394. COPD mechanisms

P3581 Fibroblast growth factor 23 (FGF23) and hypophosphatemia in patients with COPD
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Introduction: Previous studies highlighted the importance of phosphate depletion in COPD patients and the association between correction of hypophosphatemia and improvement in respiratory muscle function. Fibroblast Growth Factor 23 (FGF23) is a recently discovered circulating protein that plays a crucial role in renal phosphate reabsorption and body phosphate regulation. FGF23 has been investigated in several diseases but there is currently no published data about FGF23 in COPD.

Aims and objectives: The aim of this study was to evaluate whether FGF23 levels correlate with serum phosphate levels and disease severity in COPD patients.

Methods: 70 COPD patients aged 63 ± 4.6 years and 34 age and sex matched randomly selected controls were studied. Criteria for diagnosing COPD and assessing severity were according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines. Serum samples were analyzed for routine tests including calcium, phosphate, renal/lytes, and FGF23 levels were measured by a commercially available Eliza kit.

Results: There were no differences in serum calcium and Vitamin D levels in COPD patients and controls (P > 0.05). COPD patients had significantly lower serum phosphate levels compared to controls (P < 0.01). Plasma FGF23 was significantly higher in patients compared to controls: 280 (51-968) versus 140 (21-200) RU/ml (P < 0.001). As expected plasma FGF23 levels correlated negatively with serum phosphate (r = -0.799 & P < 0.001). Furthermore plasma FGF23 correlated negatively with FEV1 (r = -0.352 & P = 0.003)

Conclusion: This study illustrates a significant increase in plasma FGF23 levels that may contribute to low phosphate levels and disease severity in COPD patients.

P3582 Low testosterone in chronic obstructive pulmonary disease
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Aim: Among other comorbidities, COPD patients have fatigue and a low physical activity level. A low level of testosterone may explain some complains mentioned by COPD patients. In this study we compared the testosterone level in COPD patients with that of elderly men with a normal pulmonary function.

Methods: Circulating levels of testosterone and luteinizing hormone were determined using chemiluminiscence technique in 34 patients (FEV1: 34.9% of the predicted values) and 20 control subjects. Moreover, the relationship of hypogonadism with 6-min walking distance, number of pack-year, systemic inflammation and LDL level has been studied in men with COPD.

Results: The testosterone level was lower in the COPD patients (p=0.001; <0.05). Low androgen status was related to LDL level and 6-min predicting walking distance. No correlation was observed between testosterone level and FEV1, CRP level, and number of pack-year.

Conclusion: Testosterone level is significantly lower in COPD patients comparing with control subjects. A restricted activity level is in correlation with testosterone level. Further studies are necessary to clarify the hypothesis that testosterone treatment could enhance the COPD patients activity level.

P3583 WITHDRAWN
P3584
The study of proton magnetic resonance spectroscopy on hippocampus in rats with chronic obstructive pulmonary disease
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Objective: To employ in vivo proton nuclear magnetic resonance spectroscopy to investigate the hippocampal metabolism of rats with Chronic Obstructive Pulmonary Disease and to assess if there is a relationship between brain metabolism and chronic brain injury in COPD.
Methods: Rats COPD model (model group, n=6) were established by passive smoking and intratracheal instillation of lipopolysaccharide (LPS). All subjects underwent brain micro-magnetic resonance imaging (micro-MRI) and bilateral hippocampal proton nuclear magnetic resonance spectroscopy (1H-NMRIS) in vivo at 7.0 T. A neurological profile consisting of metabolite concentrations, N-acetylaspartate (NAA)/creatine (Cr) and choline (Cho)/Cr metabolite ratios in the hippocampus were evaluated and analyzed.
Results: 1. Rats COPD model were successfully established by passive cigarette smoking plus intratracheal instillation of LPS. 2. Compared with the normal group, the mean value of Cho/Cr is significantly altered in the bilateral hippocampal of COPD rat model (p < 0.05), but The mean value of NAA/Cr without difference (p > 0.05).
Conclusion: Our results demonstrate that the metabolism is significantly altered in rats COPD model bilateral hippocampal, it is possibly one of pathophysiologies for the COPD complicated with chronic brain damage.

P3585
COPD: Different psychology status (PS) in the patients with different co-morbidity rate
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Aim: To evaluate whether and in which extent co-morbidity influence on the PS in patients with COPD.
Study population: 120 outpatient patients with COPD, stage III made the study sample. Exclusion criteria were 1) mental diseases; 2) presence of acute infections.
Methods: For the evaluation of the PS the depression (by Zung scale), the anxiety (by Ch.D. Spilberger questionnaire) and the vegetative lability (by VELA test) were used. The results of 120 patients were included in the analysis.
Results: In accordance with co-morbidity rate all patients were divided in three groups (GR): GR I without any co-morbid condition, GR II – with 1–2 and GR III – with more than 3 co-morbidity conditions. All groups were similar regarding to age and smoking status. One or more abnormalities in PS were found in 21 (20,3%) patients of Group I, in 63 (74,11%) – of Group II and 13 (81,25%) persons in Group III. The data of psychological status are tested in the table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>Depression (M ± m)</th>
<th>Personal anxiety (M ± m)</th>
<th>Situational anxiety (M ± m)</th>
<th>Vegetative lability (M ± m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (n=19)</td>
<td>28 ± 9,1</td>
<td>25 ± 1,3</td>
<td>22 ± 1,4</td>
<td>22 ± 4,5</td>
</tr>
<tr>
<td>II (n=85)</td>
<td>40 ± 4,5</td>
<td>39 ± 4,5</td>
<td>21 ± 1,6</td>
<td>20 ± 4,3</td>
</tr>
<tr>
<td>III (n=16)</td>
<td>63 ± 10,5*</td>
<td>43 ± 4,5</td>
<td>23 ± 4,0</td>
<td>38 ± 5,2*</td>
</tr>
</tbody>
</table>

*p (II-III) < 0.05, * (III-III) < 0.05, p (II-I) = 0.002, *p (III-I) = 0.004

Conclusion: Co-morbid condition significantly impair psychology status in patients with COPD, and the most significant changes concerns depression, personal anxiety and vegetative lability level.

P3586
Arterial hypertension (AH) and endothelial function (EF) in patients with COPD
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Objective: To investigate the influence of co-morbid AH at the EF in patients with COPD.
Materials and methods: A total of 41 men with stable COPD stages I–was observed. Mean age – 61 ± 4.1 years; mean disease duration – 54.5 ± 8.3 years. Group I consisted of patients without concomitant AH – 21 patient, Group II – with AH – 20 patients. Pulmonary function was evaluated by spirometry Master-Lab (Jeger, Germany), endotelin-1 plasma level (ET-1) – by reagents “Diambe 86” (DRG, USA), the concentration of exhaled NO (FeNO) – by Niox Mino (Acronic, Sweden), Sa O2 – by pulse oximeter (NONIN, USA).
Results: Both groups were comparable. In Group II the concentration of FeNO was significantly higher than in group I (14.8 ± 1.39 ppb and 9.7 ± 1.41 ppb, respectively (p < 0.05)). In group II the level of EF-1 was similar to data in group I (0.81 ± 0.02 nmol/ml and 0.78 ± 0.03, respectively (p > 0.05)). In group II the level of EF-1 significantly correlated with Sa O2 (r = -0.38, p = 0.025). We didn’t found any significant correlation between EF and airflow obstruction.
Conclusions: High concentration of FeNO in COPD patients indicates the presence of more pronounced endothelial dysfunction in patients with concomitant AH; plasma levels of ET-1 increases with an increase in hypoxia in patients with COPD only if there is concomitant AH; NO concentration in exhaled air and plasma levels of ET-1 in patients with COPD, regardless of the presence of an accompanying AH, does not correlate with indices of airflow obstruction.

P3587
The impact of comorbidities related to BMI in COPD patients
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Objective: To investigate the impact of co-morbidities related to BMI in COPD patients.
Methods: We followed 1664 COPD patients of the BODE cohort. A total of 80 comorbidities were systematically recorded. Comorbidities prevalence and association with mortality was explored using Cox proportional hazard stratified by BMI.
Results: COPD patients with BMI ≥ 36 had significantly more comorbidities than the other groups but they had lower mortality, better FEV1 and lower BODE.
Conclusion: COPD patients with BMI ≥ 36 have a better survival than the obesity paradox. The mechanism of this paradox is not well understood. We explored whether different co-morbidities related to survival in patients with different BMI.

No specific co-morbidities had an independent association with mortality in this group whereas they did in the other subsets. Patients with a BMI between 22 and 25 had the most number of comorbidities associated with death.

Conclusions: In COPD, obese patients (BMI ≥ 36) have a better survival than non-obese patients, in spite of having more co-morbidities. In these obese patients there was no co-morbidity that was significantly and independently associated with mortality.
P3588
Fibrinogen, health status and hospitalization in patients with moderate to severe COPD
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Background: There is evidence that COPD is a systemic illness. Serum biomarkers have been associated with clinically relevant variables.

Aim: To investigate the relationships between the blood level of fibrinogen and large group of clinical and functional parameters.

Patients and methods: Twenty-nine stable patients (age [yr] = 63.4±8.6; FEV1 [% predicted] = 37±11%; BODE index = 3.7±1.8) were enrolled in the study. Pulmonary function tests, blood-gas measurements; echocardiography, brain natriuretic peptide (BNP), 6-minute walking test (6MWT) and cardiopulmonary exercise test (CPET) on a treadmill were performed. In addition, health status was evaluated by SGRQ (St George’s Respiratory Questionnaire) and CAT (COPD assessment test).

RESULTS: The number of hospitalization, the need of antibiotic treatment and oral/intravenous corticosteroids (OICS) in the 12 months prior to evaluation were recorded.

Results: The mean value of fibrinogen was 3.06±0.8 [g/L]. Fibrinogen correlated significantly with health status - SGRQ (r = -0.49, p = 0.008), CAT (r = -0.44, p = 0.016) and hospitalizations (r = 0.50, p = 0.006), and OICS application (r = -0.48, p = 0.012). Differentiation of patients by value of fibrinogen (> 3 g/L ≤) discriminated them with respect to last year hospitalisations (1.8±1.9 vs 0.6±1.3; p < 0.05). A general linear model analysis was performed for SGRQ and hospitalisations and the following equations were derived: SGRQ = 146.7-2.56*VO2max–ps–0.48, p = 0.012) and Differentiation of patients by value of fibrinogen (> 3 g/L ≤) discriminated them with respect to last year hospitalisations (1.8±1.9 vs 0.6±1.3; p < 0.05). A general linear model analysis was performed for SGRQ and hospitalisations and the following equations were derived: SGRQ = 146.7-2.56*VO2max–ps–0.48, p = 0.012) and hospitalizations (r = 0.50, p = 0.006), and OICS application (r = -0.48, p = 0.012).

Conclusions: Blood level of fibrinogen was related to health status and hospitalization in patients with moderate to severe COPD.

P3589
Ego defense mechanisms in COPD: Impact on health-related quality of life and dyspnoea severity
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Purpose: To assess chronic obstructive pulmonary disorder (COPD) patients’ defensive profile compared to healthy participants and to test whether specific ego defense mechanisms are associated with health-related quality of life (HRQoL) and self-reported dyspnoea severity.

Methods: In a cross-sectional study, we assessed in 80 patients with COPD and 80 age and gender matched healthy participants, psychological distress (Hospital Anxiety and Depression Scale) and defense mechanisms/styles (Defense Style Questionnaire). Patients had their HRQOL evaluated with the St. George’s Respiratory Questionnaire and underwent a comprehensive clinical evaluation with 6MWT and self-reported dyspnoea severity.

Results: COPD patients presented higher scores in undoing, acting out, autistic fantasy, denial and splitting defenses compared to healthy-controls. Overall, patients showed a more immature (p<0.001) and neurotic (p=0.006) defensive profile. Higher scores of denial (p=0.044), somatization (p=0.009) and undoing (p=0.032) were associated with poorer HRQoL, independently of the anticipated significant associations of clinical and psychological distress variables with impaired HRQoL. Somatization was strongly independently associated with more severe self-reported dyspnoea.

Conclusions: COPD patients exhibit a relatively immature and neurotic defensive profile. Pneumologists and consultation-liaison psychiatrists should consider the patients’ underlying personality structure, especially somatization tendencies, since it is independently associated with HRQoL and dyspnoea severity.

P3590
Heart rate variability during the night in chronic obstructive pulmonary disease
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Patients with chronic obstructive pulmonary disease (COPD) could have a lower oxygen saturation during the night compared to the day-time and it could affect autonomic modulation of heart rate. We studied the behaviour of heart rate variability (HRV) during the day-time versus the night in COPD patients. 30 stable outpatients were recruited and classified by BODE index. A 24 h electrocardiographic Holter recording and a transcutaneous measurement of oxygen saturation were performed at the same time. Lung function was also measured. Statistical analysis was made by linear regression. According to BODE index, 13 patients belonged to first group (BODE 1=0-2), 8 to second group (BODE 2=3-4) whereas 9 were included in the third group (BODE 3=5-10).

During the night, we observed, compared to the day-time, a significant increase of both normal-to-normal (NN) intervals (r.e. a reduction of heart rate, 831 vs 720 msec, p<0.000), and Standard deviation of all RR intervals (SDNN, 94.3 vs 85.5 msec, p=0.03), and High Frequency band (HF; 14.86 vs 10.97 msec p=0.0004) with reduction of ratio of low frequency to HF band (LF/HF ratio, 1.54 vs 1.96 p=0.09). Mean oxymoglobin saturation (SpO2) during the night was directly and significantly related to both SDNN (p=0.0018) and HF (p=0.057). Subjects with mean SpO2 lower than 90% showed lower SDNN (60 vs 100 msec, p=0.012) and lower HF (8.2 vs 16.2 msec, p=0.04). LF/HF ratio was found unrelated to mean SpO2 during the night, but a close inverse relationship was found with RV/TLC ratio (p=0.0058).

Our data demonstrated that in COPD patients both level of oxygen saturation of haemoglobin and impairment of static lung volumes could affect the cardiac autonomic modulation.

P3591
Changes in bronchial mucous membrane depending on the stage of COPD (I, II)
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Aim: To determine immune-histochecmical characteristics of bronchial mucous membrane depending on the stage COPD (I, II).

Methods and population: 78 patients (pts) (mean age 54±2±2 years) with stage COPD were divided on two groups (Gr): Gr I – 32 pts with stage I (22 male), Gr II – 46 pts with stage II (31 male). Bronchoscopy with consequent histology sampling. There were not any microscopically signs of hyperplasia. In Group II all pts took place intensive positive membrane and cytoplasmatic reaction with Ctk 8 in goblet and basal cells with morphologically signs of hyperplasia. Besides, in every sample there were fiti with high Ctk 4E12 expression in basal cells.

Conclusion: 1. Pts with COPD, stage I have significantly higher potential for the bronchial epithelial cells’ regeneration in comparison with COPD, stage II. Co-expression of both Ctk 8 and 4E12 in COPD pts, stage II allows to suppose high risk of irreversible metalasisis in bronchial epithelium.

P3592
GERD and anxiety in patients with severe COPD
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Objectives: To detect the impact of anxiety on shaping the prevalence of gastro-intestinal reflux disease (GERD) in patients with severe chronic obstructive pulmonary disease (COPD).

Methods: We examined the prevalence of symptomatic GERD, using the Vigneri score, in 29 male patients with COPD. Esophageal 24 h pH monitoring was used to document the diagnosis of GERD in symptomatic group. Beck Anxiety inventory was used to detect the impact of anxiety on expressing GERD symptoms.

Results: Reflux disease symptoms were recorded in eighteen patients of the studied group (62%). GERD was diagnosed, based on esophageal 24 h pH monitoring, in only 11 patients of those who expressing symptoms of GERD. Mean of Anxiety score was correlated significantly with the number and frequency of symptom presentation in patient with symptoms of GERD reflecting the attribute of different symptoms of anxiety to the GERD syndrome. Also Anxiety scores correlated positively with time (total) PH reflecting the effect of anxiety on the severity of GERD syndrome.

Conclusion: Patients with severe chronic obstructive pulmonary disease have a high prevalence of symptomatic gastro-oesophageal reflux. However True GERD was documented in a fewer number of them. Psychological factors, such as anxiety and somatisation may play a role, particularly in those patients without esophageal inflammation.
Is COPD a risk factor for thyroid disorders?
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Introduction: Multiple endocrinological disorders are induced by COPD through hypoxemia, hypercapnia, systemic inflammation and glucocorticoid administration; thyroid structural and functional derangements are amongst them.

Objectives: Our aims were to find out if COPD is a risk factor for thyroid disorder and what type of thyroid derangement is more specific to different COPD stages.

Methods: 2 groups of patients were assessed for age, gender, environment, smoking, alcohol intake, diabetes, dyslipidemia and thyroid disorder (autoimmune thyroid disease, nodular and nodulocystic goitre). First group was compounded by non-COPD pts (N = 148, 19 M/128, 19 F; 61 ± 8.0 years, mean age 61.33, SD 10.21) and the second one by COPD pts (N = 137, 79 M/57, 66% male and female; 68 ±42.33% male, mean age 64.34, SD 10.94). COPD pts were staged according to GOLD criteria in stage I 104/75.9% pts, stage II 22/16.1% pts, stage III 10/7.3 pts and stage IV 1/0.7% pts.

Results: There is a significant correlation between COPD and the presence of a thyroid disorder 0.123 (p < 0.05, 95% CI 0.24-0.67). There is also a low relative risk of 1.043 (p<0.05, 95% CI 0.24-0.63) for the COPD stage I pts to develop autoimmune thyroid disease.

Conclusions: COPD pts have a relative low risk to develop a thyroid disorder. In COPD stage I, with more individuals in this study, the risk was found higher for autoimmune thyroid disease. Because of this, we can consider that in the statistical significant influence of COPD on thyroid dysfunction the most probable link is their development on the basis of autoimmune process, and low risk of thyroid dysfunction in COPD pts is rather small (p < 0.05, 95% CI 0.24-0.67). There is also a low relative risk of 1.043 (p<0.05, 95% CI 0.24-0.63) for the COPD stage I pts to develop autoimmune thyroid disease.

Alpha-1-antitrypsin deficiency: an analysis of patient subgroups of the German registry
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Objectives: Alpha-1-antitrypsin deficiency (AATD) is a rare hereditary disorder that affects 1 in 1920 in the Caucasian population. AATD is associated with COPD. In the present study, we analyzed the distribution of the two common AATD mutations, A1S and A1T, in COPD patients and controls in a large cohort of patients and healthy controls of German origin.

Methods: COPD (mean age: 54 ± 10 years) and control (mean age: 40 ± 11 years) participants were recruited from the German AATD registry. The A1S and A1T mutations were genotyped by PCR-SSCP and sequence analysis.

Results: The frequency of the A1S mutation was significantly higher in COPD patients than in controls (9.7% vs 2.7%, p = 0.004). The frequency of the A1T mutation was also higher in COPD patients than in controls (5.5% vs 2.4%, p = 0.038).

Conclusions: Our study provides evidence that AATD is a risk factor for COPD. Further studies are needed to determine the exact mechanism by which AATD influences COPD development.
were linked. There was no relationship with genotyping and exacerbation frequency for any of the polymorphisms.

There was a seasonal difference in vitD levels but this was the same for all polymorphisms; all p > 0.05.

**Conclusions:** FokI, BsmI and TaqI VDR polymorphisms are not associated with exacerbation frequency and do not affect vitD levels in COPD.

**P3598**

Is there any correlation between apoptosis of the cells from bronchoalveolar lavage fluid (BALF) and the progression of chronic obstructive pulmonary disease (COPD)?

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**Background:** It has been already well known that neutrophilic inflammation, oxidative stress and protease/antiprotease imbalance play a significant role in the pathogenesis of COPD. In recent years some data were published, showing that also apoptosis may be one of the processes concerned in the pathogenesis of this disorder.

**Objectives:** We presumed that apoptosis of the cells (granulocytes, lymphocytes, macrophages) from COPD patients’ bronchoalveolar lavage fluid increases along with the decline of FEV1 (forced expiratory capacity in 1 second).

**Methods:** 19 patients (16 men and 3 women), smokers or former smokers, diagnosed with COPD (stages 2-4) were enrolled into the study. The mean age was 64.9 ± 8.3. In all subjects spirometry after the inhalation of beta-2-agonist was performed, to confirm the diagnosis of COPD according to GOLD criteria and to estimate FEV1. BALF during fiberoptic bronchoscopy was taken in all patients. We used annexin V to assess apoptosis of the cells concerned in BAL fluid. (BD Biosciences, Annexin V - FITC Apoptosis Detection Kit I)

**Results:**

The median FEV1 was 38.6%. Only the patients with advanced COPD were enrolled into the study (max FEV1 55.3%, min FEV1 15.3%). In the group of patients with FEV1 lower than 38.6% median for apoptosis was 4% (0-59%), in the group with FEV1 higher than 38.6% median for apoptosis was 5% (3-16%). No correlation between FEV1 and apoptosis of the cells concerned in COPD patients BALF was found (p = 0.74).

**Conclusions:** Our data suggest that there is no correlation between apoptosis and the progression of COPD.

**P3599**

The regional distribution of body fat mass (BFM) in men with chronic obstructive pulmonary disease (COPD)

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**Introduction:** COPD is associated with abnormal body composition and weight loss.

**Aim:** To evaluate the relations between BFM distribution and lung function in men during COPD progression.

**Methods:** We used dual-energy X-ray absorptiometry for analyze of a body composition, the regional distribution of BFM as well as fat mass ratios of Android/Gynoid (A/G) and Arms+Legs/trunk. COPD pts (aged 40-69 yrs) were divided into the 3 groups according to disease severity: the 1st was made of 14 men (GOLD I stage; mean age 55 yrs; FEV1 78%; BMI 27 kg/m², smokers 68%, packs/yrs 20); the 2nd - 43 pts (GOLD II stage; mean age 57; FEV1 63%; BMI 28 kg/m², smokers 80%, packs/yrs 21); the 3rd - 20 pts (GOLD III stage; mean age 60 yrs; FEV1 41%; BMI 24 kg/m², smokers 84%, packs/yrs 28). The control group was formed of 15 healthy men (mean age 56 yrs and BMI 26 kg/m², smokers 66%, packs/yrs 20).

**Results:**

The A/G ratio was significantly lower in 3rd group vs. the control (1.1 ± 0.3 vs. 1.3 ± 0.2 respectively). This ratio in the 1st and 2nd groups did not differ from the control. The similar picture was observed concerning Fat trunk%. Thus this level was 25.1 ± 10 in 3rd group vs. 34.8 ± 8 in the control group (p=0.02). The Arms + Legs/trunk ratio was higher in 3rd group as compare with the control (0.76±0.3 vs. 0.60±0.1; p=0.03). This ratio in the 1st and 2nd groups did not differ from the control. We detected the negative significant correlations between A/G ratio and packs/yrs index (r = -0.44) as well as among Arms+Legs/trunk ratio and FEV1 (r = -0.33).

**Conclusions:** BFM redistribution (decrease A/G ratio and increase Arms+Legs/trunk ratio) take place in the course of COPD progression.