

## 206. The best abstracts in pulmonary rehabilitation

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### Characterizing metabolic abnormality and adipose tissue infiltration in skeletal muscle of COPD patients using 31P MR spectroscopy and MRI imaging

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**Background:** Anaerobic metabolism (AM) is an extra-pulmonary manifestation of COPD. 31P Magnetic Resonance Spectroscopy (<sup>31</sup>P MRS) is an established technique to assess the oxidative capacity of skeletal muscles, but is unknown whether similar changes occur in the upper and lower limbs. Dixon MRI has been demonstrated as a quantitative technique to determine water and fat levels in tissues.

**Objective:** We hypothesised that AM would occur predominantly in the legs and that intermuscular adipose tissue (IMAT) infiltration would be a predictor of AM. **Methods:** 31P – MRS data for the quadriceps (quads) and biceps were obtained during 2 min. and 8 secs of endurance exercise and pre and post-exercise. Quads and its sub-muscle group cross-sectional area and IMAT were measured using Dixon MR imaging. Quads maximal voluntary strength (QMVC), six minute walking test (6MWT) and fat free mass index (FFMI) were additionally performed.

**Results:** Data were obtained for 14 patients with COPD (age 66±5.73) with a mean ±SD percentage predicted of forced expiratory volume in 1s (FEV<sub>1</sub>) of 36.5±12.7 and 14 age matched healthy controls (age 65±6, FEV<sub>1</sub> pred% 110±6.5). Patients with COPD had prolonged quads phosphocreatine recovery time [PCr (t<sub>1/2</sub>)], (p=0.006) and lower nadir intramuscular pH (p=0.002) as compared to controls. Biceps metabolism was not different between COPD patients and controls. Quads IMAT was 32% greater in COPD patients than controls (p=0.033). **Conclusion:** AM activation appears confined to the quads in COPD. We also suggest that IMAT, as measured by Dixon MRI, is a sensitive biomarker for AM.

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### Reduced mitochondrial density in the vastus lateralis muscle of COPD patients with low fat free mass

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Muscle wasting affecting a subgroup of patients with COPD, is a predictor of health related quality of life and survival. These patients have a further reduction in exercise capacity and evidence of decreased limb muscle oxidative capacity. We hypothesise that a further decrease in mitochondrial density occurs in patients with muscle wasting and may contribute to a lower oxidative capacity of the muscle. Mitochondrial ultrastructure was analysed using transmission electron microscopy

in the *vastus lateralis* of seventeen COPD patients, ten with low fat free mass index (FFMI) (COPD<sub>L</sub>) (FEV<sub>1</sub> 33±4.3%pred, FFMI 15±0.2 kg m<sup>-2</sup>), seven with preserved FFMI (COPD<sub>N</sub>) (FEV<sub>1</sub> 47±7.3%pred, FFMI 19±0.6 kg m<sup>-2</sup>) and compared with nine age and gender-matched healthy sedentary subjects (C) (FEV<sub>1</sub> 96±4.0%pred, FFMI 20±0.9 kg m<sup>-2</sup>). Mitochondrial density was reduced in COPD<sub>L</sub> in comparison to COPD<sub>N</sub> (1.82±0.25% and 2.72±0.34% respectively, p<0.05). In comparison to C, only COPD<sub>L</sub> showed a reduction in mitochondrial least diameter (0.15±0.0µm and 0.13±0.00 µm respectively, p<0.05) reflecting a reduction in mitochondrial size.

Mitochondrial density correlated with parameters of lung function, muscle function, exercise capacity and exacerbation frequency. Only exacerbations frequency remained independently related to mitochondrial density in a multiple regression analysis.

We conclude that peripheral muscle of COPD<sub>L</sub> patients have a reduced mitochondrial density that is likely to contribute to a decreased oxidative capacity of the muscle.

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### Blunted muscle angiogenic response after exercise training in COPD patients

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In chronic obstructive pulmonary disease (COPD) patients, the skeletal muscle impairment reduces the exercise capacity. Systemic factors (i.e oxidative stress, low grade inflammation ...) have been incriminated. Then, as for the muscle oxidative fibers, the muscle angio-adaptive response to training could also be blunted in COPD, like in other chronic conditions. Therefore, we aimed to compare the muscle functional response, myofiber remodeling and angio-adaptations to training in COPD patients and sedentary healthy subjects (SHS).

21 COPD patients and 23 SHS completed a 6-week rehabilitation program based on individualized moderate-intensity endurance and resistance training. Histomorphological muscle analysis and measurements of pro-angiogenic vascular endothelial factor-A (VEGF-A) and antiangiogenic thrombospondin-1 (TSP-1) were conducted before and after training.

Both COPD patients and SHS improved their peak oxygen consumption (respectively, +0.96±2.4 and +2.9±2.6mL/kg/min, p<0.001) and muscle endurance (respectively, +65% and +108%, p<0.001), although improvements were lower in COPD patients (group-time interaction: p<0.05 and p=0.06 respectively). Whereas the capillary-to-fiber ratio (C/F) and the angio-adaptive VEGF-A/TSP-1 ratio increased in COPD patients and SHS (C/F: p<0.01 and VEGF-A/TSP-1: p<0.05), the improvement in C/F was significantly reduced in COPD patients vs. SHS (p<0.05), and no fiber type switch occurred in patients. Absolute changes in C/F and in VO<sub>2SL</sub> were correlated (r=0.51, p<0.05).

The angiogenic response may drive the functional improvements. In addition to a lack of fiber switch, the angiogenic response to training was blunted in COPD patients.

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### Effects of a 3-week inpatient pulmonary rehabilitation (PR) on muscle remodelling in patients with emphysema

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**Rationale:** Exercise training of at least 10 weeks duration induces significant changes in myofiber size, capillarization and distribution in patients with emphysema. Up to date it is unknown which changes in muscle structure can be achieved by a German inpatient PR with a standard duration of 3 weeks.

**Methods:** Ten patients with emphysema (age: 57m5y; BMI: 24m3kg/m<sup>2</sup>; FEV<sub>1</sub>: 31±9%pred.) were included in this prospective trial. All patients performed an incremental cycle test to determine the peak work rate (PWR). The PR included daily supervised exercise training sessions (strength- and endurance training). Pre and post PR, biopsies from vastus lateralis muscle were taken.

**Results:** PWR improved significantly during PR (+17Watt [95% CI, 6.3 to 27.7] p<0.01). We observed a significant increase in the capillary to fibre ratio in fibre types I and IIa respectively (+0.5% [95% CI, 0.1 to 1.0] p=0.03; +1.0% [95% CI, 0.6 to 1.4] p<0.01) in skeletal muscle. We found a significant negative correlation between FEV<sub>1</sub>% pred. and the change in capillary to fibre I ratio (r=-0.633, p<0.05).

A non-significant but notable increase in the quantity of fibre type I (+6.5%), IIa (+2.2%) and IIx (+2.6%) was detected. Hybrid fibres decreased during PR (type I/IIa: -1.3% [95% CI, -2.21 to -0.39] p<0.01; type IIa/IIx: -5.2%, p=0.09).

**Conclusions:** These preliminary data show that an inpatient 3-week PR is able to exert relevant adaptations in peripheral muscle of COPD patients. This includes an increase in capillarization and an augmented type I myofiber distribution. To confirm these first results, further patients will be investigated.

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**Changes in fatigue index during an 8 week quadriceps resistance training programme for patients with COPD & healthy controls**

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**Introduction:** Fatigue index (FI) measures the reduction in muscle force during muscle testing/training & can be altered by resistance training (RT). FI is seldom reported in patients with COPD. In isokinetic testing 2 variables are of interest: peak torque (PT) & total work (TWor).

**Aim:** To evaluate changes in FI for PT & TWor during 8weeks of RT in patients & healthy controls.

**Methods:** 70 patients [mean (SD) age 68.6 (9.1)yr, FEV<sub>1</sub>44.8(15.2)% pr, 42 men] & 22 controls [age 66.6 (5.1)yr, FEV<sub>1</sub>103.4(15.9)% pr, 12 men] completed quadriceps RT for 8weeks. RT was 5x30 knee extensions; 3times/week on a cybex dynamometer (speed=180°/sec). PT (Newton-metres:Nm) & TWor (Joules:J) were recorded for each set & FI was calculated as: set5/set1x100 for the right leg (weekly average). A high FI=less fatigue.

**Results:** There were no significant differences between/within-groups for PT FI over 8 weeks (FI approx 90% in both groups for all weeks).

TWor FI in the COPD group did not significantly change over 8weeks. Control subjects displayed improvements in TWor FI & the difference in FI at week8 was significant compared to baseline & week4. However there were no significant differences between the 2 groups for TWor FI (Fig. 1).

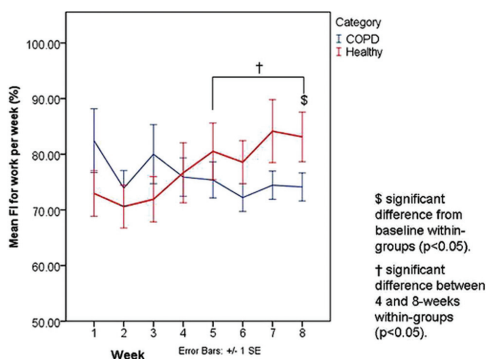


Figure 1

**Conclusions:** Healthy controls experienced less fatigue in TWor as RT progressed. This did not occur in the COPD group & may be related to muscle dysfunction. TWor seems a more sensitive measure than PT.

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**Effects of home-based pulmonary rehabilitation on the time spent in active- and passive- walking in elderly patients with COPD**

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**Purpose:** The objective of this study was to evaluate the effect of home-based pulmonary rehabilitation (PR) including a chair-walking exercise and lower muscle training on daily active- and passive-walking time in elderly patients with COPD.

**Methods:** We assessed walking time according to the walking speed using a newly developed triaxial accelerometer (A-MES activity monitor, Kumamoto, Japan), which could measure the time spent in walking, standing, sitting and lying separately and also could discriminate active walking (≥2 km/hour) from passive walking (< 2 km/hour). Twenty elderly patients with COPD (Age 76±7 years; FEV<sub>1</sub> 56.6±18.7% pred) were evaluated using this activity monitor for 3 consecutive days before and after PR. The home-based PR program included a chair-walking exercise, lower muscle training, stretch of body trunk, respiratory muscle training and education of self management. Pulmonary function, exercise

capacity (6-min walking distance; 6MWD), quadriceps muscle force (QF), and health-related QOL (CRQ) were evaluated before and after PR.

**Results:** Active-walking time increased (pre PR: 27±23 vs. post PR: 52±31 min/day) and lying time decreased (pre PR: 53±18vs. post PR: 38±18 min/day) significantly after PR. Frequency of standing increased (pre PR: 80±42 vs post PR: 117±63 times/day) significantly after PR. The degree of improvement of active-walking time after PR was correlated with 6MWD and QF.

**Conclusions:** These data suggested that home-based PR consisting of a chair-walking exercise and lower muscle training was effective in improving active-walking time in elderly patients with COPD.

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**The effect of post operative physical training on activity after curative surgery for non small cell lung cancer (NSCLC) – RCT**

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**Background:** In England and Wales the incidence of lung cancer is around 0.05%, 13.5% of patients receive surgery with curative intent. Strategies addressing quality of life (QoL) and activity post op are lacking.

**Aims and objectives:** To evaluate the effect of in-patient, cycle training, provided post op for NSCLC on physical activity at 4 weeks post op.

**Methods:** This RCT recruited patients undergoing curative lung resection. The control group received usual care. The active group additionally received daily cycle training a home walking programme with diary. Outcomes, measured pre, 5 days and 4 weeks post op, activity monitor data, muscle strength, exercise tolerance and QoL (SF36). ANCOVA was used to test for differences between groups.

**Results:** 131 patients (72 female), mean age 67.5 (SD: 10.97) years, FEV<sub>1</sub> 2.4 (1.13) l, median ISWT m 290 (IQR: 190-440) were randomised. 63 (48%) had evidence of spirometric obstruction (OB). Physical activity was not significantly different between groups nor in those with OB. There were no significant differences in any secondary outcomes for the groups as a whole. However, in those with OB, physical and mental component scores for the SF36 were 11.7 (p = 0.04) and 19.6 (p=0.01) higher in the active group compared to controls at 4 weeks post op and muscle strength was significantly different between groups in favour of active (p = 0.04).

**Conclusions:** Compared with a control group, a cycle and home walking programme prevented decline in QoL and quadriceps muscle strength seen at 4 weeks post op in people with OB. These data support the need for further exercise interventions aimed at patients with OB undergoing surgery for NSCLC.

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**Atherosclerosis in subjects with COPD is independently determined by the degree of airflow limitation**

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**Background:** Subjects with COPD have an increased cardiovascular risk that may be related to shared risk factors. To date, it is not clear whether this is a consequence of the severity of COPD itself.

**Objective:** We aimed to determine independent predictors of the presence of atherosclerosis in patients with COPD and establish whether and to what extent the degree of airflow obstruction is independently predictive for the degree of atherosclerosis in a model including all traditional cardiovascular risk factors.

**Method:** Pulmonary function, blood gases, packyears, body composition (BMI, FFMI), lipids, glucose, hsCRP, renal function (eGFR) and blood pressure were determined in 197 patients (mean±SD) age: 64±7 year, 60% male, FEV1: 51±17% pred., BMI: 26.2±5.2 kg/m<sup>2</sup> with stable COPD prior to pulmonary rehabilitation. Carotid-wall intima-media thickness (c-IMT) was assessed in all patients (mean±SD: 0.93±0.18 mm) as an ultrasonographic surrogate measure of atherosclerosis. Independent predictors of an increased c-IMT were assessed using multivariate backward linear regression.

**Results:**

Independent predictors of an increased c-IMT	Beta	t-test	p-value
BMI, kg/m <sup>2</sup>	0.450	6.830	<0.001
Age, years	0.237	3.886	<0.001
FEV1, % predicted	-0.174	-2.865	0.005
Mean blood pressure, mm Hg	0.142	2.330	0.021
Triglycerides, mmol/L	0.143	2.262	0.025

Other variables included in the model: Gender, FFMI, packyears, pCO<sub>2</sub>, pO<sub>2</sub>, TLC%, HDL, LDL, hsCRP, glucose and eGFR.

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**Conclusion:** In addition to traditional cardiovascular risk factors, such as obesity, older age, higher blood pressure and higher fasting triglycerides, atherosclerosis (c-IMT) is independently predicted by increasing airflow limitation in patients with COPD.