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Title: Serological detection of elastin fragments in COPD and IPF patients

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Body: Introduction: Elastin plays a critical role in the development of respiratory system disorders including COPD and IPF, whose pathogenesis involves an inflammatory response and tissue turnover mediated by proteases, especially matrix metalloprotease (MMP)-12 secreted by activated macrophages. Aims and objectives: Our aim was to evaluate whether a novel biochemical marker of elastin degradation mediated by MMP-12 may provide information in relation to lung tissue destruction during pulmonary disease and aid in the diagnosis of respiratory disease. Methods: Human elastin was in vitro cleaved by different proteases and the resulting peptides were analyzed by LC-MS/MS. Among more than 400 fragments, the MMP-12 generated elastin neoepitope cleaved at the amino acid position 444 (ELN-441/ELM) was chosen as candidate for antibody generation for its uniqueness for human elastin following assay development. This novel marker was assessed in serum collected in a small cohort of COPD (n=10), IPF (n=29) patients and controls (n=11) using a competitive enzyme linked immunosorbent assay (ELISA). Results: Serum levels of ELM were significantly higher in patients diagnosed with COPD ($p<0.0003$) and with IPF ($p<0.0001$) compared to controls. The diagnostic value, measured by means of the area under the curve of receiver operating characteristic (AUROC) was best in COPD patients (AUROC 97%, $p=0.00025$) and lower but still significant in IPF patients (AUROC 90%, $p=0.00011$). Discussion: Even though these findings need to be validated in larger clinical settings, the ELM marker described showed potential for the separation of controls from COPD or IPF patients.