

Certain inflammatory biomarkers associated with increased risk of COPD exacerbations

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Simultaneously elevated levels of the biomarkers C-reactive protein, fibrinogen and leukocyte count in individuals with chronic obstructive pulmonary disease (COPD) were associated with increased risk of having exacerbations, even in those with milder COPD and in those without previous exacerbations, according to a study in the June 12 issue of *JAMA*.

"[Exacerbations](#) of respiratory symptoms in COPD are of major importance because of their profound and long-lasting adverse effects on patients. Frequent episodes accelerate loss of lung function, affect the quality of life of the patients, and are associated with poor survival," according to background information in the article. Some patients with COPD have evidence of low-grade [systemic inflammation](#) with increased levels of certain inflammatory biomarkers during stable conditions, and previous studies have found that elevated levels of inflammatory biomarkers like C-reactive protein (CRP), fibrinogen, and leukocytes during stable COPD are associated with poor outcomes.

Mette Thomsen, M.D., of Herlev Hospital, Copenhagen University Hospital, Herlev, Denmark, and colleagues tested the hypothesis that elevated levels of inflammatory biomarkers in individuals with stable COPD are associated with an increased risk of having exacerbations. The prospective study examined 61,650 participants with spirometry measurements from the Copenhagen City Heart Study (2001-2003) and the Copenhagen General Population Study (2003-2008). Of these, 6,574 had COPD. Baseline levels of CRP, [fibrinogen](#) and leukocyte count were

measured in participants at a time when they were not experiencing symptoms of exacerbations. Exacerbations were recorded and defined as short-course treatment with [oral corticosteroids](#) alone or in combination with an antibiotic or as a [hospital admission](#) due to COPD.

During a median (midpoint) 4 years of follow-up time, 3,083 exacerbations were recorded (average, 0.5/participant). The researchers found that the risk of having frequent exacerbations was increased approximately 4-fold in the first year of follow-up and 3-fold using maximum follow-up time in individuals with 3 high inflammatory biomarkers compared with individuals who had no elevated biomarkers. "Importantly, relative risk estimates were consistent even in those with milder COPD and in those with no history of frequent exacerbations, suggesting that these biomarkers provide additional information to the latest Global Initiative for Chronic Obstructive Lung Disease [GOLD] 2011 grading."

The highest 5-year absolute risks of having frequent exacerbations in those with 3 high biomarkers (vs. no high biomarkers) were 62 percent (vs. 24 percent) for those with GOLD grades C-D (n=558), 98 percent (vs. 64 percent) in those with a history of frequent exacerbations (n=127), and 52 percent (vs. 15 percent) for those with GOLD grades 3-4 (n=465).

"... our study provides novel information that may lead to a simpler assessment using measurements of inflammatory [biomarkers](#) in individuals with stable COPD to further stratify preventive therapies based on absolute risk of frequent exacerbations. The potential benefits of such stratification should be tested in future clinical trials that could include drugs of particular current interest, such as macrolides or statins," the authors write.

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