

Frequency of exacerbations in patients with chronic obstructive pulmonary disease: an analysis of the SPIROMICS cohort

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SUMMARY

Background Present treatment strategies to stratify exacerbation risk in patients with chronic obstructive pulmonary disease (COPD) rely on a history of two or more events in the previous year. We aimed to understand year to year variability in exacerbations and factors associated with consistent exacerbations over time.

Methods In this longitudinal, prospective analysis of exacerbations in the Subpopulations and Intermediate Outcome Measures in COPD Study (SPIROMICS) cohort, we analysed patients aged 40–80 years with COPD for whom 3 years of prospective data were available, identified through various means including care at academic and non-academic medical centres, word of mouth, and existing patient registries. Participants were enrolled in the study between Nov 12, 2010, and July 31, 2015. We classified patients according to yearly exacerbation frequency: no exacerbations in any year; one exacerbation in every year during 3 years of follow-up; and those with inconsistent exacerbations (individuals who had both years with exacerbations and years without during the 3 years of follow-up). Participants were characterised by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometric category (1–4) on the basis of post-bronchodilator FEV1. Stepwise logistic regression was used to compare factors associated with one or more acute exacerbations of COPD every year for 3 years versus no exacerbations in the same timeframe. Additionally, a stepwise zero-inflated negative binomial model was used to assess predictors of exacerbation count during follow-up in all patients with available data. Baseline symptom burden was assessed with the COPD assessment test. This trial is registered with ClinicalTrials.gov, number NCT01969344.

Findings 2981 patients were enrolled during the study. 1843 patients had COPD, of which 1105 patients had 3 years of complete, prospective follow-up data. 538 (49%) of 1105 patients had at least one acute exacerbation during the 3 years of follow-up, whereas 567 (51%) had none. 82 (7%) of 1105 patients had at least one acute exacerbation each year, whereas only 23 (2%) had two or more acute exacerbations in each year. An inconsistent pattern (both years with and without acute exacerbations) was common (456 [41%] of the group), particularly among GOLD stages 3 and 4 patients (256 [56%] of 456). In logistic regression, consistent acute exacerbations (≥ 1 event per year for 3 years) were associated with higher baseline symptom burden, previous exacerbations, greater evidence of small airway abnormality on CT, lower interleukin-15 concentrations, and higher interleukin-8 concentrations, than were no acute exacerbations.

Interpretation Although acute exacerbations are common, the exacerbation status of most individuals varies markedly from year to year. Among patients who had any acute exacerbation over 3 years, very few repeatedly had two or more events per year. In addition to symptoms and history of exacerbations in the year before study enrolment, we identified several novel biomarkers associated with consistent exacerbations, including CT-defined small airway abnormality, and interleukin-15 and interleukin-8 concentrations.

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