## 320. COPD: mechanisms and biomarker

**2931**

**Association of testosterone level with phenotypic characteristics and long-term outcomes of men with COPD in the ECLIPSE cohort**

Richard Casaburi[1], Richard V. Clark[2], Bruce Miller[3], Lisa Edwards[4], Stephen Rennard[5], Ruth Tal-Singer[3], Ronald Swerdloff[6], Christina Wang[6]. *[1]Rehabilitation Clinical Trials Center, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, United States; [2]Muscle Metabolism DPU, GlaxoSmithKline R&D, Research Triangle Park, NC, United States; [3]COPD Clinical Discovery, GlaxoSmithKline R&D, King of Prussia, PA, United States; [4]Biomedical Data Sciences, GlaxoSmithKline R&D, Research Triangle Park, NC, United States; [5]Pulmonary & Critical Care Medicine, University of Nebraska Medical Center, Omaha, NE, United States; [6]Department of Medicine, Harbor-UCLA Medical Center and Los Angeles Biomedical Research Center, Torrance, CA, United States*

The impact of plasma total testosterone (T) level, measured by liquid chromatography tandem mass spectrometry, was evaluated in 1296 male COPD patients from the "Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints" (ECLIPSE) study in which GOLD II-IV COPD patients were followed without additional intervention for three years.

Median T level was 439 ng/dL. T level was not correlated with% pred $FEV_1$ but was inversely correlated with body mass index (BMI) (Spearman's r=-0.47) and positively correlated with% predicted total lung capacity (r=0.21), each $p<0.001$. We detected weaker but statistically significant ($p<0.05$) negative correlation of T with age, and positive correlation with 6 minute walk distance and emphysema score on CT scan. In univariate analysis, subject death tended to be higher in those with low T levels (OR 0.51, p=0.054); lower T level significantly predicted subject death among those with stage II disease [OR 0.24, p=0.003]. In multivariate linear regression analyses that included age,% predicted $FEV_1$, BMI, smoking status and T level, both COPD hospitalization and subject death were predicted by age and% predicted $FEV_1$ but T level was not predictive of COPD hospitalization and was only predictive of higher subject death in stage II patients (OR 0.25 p=0.007).

In a large cohort of men with COPD, T level correlated with several COPD phenotypic characteristics. Low T tended to predict higher death rate particularly in subjects with moderate disease. The ECLIPSE Study was funded by GlaxoSmithKline (SCO104960, NCT00292552)

**2932**

**Relation of health-related quality of life, frequent exacerbation phenotype and circulating systemic biomarkers in stable COPD**

Daiana Stolz[1], Francesco Blasi[2], Renaud Louis[3], Wim Boersma[4], Alicia Lacoma[5], Kostantinos Kostikas[6], Paola Castellotti[2], Lucas Boeck[1], Branislava Milenkovic[7], Tobias Welte[8], Janko Rakic[1], Emiel Wouters[9], Joachim Aerts[10], Arturo Huerta[11], Markos Minas[6], Antoni Torres[11], Michael Tamm[1]. *[1]Clinic of Pulmonary Medicine, University Hospital, Basel, Switzerland; [2]IRCCS Policlinico Milan, University of Milan, Milan, Italy; [3]Pneumology, University of Liege, Liege, Belgium; [4]Pneumology, Medisch Centrum, Alkmaar, Netherlands; [5]Microbiology, Hospital Universitari Germans Trais i Pujol, Badalona, Spain; [6]Pneumology, University of Thessaly Medical School, Larissa, Greece; [7]Institute for Pulmonary Diseases, Clinical Centre of Serbia, Belgrade, Serbia; [8]Pneumology, Medizinische Hochschule Hannover, Hannover, Germany; [9]Pneumology, University Hospital Maastricht, Maastricht, Netherlands; [10]Pneumology, Amphia Hospital, Breda, Netherlands; [11]Pneumology, Hospital Clinic, Barcelona, Spain*

**Background:** We have evaluated the impact of the frequent exacerbation phenotype and circulating systemic biomarkers in the HRQL in a well characterized cohort of COPD patients.

**Methods:** Data of 636 patients with stable COPD (GOLD II-IV) for $\geq$ 6 weeks seeking care in pulmonary tertiary care hospitals in 10 European centers were analyzed. Assessment included frequency of exacerbations in the previous year, systemic biomarkers (procalcitonin, proANP, copeptin, proadrenomedullin), lung function, SF-36, SGRQ, MMRC dyspnea score, and 6MWD test.

**Results:** Patients had a mean age of 66 yo $\pm$ 11; 74.1% were male; mean FEV1% pred 48.2% $\pm$ 18.5. 205 (32.3%) were current smokers and 142 (22.32%) reported frequent exacerbations ($\geq$ 2/y). Median [95% CI] MMRC was 3 [2-3], 6MWD was 390 m [325-445]. The mean SGRQ scores were: total 43.0$\pm$38.9; symptoms 48.6$\pm$23.1, activity 57.4$\pm$23.3, and impact 32.9$\pm$19.8. In a linear, univariate regression analysis, frequent exacerbation phenotype, SaO2 at rest, desaturation (< 88%) at exercise, FEV1% pred, MMRC, 6MWD, and Borg scale, but neither current smoking nor circulating biomarkers were associated with the total SGRQ score. In the multivariate analysis, frequent exacerbation phenotype [95%] 6.55 [3.04-10.06], FEV1% pred -0.09 [-0.17–0.003], MMRC 6.46 [4.83-8.00], 6MWD -0.021 [-0.036- -0.006], Borg 1.35 [0.64-2.05] were independently associated with the HRQL as assessed by the SGRQ total score.

**Conclusions:** Additionally to the variables related to COPD severity, the frequent exacerbation phenotype is independently associated with the HRQL. Conversely, systemic biomarkers are not related to HRQL in COPD at stable state.

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**Anti-elastin immunity in COPD patients**

Manuela Rinaldi, An Lehouck, Marc Decramer, Ghislaine Gayan-Ramirez, Wim Janssens. *Respiratory Research Unit, Katholieke Universiteit Leuven, Leuven, Belgium*

**Introduction:** The contribution of anti-elastin immunity in COPD is subject of intense debate. Conflicting data are reported on the presence of serum auto-antibodies against elastin fragments correlating with COPD severity. As auto-immunity is driven by antigen-specific T cells, we investigated the presence of B cell and T cell responses against elastin fragments in a large sample of COPD patients and controls.

**Material and methods:** Anti-elastin antibodies were analyzed with indirect ELISA on plasma samples of 352 COPD patients (GOLD 1-4) and 168 age-matched smoking controls. In a random subgroup of 25 patients, T-cell responses against elastin fragments were further determined with ELISPOT (IFN-g and IL-2) on peripheral blood mononuclear cells (PBMC) and compared with responses of 5 non-smoking age-matched controls.

**Results:** Increased titers of anti-elastin antibodies were found in 14.2% (24/168) of smoking controls compared to 12.5% (44/352) of the COPD population (p=0.07).

No significant correlation was found between anti-elastin antibodies and FEV1% predicted (p=0.699), nor with the presence of emphysema on CT scan (p=0.150). Despite significant responses to control antigen, ELISPOT analysis could not detect increased T cell responses against elastin in any of the individuals.
**Conclusion:** Anti-elastin antibodies are not specific for COPD patients and do not correlate with disease severity. The absence of elastin-specific T cell responses further weakens the role of anti-elastin auto-immunity in the pathogenesis of COPD.
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**2934**

**Resting energy expenditure and adipose tissue leptin expression in patients with COPD**

Miroslav Brusik[1], Peter Skyba[1], Pavol Pobeha[1], Jozef Ukropec[2], Barbara Ukropcova[2], Daniela Gasperikova[2], Ruzena Tkacova[1], Pavol Joppa[1]. *[1]Department of Respiratory Medicine, and Tuberculosis, Faculty of Medicine, P.J. Safarik University and L. Pasteur University Hospital, Kosice, Slovakia (Slovak Republic); [2]Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava, Slovakia (Slovak Republic)*

**Aim:** Increases in resting energy expenditure (REE) have been previously shown in wasting COPD patients. Decreased leptin levels have been associated with weight loss in patients with emphysema, however, adipose tissue (AT) leptin expression has not been studied previously in COPD. Our scope was to investigate the REE, leptin AT expression and serum levels in patients with COPD and different BMI.
**Methods:** 44 patients with stable COPD were divided into 3 groups: Group 1 with BMI $\leq$20kg/m$^2$ (n=9, 9 males, 61.4$\pm$8.2 years, $FEV_1$ 33.8$\pm$19.8%), Group 2 with BMI 20-30kg/m$^2$ (n=24, 20 males, 62.8$\pm$5.9 years, $FEV_1$ 59.4$\pm$22.7%) and Group 3 with BMI >30kg/m$^2$ (n=11, 9 males, 60.2$\pm$8.0 years, $FEV_1$ 60.5$\pm$19.0%). REE was measured by indirect calorimetry using a ventilated hood system. Samples of subcutaneous AT were obtained by percutaneous biopsy. AT gene expression was measured in duplicates with aid of the real-time PCR using the TaqMan gene expression assays.
**Results:** REE per kg of body weight (REE/kg) decreased from Group 1 to Group 2 and 3 (32.9$\pm$6.1 vs 26.2$\pm$5.8 vs 23.9$\pm$6.6 kcal/kg/24 h, p=0.006), whereas leptin AT expression ($\Delta\Delta$Ct) and serum leptin levels increased (8.8$\pm$9.4 vs 44.1$\pm$20.9 vs 58.1$\pm$15.8, p<0.001; 0.8$\pm$0.9 vs 11.9$\pm$16.5 vs 28.9$\pm$21.5 $\mu$g/ml, p<0.001; respectively). There was a significant inverse relationship between REE/kg and both AT leptin expression and serum leptin levels (R= -0.458, p=0.002; R= -0.522, p<0.001, respectively).
**Conclusion:** In patients with stable COPD resting metabolic rate increased with decreasing BMI, in association with reductions in AT leptin expression. Low leptin AT production is associated with hypermetabolism in lean COPD patients.
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**2935**

**Prevalence of anaemia in COPD: Less than what has been published before**

Lorena Comeche Casanova[1], Mª Jesus Llorente Alonso[2], Irene Albarrán Lozano[3], Mª Paz Rodríguez Bolado[1], Asunción Flórez Horcajada[1], Dolores Álvaro Álvarez[1]. *[1]Respiratory, Hospital Universitario de Móstoles, Móstoles, Madrid, Spain; [2]Biochemistry, Hospital Universitario de Móstoles, Móstoles, Madrid, Spain; [3]Statistical, Carlos III University, Madrid, Spain*

**Objectives:** To determine the prevalence of anaemia in stable-phase COPD patients. To ascertain the differences in serum values of some biomarkers between COPD patients with and without anaemia.
**Population and methods:** COPD stable outpatients were included. These patients were followed up in the respiratory clinic and none of them could meet any of de following exclusion criteria: moderate-severe exacerbations in the last two months; asthma, thyroid disease, cancer in the last 5 years, liver disease, chronic heart or renal failure, any origin blood loss background, B12 vitamin and folic acid deficit. A set of tests were performed, including lung function test, blood samples for hemogram and biochemistry and serum values of ultrasensitive CRP, IL6, IL8 and TNFalfa. Bootstrap methodology has been used in order to test differences between with and without anaemia group.
**Results:** 130 patients were included, 116 (89,2%) were men, with an average age of 64,2 years (DS 8,4) and a FEV1% postbronchodilatador of 49,7% (DS 15,6). 8 patients showed anaemia (6,2%). A summary of the biomarkers results for each group is presented below.

| Biomarkers | COPD without anaemia group (n=122) | COPD with anaemia group (n=8) | p value |
|---|---|---|---|
| IL6 | 23,7 (DS 91,4) | 5,3 (DS 5) | 0,003 |
| IL8 | 32,8 (DS 72,8) | 28,8 (DE 21,7) | 0,72 |
| TNF$\alpha$ | 5,5 (DS 2) | 6,1 (DS 2,1) | 0,41 |
| CRP | 7,1 (DS 17,1) | 16,8 (DS 26,9) | 0,28 |

**Conclusions:** The anaemia prevalence in COPD is 6,2% in our study. We have found significant differences in serum values of IL6 between COPD patients with and without anaemia. The CRP serum values in patients with COPD and anaemia were higher than the values in patients without anaemia.
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**2936**

**Can brain MRI explain cognitive decline in COPD? A pilot study**

Rebecca A. Charlton[1], James W. Dodd[1], Martin van den Broek[2], Franklyn A. Howe[1], Thomas R. Barrick[1], Paul W. Jones[1]. *[1]Clinical Sciences, St George's University of London, London, United Kingdom; [2]Department of Neurospychology, St George's NHS Trust, London, United Kingdom*

**Background:** Cognitive deficits have been described in patients with COPD. We used MRI to investigate brain structure in COPD patients with and without evidence of cognitive decline and in healthy controls.
**Methods:** Participants (n=27) completed a full cognitive assessment and MRI scan. Two groups of COPD patients were selected; those who demonstrated evidence of cognitive decline (COPD-D; n=9) or who did not (COPD-ND; n=9). Age-matched healthy controls (HC; n=9) were studied. Volumes of grey matter (GMV), white matter (WMV), and white matter lesions (LV), were calculated. The presence of lesions in the brain stem (BSL) and external capsule (ECL) was noted.
**Results:** Groups did not differ on measures of GMV or WMV. LV was significantly greater in patients versus controls (t=-3.47, p=0.002); there was no difference between LV in COPD-ND and COPD-D (t=.342, p=.737). No significant group difference in the presence of BSL was observed (X2(df2)=3.0, p=0.223), but ECL was numerically more frequent in the COPD-D group (X2(df2)=5.64, p=0.060). See Table 1.

Table 1. Demographics & MRI data

| | Controls (n=9) | COPD-ND (n=9) | COPD-D (n=9) |
|---|---|---|---|
| Age, years: Mean (SD) Range | 70 (10) 57–88 | 70 (7) 60–82 | 70 (6) 60–81 |
| Sex (m, f) | 6, 3 | 5, 4 | 5, 4 |
| GMV, mm$^3$ | 736,164 (39,035) | 741,856 (49,877) | 729,649 (47,252) |
| WMV, mm$^3$ | 683,854 (60,910) | 688,437 (29,210) | 686,654 (47,087) |
| LV, mm$^3$ | 4,891 (3568) | 18,220 (14,979) | 15,901 (13,754) |
| % BSL | 11% | 44% | 44% |
| % ECL | 22% | 44% | 77% |

**Conclusion:** COPD-D and COPD-ND patients both have more white matter lesions than HC, possibly due to increased vascular risk. The significance of BSL and ECL requires further exploration. Future analysis will use methods that detect change in tissue microstructure, and associations between brain damage and cognition.

**2937**

**Iron deficiency in non-anemic patients with chronic obstructive pulmonary disease**

Matthias Urban[1], Otto Chris Burghuber[1], Wolfgang Hübl[2], Georg-Christian Funk[1]. *[1]Ludwig-Boltzmann Institute for COPD and Respiratory Epidemiology and Department for Respiratory and Critical Care Medicine, Otto Wagner Spital, Vienna, Austria; [2]Department of Laboratory Medicine, Wilhelminenspital, Vienna, Austria*

**Background:** Iron deficiency contributes to reduced exercise capacity in patients with heart failure. The repletion of iron improves cognitive, symptomatic, and exercise performance in these patients independent of hemoglobin. COPD shares many functional features of heart failure. Thus iron deficiency could be a potential therapeutic target in COPD.
**Aims and objectives:** The aim of this study was to determine the prevalence of iron deficiency in non-anemic patients with COPD.
**Methods:** Serum markers of iron status were measured in 53 stable non-anemic (hemoglobin>12 g/L) COPD patients (53% males; mean age 64$\pm$8 years, mean FEV1predicted 41$\pm$18%; GOLD stage II, III, and IV was 34%, 32%, and 34%, respectively). Iron deficiency was diagnosed when the serum ferritin level was either <100 $\mu$g/l or was between 100 and 299 $\mu$g/l with the transferrin saturation <20%.
**Results:** The serum ferritin level was <100 $\mu$g/l in 20 patients. The serum ferritin level was between 100 and 299 $\mu$g/l and transferrin saturation was <20% in 6 patients. Thus iron deficiency was present in 49% of the patients. The median soluble transferrin receptor to log_ferritin ratio was higher in patients with iron deficiency (1.7, 1.0 to 1.4) compared to patients without (1.7, 1.4 to 2.0), p<0.001.
**Conclusions:** Iron deficiency is present in half of the patients with stable COPD. A randomized, placebo-controlled trial should clarify whether repletion of iron stores improves functional performance in COPD patients with iron deficiency.