P3525
Temporal analysis of oscillatory mechanics and lung morphometry in mice after nasal instillation of papain
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Introduction: Few studies have evaluated the progression of pulmonary emphysema and lung remodeling after nasal instillation of proteolytic enzymes. Objectives: To study the progression of emphysema after papain nasal instillation. Methods: 55 adult male Balb/c mice received either a nasal drop of 50 ul (20 mg/ml) of papain solution (P) or normal saline (S) and were studied on days 3, 15, and 28 after instillation. Mice were anesthetized, tracheostomized and connected to an animal ventilator to measure tissue elastance (Htis), tissue damping (Gtis), and linear intercept (Lm). Results: There was a significant increase in volume proportion of collagen in lung parenchyma (0.004) after 28 days in papain group when compared to saline group, but there were not significant differences in elastin fibers content. Conclusions: In this murine model, nasal administration of a single dose of papain solution results in pulmonary emphysema and alveolar septa remodeling that are evident after 28 days. Supported by FAESP and CNPq, Brazil.

P3532
Intracerebroventricular serotonin reduces the degree of acute hypoxic ventilatory depression in peripherally chemodenervated rabbits
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Introduction: In this murine model, nasal administration of a single dose of papain solution results in pulmonary emphysema and alveolar septa remodeling that are evident after 28 days. Supported by FAESP and CNPq, Brazil.

P3527
Quantifying the physiology of upper airway stenosis: changes in ventilatory mechanics with extrathoracic inspiratory resistive loading
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Background: We created a model of airway obstruction to study the impact of resistance changes on ventilatory dynamics. Quantitative indices of airway obstruction were derived and their diagnostic and monitoring utility were studied.
Methods: Six resistors, mirroring the selective impairment to inspiratory airflow occurring in LTS were developed and calibrated. Maximum-effort flow-volume loops were obtained from 15 volunteers with resistors placed in series. Diagnostic and monitoring performances of flow-volume indices were assessed with Receiver Operator Characteristic and Analysis of Variance respectively.
Results: The ratio of midcapillary capacity to inspiratory flow (MEF50/MEFmax) and peak expiratory to inspiratory flow ratio (PEF/PIP) had diagnostic sensitivities of 87% and 89% respectively. The best index both experimentally and clinically was the ratio of area under the expiratory and inspiratory curves (ratio of integrals), having experimental and clinical sensitivities of 97% and 100% respectively. A clinical specificity of 95% was achieved. Both PEF/PIP and the ratio of integrals could identify changes in airway resistance over 10cmH2O.sec.L−1 (p < 0.05; ANOVA).

Conclusions: Flow-volume testing is simple and non-invasive, and can be used to quantify the diagnosis and monitoring of LTS patients. The ratio of integrals is the optimal index for this purpose.

P3528
Intracerebroventricular serotonin reduces the degree of acute hypoxic ventilatory depression in peripherally chemodenervated rabbits
G. Sahin, I. Guner, N. Yelmen, U. Aksu, T. Oruc, Z. Yildirim. Physiology, 1Department of Pulmonary Medicine, Cerrahpaşa Medical School, Istanbul, Turkey; Physiology, 1Cerrahpaşa Medical School, Istanbul, Turkey; Physiology, 1Cerrahpaşa Medical School, Istanbul, Turkey; Physiology, 1Cerrahpaşa Medical School, Istanbul, Turkey; Physiology, 1Cerrahpaşa Medical School, Istanbul, Turkey.

Hypoxia causes changes in the rate of synthesis or release of neurotransmitters in the brain, and the accumulation of serotonin (5-HT) in the central nervous system might cause hypoxic respiratory depression. In the present study, we aimed to examine the role of 5-HT on acute hypoxic ventilatory depression (AHVD) in peripheral chemoreceptors denervated rabbits. All experiments were performed in peripherally chemodenervated rabbits anesthetized with intravenous injection of urethane (400 mg/kg) and alphachloralose (40 mg/kg). For intracerebroventricular (ICV) administration of 5-HT, a cannula was placed in left lateral ventricle by stereotaxic method. Respiratory frequency (fR), tidal volume (VT), ventilation minute volume (Vt) and systemic arterial blood pressure (BP) were recorded during air breathing and breathing of hypoxic gas (8% O2 - 92% N2) and mean arterial pressure was calculated (MAP). During hypoxia, ICV injection of serotonin caused significant increases in VT and ICV injection of 5-HT (20 mg/kg) during normoxia caused significant increases in VT in ICV injection of 5-HT (20 mg/kg) and in VT in ICV injection of 5-HT (20 mg/kg). On the other hand, 5-HT injection reduced the degree of AHVD in rabbits during hypoxia (p < 0.05; VT in ICV injection of 5-HT (20 mg/kg) and in VT in ICV injection of 5-HT (20 mg/kg)). ICV injection of serotonin (10 mg/kg), a 5-HIAA, receptor antagonist, prevented the enhancing effect of 5-HT on ventilation during normoxia. On the breathing of hypoxic gas after ketanserin administration, the degree of AHVD was augmented. In conclusion, our findings suggest that central 5-HT increases normoxia ventilatory depression and reduces the degree of AHVD during hypoxia via 5-HT2 receptors.
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Thematic Poster Session
Tuesday, September 18th 2007

P3529
The effect of dexamethasone on the pulmonary fibrosis of acute lung injury induced by lipopolysaccharide in rats
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Background: Persistent acute lung injury (ALI) is characterized by excessive fibroinflammation and a substantial risk of death. The aim of this study was to evaluate the effect of dexamethasone on the pulmonary fibrosis of lipopolysaccharide (LPS)-induced ALI in rats.

Methods: Rats were experimented in three groups, i.e., control, ALI and ALI with dexamethasone treatment (8 mg/kg, respectively). ALI was induced by intraperitoneally injection of LPS (5 mg/kg) every day. After 3 days, the rats of dexamethasone groups were treated with intraperitoneal injection of dexamethasone solution (0.5 mg/kg) at 8:00 AM every day. Control and ALI rats were treated with saline. On the 14th day, airway resistance and elastance were extracted from forced oscillatory respiratory input impedance spectra by model fitting. The concentration of procollagen aminoterminal propeptide type I (PINP) in bronchoalveolar fluid (BALF) was examined. The lung hydroxyproline content was measured and histological examination was performed with Victoria blue and Ponceau for all groups.

Results: The resistance of lung paranchyma of dexamethasone-treated rats were significantly decreased in comparison with ALI group (0.59±0.07 kPa/ml/s vs 0.68±0.25 kPa/ml/s, P<0.05). PINP in BALF decreased significantly after dexamethasone administration (74.00±2.59 pg/ml vs 89.10±4.96 pg/ml, P<0.05). Treated animals showed reduced pulmonary fibrosis at day 14 compared to the ALI group as shown by histology and hydroxyproline content (2.24±0.21 mg/g vs 2.73±0.36 mg/g, P<0.05).

Conclusions: We propose that an early course treatment with dexamethasone may be useful in inhibiting pulmonary fibrosis of LPS-induced ALI.

P3530
Vascular remodeling and inhaled beclomethasone dipropionate in COPD patients
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Background: An increase in airway wall vascularity has been demonstrated in asthma that can be reduced by inhaled corticosteroids. Recent studies in COPD patients, have shown an over expression of VEGF and an increased vascularity in bronchial mucosa, but the effects of treatment on mucosal microvascularity in COPD are still unknown.

Aim: This study was designed to evaluate vascular remodelling and treatment effects in COPD patients.

Methods: All patients were ex-smokers with stable moderate to severe COPD, aged 50−90. The study included 10 COPD patients, mean FEV1 49.9% of predicted treated with nebulized BDP (TP) 1600–2400 mcg daily (equivalent to predicted not treated with BDP (NT), 10 COPD patients mean FEV1 50.8% of predicted. Both patients groups were compared with healthy subjects (HS). Bronchial biopsies were collected and vessels number and size, vascular area, VEGF and b-FGF expression were evaluated.

Results: See table.

Comparison of vascular remodelling in COPD patients is more likely due to vessels morphological changes than neo-angiogenesis and seems to be affected by BDP therapy.

<table>
<thead>
<tr>
<th>HS</th>
<th>TP</th>
<th>NT</th>
</tr>
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| Vessels number (n/mm²) | 140±1.286 | 135±0.527 | 130±0.48 ²
| Vessel area (%) | 3.41±0.71 | 4.87±1.53 | 5.94±1.07 ²
| Vessels size (μm) | 229±4.47 | 335±0.78 | 487±2.03 ²
| VEGF* (cell/mm²) | 53±6±33 | 171±0.95 | 263±3.112 ²
| b-FGF* (cell/mm²) | 20.58±3.40 | 38.6±7.8 | 55.92±20.24 ²

Values are mean±SD; *p<0.05 vs HS; †p<0.05 vs TP

P3531
Change of induced sputum TNF-α and sTNF-R55.75 levels in patients with acute exacerbations of COPD
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Objective: To investigate the changes of pro- and anti-inflammatory mediators in local airway of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) before and after treatment.

Methods: Levels of soluble tumor necrosis factor receptor 55.75 (sTNF-R55.75), tumor necrosis factor α (TNF-α) in induced sputum and their airway function were made in 48 patients with AECOPD on admission and after treatment, in 28 healthy volunteers.

Results: Airway function was significantly improved after treatment in AECOPD but still worse than that of volunteers (p<0.05). Levels of TNF-α and sTNF-R55.75 before and after treatment were higher than those of volunteers (p<0.01). After treatment, TNF-α levels were markedly reduced in AECOPD (478±2.656 mg/ml 8 30±1±3.43 pg/ml, p<0.05). Levels of TNF-α and sTNF-R55.75 in AECOPD were found in good correlation with airway function (r(TNF-α,sTNF-R)55.75=0.547, p<0.001). Levels of TNF-α level was found in negative correlation with sTFE (r(TNF-α,sTNF-R)55.75=-0.524, p<0.01). Volunteers there was no significant relationship between sTNF-R55.75 and airway function.

Conclusions: Our data suggest that AECOPD may be due to local imbalance of inflammatory and anti-inflammatory mediators. Patients with AECOPD had higher levels of pro and anti-inflammatory mediators than volunteers. Levels of pro-inflammatory mediators were decreased while anti-inflammatory mediator was increased after treatment; in the meantime airway function was improved. The increase of anti-inflammatory mediators may contribute to the improvement of airway function.

P3532
Hypoxia ventilation in diabetic rats
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There are reasons to believe that the hypoxic ventilatory response (HVR) is decreased in diabetes. In this study we hypothesized that tissue hypoxia, a feature of diabetes, if present in the carotid body (CB), where the hypoxia sensing takes place, might actually mitigate a possible decrease in the diabetic HVR by resetting basal CB excitability to a higher level. We addressed this issue by comparing CB function and ultrastructure in 6 diabetic and 6 normal Wistar rats. Diabetes was induced by streptozocin (80 mg/kg, ip). The experiment was performed 1 month after the induction. The HVR was increased 14% and 14% O2 in N2, in conscious poikilocapnic animals using a whole body plethemograph. Ventilatory changes were expressed as a percentage of the baseline prehypoxic level. After the completion of ventilatory measurements, the animals were anesthetized and CBs were dissected. The organs were subjected to the post-embedding procedure for transmission electron microscopy. We found that resting minute ventilation (Vr) was comparable in diabetic and control rats, 316±79 and 331±32 ml/min, respectively. The HVR profile was overall decreased in diabetic rats (P<0.02). Moreover, the peak hypoxic Vr was about the same at 11% and 14% hypoxia; thus the hypoxic sensitivity decreased in diabetes. At the ultrastructural level, the most striking feature of the diabetic CB was hypoplasia of interglomerulare connective tissue, clearly lengthening the O2 diffusion path from capillaries to chemoreceptor cells. We conclude that the stagnant hypoxia developing in diabetic CB tissue cannot offset the functional handicap, which also is due to CB-unrelated mechanisms.

P3533
Nasal mucosa morphometry in tobacco smoking COPD patients
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Introduction: As evidences have shown, tobacco smoking can damage lower airways (LA), likewise, it is expected to do with upper airways (UA). This is the first study trying to demonstrate such events concerning nasal mucosa biopsies in COPD patients.

Objective: To describe possible structural changes in UA by employing morphometry in nasal mucosa.

Methods: Middle turbinate biopsies were taken from 13 stable COPD patients (M/F ratio 11/2, Age 65±18 yrs, pack-years 41±21, FEV1 47±25 and sTFE/VF48±15), H&E stained and epithelial, inflammatory infiltrate, basement membrane (BM) and submucosal layer were evaluated by pathologist.

Results: The following morphological characteristics were found in percentage of total biopsies: Epithelial metaplasia 69%, <25% total length Epithelia Disruption in 54% and >25% in 23%; scarce inflammatory infiltration in epithelia in 92% and in 46% moderate inflammation in submucosa. BM thickness 7.3±5.4μ and sub-mucosal gland hyperplasia and numerous blood vessel in 63%.

Conclusion: All morphometric parameter were affected. These evaluations shows a strong chronic inflammation in most of patients. This structural changes considered as "remodeling" are so similar to such tissue changes observed and described in bronchial and bronchiolar sites. In certain manner UA reflects what is happening in LA.
P3534
The role of inflammation in prevalence of chronic obstructive pulmonary diseases in wood workers
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In this study the research has been directed mainly towards defining the relationship between exposure to air pollution (wood dust, smoking) and development of respiratory disorders and the validation of low dose cough as index of bronchial secretion and inflammation in wood workers. Since the smoke induces inflammatory bronchial alterations leading to hypersecretion, the aim of this study was: a) to determine humidity of voluntary cough and the quality of cough (productive or nonproductive) in patients with chronic obstructive pulmonary diseases (COPD) exposed to wood dust pollution and smoking, and b) to determine the correlation coefficients in comparisons of different tests used in diagnosis of airway obstruction (FEV1 and FVC) versus indirect tests (FEV1; MEF 25%/FVC; MEF 50% FVC) in relation to exposure to wood dust and smoking index. The results of our investigation observed in 212 wood workers, and 117 control subjects from industry in the same geographical area (23 to 58 years of age), showed that workers exposed to wood dust of beech-tree prove to have a significantly higher prevalence of bronchial asthma and ventilator impairment than did control group. The relationship between flow and volume during maximal force expiration suggests that expiratory flow at 25 and 50% of the volume in the lung (MEF 25% FVC; MEF 50% FVC) in smokers are lower than in non-smokers (p < 0.001). In smokers was significant negative correlation between MEF 25%/FVC; MEF 50% FVC and smoking index (p < 0.01). In smokers with productive cough, MEF 25%FVC and MEF 50% FVC are significantly lower than obtained values in non-smokers with the same symptoms (p < 0.01).

P3535
The reversibility of bronchial obstruction and hyperinflation at COPD

The measure of the FEV1 may not be the optimal method to assess the response to bronchodilator therapy in COPD patients.

Aim: To compare the reversibility of bronchial obstruction and hyperinflation in the bronchodilator test for COPD patients depending on a degree of severity.

Methods: The FEV1, residual volume – RV; inspiratory capacity – IC of the 115 COPD patients (I = n = 21, II in n = 36, III in n = 58, GOLD, 2005) were analyzed before and after inhalation of 400 mcg Salbutamol.

Results: The reversibility (A%) is reduced with increase of a degree of bronchial obstruction – AFEV1 (%) is decreased with increase of COPD severity: 9.1 ±3.6; 6.4 ±4.4 and 5.8 ±4.1 at the I, II and III stages accordingly (p < 0.05 II-I stage). The analysis of A RV revealed the same regularity. The median of values A RV worked out 18.6 % at the II and 8.2 % at the III COPD (p < 0.05). In comparison to AFEV1 and A RV, the parameter of AIC is characterized with higher values after bronchodilator and its median value worked out 20.8 % for the II and 20.1 % for the III in COPD.

Conclusion: With increase of COPD severity both the reversibility of the bronchial obstruction and the hyperinflation of the lungs are reduced. However significant increase of IC at severe COPD can reflect expressed dynamic hyperinflation which can be viewed as one of the application points bronchodilator therapy for this disease.

P3536
Postexpiratory pause reflects breathing control in patients with community acquired pneumonia
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Previous studies showed that postexpiratory pause (PEP) duration is a sensitive index of breathing control in patients with COPD. Aim of the study: to evaluate PEP for diagnostic purpose in patients with community acquired pneumonia (CAP). The study included 50 CAP patients (25 (50%) male, 25% of them had severe CAP (70.6 ± 15.1 PORT score), 207 healthy control subjects were evaluated for breathing pattern analysis. Breathing rate (BR), interbreathing interval (TI), and mean PEP duration, individual coefficient of variation (PEPVC%), mean ratio PEP/Ttot were obtained from a 10-min resting impedance pneumography records.

Table 1: PEP values in patients with CAP and controls

<table>
<thead>
<tr>
<th>BR (min)</th>
<th>Controls</th>
<th>Nonsevere CAP</th>
<th>Severe CAP</th>
</tr>
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<tbody>
<tr>
<td>15.7(3.3)</td>
<td>20.1(5.1)*</td>
<td>28.5(5.5)*</td>
<td></td>
</tr>
<tr>
<td>0.51(0.43)</td>
<td>0.34(0.17)*</td>
<td>0.16(0.07)*</td>
<td></td>
</tr>
<tr>
<td>89.3(72.1)</td>
<td>44.7(30.1)*</td>
<td>26.7(13.7)*</td>
<td></td>
</tr>
<tr>
<td>12.9(6.6)</td>
<td>10.0(6.2)*</td>
<td>7.1(1.4)*</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation. * p < 0.01 compared with controls. 1 = p < 0.01 compared with nonsevere CAP.

In both CAP groups, PEP as well as PEPVC% and PEP/Ttot values were significantly lower than in the control group. Severe COPD group demonstrated lowest values of PEP parameters. PEP was significantly correlated with dyspneic Borg score (r = -0.44, p < 0.02).

Conclusion: postexpiratory pause seems to be a sensitive index of breathing control in patients with CAP.

P3537
COPD in male patients and the assessment of domiciliary exposure to wood smoke
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A recent study has shown a strong association between wood or charcoal (biomass) smoke exposure and chronic obstructive pulmonary disease (COPD) in European females (Orozco-Levi et al. Eur Respir J. 2006). Studies assessing whether this association also exists in males are warranted.

The present study was aimed at determining the frequency and magnitude of exposure to domiciliary biomass smoke in male smokers (n=319) requiring hospitalization due to a COPD exacerbation (PAC-COPD project). All patients answered a standardized questionnaire.

Results: Exposure to wood or charcoal smoke for longer than 10 years (mean, 21±8 years) was present in 72% (77% cooking, 57% heating) of the study population. The length of time exposed to cigarette smoke only (i.e., free of exposure to biomass smoke) was significantly lower in subjects exposed to biomass smoke when compared with non-exposed subjects (13.1±30 vs. 52.2±5 years, p < 0.001). On the other hand, the sum of years of exposure (78±25 vs. 98±25 years) and the product of time of exposure (3150±2486 vs. 2701±2374 years²) to either cigarette or domiciliary biomass were greater in the cases (p < 0.001, both).

Conclusions: This study shows that domiciliary exposure to biomass fuel smoke is highly frequent (>70%) and has been clearly underestimated in males, and (2) it must be taken in mind as a potential (interacting) risk factor for COPD in male smokers.

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P3538
Gender differences in exertional breathlessness in healthy older subjects
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We postulated that healthy older females would perceive greater respiratory difficulty due to greater ventilatory constraints during exercise compared with their male counterparts.

Methods: We studied 39 healthy subjects (FEV1, and FEV1/FVC > 80% predicted): 23 females (68±1 years) and 16 males (67±2 years) (mean±SD). We computed ventilation for COPD (Ve), breathing pattern, operating lung volumes and intensity of breathing discomfort (dyspnea) during symptom-limited incremental treadmill exercise.

Results: At a standardized oxygen uptake (V’O2) of 20 ml/kg/min, dyspnea intensity was greater in females than males: 2.3±0.4 and 8.8±0.2 Borg scale units, respectively (p < 0.05). However, gender differences in dyspnea intensity were not significant when corrected for predicted values of Ve and V’O2.

Conclusion: Older females perceived greater breathing discomfort during physical exertion compared to age-matched males. This reflected (1) a relatively reduced maximal ventilatory capacity (MVC) with higher Ve/MVC ratios at a given V’O2 and (2) greater mechanical constraints on tidal volume expansion during exercise in females.

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P3539
Ventilatory response to incremental dead space loading
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Background: Oxygen consumption of respiratory muscle has been reported to be able to estimate using incremental dead space (DS) loading. However, little is known about the ventilatory response to the incremental DS loading.

Aim: To examine the response of respiratory pattern to incremental DS loading.

Methods: Seven healthy young adults (Age: 23±3.5 years, MF 4:3) were examined using DS loading apparatus, which we originally developed. The apparatus produces stepwise increase of DS by 100 ml per 20 seconds from 0 to, at the breathing frequency (29±1 vs 23±2 min⁻¹); and a higher ratio of V’E to maximal ventilatory capacity (48±3 vs 38±6%MVC) respectively (all differences p < 0.05). However, gender differences in dyspnea were not significant when corrected for predicted values of Ve and V’O2.

Conclusion: Older females perceived greater breathing discomfort during physical exertion compared to age-matched males. This reflected (1) a relatively reduced maximal ventilatory capacity (MVC) with higher Ve/MVC ratios at a given V’O2 and (2) greater mechanical constraints on tidal volume expansion during exercise in females.

Supported by: Ontario Thoracic Society.

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Conclusions: FOT, and particularly X6Hz is able to detect relevant changes after BDL in COPD. These are potentially related to changes in the elastic properties of the respiratory system which affect dyspnea.

P3542 Cold preservation of the rat lung induce the parenchymal airway inhomogeneity; evaluated by the forced oscillation technique (FOT) method

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Background and Purpose: The dynamic mechanical property under cold preservation, before re-perfusion is not fully examined. We used Forced Oscillation Technique (FOT) and evaluated the change of lung mechanical property under cold preservation.

Methods: Rats were assigned to two groups. In the control group, the lungs were not preserved (n=6). In 90 minutes after 12 cmH2O PEEP for 9 hours (n=6). Input impedance (Z) data was collected using the computer-controlled small animal ventilator (flexiVent; SIRCQ). All data were analyzed using homogeneous linear model, which includes airway resistance (Raw), tissue elasticity (EI) and tissue damping (G). Hysteresis (η) was calculated as G/H.

Results: In the cold preservation group, the value of G and H was lower than those of the control group at the Fc=2Hz range respectively. (G: 0.164±0.015, 0.197±0.015: H:1.714±0.128 1.992±0.178) A significant change was not appeared in Raw and Hysteresis.

Discussion: The change of the value in G and H suggested that the lungs became stiffer because of the increase of airway inhomogeneity. The increase in parenchymal airway inhomogeneity causes the increase in Shear-Stress during inflation.

Conclusion: During cold preservation, lungs have already started the change in the mechanical property of lung parenchyma, and these change can be detect by the FOT. To check these phenomena may become new index of the preservation stage of the Graft before transplantation.

P3543 Diffusing capacity and oxygen saturation response to bronchodilator response (BDLR) in COPD

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Background: Pulmonary function tests including the single-breathe diffusing capacity of the lung (DLCO) and measurement of oxygen saturation by pulse oximetry (SpO2) are well-recognized tools for any lung presoratory disorder. Objectives: The purpose of this study was to determine in patients with FEV1 <50%, response of DLCO and SpO2 to a short acting inhaled ([2-agonist. Setting: University Hospital-based pulmonary function laboratories

Methods: Patients referred for spirometry with FEV1 <50% underwent baseline measurement of DLCO and SpO2. Lung function tests and pulse oximetry were repeated within fifteen minutes of 400 mg of inhaled salbutamol administration. This study was carried out over a 3-month period.

Results: A total of 38 consecutive patients were assessed. According to ATS/ERS guidelines 30 patients had severe obstructive disease (FEV1 <34%) and 8 had very severe obstruction before (FEV1 <34%). The mean variation between the two measurements was an increase of 14.6% (169 ml) for FEV1, 4% for DLCO and 0, 6% for SpO2. The coefficient of correlation (CC) between baseline FEV1 and DLCO was 52% which increased to 77% post bronchodilatation.

Other patient factors such as gender and age were not associated with measurement variability.

Conclusions: A positive correlation between baseline DLCO and post bronchodilator response was found even though the mean variation increase was low. It seems that there is no significance in clinical testing of SpO2 response to bronchodilatation. The CC between FEV1 and DLCO increased significantly after bronchodilatation.

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**Hall C-14 - 12:50-14:40**

**Thematic Poster Session**

Tuesday, 18th July 2017