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Title: Inflammatory biomarkers and comorbidities in chronic obstructive pulmonary disease

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Body: Background Patients with chronic obstructive pulmonary disease (COPD) have evidence of systemic inflammation that may be implicated in the development of comorbidities. We tested the hypothesis that elevated levels of three inflammatory biomarkers are associated with increased risk of comorbidities in COPD. Methods We measured baseline C-reactive protein (CRP), fibrinogen, and leukocyte count in 10,052 COPD patients from two large population studies. During a median 5-years follow-up we recorded hospital admissions due to ischemic heart disease, myocardial infarction, heart failure, type II diabetes, lung cancer, pneumonia, pulmonary embolism, hip fracture, and depression as endpoints. Results Multifactorially adjusted risk of ischemic heart disease was increased by a factor of 2.19 (95% confidence interval 1.48 to 3.23) in individuals with three biomarkers elevated (CRP above 3 mg per liter, fibrinogen above 14 μ mol per liter, and leukocyte count above 9×10^9 per liter) versus individuals with all three biomarkers at or below these limits. Corresponding hazard ratios were 2.32 (1.34 to 4.04) for myocardial infarction, 2.63 (1.71 to 4.04) for heart failure, 3.54 (2.03 to 6.19) for diabetes, 4.00 (2.12 to 7.54) for lung cancer, and 2.71 (2.03 to 3.63) for pneumonia. There were no consistent differences in risk of pulmonary embolism, hip fracture, or depression as a function of these three biomarkers. Conclusions Simultaneously elevated levels of CRP, fibrinogen, and leukocyte count are associated with a 2 to 4-fold increased risk of major comorbidities in COPD. These findings may enable clinicians to conduct stratified management of comorbidities in COPD patients.