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Title: Evaluation of mechanisms determining endothelial function in patients with COPD

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Body: Background: COPD is associated with increased cardiovascular mortality. Factors contributing to vascular damage in patients with COPD are mostly unknown. However, it has been suggested that airflow limitation, systemic inflammation, oxidative stress, sympathetic activation, hypoxia and impaired physical activity may lead to endothelial dysfunction and underpin this association. Objective: To determine the impact of airflow obstruction, systemic inflammation, oxidative stress, sympathetic activation, hypoxia and physical activity on endothelial function in COPD. Methods: In patients with stable COPD (GOLD stage I-IV) assessments of endothelial function by flow-mediated dilatation (FMD), conventional cardiovascular risk factors (Pocock-score), airflow obstruction (FEV1), systemic inflammation (CRP), oxidative stress (malondialdehyde), sympathetic activation (baroreflex-sensitivity), hypoxia (blood gases) and physical activity (steps per day) were performed. Associations between endothelial function and these potential underlying mechanisms were assessed in univariate and multivariate analysis. Results: 106 patients (35% GOLD stage I/II, 25% III, 40% IV) were included. In univariate analysis FMD correlated with FEV1 ($r=0.53$, $p<0.001$), baroreflex-sensitivity ($r=0.25$, $p=0.01$), and steps per day ($r=0.27$, $p=0.01$) but not with CRP, malondialdehyde, hypoxia or Pocock-score. In multivariate analysis including all proposed mechanisms only FEV1 and steps per day were independently associated with FMD. Conclusions: Endothelial function in COPD seems to be primarily determined by the severity of airflow obstruction and the level of physical activity.