cardiovascular magnetic resonance (CMR) has become a very valuable diagnostic tool in patients with suspected CS, but usually a combination of different tests is used. Oxygen uptake efficiency slope (OUES) is a parameter of cardiopulmonary exercise testing (CPET), which is used as an indicator for cardiovascular impairment. We investigated the predictive value of OUES for the diagnosis of myocardial involvement in sarcoid patients.

**Methods:** Retrospectively 37 consecutive patients (44.9 $\pm$ 13.8 years) with histologically confirmed sarcoidosis and clinical suspicion of heart involvement underwent noninvasive diagnostic testing including CMR. CS was diagnosed according to the guidelines from the Japanese Society of Sarcoidosis and other Granulomatous Disorders with additional consideration of CMR findings. Furthermore, CPET with calculation of predicted OUES according to equations by Hollenberg et al. was carried out.

**Results:** Patients with CS (11/37; 30%) had a worse cardiovascular response to exercise. OUES was significantly lower in CS-group compared to non-CS-group (59.3±19.1 vs 88.0±15.4%pred., p < 0.0001). ROC curve method identified 70%pred. as the OUES cut-off point, which maximized sensitivity and specificity for detection of CS (96% sensitivity, 82% specificity, 89% overall accuracy). OUES < 70%pred. was the single best predictor of CS (OR: 67, 95% CI: 6.05 to 734.27, p < 0.001) even in multivariate analyses.

Conclusion: Cardiac involvement of sarcoidosis can be predicted by CPET using

OUES. Patient selection for CMR can probably be guided by CPET findings in patients with sarcoidosis.

#### P4436

#### Prognostic implications of delayed heart rate recovery from maximal-incremental exercise in patients with pulmonary arterial hypertension

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**Rationale:** Early recovery from exercise is characterized by a marked reduction in heart rate (HR) due to sudden reintroduction of vagal tone and progressive withdrawal of sympathetic stimulation. HR recovery (HRR) is delayed in pulmonary arterial hypertension (PAH), a disabling condition associated with autonomic imbalance.

**Objective:** To investigate the usefulness of HRR to estimate exercise impairment and prognosis in PAH patients.

**Methods:** We evaluated 72 patients with PAH of varied aetiology (NYHA class I to IV) and 21 age- and gender-matched controls who underwent a maximal incremental cardiopulmonary exercise test (CPET) with HR being recorded up to the 5th minute of recovery.

**Results:** HRR was consistently lower in patients compared to controls (p<0.05). The best cutoff for HRR in one minute (HRR<sub>1min</sub>) to discriminate patients from controls was 18 beats (AUC 0.76 [0.66-0.86], p<0.05). "Normal" HRR<sub>1min</sub> was associated with a range of maximal and sub-maximal variables indicative of better preserved exercise tolerance (p<0.05). On a multiple regression analysis which considered only CPET-independent variables (6-minute walking distance, NYHA class and PAH treatment), HRR<sub>1min</sub> was the single predictor of mortality (hazard ratio (95% confidence interval)= 1.19 (1.03-1.37); p<0.05).

**Conclusions:** Preserved HRR<sub>1min</sub> (>18 beats) is associated with less impaired responses to exercise in patients with PAH. Conversely, an abnormal HRR<sub>1min</sub> response has negative prognostic implications, a finding likely to be clinically useful when more sophisticated analyses provided by a full CPET are not readily available.

#### P4437

# Portioning out the contribution of dead space ventilation and low $\mathrm{CO}_2$ set point to ventilatory inefficiency during exercise in chronic thromboembolic pulmonary hypertension

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**Rationale:** The individual relevance of enlarged dead space ventilation as a fraction of tidal volume (VD/VT) and low CO<sub>2</sub> set-point in promoting exercise ventilatory inefficiency in chronic thromboembolic pulmonary hypertension (CTEPH) remains controversial.

**Objective:** To determine the contributing role of VD/VT and  $PaCO_2$  on the excessive ventilatory response to exercise in patients with CTEPH.

**Material and methods:** 20 patients  $(47\pm14 \text{ yrs}, \text{ mean pulmonary artery pressure} = 52\pm10 \text{ mmHg})$  underwent an incremental exercise test and a steady-state test with arterial blood gases measurements.

**Results:** Compared to normal standards, patients showed lower resting PaCO<sub>2</sub> and peak V'O<sub>2</sub> but greater  $\Delta V'E/\Delta V'CO_2$  slope (68±16). Peak V'O<sub>2</sub> and  $\Delta V'E/\Delta V'CO_2$  were inversely correlated (r= -0.70; p<0.05). V'E/V'CO<sub>2</sub> ratio during the constant work rate test was also abnormally high (62±15). VD/VT increased from 0.31±0.08 at rest to 0.39±0.11 during exercise; on the other hand, end-tidal partial pressure (PET) for CO<sub>2</sub> decreased despite a stable PaCO<sub>2</sub> (p>0.05). Consequently, P(a-ET)CO<sub>2</sub> became wider (4±3 mmHg to 8±5 mmHg), a finding related to greater V'E/V'CO<sub>2</sub> (r= 0.81; p<0.05). On a multiple regression analysis VD/VT (partial r = 0.89) and PaCO<sub>2</sub> (partial r = -0.37) explained up to 90% of V'E/V'CO<sub>2</sub> variability (125.9 VD/VT - 2.3 PaCO<sub>2</sub> + 77.1; p<0.001).

**Conclusion:** Increased VD/VT is the main pathophysiological mechanism leading to an excessive ventilatory response to exercise in patients with CTEPH. Low  $CO_2$  set-point responds for a relatively minor portion of this abnormal feature.

#### P4438

Association of 6-minute walk distance and maximal work capacity assessed by ergometry in patients with obstructive and restrictive lung diseases <u>Uta Ochmann<sup>1</sup></u>, Nicola Kotschy-Lang<sup>2</sup>, Wolfgang Raab<sup>3</sup>, Jessica Kellberger<sup>1</sup>, Dennis Nowak<sup>1</sup>, Rudolf Jörres<sup>1</sup>. <sup>1</sup>Institute of Occupational, Social and Environmental Medicine, Ludwig-Maximilians-University, Munich, Germany; <sup>2</sup>Rehabilitation Clinic Falkenstein, Falkenstein, Germany; <sup>3</sup>Rehabilitation Clinic Bad Reichenhall, Bad Reichenhall, Germany

Background and objective: In patients with chronic lung diseases work load for

endurance training is calculated from maximal load. If this is not known, it might be predicted on the basis of 6-minute walk distance (6MWD). We addressed the reliability of such prediction.

Methods: Within a longitudinal clinical study on the efficacy of rehabilitation, baseline data including 6MWD, maximal work load (Wmax), peripheral muscle force, lung function, fat-free mass (FFM) and dyspnoea (MMRC score) of 255 men with occupational lung diseases (asthma, asbestosis, silicosis, COPD) were evaluated.

Results: 6MWD (mean 502m, SD 92m) correlated (r=0.51, p<0.05) with Wmax (mean 112Watt, SD 35Watt), without systematic differences between asthma, silicosis and COPD. The asbestosis group was evaluated separately since the regression line was different. Muscle force, lung function parameters and MMRC score correlated moderately with Wmax (p<0.05 each). Including all statistically significant predictors the correlation was r=0.76 in patients with obstructive lung function impairment and r=0.61 in asbestosis patients. The residual standard deviations of predicted Wmax were 20-28 Watt, depending on the predictors used, and the 95% prediction intervals of Wmax based on the predictor 6MWD 47-65 Watt.

Conclusions: Compared to literature data we observed weaker correlations indicating that a sufficiently reliable prediction of individual Wmax by 6MWD or related measures is not possible. Despite this, the regression lines based on a large sample of subjects might be useful for the comparison of epidemiological studies.

#### P4439

#### The relationships between hyperinflation during exercise and symptoms in adults with cystic fibrosis

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Exercise tolerance is reduced in patients with Cystic Fibrosis (CF). Ventilatory limitation, peripheral skeletal muscle weakness and poor nutritional status may contribute to exercise intolerance. The mechanisms of exertional dyspnoea are less understood, but it seems that dynamic hyperinflation may play a role. So we wonted to investigate the role of exercise dynamic hyperinflation on breathlessness (DYS) and leg fatigue (LEG) in CF patients. 17 stable CF patients (32±8SD yrs; FEV1  $2.66\pm0.7$  l;  $68\pm16\%$  pred; IC  $3.4\pm1.0$  l), during constant load cycle ergometry at 80% V'O2 max were studied. Intensity of breathlessness and leg fatigue, by Borg scale, and IC were recorded every 2 minutes. The individual slopes of the change in IC vs DYS and IC vs LEG were also computed.

Results: In most patients we did not observe a correlation between changes in IC during exercise vs either DYS ( $r^2 = 0.30 \pm 0.28$ ) or vs LEG ( $r^2 = 0.35 \pm 0.26$ ). In addition, resting IC did not predict the rate of change in DYS or LEG. Conversely, we found a close relathionship between the rate of increase in DYS per unit change in IC and the rate of increase in LEG per unit change in IC (r<sup>2</sup>=0.85 p<0.0001). Importantly, we found a good relationship between the baseline IC and T<sub>LIM</sub> ( $r^2$ =0.44 p<0.005), but not between baseline FEV1 and T<sub>LIM</sub>.

Conclusions: CF patients show considerable variation in the rate at which symptoms develop during exercise, suggesting that different physiological processes underline these symptoms. Baseline IC strongly predict the duration of the endurance tolerance, while the degree of resting hyperinflation is poorly predictive of exercise induced changes in DYS and LEG.

#### P4440

#### Exercise capacity and limiting factors in older patients with post infectious bronchiolitis obliterans

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Exercise capacity has been poorly studied in patients with post-infectious bronchiolitis obliterans (PBO) and main studies evaluated children with follow-up in older subjects lacking.

We evaluated exercise capacity in older patients with PBO and mechanisms of exercise limitation.

This was a cross-sectional study including the oldest patients of our tertiary care center. Cycle incremental cardiopulmonary exercise tests with investigation of dynamic hyperinflation and exercise induced bronchoconstriction (EIB) were performed.

Sixteen patients were studied with a mean age of  $15.3\pm3.9$  (range 10-23) years, and post-bronchodilator (BD) resting lung function (%pred): FVC 88.9±19.3; FEV<sub>1</sub> 67.4±27.5, TLC 115.3±10.7; RV 234.3±87.1, D<sub>1</sub> CO 73.6±11.9. Only 7 patients (43.8%) had reduced exercise capacity (VO2peak<84%pred), of these 5 (71.4%) was <16 years-old. VO2peak was only correlated with age (r=0.58; p=0.01) and DLCO% pred (r=0.66; p=0.01).

Patients with reduced exercise capacity tended to be younger  $(13.4\pm3.3 vs \ 16.8\pm3.9$ years; p=0.09), with greater FEV<sub>1</sub> response to BD (18.9 $\pm$ 12.8 vs 7.0 $\pm$ 11.9%; p=0.08) and lower D<sub>L</sub>CO (67.8 $\pm$ 12.9 vs 81.2 $\pm$ 9.2%; p=0.053). No difference were found in relation to ventilatory reserve and dynamic hyperinflation during

exercise. Of the 4 patients who presented EIB, 3 (75%) had reduced exercise capacity. Nevertheless, FEV1 alteration post-exercise was not significantly different from those with preserved exercise capacity (-17.0±20.3 vs -5.7±6.7%, p=0.20). In conclusion, it seems that functional alterations of POB tend to ameliorate with aging. Those with reduced exercise capacity present lower lung diffusion capacity and greater airway obstruction variability.

#### P4441

#### Estimation of the exercise ventilatory compensation point by the analysis of the relationship between minute ventilation and heart rate in patients with pulmonary hypertension

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Background: Incremental cardio-pulmonary exercise test with gas exchange measurement is the gold standard for the identification of the ventilatory compensation point (VCP). It has previously been demonstrated that the change in the slope of increment of minute ventilation over heart rate ( $\Delta V'E/\Delta HR$ ) can be utilized alternatively to the ventilatory equivalent for CO2 (V'E/V'CO2) method for detection of VCP in healthy subjects. The reliability of this parameter in patients affected by cardiac and pulmonary diseases is still not well elucidated.

Aim: To evaluate the efficacy and reliability of the  $\Delta V'E/\Delta HR$  in patients with pulmonary hypertension.

Methods: Twenty subjects (11F - 9M; mean age 44±15.8 SD) with a diagnosis of pulmonary hypertension underwent an incremental maximal exercise test on a cycle-ergometer. V'O2, V'CO2, V'E were measured breath-by-breath. Heart rate was also registered. Results are expressed as mean±SD.

Results: All patients reached the VCP showing a mean VO2 max % predicted of 55±15%. As in healthy subjects it was possible to identify two different slopes (S1 – S2) of increment in the  $\Delta V'E/\Delta HR$  in 14 out of the 20 patients tested (0.78±0.2 vs 1.83±1.0 p=0.002). The remaining 6 patients in whom was not detected a significant difference between the two slopes interestingly showed an altered cardiac function, as shown by the O2 pulse in the final phase of exercise. Conclusions:  $\Delta V'E/\Delta HR$  as a predictor of the VCP, appears to be a useful and

reliable method to identify more severe IP patients with an altered cardiac function.

#### P4442

Critical power for upper limb in patients with COPD Carla Malaguti<sup>1</sup>, Eduardo Colucci<sup>2</sup>, Talita Stuchi<sup>3</sup>, Roberta Ramos<sup>3</sup>, Luiz Nery<sup>3</sup>, Simone Dal Corso<sup>2</sup>. <sup>1</sup>Physiology, Federal University of Juiz de Fora, MG, Brazil; <sup>2</sup>Pneumology, Federal University of São Paulo, SP, Brazil; <sup>3</sup>Rehabilitation Sciences Program, Nove de Julho University, São Paulo, SP, Brazil

Introduction: The determinants of the critical power (CP) for whole-body exercise (lower limbs) in patients with COPD have been previously identified. There are no data concerning to its determinants for upper limbs (UL) in this population. Objective: To characterize the determinants of the CP for UL in patients with COPD.

Methods: Eight patients with COPD (FEV1: 45.1±1.2% of predicted) and seven healthy subjects were assessed. After an arm incremental test on cycle ergometer, three constant workload tests were performed (100-120%, 90% and 80% of peak workload). From these tests the CP was estimated and an additional test was performed (5-20% above the workload of the estimated CP). Then, CP was determined by the intercept of the linear regression between workload and reciprocal of time for the four tests and was confirmed in a new test. The inspiratory capacity (IC) was measured before and immediately after each test.

Results: There was no significant difference in the CP workload between patients and controls (30.2±12.7 Watts - 59.8±11.4% of peak workload vs 42.2±16.7 Watts - 66.7±9.3% of peak workload, respectively). The oxygen uptake in CP was lower in the COPD group than controls (0.79±0.28 L/min vs 1.20±0.37 L/min, respectively, p < 0.05). The patients presented dynamic hyperinflation and substantial reduction of ventilatory reserve for all tests, including the CP test. Despite the ventilatory limitation, all patients were able to sustain exercise at CP for 20 minutes.

Conclusion: The present study shows that the ventilatory constraint is the most important determinant of the CP for UL exercise in COPD patients.

#### P4443

#### Physiological responses at critical load on resistance exercise - Effects of aging process

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Background: Critical load (CL) is a theoretical analysis derived from a series of constant load repetitions until concentric failure during resistance exercise (RE), which indicates the transition of moderate to intense exercise. However, it appears the influence of age on differences in CL remains to be investigated.

Aims: The objectives of the study were to; 1) determine the intensity of CL during RE, and 2) evaluate the behavior of cardiorespiratory and metabolic responses during RE at the CL in young and older subjects.

Methods: We evaluated 12 young  $(23\pm3)$  years) and 10 elderly  $(70\pm2)$  years) apparently healthy males, who underwent: 1) a 1 repetition maximum (1RM) test on Leg Press and, 2) on different days, three high-intensity resistance exercise constant load tests (60%, 75% and 90% 1RM) in order to obtain CL by linear regression: load X reverse of time (Tlim = duration of exercise until fatigue).

Results: Absolute values of both the CL asymptote and curvature constant (kg) were significantly lower in elderly subjects (p<0.05). In contrast, both groups have the same value for CL  $\sim$  52%RM. As expected, actual oxygen consumption (VO2) and heart rate (HR) values obtained during CL exercise testing were significantly reduced in older subjects. However, percent-predicted aerobic capacity values were significantly higher in older subjects (P<0.05). In addition, blood lactate ([La-]) corrected to Tlim were greater in younger subjects at all intensities (p <0.05). Conclusion: These findings suggest that the despite reduced force production

in older subjects, endurance-related parameters are well preserved according to age-adjusted percent-predicted values in apparently healthy males. Financial support: FAPESP No. 2009/01842-0.

#### P4444

#### Impaired cardiac output responses to incremental exercise measured by signal-morphology impedance cardiography in advanced COPD

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Background: There is renewed interest in the continuous evaluation of cardiac output (Q'T) during exercise in patients with chronic obstructive pulmonary disease (COPD). Signal-morphology impedance cardiography  $(SM_{ICG})$  has some advantages over previous impedance approaches and it might be useful to track relative changes in exercise Q'T in this patient population.

**Objective:** To contrast the dynamic changes  $(\Delta)$  in Q'T as a function of metabolic demand (O<sub>2</sub> uptake,  $\Delta V'O_2$ ) in patients with advanced COPD and healthy controls. Methods: 15 males with COPD (11 GOLD stages III-IV) and 9 gender-matched controls underwent a ramp-incremental test with Q'T being measured by a commercially-available SM<sub>ICG</sub> system (Physioflow™ PF-05, Manatec, France).  $\Delta Q'T/\Delta V'O_2$  relationship was calculated by linear regression.

Results: Patients were significantly younger than controls (61±6 yrs vs. 72±5 yrs, respectively; p<0.01). As expected, patients had lower peak V'O2 (% predicted) compared to controls (p<0.05). There were no significant between-group differences in the y-intercept or the slope of  $\Delta Q'T$  (L/min)/ $\Delta V'O_2$  (L/min) (p>0.05). Interestingly, however, both parameters were lower in patients than controls when Q'T was expressed as fold-changes (0.90±0.30 vs. 1.22±0.18 and 0.43±0.17 vs.  $0.61\pm0.10$ , respectively; p<0.05).  $\Delta Q$ 'T at maximal exercise was associated with peak V'O<sub>2</sub> in controls (r= 0.73; p<0.05) but not in patients (r= 0.12).

Conclusions: Semi-quantitative SMICG measurements indicated blunted Q'T adjustments to rapidly-incremental exercise in patients with advanced COPD - even when compared to older healthy controls.

#### P4445

## Exercise ventilatory inefficiency is an independent predictor of mortality in

patients with pulmonary arterial hypertension <u>Eloara Ferreira</u><sup>1,2</sup>, Roberta Ramos<sup>1,2</sup>, Jaquelina Arakaki<sup>1,2</sup>, Priscila Barbosa<sup>2</sup>, Erika Treptow<sup>1</sup>, L. Eduardo Nery<sup>1</sup>, Fabrício Valois<sup>1,2</sup>, J. Alberto Neder<sup>1</sup>. <sup>1</sup>Respiratory Division, Pulmonary Function and Clinical Exercise Physiology Unit (SEFICE), Federal University of São Paulo, SP, Brazil; <sup>2</sup>Respiratory Division, Pulmonary Vascular Group, Federal University of São Paulo, Brazil

Rationale: An excessive ventilatory (V'E) response to CO2 output (V'CO2) during incremental exercise is a strong prognosticator in cardiovascular diseases. The role of  $\Delta V'E/\Delta V'CO_2$  to predict mortality in pulmonary arterial hypertension (PAH), however, remains to be demonstrated.

**Objective:** To investigate the value of increased  $\Delta V'E/\Delta V'CO_2$  as a negative prognostic marker in PAH.

Methods: 80 patients with PAH who underwent a ramp-incremental cardiopulmonary exercise test (CPET) were followed-up for 5 yrs.  $\Delta V'E/\Delta V'CO_2$  slope was calculated to the respiratory compensation point  $(\Delta V'E/\Delta V'CO_{2(start-RCP)})$  or to peak exercise  $(\Delta V'E/\Delta V'CO_{2(start, PEAK)})$ . **Results:** 14 patients (17.5%) died of PAH-related causes. Compared to sur-

vivors, deceased patients were younger and had lower peak O2 uptake, O2 pulse, and oxyhemoglobin saturation but, regardless the method of calculation, higher  $\Delta V'E/\Delta V'CO_2$  (p<0.05). None of the other variables (including the six-minute walking distance) was related to mortality (p>0.05). The best cutoff to death prediction was higher for  $\Delta V'E/\Delta V'CO_{2(start-PEAK)}$  (>55) than  $\Delta V'E/\Delta V'CO_{2(start-RCP)}$ (>45). An univariate analysis revealed that the former variable was superior to the later on this regard (p= 0.004 vs. 0.02).In fact, a multiple regression analysis showed that resting heart rate (hazard ratio (95% CI)= 1.04 (1.00-1.08); p=0.03) and  $\Delta V'E/\Delta V'CO_{2(start-PEAK)}$  (1.04 (1.01-1.07); p= 0.006) were the only independent predictors of mortality.

Conclusions: A resting variable (heart rate) and an effort-independent marker of ventilatory inefficiency ( $\Delta V'E/\Delta V'CO_{2(start-PEAK)}$ ) are clinically-useful markers of poor prognosis in patients with PAH.

#### P4446

#### Clinical and functional determinants of exercise limitation in adult patients with cystic fibrosis

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Objective: Exercise tolerance is reduced in adult patients with cystic fibrosis (CF). The aim of this retrospective analysis was to determine the mechanisms of this limitation

Patients and methods: Cardiopulmonary exercise testing (CPET) with peak exercise blood gas was performed in 102 patients (Sex Ratio M/F=0.51) aged  $28\pm11$ years old (FEV1<50%: 48 patients; FEV1 between 50 and 80%: 22; FEV1>80%: 32). VO2 peak was correlated with clinical, biological and functional parameters. Results: VO2 peak was decreased (<84%) in 85% of patients (25±9 ml/kg or  $65{\pm}21\%$  predicted) and was correlated with Body Mass Index (r = 0.26), CRP (r = -0.34), FEV1 (r = 0.71), FVC (r = 0.69), RV (r = -0.63) and DLCO (r = 0.56). Upon exercise parameters, VO2 peak was correlated with VE/VO2 at ventilatory threshold, peak VD/VT, peak PaO2, PaCO2 and P(A-a)O2, and ventilatory reserve (r= -0.50 respectively, -0.64, 0.54, 0.64, -0.54 and 0.37). In multivariate analysis, FEV1 was the most predictive parameter of VO2 peak impairment, accounting for 48% of VO2 peak alteration. Reduced or absent ventilatory reserve and excessive hyperventilation (VE/VO2 threshold) accounted for respectively 10 and 8% of VO2 peak alteration. Peak VD/VT and P(A-a)O2 explained only 1% each of the VO2 peak value.

Conclusion: Limiting aerobic capacity in adult patients with cystic fibrosis is correlated with nutritional status, inflammation and lung function. This limitation is largely dependent, not only on FEV1, but also on the importance of ventilatory response to exercise. CPET is useful for a better management of CF patients.

#### P4447

#### Exercise training affects alveolar to arterial oxygen partial pressure difference in obese subjects: Preliminary data

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Background: Obesity is often associated with decreased lung volumes and daytime hypoxemia. The decrease in lung volumes and the decrease in physical activity may favour microatelectasis that may account for at least a part of the decreased observed davtime paO2.

Objectives: The aim of the study was to investigate the effect of a course of exercise training on the alveolar-to-arterial oxygen partial pressure difference (AaDO2) in obese subjects.

Methods: Seventeen obese subjects (BMI>30) with no evident respiratory diseases (FEV1/FVC > 0.7) were divided in 2 groups. Group I (n=8) underwent to a 15 days exercise training program associated to an educational program; group II (n=9) underwent to a 15 days educational program. All patients performed blood gases analysis, spirometry, body pletismography and 6MWT before and after the treatment

Results: Both groups displayed mild baseline hypoxemia (mean PaO2=71±9 mmHg, and 74±10 mmHg for the control and treated group respectively) and an elevated BMI (43±8 and 38±5 respectively). In the treated group, preliminary data, show a decrease in AaDO2 after the exercise training program (15±5 vs. 24±5 mmHg, p<0.05).

Conclusions: Our data suggest that daytime hypoxemia in obese patients may be partially corrected by a program of exercise training. The mechanism may be related to reopening of microatelectasis.

#### P4448

#### Obese asthmatics have reduced exercise capacity and higher ventilation than non-obese asthmatics

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Obesity is a modifiable risk factor of asthma (Beuther 2007). Regular exercise is associated to better asthma control but little is known about the exercise capacity and physical activity level (PAL) in obese asthmatics.

Aim: Analyze exercise capacity, ventilation (VE) during exercise, physical activity and QoL in obese compared with normal weight asthmatics.

Methods: 48 asthmatics (29F), age 57,4±11, regularly visited at Asthma Center of Ferrara University Hospital were submitted to spirometry, 7 days PAL monitoring (Armband<sup>®</sup>), QoL questionnaire (AQLQ) and walking test (6MWT) with VE analysis (Spiropalm, Cosmed).

**Results:** 19 subjects were obese (OB), 17 overweight (OW), 12 normal weight (NW). FEV<sub>1</sub>% was < in subjects with BMI  $\ge 25$  (72.1 $\pm$ 17 vs 81.5 $\pm$ 17, ns). PAL (METs) in OB was < OW and NW(1,3 $\pm$ 0,2 vs 1,5 $\pm$ 0,3; 1,5 $\pm$ 0,2,\*) independently from the severity of obstruction. No difference in QoL was found.

OB and OW showed a reduced exercise capacity and  $\ensuremath{\text{SpO2\%}}$  in comparison to NW.

Table 1

	SpO2%	Meters	Dyspnea (Borg)
OB	95,7±0,3§	454,7±87,2§	2,5±2,3
OW	95,6±0,5¶	456±96,4 <sup>¶</sup>	2,5±2,1
NW	97,2±0,3	$548 \pm 52,5$	1,2±1,3

<sup>§</sup>p<0,05 OB vs NW; <sup>¶</sup>p<0,05 OW vs NW.

No difference in dyspnea Borg scale (0-10).

VE analysis during 6MWT: OB showed a higher maximal increase (%) in VE than NW, independently from the level of obstruction and mainly due to the increase in tidal volume (TV).

Table 2	Ta	bl	e	2	
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	Increase VE (%)	Increase TV (%)	
OB	108,3±38,8 <sup>§</sup>	93,6±34§	
OW	93,7±38,3¶	56,9±41 <sup>¶</sup>	
NW	67,9±6,3	59,8±10,2	

 $^{\$}p{<}0{,}05$  OB vs NW;  $^{\P}p{<}0{,}05$  OW vs NW.

**Conclusions:** In asthmatics, obesity influences negatively the daily physical activity and exercise capacity through mechanisms which appear independent from the severity of bronchial obstruction.

## P4449

## Laboratory exercise tests are not representative of the real physical activity in more severe COPD patients

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**Background:** Cardiopulmonary exercise test (CPET) is the gold standard to evaluate the exercise tolerance. Incremental shuttle walking test (ISWT) has ventilatory and metabolic responses similar to those of CPET in moderate-severe COPD. Sensewear Armband is a new device to quantify the physical activity of daily life. Aim: To evaluate the correlations among CPET, ISWT and daily physical activity, measured by Armband, in patients with COPD of different severity.

Subject and methods: In cross sectional study 45 COPD patients (FEV1%:  $52.5\pm17$ , 36 male) evaluated: CPET, ISWT, pulmonary function test (PFT), dyspnea scale (MRC), steps/day and total energy expenditure (TEE) by Armband (as a mean of a 7-day monitoring period). The patients were divided according to FEV1 (>50% or  $\leq$  50%) and MRC ( $\leq$  2 or > 2).

**Results:** CPET and ISWT significantly correlated between them, better in patients with FEV1 <50% and in those with MRC > 2. In COPD patients with FEV1 >50%, steps/day (r=0.405, r=0.582) and TEE (r=0.494, r=0.615) significantly correlated with CPET and ISWT, respectively, while this did not occur in COPD patients with FEV1 <50%. Similarly, steps/day (r=0.423, r=0.575) and TEE (r=0.319, r=0.494) significantly correlated with CPET and ISWT in COPD patients with a MRC <2, respectively, while this did not occur in COPD patients with MRC >2.

**Conclusion:** Exercise tolerance evaluated in laboratory by CPET and ISWT is representative of the real physical activity, as expressed by steps/day and TEE, in patients with moderate COPD but not in patients with severe COPD. In these patients, physical activity evaluation may offer complementary informations to the laboratory exercise assessment.