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Angiogenic proteome profiling of pulmonary hypertension in chronic obstructive pulmonary disease (COPD)

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Background. Pulmonary hypertension (PH) associated with COPD (COPD-PH) may lead to right heart failure with a very poor prognosis. However, reliable predictive/prognostic biomarkers of PH in COPD have not been established. In severe COPD-PH, vascular remodeling includes a distinctive loss of alveolar capillaries, and dysregulated angiogenesis may provide a clue for biomarker research. Therefore, we aimed to characterize the profiles of circulating angiogenesis-related factors (levels of pro- and anti-angiogenic proteins) in COPD patients with or without PH. Methods. Blood plasma samples from COPD patients were obtained from Graz biobank and divided into 3 groups: COPD (mPAP ? 24 mmHg, n=6), COPD-PHlow (mPAP = 25-34 mmHg, n=7) and COPD-PHhigh (mPAP ? 35 mmHg, n=7). Control group included 10 healthy donors. All groups were age- and gender-matched. Angiogenesis-associated proteins were measured with the Proteome Profiler Human Angiogenesis Array (ARY007, R&D Systems). Pixel densities of the membranes were analyzed by HLImage+ software (QuickSpots, R&D Systems). Group comparisons were performed with the Kruskal-Wallis H test. Correlations were calculated with the Spearman´s rank test. SPSS software (IBM SPSS Inc.) was used for statistical analysis. A p-value <0.05 was considered significant. Results. Thrombospondin-1 and prolactin may be suggested as candidate biomarkers of COPD, as their levels were significantly elevated in COPD groups (with and without PH), compared to healthy controls. We were not able to distinguish COPD-PH from COPD, although EGF and PDGF-AA levels were significantly decreased in COPD-PH compared to healthy controls. MMP-9 in COPD-PHhigh was significantly increased compared to COPD-PHlow, thus suggesting this enzyme to be a potential biomarker of severe PH. Among 55 angiogenesis-associated proteins, only IGFBP1 was correlated with age. Correlations with mPAP were not found. Further studies are required to validate the selected candidate biomarkers