P2124

Relationships between bronchial obstruction and differential NO parameters after methacholine challenge testing

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The aim of the study was to investigate whether methacholine-induced changes of FEV1/FVC on the one hand, and of the alveolar NO concentration (Calv) and the NO flux from the bronchial wall (Jaw) on the other hand, are associated.

Patients and methods: 65 patients (all non-smokers) with work-related symptoms underwent a methacholine challenge test. Bronchial hyperresponsiveness (NSBHR) was defined as a decrease of FEV1 of 20% induced by ≤0.3mg of methacholine. Measurements of FeNO were performed at five flow rates. Calv and Jaw were calculated.

Results: There was a positive association between lung function changes after methacholine challenge and Jaw decrease with a stronger Jaw decrease in the NSBHR group:

\[ \Delta \text{Jaw: } -0.73 \pm 0.27 \text{ vs. } -0.25 \pm 0.07 \text{ nL/s, p=0.1.} \]

Contrary to this, Calv increased in the NSBHR group (n=22) and decreased in the group without NSBHR (n=43) (\[ \Delta \text{Calv: } 0.3 \pm 0.1 \text{ vs. } -0.2 \pm 0.07 \text{ ppb, p<0.001} \] with a significant negative correlation between the changes of FEV1/FVC and of Calv in the NSBHR group (r= -0.65, p<0.005), but no correlation in the group without NSBHR.

Conclusions: The increase of Calv in the NSBHR group is related to the degree of bronchial obstruction and evidently due to mixing alveolar and bronchial NO. The stronger airways obstruction (\[ \Delta \text{FEV1/FVC,} \] the more NO of bronchial source does not reach the alveoli and is exhaled late during the alveolar phase. Our results confirm the thesis of Höggman et al. (2002), who interpreted elevated Calv of COPD as a poor ventilation-perfusion matching. Correspondently, elevated Calv can be considered not only as a marker of alveolar inflammation but also as an indicator of peripheral airways obstruction.

P2125

Minor local alveolar edema in an in vivo human model can be detected by changes in respiratory mechanics by impulse oscillometry (IOS)

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Aim: We assessed the sensitivity of the impulse oscillometry methods (IOS) to detect residual alveolar edema in a lung segment after broncho-alveolar lavage (BAL).

Methods: 15 patients of both sexes undergoing BAL in different lobes for diagnosis of interstitial lung disease were studied. IOS was applied before and after withdrawal of BAL fluid, leaving in the alveoli a volume (V0) of 86.6±23.6 (mean ± DS), and continued up to 150 min. From IOS data we derived the corresponding values of respiratory resistance (Rrs) and reactance (Xrs) at frequencies from 5 to 35 Hz. We also estimated the “area of reactance” (AXrs) as defined in Fig. 1A.

Results: After withdrawal of BAL fluid, the remaining V0 caused a 30% significant increase of Rrs at 5Hz: a significant increase in resonance frequency (fres) from 11.9 Hz ± 3.3 to 15.2 Hz ± 4.9; and minor changes in Xrs. The increase in fres led to a significant 90% increase in AXrs. Rrs, fres and AXrs returned towards baseline values through an exponential decay function within 150 min (data of AXrs and regression equation are shown in Fig. 1B).

Conclusion: IOS technique is sensitive enough to detect minor localized increase in extravascular lung water.

P2126

Distribution and determinants of restrictive functional pattern

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P2128 Effects of gastric bypass surgery compared to intensive lifestyle treatment on blood gases and lung function in morbidly obese subjects

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Objective: We aimed to compare the effect of Roux-en-Y gastric bypass surgery (RYGBP) with intensive lifestyle intervention (ILI) on blood gases and lung function in morbidly obese subjects.

Design: One year non-randomized controlled clinical trial (ClinicalTrials.gov identifier: NCT00273104).

Methods: 139 morbidly obese subjects, (103 women); mean (SD) age 44 (11) years, BMI 38.6 (5.6) kg/m², and mean (SD) weight 131.8 (18) kg were treated with either RYGBP (n=76) or ILI (n=63), were included. Blood gases and lung function tests were registered before and after treatment.

Results: Mean (SD) 1-year weight loss was -30 (8)% and -8 (9)%, and mean (SD) age increased 1.4 (1.5) kg and 0.8 (1.5) kg in the RYGBP- and ILI-group, respectively (all P<0.001). Mean pCO2 decreased by 0.16 (0.4) kPa in the ILI-group (P=0.005) and 0.8 (1.5) kPa in the RYGBP-group (P=0.51). Mean ERV increased from 44 (32)% to 89 (39)% of predicted value (P<0.001) in the RYGBP-group, while there was no significant change in the ILI-group. We also found significantly improved mean values for FVC, FEV1, DLCO/VA, TLC, IC, and RV in the RYGBP group (all P<0.001, data not shown). In the lifestyle group there were significant changes in mean TLC and RV (P<0.001), DLCO/VA (P=0.010) and FVC (P=0.049). There were no significant changes in mean DLCO in either group.

There were significant between-group changes for mean FVC, FEV1, DLCO/VA, IC and ERV (all P<0.001), TLC (P<0.007) and pO2 (P=0.032). Conclusion: Blood gases and lung function improved in both treatment groups. However, the greatest effects were seen in the RYGBP group.

P2129 Reproducibility and repeatability of tidal breathing parameters derived from structured light plethysmography when compared to spirometry

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Introduction: This study aimed to test the reproducibility and repeatability of data collected by Structured Light Plethysmography (SLP) when compared to pneumotach. SLP is a non-invasive method of pulmonary function assessment. A grid of black and white squares is projected onto the thoraco-abdominal surface. 2 digital cameras image the grid’s movement and enable a stereoscopic representation of thoracic volume change enables Volume -Time; Flow-Time and Flow-Volume to be derived.

Method: 120 datasets of 45 seconds were captured from 10 healthy adults. Spirometry data were taken simultaneously with SLP Subjects took 5 tidal breaths. To assess reproducibility, 3 operators collected consecutive data. Data was collected in sitting and standing positions. Repeatability was assessed by collecting data a second time after 40 mins.

Results: The inspiratory (TI), expiratory (TE) times and tidal volume (TV) were measured with body plethysmograph or oscillometer will be required to further test reproducibility and repeatability of data to help confirm patient effort with FVLc.

Discussion: While there was a significant difference in FIV1 between control and the 2 asthma groups, they identified obstruction alone. The only other discrimining spirometric parameter was FIFS50/FEF50% which was significantly different between the control group and those with AVCVM.

Conclusion: Spirometric parameters appear to be poor discriminators for detecting AVCVM. It may be that more sensitive lung function measures, such a resistance measured with body plethysmograph or oscillometer will be required to further discriminate between obstruction of the upper and lower airways.

P2131 Compression artifact free flow-volume loops used to establish objective measurements in patient effort with spirometry

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Background: Flow-volume loops (FVL) measured by using pressure-compulsion volume plethysmography has been described in the literature and is commonly called compression artifact free flow-volume loops (FVLc). The utility of this technique has been to help demonstrate good patient effort and to help identify upper airway obstruction. There are no studies demonstrating measurable objective data to help confirm patient effort with FVLc.

Goal: Our study looks to identify the utility of FVLc by trying to establish a percentage cut off point for FVLc peak expiratory flow and what normal flow should be at 25, 50, and 75% intervals of the FVLc that can demonstrate good patient effort.

Methods: 76 patient’s charts that had FVLc in our lab were randomly reviewed. We looked to see if the peak flow on the FVLc was 25% higher than the traditional FVL. We recorded the flow percentages at the 25, 50, and 75% intervals of each patient’s FVLc. Patients were divided by having a peak flow greater than 25% (group A) or less than 25% (group B).

Results: 57 subjects peak flows on FVLc were greater than 25% and 19 patients were less than 25%. Comparing groups, the flow at the 25% interval in group A were statistically higher (mean 0.58 vs 0.35, P=0.0001). All patients with peak flow greater than 25% had higher flow rates at the 25% and 50% flow intervals (P=0.0001).

Conclusion: Evaluating patient effort with FVLc may be helpful if the peak flow is 25% greater than seen on traditional FVL and if the 25% interval flow is greater. Further study is needed to establish the validity of this technique.
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P2137
Impact of bronchodilator on pulmonary function and exercise tolerance in LAM
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Rationale: Reduced exercise capacity in LAM patients is still slightly understood. As many patients have airflow obstruction and dynamic hyperinflation (DH) (abstract 4576, ATS 2010), bronchodilator (Bd) might be a plausible option.

Objective: To evaluate the improvement with inhaled salbutamol in resting airflow obstruction, exercise tolerance and reversal of DH.

Methods: 37 LAM patients (mean age 41±10 years; FEV1 79±24%pred; DCO 68±24%pred) performed incremental CPET (incCPET) on cycle; decrease ≥ 10% in IC defined DH. So, a randomized double-blind crossover study (inhaled salbutamol x placebo) was done. After each intervention, they performed lung function (PFT) and endurance CPET (endCPET) (75% max work-rate). Exercise duration, Borg scale and IC were compared at isoitre in endCPET after Bd and placebo.

Results: 19 patients (51%) showed DH in incCPET, with max work-rate lower in DH group (93 ± 11.5W, p=0.16) and higher values in Borg dyspnea (7 ± 5, p=0.02). Compared to non-DH, DH group had lower DCO (56 ± 81%pred, p=0.001), lower FEV1 (76 ± 89%pred, p=0.002) and greater RV/TLC (0.43 ± 0.29, p<0.001). In general, Bd increased FEV1 (2.39 ± 2.40L, p<0.001), with no effects on exercise duration (325 ± 329s, p=0.75), delta IC (0.22 ± 0.22L, p=0.99) or Borg dyspnea (5 ± 5, p=0.99). In DH group, Bd reduced RV/TLC (p=0.006) and Borg dyspnea (-1 ± 1, p=0.003) more significantly, with no effects in the variation of duration (4 ± 2s, p=0.82) and of IC during CPET (60 ± 60 mL, p=0.99). In DH group, Bd reduced RV/TLC (p=0.006) and Borg dyspnea (-1 ± 1, p=0.003) more significantly, with no effects in the variation of duration (4 ± 2s, p=0.82) and of IC during CPET (60 ± 60 mL, p=0.99).

Conclusion: DH during exercise is frequent in LAM and is associated with resting airflow obstruction, reduced exercise capacity and higher breathlessness. Short-term Bd may exert a potential beneficial effect in DH patients.

P2138
A case of double aortic arch suggested by the analysis of the flow-volume curve
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A twenty-one year old female with a history of recurrent pneumonia and airway infections since infancy, chronic cough, gastrointestinal reflux symptoms, and persistent allergic rhinitis was referred to our asthmatic centre. She exhibited a normal sweat test, skin prick test positive to common allergens, and gastroscopy showing hiatal hernia and reflux esophagitis. We performed spirometry for the first time. The flow-volume curve showed a plateau of forced expiratory flow suggesting a variable intrathoracic airway obstruction. We then carried out bronchoscopy that showed a compression of the distal trachea. A computed tomography angiogram revealed a vascular ring consisting of a double aortic arch with right-arch dominance compressing the trachea and esophagus. Echocardiography confirmed the presence of the vascular ring. The patient had been referred for surgery. This report underscores the importance of spirometry and the analysis of the flow-volume curve morphology in the evaluation of patients with respiratory symptoms.

P2139
Pulmonary and liver injury after exposure to sublethal doses of microcystin-LR
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Rationale: Biological pollution caused by cyanotoxins leads to respiratory function impairment.

Aim: Study pulmonary mechanics, lung and liver histology in mice submitted to sublethal doses of microcystin-LR (MCLR) and evaluate whether the results depended on the doses.

Methods: Male Swiss mice were divided into 2 groups: CTRL (n=6) received distilled water intraperitoneally (ip, 100 mL) and TOX (n=30): injected with sublethal doses of MCLR (5, 10, 15, 20 and 25 μg/kg ip in 100 mL of distilled water). 24 h later pulmonary mechanics [static elastance (Ea), resistive (ΔP1), viscoelastic (ΔP2), and total (ΔPtot) pressures] were determined, and lungs and livers were prepared for histopathology. ANOVA was used to test differences among the groups.

Results: ΔP2, ΔE and ΔPtot were significantly higher than CTRL in all MCLR doses, but did not differ among them. Only TOX25 showed significantly higher Ea and ΔP1 than CTRL. Alveolar collapse was higher in TOX10 (18.95%), TOX15 (17.56%), TOX20 (19.11%) and TOX25 (21.63%) than in CTRL (11.57%). The lung inflammatory cell content (cells/mm3) gradually increased: TOX10 (120.90 ± 101.3), TOX15 (140.40 ± 103.1), TOX20 (206.40 ± 105) and TOX25 (5.30 ± 103) in relation to CTRL=141 ± 103. All TOX mice showed a complete loss of liver architecture with hyalinization, steatosis, dilated sinusoidal spaces and a high degree of binucleated hepatocytes. Necrosis began in TOX15, whereas only TOX 25 showed inflammation.

Conclusion: MCLR impaired pulmonary mechanics, lung and liver histology. These findings depended on the degree of exposure.

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P2140
Respiratory function in rats submitted to pharmacological hypothyroidism
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Hypothyroidism has been associated with hypventilation, decreased respiratory muscle strength and fatigue. However, the impact of chronic hypothyroidism on respiratory mechanics has not been described so far. Male Wistar rats were divided in 3 groups: Control (C, n=3), hypothyroidism (H, n=5), and hypothyroidism + T4 replacement (HR, n=5). H and HR groups received 0.03% methimazole (MMI) in drinking water for 21 days, followed by saline or T4 (1 μg/100 g BW) injections daily during the last 10 experimental days, respectively. Then, respiratory mechanics was determined during spontaneous breathing [respiratory system (RS)] and under mechanical ventilation after muscle paralysis (RS, lung and chest wall). Total lipid content in bronchoalveolar lavage fluid (BALF) and lung histology were assessed. During spontaneous breathing, RS elastic recoil and intrathoracic pressure make (Pmus,i) were lower in H group than in C (p=0.016 and p=0.011, respectively). The time required for Pmus,i to decay to zero was higher in H animals than in C or HR groups (p<0.001). Under mechanical ventilation, H group showed a smaller lung viscoelastic component of elastance (p=0.006) and viscoelastic pressure dissipation (p=0.042) than HR, and lower lung resistive pressure (p=0.015) than C rats. Chest wall and RS parameters did not differ among groups. H rats also showed a 3-fold increase in lipid content in BALF in comparison to C and HR rats. Alveolar collapse was less important in H group than in HR (p=0.026). Hence, in rats pharmacological hypothyroidism diminished RS impedance possibly because of an increased lipid content in BALF and hormonal replacement could revert these findings.

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P2141
Exercise tolerance is related to lung density in patients with COPD
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In patients with COPD, the peak oxygen uptake (peakVO2) measured during car diopulmonary exercise test (CPET) has been associated with lung hyperinflation and survival. However, no study has compared exercise tolerance relative CT measures of emphysema.

Aims: In patients (10 females) with moderate to very severe COPD (FEV1 53.3±8.5% pred., RV/TLC 53.6±10.5%) underwent measuring of pulmonary function tests (F-V curve, static lung volumes, transferfactor of the lung for carbon monoxide) and breath-by-breath measurement of flow, volumes and O2 and CO2 concentration during standard CPET. The extend of emphysema was assessed using the percentage of lung voxels with X-ray attenuation values less than -950 HU (50%LAA).

During pulmonary function tests the TLCO had the closest relationship to 50%LAA (p=0.0017), followed by the RV (p=0.0044) and the ratio of FEV1 to VC

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(p=0.0124). PeakVO₂ (both in absolute values and%predicted) showed negative correlation to%LAA (p=0.0178, resp. p=0.0337). We also found significant correlation between%LAA and O₂ pulse (p=0.0017) and slope of VO₂ (p=0.0232), reflecting decreased left ventricular stroke volume and slower dynamic of cardiac output. Quantitative CT measures of emphysema seem to be closely related to exercise tolerance, namely to decreased left heart function during CPET.

**P2142**

*Exhaled nitric oxide and lung function in winter sports elite athletes*

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**Background:** Little is known about the role of nitric oxide (NO) in pathogenesis of exercise-induced bronchoconstriction and its association with lung function in athletes.

**Aim:** The aim of the study was to investigate whether airway NO is associated with lung function in elite athletes of winter sports.

**Methods:** A total of 86 elite athletes (biathlon, ski, ice hockey, snowboard) aged 14–35 were included in the study. FEV₁, FVC, PEF (MasterScreen Pneumo, Viasys) were analyzed at the baseline and 1, 5, and 10 minutes after the exercise challenge test. NO was measured in the exhaled air (fractional exhaled NO (FeNO)) pre and between 1 and 5 min after the exercise using CLD 88 apparatus (EcoMedics). All tests were performed according to ATS/ERS recommendations before the competition phase.

**Results:** 21% of athletes had a post exercise decrease in FEV₁ of ≥ 10%. Baseline and post exercise FeNO levels were 15.1 ppb and 14.5 ppb, respectively. Most athletes had a post exercise decrease in FeNO (63.6% in males and 72.7% females). In athletes with the decreased post exercise FeNO level, the mean change was -26.8% from the baseline, in contrast to +70% increase in those who had a post exercise FeNO level unchanged or increased (p<0.01). We found the following correlations between (i) baseline FeNO and baseline absolute FEV₁ (rs=0.41; p<0.01); (ii) post exercise FeNO and ΔFEV₁% 1 min post exercise (rs=0.38; p=0.04); (iii) post exercise FeNO and ΔFEV₁% 5 min post exercise (rs=0.58; p<0.01); (iv) post exercise FeNO and PEF% 5 min post exercise (rs= -0.56; p<0.01).

**Conclusion:** The present data suggest a role of airway NO in lung function and in exercise induced bronchoconstriction in elite athletes.

**P2143**

*Exercise-related perceptions do not affect exercise response in subjects with OSA*

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Lean and obese subjects have similar exercise capacity and intensity of dyspnea and leg effort. Obese individuals with OSA have a reduced exercise capacity (Vanhecke et al. 2008); if this depends on exercise-related perceptions needs to be defined. Sixteen subjects with OSA, 8 lean (BMI:25.6±2.5) and 8 obese (BMI:40.8±10.1) and 14 subjects without OSA, 8 obese (BMI:44.8±7.5) and 6 lean subjects (25.5±7.5) underwent spirometry, polysomnography, and incremental exercise test. FRC (%pred) was similar in obese with and without OSA (84.4±9.8 vs 88.6±24.2 respectively; p=ns). The severity of OSA (AHI:51.1±7.1 vs 24.2±10.5; p=ns) was the same in obese and lean subjects. At VO₂Peak (l/min: 2.62±0.6; 2.4±0.7; 2.5±0.6; 2.2±0.5 in obese with OSA and non OSA, and lean with OSA and non OSA subjects, respectively; ANOVA: p=ns). VO₂peak (ml/kg/min) was similar between obese subjects (OSA vs non OSA) and between lean subjects (OSA vs non OSA). End-expiratory-lung-volume (EELV) decreased in lean subjects with (290±420ml), and without OSA (330±184ml), while increased in Obese with (279±330ml) and without OSA subjects (304±330ml). Peak BORG was similar (ANOVA: p=ns) in the four groups (7.5±1.6; 6.25±1.75; 5.9±2.4; 6.8±2.3 for obese OSA and non OSA, and lean OSA and non OSA subjects, respectively). Peak leg effort did not significantly differ in obese and lean subgroups: (8.6±1.69; 7±1.9; 7.1±2.1; 8.5±0.8 for obese with and without OSA, and lean with and without OSA, respectively; ANOVA: p=ns). The qualitative difference in EELV response indicates respiratory mechanical limitation during exercise in obese subjects with and without OSA. Exercise-related perceptions do not affect exercise response in obese with OSA.