European Respiratory Society
Annual Congress 2012

Abstract Number: 4953

Publication Number: P3622

Abstract Group: 1.5. Diffuse Parenchymal Lung Disease

Keyword 1: Idiopathic pulmonary fibrosis **Keyword 2:** Bronchoalveolar lavage **Keyword 3:** Biomarkers

Title: BAL markers of alveolar/capillary abnormality in IPF

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Body: Several lines of evidence suggest that alveolar-capillary abnormalities, including increased alveolar septal capillary density and pulmonary veno-occlusive disease,are characterizing feature of IPF and may play a role in its progression.This study assess altered capillary permeability,abnormal intra-alveolar coagulation and alveolar hemorrhage as markers of alveolar/capillary abnormality. Methods: Bronchoalveolar lavage (BAL) samples from 62 subjects (53 IPF patients and 14 healthy volunteers) were evaluated for α2-macroglobulin (α2-M) and fibrinogen D-dimer (D-d) concentration by ELISA.D-d levels were comparatively assessed in blood as well.The numbers of haemosiderin laden macrophages were measured by Perls' stain and the intensity thereof assessed by the Golde score. Results: IPF patients had markedly increased α2-M levels (mean 10000 vs 50 ng/ml, p<0,0001) and D-d were elevated with significantly higher frequency (39/62 vs 1/14, p<0,05) with no blood elevation.Golde scores were elevated (69 vs 19, p<0,001) compared to controls. α2-M concentration positively correlates with the Golde score (p<0,05) and D-d concentration (p<0,05).In patients with a high Golde score (Golde score>59) the D-d concentration (125 vs 17 p<0,05) was increased and both DLCO (43 vs 56%,p<0,05) and exercise capability (6MWTD 273 meters vs 415,p<0,05) were reduced vs patients with low score,while the FVC was not significantly different (82 vs 66%).Golde score and arterial pulmonary pressure showed significant correlation (R=0,39). Conclusions: leak of α2-M,intra-alveolar hemorrage and coagulation,indicate that alveolar-capillary abnormalities are important in the pathogenesis and progression of pulmonary fibrosis, and likely pulmonary hypertension in IPF.