

Suppression of the anti-inflammatory cytokine IL-38 in moderate to severe COPD

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Rationale

Interleukin (IL)-38 is an anti-inflammatory cytokine that is upregulated in several chronic inflammatory disorders and acts as an endogenous antagonist of neutrophil-mobilising IL-36 cytokines. Its role in COPD, however, remains largely unknown. This study aimed to determine whether systemic IL-38 is involved in COPD.

Methods

Patients with COPD and lung-healthy controls (LHC) were recruited. All participants underwent spirometry, body plethysmography, and DLCO measurement. Sarcopenia was assessed using hand-grip strength. COPD patients also underwent chest CT imaging, and emphysema was evaluated and graded by a pulmonology specialist. Serum IL-38 concentrations were quantified by ELISA.

Results

The COPD group (n=25) included 60% females, median age 68 (64–73) years; 80% were ex-smokers, 16% current smokers, and 4% never-smokers. Most were GOLD stage III (64%). LHC (n=15) included 80% females, age 42 (36–62) years; 68% were never-smokers and 33% ex-smokers. Emphysema was present in 78% of COPD patients, of whom 30% had severe disease. Hand-grip strength was 27 (17–37) kg in COPD and 35 (27–40) kg in LHC.

Serum IL-38 concentrations were markedly lower in COPD patients compared with LHC. Within the COPD group, IL-38 levels were higher in those with severe emphysema than in those with mild or no emphysema. Across the pooled study population, IL-38 concentrations correlated positively with hand-grip strength, with a similar but non-significant trend within the COPD subgroup.

Conclusion

Systemic IL-38 concentrations were reduced in COPD, suggesting impaired endogenous anti-inflammatory protection. The positive association between IL-38 and hand-grip strength supports a potential protective role against sarcopenia. Elevated IL-38 levels in COPD patients with severe emphysema may reflect a reactive, yet still protective, response. These findings support further investigation into IL-38 as a protective mediator in COPD and emphysema and warrant mechanistic studies to clarify its role.

Figure 1. A: Serum IL-38 levels in lung healthy controls (LHC) and in patients with COPD. Bars are means with standard error of the mean (SEM). **B (COPD group):** Serum IL-38 levels according to the severity of emphysema as assessed through imaging. The dotted lines indicate the lower limit of detection for the ELISA. Significant differences are indicated by *. **C:** Correlation between serum IL-38 levels and hand grip strength. Only subjects with IL-38 values within the ELISA detection limits were included (n = 11). A linear trend line is shown for visual guidance (assessed with Spearman's rank correlation test). Abbreviation: LHC: lung healthy controls.

