418. Treatment strategies, systemic manifestations and biomarkers in airway diseases

P4052

Markers of airway inflammation and airway hyperresponsiveness remain stable in untreated asthmatics over time

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Introduction: Airway hyperresponsiveness (AHR) and airway inflammation are important hallmarks of asthma that may be used in asthma monitoring, but may also vary between asthmatics as a potential indication of different clinical asthma phenotypes. The aim of this study was to assess whether two commonly used measures, AHR to mannitol and exhaled NO (eNO), were stable over a period of time in asthma patients who were not treated with steroids.
Materials and methods: A total of 54 non-smoking, asthmatics not treated with steroids were enrolled in the study and assessed at baseline and again three to six months later, where spirometry, skin prick test and induced sputum was performed as well as measurements of hyperresponsiveness to mannitol and eNO. Subjects were excluded if they experienced a worsening of their asthma or commenced on steroid treatment.
Results: A total of 41 subjects (21 females, mean age; 41 years, 70,70% atopics) completed both visits. Mean FEV1% predicted at baseline was 94,13% (SD 17,71).There was a significant correlation between the degree of AHR, defined by the Response Dose Ratio (RDR:% change/mg mannitol) at visit 1 and visit 2 (LogRDR, r = 0,80, p<0,001) as well as between the levels of eNO at visit 1 and 2 (LogeNO, r = 0,59, p<0,001).
Conclusion: In asthmatics not treated with steroids, markers of AHR and airway inflammation remains at the same level over a three to six months period of observation, suggesting that these are stable markers of clinical disease.

P4053

Airway resistance and reactance in COPD patients and healthy smokers, and effect of bronchodilators

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Background: Little is known about the reversibility response of the obstructive patterns to therapies in COPD. Impulse oscillometry (IOS) is a method to measure resistance and reactance of both the central and peripheral airways.
Aim: The aim of this study was to investigate how salbutamol and ipratropium, commonly used therapies in COPD, affect obstructive airway patterns measured by impulse oscillometry.
Methods: Twenty two healthy smokers and 24 patients with COPD, with matched pack years were included in this study. Spirometry and impulse oscillometry were performed at baseline, after inhalation of salbutamol and after additional ipratropium.
Results: Medication increased FEV1 as expected. COPD patients had significantly higher total (R5), central (R20) and peripheral (R5-R20) resistance (% predicted) at baseline compared to healthy smokers. After medication with salbutamol, R5, R20 decreased in both COPD patients and healthy smokers. Salbutamol only decreased R5-R20 in COPD patient, but after additional ipratropium the R5-R20 in healthy smokers also decreased. The COPD group showed a higher reactance (X5, AX and Fres) at baseline compared to the healthy smokers. After inhalation of salbutamol, X5, AX and Fres was significantly decreased in the COPD group as well as in healthy smokers. Additional inhalation of ipratropium showed a tendency of decreasing X5 and AX in both COPD patients and healthy smokers.
Conclusions: COPD patient have higher resistance and reactance compared to healthy smokers at baseline. Both airway resistance and reactance was affected by inhalation of salbutamol and additional ipratropium, and more pronounced in COPD patients compared to healthy smokers.

P4054

Monitoring of efficacy of therapy with monoclonal antibodies – Omalizumab – Using the Recovery-ELISA

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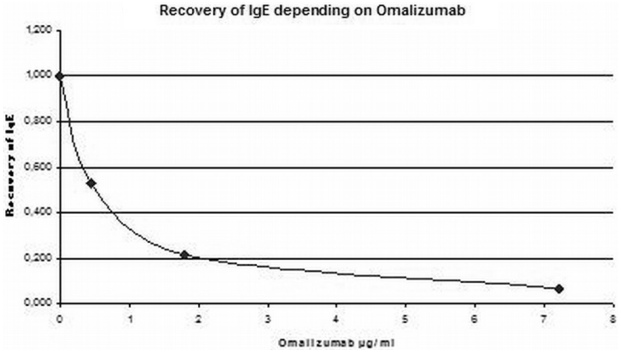
The Revovery-ELISA (R-ELISA) resembles a combination of a Sandwich-ELISA for the antigen and a competitive ELISA for the therapeutic antibody.
The R-ELISA is a special ELISA application for presence of an additional TAb in the measuring system. The special feature is a two-dimensional calibration, which performs a calibration for the antigen without and with addition of the therapeutic antibody and a calibration of the antigen-recovery in dependence of the therapeutic antibody.
Addition of Omalizumab to the IgE-Sandwich-ELISA reduced the optical density of the signal in a non-linear manner for the detection of IgE. At 7,2 µg/ml Omalizumab the IgE-signal is reduced for 75%. The addition of substrate to the assay enables the re-calculation for real samples. The Fig. shows the antigen recovery in dependence of Therapeutic antibody.



The therapeutic effect of the therapeutic antibody is visible on recovery curve. This curve shows the remaining percentage of free antigen = recovery under therapy. The assay runs in serum dilutions of 1:20.
This recovery curve demonstrates that the efficacy of antibody therapy in concentrations higher than 2 µg/ml Omalizumab (=40 µg/ml in undiluted serum) becomes rather low. In clinical samples was found similar IgE concentration within a wide range of high Omalizumab activity.
Using the R-ELISA it will be possible to calculate a maximal effective dose of TAb.

P4055

Predicting performance of cough reflex sensitivity, exhaled nitric oxide (eNO) and bronchial responsiveness for efficacy of bronchodilator therapy on isolated chronic non-productive cough

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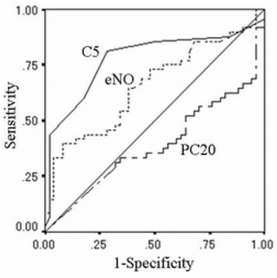
Background: Chronic cough responding to bronchodilator therapy (BDT) was originally reported as cough variant asthma (CVA), in which bronchial responsiveness was shown to be mildly increased. Our aim was to elucidate whether cough reflex sensitivity, exhaled nitric oxide (eNO) and bronchial responsiveness could predict efficacy of BDT on chronic non-productive cough.
Methods: Consecutive patients with non-productive cough lasting at least 8 weeks who visited our respiratory medicine clinic from 2005 to 2010 and gave informed consent for participating in this study were enrolled. Exhaled NO, capsaicin cough sensitivity (C5) and bronchial reversibility were measured in this order at their first visit. Bronchial responsiveness (PC20) was measured at their second visit following 6-day BDT.
Results: The study protocol was fully completed in 117 patients. Multivariate regression analysis revealed that only C5 was significantly (r=0.430, p<0.0001) correlated with the VAS scale. The ROC curve showed that the optimal cut-off

value of C5 to predict MI on the efficacy of BDT on cough was solution number of 4.5 (2.8 mmol/L) with a sensitivity of 0.81 and specificity of 0.72.

ROC curve for efficacy of bronchodilator (BD) therapy (excellent and good response (cough scale 5 to 0 points) vs. poor response (cough scale 10 to 8 points) at the second visit following 6-day BD therapy)



*The efficacy of treatment on cough was assessed with a subjective cough symptom scale (cough scale). Cough symptom was scored on a scale from 0 to 10 points, based on the severity and frequency of their cough for 24 h at the first visit and after the 6-day BDT (the second visit). A scale of 0 meant "no cough," whereas a scale of 10 denoted "cough as bad as at first visit".
Efficacy: excellent: 0,1,2, good: 3,4,5, fairly good: 6,7, poor: 8 or more points of cough scale at the second visit.
Positive effect was defined as excellent and good and negative effect was defined as poor. Patients showing fairly good was excluded from this analysis.

Conclusions: Measurement of C5 may be useful for predicting efficacy of BDT on chronic non-productive cough, in other words for diagnosis of CVA.

P4056

Systemic inflammation in COPD: Is there a link with body composition?

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Introduction: COPD is characterized by a low grade systemic inflammation which has an effect on body composition. We examined the relationship between systemic inflammation and body composition using the Body Mass Index (BMI) and Fat Free Mass Index (FFMI).
Methods: A cohort of 37 stable COPD patients (GOLD I-IV) was included. BMI was calculated as weight/height^2 and the FFMI as fat free mass/height^2. Systemic inflammation was visualized by expression of activation markers on peripheral blood neutrophils using flow cytometry.
Results: The responsiveness of neutrophils for formyl peptides (like fMLF) is one of the most sensitive markers for detecting in vivo activation of neutrophils. Peripheral blood neutrophils are less responsive for fMLF under conditions of systemic inflammation, which is associated with disease severity. This responsiveness in the context of expression of CD11b and the active form of FcγRII was positively correlated with BMI (Table 1). We also found that CCR3, a marker mainly expressed on pulmonary neutrophils correlated with BMI. In addition, a positive correlation (Table 1) between FFMI and BMI was found in COPD patients.

Table 1. Indices of systemic inflammation correlate with a low BMI

Correlation between	BMI	Sig (2-tailed)
FFMI	0.870	0.000
Active form of FcγRII after fMLF stimulation	0.422	0.012
CD11b after fMLF stimulation	0.415	0.013
CCR3	–0.402	0.017

Conclusion: A low BMI is associated with a low grade systemic inflammation in COPD patients visualized by systemic activation of neutrophils. In COPD patients the FFMI correlated with BMI, which suggests that the systemic inflammation in COPD patients is associated with a muscle wasting phenotype.

P4057

The relationship between comorbidities and systemic inflammation in patients with COPD

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Objectives: Although the effect of comorbidities on morbidity and mortality of COPD is better understood, the discussion about the role of systemic inflammation on development of comorbidities is going on. We aimed to investigate the relationship between systemic inflammation and comorbidities in patients with COPD.
Methods: Comorbidities, systemic and local inflammation markers were investigated in 50-stable COPD patients and 42-healthy adults who admitted to our out-patient clinic. Venous blood samples for markers of systemic inflammation (CRP,fibrinogen,AAT, TNF-α, sTNF-R, IL-1, IL-6, IL-8, neutrophils,lymphocytes,eosinophils) and induced sputum samples for local inflammation markers (TNF-α, IL-6, neutrophils, lymphocytes, eosinophils) were examined.
Results: At least one comorbidity was determined in 80% of patients with COPD and 47.6% in the controls. The depression, cachexia, pulmonary hypertension and prevalence of coronary artery disease in patients with COPD were higher than the controls ($p<0.05$).All markers of systemic inflammation and local inflammation, except serum mean IL-6 level and mean percentage of peripheral blood eosinophils, were significantly found higher in patients with COPD. In addition, the mean serum TNF-α and IL-8 levels were found to be associated with presence of comorbidity in patients with COPD. The determined comorbidities which are anxiety, depression, anemia, heart disease, osteoporosis and metabolic syndrome were found to be associated with one or more systemic inflammatory markers.
Conclusion: The observed comorbidities in COPD is closely related to systemic inflammation however we think that the exact mechanism of each comorbidity needs to be further investigated.

P4058

Is the body mass index a determinant of inflammatory status and quality of life in asthma?

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Introduction: The aim of our study was to determine the relationship between body mass index (BMI), alveolar nitric oxide (CaNO), and the health status of asthmatics by applying the quality of life questionnaire Sydney-modified (AQLQ-S).
Material and methods: We studied 139 asthmatics (GINA) between 15 and 75 yr of age (men 45 and women 94) and several degrees of severity. We measured anthropometric variables, baseline spirometry, and nitric oxide exhaled (eNO) at multiple flows (50, 100, 150, 200 and 250 ml/s). Bronchial nitric oxide flux (JaNO) and CaNO were assessed according to Tsoukias model. All patients completed the AQLQ-S questionnaire. For comparisons between two groups, T-student test was used. The relations between NO parameters and other markers were analyzed with partial correlations adjusted for asthma severity.
Results: The mean BMI was 26.46±4.97 kg/m^2,CaNO 3.89±4,7 ppb and JaNO 2401±2307 nl/sec.There were no statistically significant differences in values of CaNO and JaNO between obese asthmatic group and non obese. The AQLQ-S scores obtained were (mean ± SD): total score: 5.62±1.08; shortness of breath: 5.73±1.14; mood: 5.21±1.24, social restriction: 5.92±1.25; and concern: 5.69±1.10

Correlations between BMI and AQLQ-S scores

	Total score	Shortness of breath	Mood	Social restriction	Concern
BMI	–0,26 (p=0,011)	–0,30 (p=0,004)	–0,15 (p=0,13)	–0,30 (p=0,003)	–0,13 (p=0,20)

Conclusions: Obesity determines deterioration in the quality of life of patients with asthma especially in two dimensions: 1) shortness of breath and 2) social restriction. CaNO and JaNO show no relation to the inflammatory state that involves obesity and have no expression in the health questionnaire score used.

P4059

A comparative study of the correlations of the COPD assessment test (CAT) scores and high sensitive CRP levels to SPO_2, FEV_1, BODE index, and exacerbation rate

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Background: High sensitive CRP is used as a marker of systematic inflammation in COPD. Results have shown an inverse relation between serum hs-CRP and FEV_1, except for small study which did not report any correlation between hs-CRP level and FEV_1. However, we hypothesize that the raised hs-CRP is not closely related to the multiple consequences of COPD. CAT is a simple questionnaire for assessing and monitoring COPD. Thus, this study was undertaken to investigate the correlations between CAT score and SPO_2, FEV_1, BODE index, and exacerbation rate, and compare it with the correlations to the serum hs-CRP.
Method: We studied 60 patients with stable COPD and 15 normal subjects as a control group. SPO_2, BODE index, pulmonary function test and exacerbation rate were determined in COPD patients. Serum level of hs-CRP was measured in all patients and the control group. Then, the CAT questionnaire was completed by patients.
Results: Hs-CRP level was significantly raised in patients (p=0.005). In these patients, correlations of hs-CRP level with BODE index appeared significant (p=0.008). However, the correlation between hs-CRP with SPO_2 and FEV_1 did not appear significant (p=0.47, p=0.17 respectively). Also, the CAT score correlations with SPO_2, FEV_1, BODE index, and exacerbation rate in the previous year were all found to be significant (p=0.000, p=0.000, p=0.000, p=0.017, respectively).
Conclusion: We conclude that SPO_2, FEV_1, BODE index and exacerbation rate are more correlated with the CAT scores than with the serum level of hs-CRP in stable COPD patients. The findings of this study should be considered in management of stable COPD.

P4060

Analysis of atherosclerosis in patients with chronic obstructive pulmonary disease by carotid ultrasonography

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Rationale: Chronic obstructive pulmonary disease (COPD) is associated with an increased risk of cardiovascular events. Atherosclerosis is an independent predictor of cardiovascular disease. We tested the hypothesis that there is a close association between atherosclerosis and disease severity of COPD.
Methods: We recruited 46 subjects with COPD (45 male-1 female, 42 ex-smokers, 4 current smokers, aged (74.7±7.9)). All subjects underwent spirometry and carotid ultrasonography. The severity of COPD was determined by GOLD Staging System for COPD Severity Definition. We measured carotid intima-media thickness, and determined the maximal intima-media thickness (IMTmax) value as the indicator of atherosclerosis.
Results: Average IMTmax value in all subjects was 1.9±1.1 mm. IMTmax value was 2.2±1.2 mm in stage I (n=3), 1.7±1.0 mm in stage II (n=15), 2.0±1.1 mm in stage III (n=16), and 2.0±1.4 mm in stage IV (n=12). There were no differences of IMTmax values among the stages of COPD. IMTmax values were higher in subjects with ischemic heart disease (n=5) compared to those without ischemic heart disease (n=41) (IMTmax value: 2.7±1.6 mm vs. 1.9±1.1 mm, $p<0.05$). 3 subjects had lower limb arteriosclerosis obliterans (IMTmax value was 2.1±0.4 mm).
Conclusions: Atherosclerosis was not associated with disease severity of COPD. This study suggests that atherosclerosis progresses even in patients with mild COPD, especially in those who are associated with ischemic heart disease.

P4061

Body composition analysis on COPD patients – Results of prospective study

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Introduction: Chronic Obstructive Pulmonary Disease (COPD) is in close relation to chronic systemic inflammation involving an extrapulmonary patholgy. The results can be weight and muscle loss and nutritional abnormalities. FFMI (Fat Free Mass-index) assessment is important, because using Body Mass Index (BMI) does not distinguish between two people with a similar BMI but different body composition (BC).
Aims: To determine FFMI and BMI in COPD patients (pts).
Methods: In 2010, we began BC analysis on COPD patients with Dual-Energy X-ray Absorbtiometry (DEXA) in a prospective study trial. We analysed BC of 30 clinically stable COPD pts in stage II-IV GOLD. There were 24 M, median age 69 yrs (49-84 yrs) and 6 F, median age 74 yrs (51-85 yrs). For body composition analysis by DEXA we used Hologic Discovery Wi including the software "Whole Body Composition Analysis". Reference intervals (by Schutz) for FFMI were used.
Results: In M median BMI was 23 (17.7-33.99) and 23.34 (14.79-37.49) in F respectively. FFMI was 17.78 (14.52-22.18) and 15.47 (12.41-20.36) respectively. 13/30 pts had FFMI under the 10th percentile for their gender and age category. 16/30 pts had FFMI under the 25th percentile. The highest prevalence of low FFMI was seen in GOLD stage IV.
Conclusions: In our group, most of pts had FFMI <25th percentile. Those pts with FFMI<10th percentile have a higher risk for future physical disability. In our opinion, pts with FFMI <25th percentile need help to change their dietary habits, physical rehabilitation and nutrition support to prevent the progression of disease. Determination of FFMI would help to create procedrulas formulas for COPD pts with muscle weakness and/or terminal cachexia.

P4062

Identification of microorganisms based on gas chromatography-mass spectrometric analysis of volatile organic compounds in headspace gases

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Background: The elucidation of volatile organic compounds specifically produced by microorganisms may assist in developing a fast and accurate methodology to determine pulmonary bacterial infections. Development of this methodology might ultimately lead to the identification of bacterial species in breath.
Methods: Over 300 bacterial headspace samples from 4 different micro organisms were analyzed by gas chromatography-mass spectrometry to identify relevant VOCs, and compose profiles of VOCs that are specific for any of the micro organisms Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Klebsiella pneumoniae. Differently abundant VOCs were determined and classification models based on support vector machines (SVM) were build to allow classification of the samples.
Findings: We were able to identify a large number of compounds that show significantly different availability in bacterial cultures compared to medium and in bacterial cultures cross-compared. We identified compounds demonstrating highly significant differences between the four E. coli strains and between the two S. aureus isolates: methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-sensitive Staphylococcus aureus (MSSA). SVM models were able to classify the micro organisms with very high degrees of sensitivity and specificity based on 6 VOCs from headspace.
Interpretation: We demonstrated that identification of the studied micro organisms is possible based on a few compounds measured in headspace of cultures. It provides a fast, non-invasive, and sensitive technique as a potential diagnostic approach in medical microbiology.

P4063

Pathological changes in the skeletal muscles in COPD patients

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Background: Peripheral muscle weakness is a major problem in COPD, contributing to exercise intolerance and decreased health status. The loss of muscle mass has been described in those patients, but, little data are reported regarding the morphology of limb muscles.
Objectives: To study the pathological changes that occurs in the peripheral skeletal muscles in COPD Patients.
Methods: 50 COPD patients were chosen from the outpatient clinic of chest diseases, Cairo University Hospitals. Muscle biopsies were taken from the left Vastus lateralis under local anesthesia by Abram's needle and subjected to histopathological examination after staining with Hematoxlin and Eosin. The biopsies were compared to specimens taken from 10 healthy control subjects of the same sex and age group.
Results: Strong correlation was found between the severity of COPD and the degree of muscle atrophy graded from zero (normal) to 4 (marked atrophy) according to number of foci of atrophy. The one patient in stage I & 69% of patients in stage II COPD were found to have normal biopsy. Stage III; showed both mild atrophy in (45.5%) & moderate atrophy in (41%) of patients. Stage IV showed moderate atrophy in (64.3%). Marked degree of atrophy were belonged to stage III; 9% and IV; 7.2% of patients. A statistically significant positive correlation was found between degree of muscle atrophy and (age, smoking index & number of exacerbations/year).
Conclusion: COPD patients showed variable degrees of peripheral skeletal muscle atrophy correlated to disease severity. Progression of COPD is associated with progression of the muscle affection.

P4064

Plasma VEGF correlates with right ventricular function in pulmonary hypertension

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Introduction: Pulmonary hypertension (PH) is a severe, progressive condition of the small pulmonary vessels that leads to increased pulmonary vascular resistance, right ventricular failure and death. Previous studies suggest the role of VEGF (vascular endothelial growth factor) in the pathomechanism of PH by several pathways. Still, the relationship between airway VEGF and right ventricular function has not been investigated yet.
Aims: We aimed to evaluate the exhaled breath condensate (EBC), as an airway sampling technique for VEGF detection in subjects with PH and to compare EBC and plasma VEGF with the best noninvasive clinical sign of advanced disease, by measuring right ventricular longitudinal function, tricuspid anular plane systolic excursion (TAPSE).
Methods: 10 PH patients (6 IPAH, 2 CTEPH, 1 scleroderma, 1 congenital heart disease, 58±17 years, mean pulmonary pressure 58±21 mmHg), and 9 healthy controls (50±13 year) participated in the study. Plasma and EBC (Rtube, Charlotteswille, US) were collected for VEGF measurements (Quantikine ELISA kit, R&D) and echocardiography was performed to assess TAPSE.
Results: In EBC the VEGF concentration was under the limit of detection in both groups. The level of plasma VEGF was significantly higher in the patient group than in controls (130±98 pg/ml, 30±40 pg/ml, p=0,004). We found significant correlation between TAPSE and plasma VEGF level in PH patients (p=0,02, r=0,69).
Conclusion: We suggest, that decrease of VEGF with advanced PAH disease can be a result of deterioration of right ventricular contractility accompanied with

decreased pulmonary flow and wall stress. However, EBC is not applicable to assess airway VEGF levels in PH patients.

P4065

Airway dimensions and pulmonary phenotypes in a heavy smoking population

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Measurements of airway dimensions using low-dose computed tomography (LDCT) may elucidate the contribution of airway and parenchymal changes to airway obstruction.
We studied the association between airway wall thickness (AWT), lung function, chronic mucus hypersecretion (CMH), emphysema and smoking behavior.
LDCT was performed in 492 male heavy smokers (59% current-smoking, pack-years 34 (20-133). 39% (n=492) had COPD (GOLD-criteria) and 30% had CMH (defined: phlegm for at least 3 months a year). LDCT cross-sections at 3.5 ±.25 mm internal airway diameters were used for computerized assessment of AWT. To determine the extent of emphysema we computed for each individual the 15th percentile of the density distribution (p15). Mean AWT was log-transformed to obtain a normal distribution. Differences between COPD and non-COPD and CMH and non-CMH were tested with t-tests. Associations between AWT, FEV_1, CMH, packyears, current-smoking, and p15 were analyzed using linear and logistic regression (adjusted for height and age).
Median AWT was increased in COPD vs non-COPD (0.72 vs 0.54 mm, $p<0.001$) and in CMH vs non-CMH (0.66 vs 0.59 mm, $p<0.001$). Thicker airway walls were significantly associated with lower FEV_1 and with higher p15 (i.e. less emphysema) in COPD and non-COPD. There was no significant association between AWT and CMH, packyears and current smoking in COPD and non-COPD. CMH was associated with current-smoking in COPD (OR=2.6, 95%CI=1.29-5.28) and non-COPD (OR=3.0, 95%CI=1.60-5.66) but not with packyears, p15, AWT and FEV_1.
Thickening of the airway wall is strongly associated with decreased FEV_1 and less emphysema but not with CMH in COPD and non-COPD. Presence of CMH is associated with current-smoking.

P4066

Interrelations between brainstem auditory evoked potential and visual evoked potential abnormalities in stable COPD patients

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Background: COPD is presently regarded as a multi-system disorder having significant extra-pulmonary manifestations in addition to its pulmonary components.
Objectives: To assess brainstem auditory evoked potential [BAEP] and visual evoked potential [VEP] abnormalities in stable COPD patients, and to evaluate for any interrelations between them.
Methods: Eighty male subjects were included: 40 stable COPD patients with no clinical neuropathy, and 40 age-matched healthy volunteers [HV]. For BAEP evaluation, latencies of waves I, II, III, IV and V along with interpeak latencies [IPL] of I-III, I-V and III-V, and amplitudes I-Ia and V-Va were studied. For VEP analysis, latency and amplitude of P100 wave were assessed. Significant abnormality was defined as a variation beyond HV mean ± 3 SD.
Results: Twenty-six COPD patients had BAEP abnormalities: prolongation in latencies wave III [50%] and wave V [37.5%], increased IPL I-V [45%] and IPL I-III [35%], and decrease in amplitudes V-Va [17.5%] and I-Ia [5%]. VEP abnormalities were observed in 23 patients: prolongation in latency P100 wave (55%), and decrease in amplitude P100 wave (7.5%). Evaluations for interrelations between BAEP and VEP variables showed latency P100 [left] correlated with latencies wave I and III [both sides] and IPL I-III [right]. Amplitude P100 [right] correlated with amplitude I-Ia [right] and V-Va [both sides]. Amplitude P100 [left] correlated with amplitude I-Ia [right] and amplitude V-Va [right].
Conclusions: A significant number of stable COPD patients had BAEP as well as VEP abnormalities and, also, many of these BAEP and VEP abnormalities were interrelated.

P4067

Comorbidities in the course of chronic obstructive pulmonary disease

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Introduction: Chronic obstructive pulmonary disease (COPD) is characterized by chronic airflow limitation and frequent co-morbid conditions.
Purpose: To evaluate the prevalence of comorbities in patients with COPD and assess correlations between Body Mass Index (BMI) and exacerbations.
Methods: Retrospective study including 120 patients with COPD. Symptoms, spirometry, peripheral oxygen saturation, BMI and comorbidities were obtained from patients records.
Results: The mean age was 63,3±23 years. All patients were smoking for more than 10 years. 65,8% of patients had comorbidities and the most frequent ones were: systemic hypertension (52,5%), diabetes (32,5%), heart failure (20,8%), renal failure (8,3%), anaemia (8,3%), lung cancer (7,5%) and sleep apnea syndrom (SAS) (3,3%). Mean rate of exacerbations was 1,6/year. Patients with comorbidities had more exacerbations (2,4/year) than those without comorbidities (0,8/year). Considering their BMI, patients were divided into three groups: 17.5% had BMI > 25 kg/m^2, 67,5% had 20 kg/m^2 <BMI< 25 kg/m^2 and 17% had BMI< 20 kg/m^2. Those with higher BMI (>25 kg/m^2) had more exacerbations (p=0,046).
Conclusion: Comorbidities are very common in COPD. They are associated with more severe exacerbations. Results indicate a relation between BMI and rate of exacerbations.

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Usefulness of a panel of sputum markers in the evaluation of lung inflammation and functional impairment in symptomatic smokers and COPD patients

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Background: The pivotal role of neutrophils and macrophages in smoking-related lung inflammation and COPD development is well-established.
Objectives: We aimed to assess whether sputum concentrations of Human Neutrophil Peptides (HNP), Neutrophil Elastase (HNE), Interleukin-8 (IL-8), and Metalloproteinase-9 (MMP-9), major products of macrophages and neutrophils, could be used to trace airway inflammation and progression towards pulmonary functional impairment.
Methods: Forty-two symptomatic smokers and 42 COPD patients underwent pulmonary function tests; sputum samples were collected at the enrolment, and 6 months after smoking cessation.
Results: HNP, HNE, IL-8, MMP-9 levels were increased in individuals with COPD ($p<0.0001$). HNP and HNE concentrations were higher in patients with severe airways obstruction, as compared to patients with mild-to-moderate COPD ($p=0.002$). A negative correlation was observed between FEV1 and HNP, HNE and IL-8 levels ($p<0.01$), between FEV1/FVC and HNP, HNE and IL-8 levels ($p<0.01$), and between HNE levels and FEV1 rate of decline after 2 years ($p=0.04$). ROC analysis, to discriminate symptomatic smokers and COPD patients, showed the following AUCs: for HNP 0.92; for HNE 0.81; for IL-8 0.89; for MMP-9 0.81; for the four variables together 0.981.
Conclusions: The data suggest that the measurement of sputum markers may have an important role in clinical practice for monitoring COPD.
Further investigations are needed to validate the potential ability of sputum biomarkers to monitor the disease in patients with COPD, and to predict which subgroup of smoking subjects could be at risk to develop functional impairment.

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Airway and inflammatory profile of ORL rats: An asthma phenotype?

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Introduction: The ORL rat is a Long Evans substrain with inherited cryptorchidism. We have observed respiratory distress and wheezing in a subset of this strain but no respiratory phenotype is available.
Objective: We hypothesized that ORL rats would exhibit airway responsiveness (AR) associated with inflammation. To address this question, we investigated

whether respiratory mechanics and biomarkers of inflammation in these rats would be different at baseline (BL) or during methacholine (MCh) challenge induced constriction.
Material and methods: Long Evans WT (n=9) and ORL (n=14) rats were anesthetized, tracheostomized, placed in a plethysmograph (Buxco, Rodent RC Site), mechanically ventilated and challenged with 0.3 to 12.5 mg/ml of aerosolized MCh. We calculated resistance (R) and compliance (C), and lung tissue homogenates were assayed for IL-4, IL-6, and TNF-α using ELISA; quantitative histomorphometry is ongoing. We performed 2-way ANOVA of physiological outcomes and inflammatory markers.
Results: Respiratory challenges with MCh increased R and decreased C as a function of dose and group (WT vs. ORL), ORL rats had increased (p=<0.0001) sensitivity to MCh for R. IL-6 and IL-4 expression was decreased by 23% (p=<0.0001) and 77% (p=<0.0001), respectively in ORL rats with no differences in TNF-α as compared to WT rats.
Conclusions: ORL rats compared with WT rats were significantly more responsive to MCh challenges, indicated large and small airway reactivity and exhibited decreased expression of IL-6 and IL-4 in lung tissue. The observed respiratory reactivity in this strain of ORL rats may provide a genetic animal model for the study of asthma and associated genetic/hormonal/environmental factors.

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Impact of pulmonary tuberculosis infection on chronic obstructive pulmonary disease
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Background: Tuberculosis (TB) and chronic obstructive pulmonary disease (COPD) are common diseases in developing world, sharing some risk factors like smoking and low socioeconomic status.
Aim: To find out whether TB is a risk factor of COPD and to investigate any changes in COPD patients having TB infection compared to non TB cases.
Method: Retrospective study of 328 pulmonary function test (PFT) diagnosed COPD cases was done. Data of 81 patients with clinical and radiological signs of COPD, multiple bullae on radiography without lung function measurements were also taken. Control cases are 414 patients who had done chest radiography from different departments besides respiratory unit.
Result: Of 328 PFT diagnosed COPD patients, 141 had radiological feature of TB but only 32 of 414 control cases had those features. Odds ratio (OR) was 9 with 95% confidence interval (CI) [5.9-13.7]. Of 134 COPD cases with multiple bullae, 94 had TB infection, with OR=2.8, 95% CI [1.8-4.3]. Likewise TB infected COPD patients had lower FEV_1/FVC (p=0.046) compared to non TB group. But in case of COPD patients having TB disease in past, diseased group had lower FEV_1, FEV_1/FVC and inspiratory capacity (p 0.046, 0.041, 0.014 respectively) compared to COPD patients without TB disease. Also TB infected COPD patients had lower serum albumin and iron, and higher high sensitive C reactive protein (hsCRP) (p 0.027, 0.035, 0.016 respectively).
Conclusion: Pulmonary tuberculosis infection increases the risk of COPD and its coincidence with COPD results in more severe lung damage and greater inflammation (determined by increase in bullae formation, lower FEV_1 value and higher hsCRP level) with decrease in nutritional status.