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## 81. Pathophysiology of COPD

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**P506****Circulating auto antibodies in patients with chronic obstructive pulmonary disease (COPD)**

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**Introduction:** It has been suggested that autoimmunity can contribute to the pathogenesis of COPD. Circulating antinuclear, (ANA) anti-tissue (AT) and anti neutrophilic cytoplasmic antibodies (ANCA) are common markers of autoimmunity.

**Hypothesis:** Circulating levels of ANA, AT and ANCA are increased in COPD.

**Aims:** To determine the prevalence of abnormal titres of ANA ( $\geq 1/160$ ), AT ( $\geq 1/160$ ) and ANCA ( $\geq 1/10$ ) and their relationship to relevant phenotypic characteristics of COPD.

**Methods:** 344 patients with stable COPD were studied ( $68 \pm 9$  yr, FEV1  $52 \pm 16\%$  ref, FEV1/FVC  $54 \pm 12\%$ , DLCO  $65 \pm 21\%$  ref, BMI  $28 \pm 5$  kg/m<sup>2</sup>, C-reactive protein (CRP)  $8.2 \pm 2$  mg/L, x $\pm$ SD). ANA, AT and ANCA levels were determined by indirect immunofluorescence. Potential relationships with FEV1, DLCO, symptoms (SGRQ) smoking status, systemic inflammation, sputum microbiology and treatment with inhaled steroids were explored.

**Results:** We found abnormal titres of ANA in 34%, AT in 25% and ANCA in 12.5% of patients. These values are higher than those determined in the control population in previous studies (ANA <10%; AT and ANCA < 5%). AT and ANCA titres were associated ( $p < 0.05$ ) with FEV1 and DLCO values but not with other variables tested.

**Conclusion:** Abnormal titres of circulating auto antibodies are often present in patients with COPD, particularly in those with more lung function impairment. These results further support a role for autoimmunity in the pathogenesis of COPD. Funded by ABEMAR, FIS PI020541, FIS PI052082, SEPAR-2003, FUCAP-2003, Marató TV3-2004 and CIBERES (ISCiii).

**P507****Arterial stiffness in COPD is not related to endothelial function**

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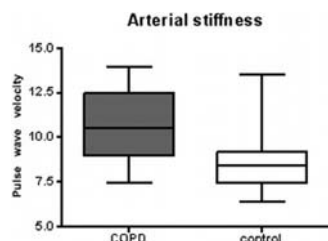
**Introduction:** COPD is associated with increased cardiovascular morbidity and mortality. Several studies have demonstrated increased arterial stiffness (a marker of cardiovascular risk) in COPD patients (McAllister 2007, Sabit 2007). Endothelial dysfunction is associated with increased cardiovascular risk and is strongly

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associated with arterial stiffness (McInerney 2006). We sought to establish if the arterial stiffness found in COPD was due to endothelial dysfunction.

**Methods:** 17 ex-smoking COPD patients and 17 age, sex and smoking history matched controls were recruited. Using forearm plethysmography we assessed vasomotor responses to 2 endothelial dependent vasodilators (acting on the endothelium) and 2 independent vasodilators (acting on the smooth muscle). Arterial stiffness was measured with carotid-femoral pulse wave velocity.

**Results:** There was a difference between the COPD and control populations as regards pulse wave velocity (10.77 vs 8.63 m/s,  $p < 0.01$ ). However, there were no differences between the groups in vasomotor responses to either the endothelial dependent or independent vasodilators.



**Discussion:** Patients with COPD do not have endothelial dysfunction compared to matched controls. This does not account for the arterial stiffness in this group of patients. Given these results, the most likely cause is differences in the extracellular matrix of collagen and elastin. This raises the possibility of elastin degradation outwith the lungs.

#### P508

##### Magnetocardiographic study of blood flow redistribution in patients with COPD

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**Background:** COPD is associated with systemic alterations including blood flow redistribution (BFR).

**Aims and objectives:** We suggested the hypothesis that adverse systemic effects (ASE) of  $\beta_2$ -agonists ( $\beta$ as) in patients with COPD were accompanied by inter-related changes in the pulmonary, intracardiac, coronary and peripheral (PICP) circulation leading to BFR.

**Methods:** magnetocardiographic (MCG) examinations were performed at rest and during the pharmacological test (PT) with a single-dose inhalation of a short acting BA. We studied 40 patients (aged 53-75 years) with COPD who had a decline in postbronchodilator FEV<sub>1</sub>. The changes in PICP circulation were assessed on the basis of comparative analysis of the hemodynamic and cardiac MCG parameters registered at rest and during the PT. We assessed: levels of the pulmonary artery pressure (PAP) and peripheral vascular resistance (PVR), severity of mitral (MR) and/or tricuspidal regurgitation (TR) as well as global contractile reserve (GConR) of the ventricles and level of myocardial ischemia of the left ventricle (LVMI) both dependent on the global coronary reserve (GCorR).

**Results:** the levels of PAP and PVR, severity of MR and/or TR had the general tendency to increase while the GCorR and GConR of the ventricles decreased during the PT leading to the increase in the level of LVMI.

**Conclusions:** the study showed that ASE of  $\beta$ as in patients with COPD were accompanied by BFR. We hypothesized that one of the systemic mechanisms of short-term as well as long-term BFR was due to "low grade" centralization of blood flow stemming from slow progressive systemic overexpression of vascular and cardiac  $\alpha_1$ -adrenoreceptors in patients with COPD.

#### P509

##### Nocturnal hypercapnia and oxygen therapy in COPD patients

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**Aim:** To analyze the prevalence of nocturnal hypoventilation (NHV) in COPD patients with conventional criteria for long term oxygen therapy (LTOT), and to determine predicted factors of this phenomenon.

**Methods:** Prospective and multicentric study enrolling 80 stable COPD patients with conventional criteria for LTOT (FEV<sub>1</sub>  $23 \pm 7\%$ , FEV<sub>1</sub>/FVC  $34 \pm 9\%$ , PaO<sub>2</sub>  $53 \pm 6\%$ , PaCO<sub>2</sub>  $54 \pm 7\%$ ). All patients had undergone pulmonary function testing, blood analysis and a polysomnographic study. Arterial blood gases samples (ABG) were obtained while awake and during sleep (3 a.m. and 7 a.m.). NHV was considered when an increased of PaCO<sub>2</sub>  $> 10$  mmHg was observed in any nocturnal ABG in relation to awake. Variables associated with NHV and those considered clinically important were included in a multivariate regression model in order to determine a predicted model.

**Results:** The mean oxygen flow administered was 1.41 L/min. Seventeen patients (21%) developed NHV. NHV was associated with BMI, hemoglobin and hematocrit, TLCO and PaO<sub>2</sub> reached after oxygen administration in the univariate

analysis. In the logistic regression analysis was considered that the BMI ( $p = 0.006$ ; OR 1,26 IC 95%: 1,068 a 1,481) and the diurnal increased of PaO<sub>2</sub> after O<sub>2</sub> ( $p = 0.010$ ; OR 0,89 IC 95%: 0,807 a 0,972) were the variables that discriminate better between both subgroups of patients with a sensitivity of 82% and specificity of 78%.

**Conclusions:** 1 – NHV is common in stable COPD patients with criteria for LTOT. 2 – NHV is related to the BMI and the increased of PaO<sub>2</sub> during awake. Patients with higher BMI and less PaO<sub>2</sub> reached after oxygen administration have a great risk for NVH.

#### P510

##### On importance of interventricular interaction under the hypoxic pulmonary hypertension due to COPD

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We examined 94 male patients with COPD complicated by secondary pulmonary arterial hypertension (PAH). The patients were divided into 2 groups. The 1<sup>st</sup> group consisted of 40 patients with PAH, but without right ventricular (RV) hypertrophy and/or dilation (mean age  $57.1 \pm 1.5$  y). The 2<sup>nd</sup> included 54 patients with PAH and RV hypertrophy and/or dilation (mean age  $57.0 \pm 1.8$  y). 15 healthy men matched by age were controls. A week before inclusion at study all vasodilators were cancelled. Two-dimensional and Doppler echocardiography was used for hemodynamics evaluation. It was revealed that peak velocity of the early diastolic filling in patients of the 2<sup>nd</sup> group was less than the same index in the control and 1<sup>st</sup> groups ( $41.4 \pm 1.1$  ms and  $49.1 \pm 1.4$  ms). Furthermore, the 2<sup>nd</sup> group, when was compared with the 1<sup>st</sup> group, demonstrated increase of the peak velocity of the late filling ( $50.7 \pm 1.2$  ms and  $41.2 \pm 1.1$  ms). Correspondingly, the peak velocity ratio  $\Delta/\bar{A}$  ( $0.83 \pm 0.03$  and  $1.2 \pm 0.02$ ) was diminished. Isovolumic relaxation time of the left ventricle in the 2<sup>nd</sup> group was more prolonged compared with the 1<sup>st</sup> and the control group ( $103.5 \pm 1.6$  ms,  $82.6 \pm 1.3$  ms and  $76.4 \pm 1.4$  ms). There were significant differences in peak velocity ratio E/A, FAF, LV IVRT between the 1<sup>st</sup> group and the controls.

**Conclusion:** LV diastolic dysfunction results predominantly from LV compression by dilated and hypertrophic RV, IVS kinetic changes and its prominence into the LV cavity with subsequent delayed opening of the mitral valve and late LV filling. The fall of the RV ejection fraction could be the additional factor (especially in RV failure), as well as reduction of LV preload, leading to decrease of LV filling pressure.

#### P511

##### Predictive factors of arterial stiffness in patients with chronic obstructive pulmonary disease (COPD)

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**Background:** Cardiovascular diseases are leading causes of mortality in COPD patients. An increased arterial stiffness could be one of the mechanisms linking systemic inflammation, oxidative stress and incident cardiovascular events in these patients.

**Objectives:** To measure arterial stiffness in stable and exacerbated COPD and to assess its relationship with inflammatory and oxidative stress markers as well as respiratory function.

**Methods:** 17 stable and 5 recently exacerbated COPD were included (age  $64 \pm 9$  yrs, FEV<sub>1</sub>  $43 \pm 16\%$  of predicted values, PaO<sub>2</sub>  $71.8 \pm 10.5$  mmHg, PaCO<sub>2</sub>  $41.8 \pm 5.3$  mmHg). We measured arterial stiffness using the pulse wave velocity (PWV), parameters of systemic inflammation (CRP<sub>us</sub>, Fibrinogen, IL-6, TNF $\alpha$ ), oxidative stress (Total antioxidant status, albumin thiols), pulmonary function (FEV<sub>1</sub>, TLC), peripheral and respiratory muscle function (sniff nasal inspiratory pressure (SNIP)).

**Results:** Arterial stiffness was severely impaired in these COPD patients ( $11.8 \pm 2.6$  m/s). There were significant correlations between arterial stiffness and systolic arterial blood pressure ( $p = 0.03$ ), systemic inflammation (CRP<sub>us</sub> and fibrinogen:  $p = 0.05$ ), respiratory function (FEV<sub>1</sub>:  $p = 0.04$ ), diaphragmatic function (SNIP:  $p < 0.05$ ) and visual analogic scale of dyspnoea ( $p = 0.04$ ).

**Conclusion:** Systemic inflammation and classical parameters reflecting the severity of COPD (FEV<sub>1</sub>, SNIP) seem to predict arterial stiffness which is a strong predictor of new cardiovascular events.

#### P512

##### Function tests during research of arterial stiffness in COPD patients

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Our purpose was to study mechanical properties of aorta in COPD patients during functional tests. We examined 60 COPD patients and 25 healthy volunteers by noninvasive arteriography (arteriograph TensioClinic TL1 (TensioMed, Hungary))

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with the physical exercise (PE) and nitroglycerine (NG) tests. Hypoxemia was assessed by digital pulseoximetry (pulseoximetry Onyx 9500 (USA)); plasma stable nitric oxide metabolites (NO) – by Greiss method. Response of aorta to PE was statistically lower in COPD patients with II-d and III-d stages of disease than healthy persons. In healthy persons aortic pulse wave velocity (aPWV) in PE test was  $+21.6 \pm 2.7\%$  from basal level. In the patients with COPD aPWV in PE test was decreased to  $+5.5 \pm 1.8\%$  from basal level ( $p < 0.05$ ). The degree of decreasing of aorta response was closely connected with disease duration and severity, lung ventilation dysfunction ( $r = 0.67$ ;  $p < 0.05$ ), hypoxia ( $r = 0.65$ ;  $p < 0.05$ ) and hyponitrooxidemia ( $r = 0.62$ ;  $p < 0.05$ ). According to noninvasive arteriography the most sensitive to COPD severity in PE test was the ratio of coronary perfusion indexes (SAI/DAI). The worsening of coronary perfusion conditions in the III-d stage of COPD was differing from healthy persons by 10 times. The degree of decreasing aPWV and augmentation index (IA) in NG test at the COPD patients does not differ from healthy persons. But in II-d stage of disease sensitivity aPWV and IA to NG test was increased. Studying of mechanical properties of aorta with functional tests essentially supplements opportunities of traditional arteriography. So, among COPD patients with “optimal” aPWV in rest, during PE test patients with statistically lowered response to PE will detect.

### P513

#### Are there gender differences of systemic inflammatory state in COPD patients?

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Systemic inflammatory state (SIS) is one of the most important branch of COPD pathogenesis, but we know little about gender features of it.

**Aim:** to study the features of SIS in COPD patients (pts) due to gender. We studied 92 pts (age –  $62.6 \pm 3.4$  yrs, male (m) – 67 (72.8%), female (f) – 25 (27.2%)) in stable phase (SP) of COPD; pts were divided into subgroups according to the stage (I-IV) of disease. Measurements included clinical status, spirometry, serum level of tumor-necrosis factor- $\alpha$  (TNF- $\alpha$ ) and soluble intercellular adhesion molecule (sICAM) by ELISA.

**Results:** are presented in Table.

Groups	TNF- $\alpha$ (pg/ml)	sICAM (ng/ml)
COPD I m	$10.8 \pm 2.5^1$ *	$714.0 \pm 90.9^{1 \approx \infty}$
COPD II m	$5.3 \pm 0.9^1$	$448.5 \pm 53.6^1$
COPD III m	$7.8 \pm 1.3^0$	$594.5 \pm 80.1^0$
COPD IV m	$5.3 \pm 1.4^*$	$460.0 \pm 75.1^*$
COPD I f	$11.7 \pm 3.2$	$392.0 \pm 92.6^{2 \dagger}$
COPD II f	$7.2 \pm 0.9^3$	$567.3 \pm 108.7^3$
COPD III f	$18.5 \pm 3.6^{3 \circ}$	$1126.0 \pm 135.0^{23 \circ}$

<sup>1</sup> $p < 0.05$  COPD I–COPD II; <sup>2</sup> $p < 0.05$  COPD I–COPD III; <sup>3</sup> $p < 0.05$  COPD II–COPD III; \* $p < 0.05$  COPD I–COPD IV; <sup>†</sup> $p < 0.05$  COPD I m–COPD I f; <sup>°</sup> $p < 0.05$  COPD III m–COPD III f<sup>†</sup>

In comparison male and female there were no differences in TNF- $\alpha$  level in COPD I ( $p > 0.05$ ). During COPD progress (from I to IV) it was registered decrease of TNF- $\alpha$  in male, and increase – in female.

As for sICAM there were differences in male and female with COPD I ( $p < 0.05$ ). During COPD progress also it was registered decrease of sICAM in male, and increase – in female.

**Conclusion:** During COPD progress male sex is associated with more significant immunology deficiency, but female sex is associated with more significant systemic inflammation.

### P515

#### Peripheral muscle weakness and exercise capacity in patients with COPD

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**Aims:** The aim of this study was to assess the correlation between peripheral muscle weakness and exercise capacity in patients with Chronic Obstructive Pulmonary Disease (COPD).

**Method:** Group of 30 patients with COPD was analyzed. Computed tomography (CT) of the right thigh halfway between the pubic symphysis and the inferior condyle of the femur was performed using Toshiba Scanner TSX 101A. The thigh muscle cross-sectional area (CSA) was obtained by measuring the surface area of the tissue with a density of 40 to 100 Hounsfield units (HU). Nutritional status was analyzed with body mass index (BMI). The exercise tolerance we assessed with 6-minute walk test distance (6-MWD).

Table 1

	Mean value of CSA (cm <sup>2</sup> )	Mean value of CSA/area of femur	Mean value of BMI (kg/m <sup>2</sup> )	Mean value of 6-MWD (m)
All group (N=30)	$99.92 \pm 14.5$	$13.31 \pm 4.2$	$23.7 \pm 5.4$	$322 \pm 108$
Male (N= 21)	$111.02 \pm 15.6$	$13.44 \pm 5.4$	$23.6 \pm 4.9$	$322 \pm 114$
Female (N= 9)	$83.91 \pm 14.3$	$13.06 \pm 4.8$	$21.3 \pm 4.2$	$321 \pm 110$

**Results:** Mean values of CSA, CSA/area of femur, BMI and 6-MWD are shown on table 1.

We found statistical significant positive correlation between CSA and 6-MWD and CSA/area of femur with 6-MWD as well. We did not find statistical significant correlation between BMI and 6-MWD (table 2).

Table 2

Correlation	r	p
CSA- 6MWD	0.412	0.026
CSA/area of femur- 6MWD	0.455	0.013
BMI- 6MWD	0.127	0.512

**Conclusion:** We concluded that alteration in body composition in COPD patients has significant impact on exercise capacity. Weakness of peripheral muscles (decreasing CSA and CSA/femur) causes significant decreasing of exercise capacity in COPD patients, independently from BMI.

### P516

#### Alpha1-antitrypsin levels and phenotypes in COPD patients in Kyrgyz population

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**Introduction:** According to the European Lung White Book (2003), mortality from chronic obstructive lung diseases (COPD) in Kyrgyzstan is the highest in Europe. Although high smoking prevalence and high-altitude are important factors, the reasons for these high mortality rates need to be investigated and the role of genetic factor is most likely underestimated.

**Aim:** to study alpha1-antitrypsin (AAT) levels and phenotypes in COPD patients in Kyrgyz population.

**Materials and methods:** 41 patients were examined (21 males and 20 females, mean age  $58.4 \pm 11.9$ ) with verified COPD. In addition to general clinical and lab investigation, serum AAT level was determined by turbidimetric method (SPIN-REACT reagents, Spain) and also AAT phenotype was determined by polymerase chain reaction (genetic testing was conducted in AAT Lab of Marburg University Hospital, Germany). The control group were 11 healthy subjects (4 males), mean age  $24.4 \pm 1.85$  years.

**Results:** AAT level in serum varied greatly from 24,0 to 308,0 mg/dl, mean level was  $148.0 \pm 69.5$  mg/dl. Among all COPD patients 7 (or 17%) were found to have low AAT levels. Their serum AAT level varied from 24,0 to 89,0 mg/dl (mean level  $66.7 \pm 25.6$  mg/dl), being significantly lower than in other COPD patients. The mean AAT level in healthy subjects was  $236.0 \pm 36.8$  mg/dl, which is significantly higher than in the COPD patients group. Out of all 41 patients genetic testing identified 39 patients with MM phenotype, one ZZ and one MZ phenotype.

**Conclusions:** AAT levels in COPD patients in Kyrgyz population are significantly lower compared to controls. AAT deficiency phenotypes are identified among Kyrgyz COPD patients, proving the hypothesis of global prevalence of AAT deficiency.

### P517

#### Findings of the central arterial pressure investigation in COPD patients

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The purpose of work was to research central arterial pressure (CAP), its interrelations with peripheral arterial pressure (PAP) and aortic stiffness parameters in COPD patients. We examined 54 COPD patients and 25 healthy volunteers by noninvasive arteriography (arteriograph TensioClinic TL1 (TensioMed, Hungary)). Aortic stiffness and aortic systolic arterial pressure (SAP) were definite. Difference between central and peripheral SAP ( $\Delta$ SAP); index of conformity CAP to PAP (IC) were estimated.

According to indirect arteriography at the patients with II-d and III-d stages of COPD was observed stable increase of the central SAP. In this patients aortic SAP was approximation to PAP ( $\Delta$ SAP =  $-2.7 \pm 3.2$ ;  $p < 0.05$ ) in comparison with healthy persons (distinction between central and peripheral the SAP =  $-10.2 \pm 2.1$  mm hg). Parameter  $\Delta$ SAP decreases and index IC increases progressively with amplify of the disease severity. It suggests that in COPD patients increases disproportion of central and peripheral SAP ratio, down to full leveling physiological distinctions between them in the severe COPD. Increase of CAP at the patients with severe COPD was associated with impairment of aortic mechanical properties and myocardial pump function. It makes certain from authentic interrelations within CAP and the left ventricular ejection time index ( $r = 0.84$ ;  $p < 0.05$ ) and key parameters of arterial stiffness: with aortic pulse wave velocity  $r = 0.68$  ( $p < 0.05$ ); with aortic augmentation index  $r = 0.66$  ( $p < 0.05$ ). CAP, indexes  $\Delta$ SAP and IC show close correlation with hypoxemia level, severity and duration of COPD. So CAP, indexes  $\Delta$ SAP and IC are the additional informative criteria of COPD severity and high cardiovascular risk.



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**P518****Systemic and pulmonary inflammation in chronic obstructive pulmonary disease (COPD)**

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**Introduction:** COPD patients can have systemic inflammation. Its relationship to pulmonary inflammation is unclear

**Material and Methods:** Tumour Necrosis Factor  $\alpha$  (TNF  $\alpha$ ), Interleukin 8 (IL-8), IL-6 and IL-10 were analyzed in induced sputum and serum in 344 patients with stable COPD (68 $\pm$ 9 yrs., FEV1/FVC 54 $\pm$ 12%, FEV1 52 $\pm$ 16% ref, BMI 28 $\pm$ 5 kg/m<sup>2</sup>, x $\pm$ SD).

**Results:** Cytokines levels (pg/ml) in serum were lower than in sputum, except for IL-10 (p<0.01): TNF  $\alpha$ , 0.83 $\pm$ 1.37 vs. 18.53 $\pm$ 61.60; IL-8, 10.08 $\pm$ 84.11 vs. 9788.5 $\pm$ 7454; IL-6, 4.57 $\pm$ 55.67 vs. 228.61 $\pm$ 382.38; and IL-10, 2.13 $\pm$ 7.32 vs. 0.74 $\pm$ 4.07. No significant correlations were found between TNF- $\alpha$  IL-8, IL-6 or IL-10 measured simultaneously in the same patient in sputum and serum.

**Conclusions:** In patients with stable COPD pulmonary inflammation is greater than and unrelated to systemic inflammation, suggesting independent regulatory mechanisms.

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**P519****Evaluation of different exercise tests and follow-up parameters in COPD patients-preliminary reports**

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Six minute walk test(6MWT) which has been used widely in chronic obstructive pulmonary disease(COPD) patients; is difficult to perform in outpatient clinics. In this study we aimed to compare 6MWT with sit to stand(STST) and timed up and go test(TUG) which could easily be performed in outpatient clinics in a short time and also with shuttle test which has been extensively used.

47 cases; 34 stable COPD patients diagnosed before (FEV1/FVC  $\leq$ 70) and 13 controls were included in the study. Cases were evaluated with pulmonary function tests(PFT) and St. George Quality of Life Questionnaire(SGQOL) following 1 hour rest time. Basal and after test, pulse, saturation, visual analog scale(VAS) and Borg dyspnea scales were recorded. Tests were performed with the same order (TUG,STST,6MWT and shuttle test) and resting periods.

Two of the patients (5,7%) had mild, 22 (62,8%) had moderate, 8 (25,7%) had severe and 2 (5,7%) had very severe disease. Each of the four tests were statistically significant related with disease stage(p<0.05). The closest relation with FEV1 was obtained with shuttle test and TUG,6MWT and STST were following it respectively(p<0.05). Any difference was not observed in VAS parameters after TUG and STST(p<0.05), while there was an increase after 6MWT and shuttle test. Pulse parameters didn't increase with respect to basal values after 6MWT, however tachycardia was observed with other tests after exercise.

Although negligible tachycardia occurs, determining a significant correlation between STST and TUG with FEV1 and diseases severity, easy feasibility and absence of feeling of dyspnea, supported us to suggest that these tests could be an alternative to 6MWT and shuttle tests.

**P520****Exercise tolerance in clinically stable COPD patients after first admission**

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Aerobic capacity is a well identified determinant of prognosis in COPD patients. As part of a follow-up study aiming at phenotyping COPD (PAC-COPD study), we assessed exercise tolerance in 309 patients three months after their first hospital admission. Their distribution by ATS-ERS COPD stages was: 6% mild (6MWD 458 $\pm$ 66 m), 48% moderate (450 $\pm$ 84 m), 38% severe (434 $\pm$ 91 m) and 8% very severe (366 $\pm$ 146m). Walking distance was negatively associated with age ( $\beta$  coef. -3.56, p<0.001), MRC scale (-18, p<0.001), HAD depression (-3.48, p<0.05),

blood TNF $\alpha$  levels (-8.90, p<0.05) and showed a positive association with PaO<sub>2</sub> (1.45, p<0.01). One third of the patients (n=108, 35%) were obese (BMI $\geq$ 30 kg.m<sup>-2</sup>) showing a negative association between 6MWD and BMI (-6, p<0.05), age (-4, p<0.001) and MRC scale (-26, p<0.001).

While 6MWD only fell in patients with very severe disease, VO<sub>2</sub>peak steadily decreased in each disease stage (90 $\pm$ 24, 78 $\pm$ 20, 61 $\pm$ 16 and 45 $\pm$ 11% pred) (p<0.001). The latter can be explained because VO<sub>2</sub>peak was significantly associated with lung function (FEV<sub>1</sub> 6.9, p<0.001; DLCO 4.85, p<0.001) and both muscle mass (FFM 6.25, p<0.05) and handgrip strength (7.62, p<0.01). Main conclusions of the current study are that exercise tolerance was relatively preserved in this cohort of COPD patients. Obesity should be taken into account in the assessment of exercise tolerance of COPD patients, particularly when using six-min walking. The impact of exercise tolerance on prognosis and admissions over a two-year follow-up period is currently under analysis. Supported by 2006 ERS-SEPAR fellowship (#191).

**P521****The comparison of carotid artery intima media thickness and inflammatory markers in patients with COPD**

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**Aim:** The aim of this study was to examine the relationship between intima-media complex of the common carotid artery and inflammatory markers and severity of disease in patients with COPD.

**Materials and method:** Fifty-three patients (38 males/15 females), median age 56.9 $\pm$ 5.4 years old, with moderate to severe COPD (in stable state) were included in the study. Their right and left carotid arteries were examined with a duplex scanner. Intima-media thickness (IMT) measurements of the carotid artery are compared to levels of CRP, fibrinogen, WBC, BMI, pro-BNP and stage of COPD, smoking habits of patients.

**Results:** There is significant relationship between the stage of COPD and the levels of CRP elevation (p:0.01). But no relationship was found between intima media thickness and the parameters we have investigated, including CRP too.

Pro-BNP levels were found significantly elevated in patients which have intima media thickness (p:0.01).

**Conclusion:** There have to be made new extended studies, to examine the effects of COPD, as a systemic inflammatory disease, on vascular system.

**P522****COPACETIC: unraveling the genetics of COPD**

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Since only about 20% of smokers develop COPD, a genetic background likely contributes to disease development. Some polymorphisms in candidate genes have been identified. So far a whole genome association study, that may identify multiple yet unidentified genes, has not been performed. Such a study needs a large sample size.

The COPACETIC study builds a population based database of  $\pm$ 4000 smokers with  $\geq$ 20 pack years without a COPD-diagnosis (the NELSON study). In these subjects pulmonary function tests and CT-scans will be obtained to establish the presence or absence of COPD (=controls versus affected). A  $\sim$ 320.000 SNP genome wide scan will be performed, and the most significant 400 SNPs will be selected. These 400 SNPs will be analysed in 5 replication cohorts. The first cohort is the Polish part of the BOLD study (Jagiellonian University School of Medicine, Krakow) which 108 of N=487 subjects are  $\geq$ GOLD stage 1. The second cohort is the Copenhagen City Heart Study with approx 8750 subjects of which 1220 were diagnosed as COPD-patients (670 in GOLD stage 1, 440 in stage 2, 95 in stage 3 and 15 in stage 4).

In the Netherlands the Vlagtwedde/Vlaardingen study sampled approx 2500 subjects of which 633 were diagnosed as COPD-patients (310 patients in GOLD stage 1, 288 in stage 2, 35 in stage 3/4). The Deutsches Krebsforschungszentrum will build a cohort of  $\sim$ 2000 participants of a lung cancer screening trial with  $\geq$ 40 pack years without a prior COPD-diagnosis.

The last cohort is the EUROSCOP study which was a 3-year multicenter study on patients with mild COPD. DNA samples are available from 700 COPD patients and 500 controls.

We will establish COPD related genes, and ultimately aim to establish a set of SNPs that could predict COPD development.