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Title: Coronary artery calcification in COPD is associated with adverse functional assessments and mortality

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Body: COPD is associated with coronary artery disease (CAD). Coronary artery calcium score (CACS) can identify and stratify risk in CAD. We evaluated CACS and its relationship with clinical outcomes using non-gated chest CT in a well-characterised cohort of COPD patients (ECLIPSE study). CACS (Agatston score) was assessed in 946 patients (COPD n=676, FEV1% predicted 48.7±16.1, age 63.2±7.0yrs; Smoker controls: n=199, FEV1% predicted 110.0±11.5, age 54.1± 8.5yrs; Non-smoker controls: n=71, FEV1% predicted 114.4±13.8, age 54.7±9.2yrs). CACS was higher in COPD patients than smoker or non-smoker controls (415±689 vs 141.7±396.4 vs 66.6±228.5, p<0.001). When corrected for pack years, the calcium score percentile based on age, sex and ethnicity was greater in the COPD group (56.5±1.6 vs 40.5±2.8 vs 30.5±5.1, p<0.001). CACS in the COPD group correlated with age (r=0.40, p<0.001), pack years (r=0.20, p<0.001), function (6 minute walking distance (=-0.13, p<0.001) and mMRC dyspnoea score (r=0.11, p=0.006)) and some biomarkers (Interleukin 6 r=0.18, p<0.001; Clara Cell secretory protein16 R=0.18, p<0.001; Surfactant Protein-d r=0.11, p=0.006) but not with emphysema (% low attenuation areas), FEV1% predicted, exacerbation frequency or decline in FEV1. CACS and calcium percentile corrected for pack years were higher in those who died during 3 years follow up (65±(SD)23 vs 39±680, p=0.003 and 68±4.6 vs 57.2±1.5, p=0.027) and a significant association between high CACS and mortality was confirmed by a COX Proportional Hazards Model. Thus in a cohort of COPD patients higher CACS was associated with poor function and increased mortality. Supported by GlaxoSmithKline (SCO104960, NCT00292552).