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Abstracts State of the Art

ASSESSING INFLAMMATION IN COPD: (NON-)INVASIVE METHODS

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Chronic obstructive pulmonary disease (COPD) is currently defined by persistent airflow limitation with enhanced and chronic airways inflammation [1]. Nevertheless, the clinical management of the disease is based on measuring symptoms, airflow limitation and exacerbation frequency [1]. Do we need to assess airways inflammation to optimize the management of COPD? When using factor analysis it appears that inflammation and airflow limitation represent partly independent features of the disease [2,3].

COPD is a heterogeneous disorder with widespread variability in airway and parenchymal histology [4]. It is close to impossible to sample this histology adequately, which has hampered progress in COPD research. The current 'silver standard' is represented by endobronchial biopsies of the large airways and bronchoalveolar lavage, which provide different and selective samples of airway inflammation [5,6]. These quantitative measurements can be used in clinical research, in which the efficacy of anti-inflammatory intervention in COPD is validated by showing *e.g.* reduction of inflammation at the airway level [7].

However, these methods are unsuitable for monitoring inflammation in COPD. Which less invasive methods are available for this? This may include peripheral blood [8], but certainly refers to (induced) sputum analysis. It has nicely been shown that guiding regular anti-inflammatory therapy in COPD by monitoring eosinophilic inflammation in sputum leads to a dramatic reduction in exacerbations [9]. This exceeds the effects of most novel drugs, and thereby points the way towards phenotype-driven, personalized medicine in COPD.

Nevertheless, even sputum analysis is laborious. Therefore, recent attempts have focused on capturing molecular signatures of exhaled air in COPD by using electronic noses. It appears that such 'breathprints' can be typical for COPD [10,11] and that the molecular constituents in exhaled air are associated with the eosinophilic and neutrophilic subtypes in COPD [12]. This is encouraging, because it may allow real-time monitoring of inflammatory phenotypes and thereby the tailoring of individual therapy in COPD.

In conclusion, at present inflammation has only a very limited role, if any, in the diagnosis and therapy of COPD. However, there is strong evidence that monitoring inflammation contributes to a better disease outcome, which may become feasible with doctor's office technology.

References

1. Vestbo J *et al*. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2012; Aug 9: EPub ahead of print: www.goldcopd.org
2. Lapperre TS *et al*. Dissociation of lung function and airway inflammation in COPD. Am J Respir Crit Care Med 2004;170:499-504.
3. Snoeck-Stroband JB *et al*. Airway inflammation contributes to health status in COPD. A cross-sectional study. Respir Res 2006;7:140.
4. McDonough JE *et al*. Small-airway obstruction and emphysema in COPD. N Engl J Med 2011;17:1567-1575.
5. Battaglia S *et al*. Differential distribution of inflammatory cells in large and small airways in smokers. J Clin Pathol 2007;60:907-911.
6. Lapperre TS *et al*. Small airways dysfunction and neutrophilic inflammation in bronchial biopsies and BAL in COPD. Chest 2007;131:53-59.
7. Lapperre TS *et al*. Effect of fluticasone with and without salmeterol on pulmonary outcomes in COPD. Ann Int Med 2009;151:517-527.
8. Gomes-Alves P *et al*. Seldi-TOF biomarker signatures for cystic fibrosis, asthma and chronic obstructive pulmonary disease. Clin Biochem 2010;43:168-177.
9. Siva R *et al*. Eosinophilic airway inflammation and exacerbations of COPD: a randomised controlled trial. Eur Respir J 2007;29:906-913.
10. Fens N *et al*. Exhaled breath profiling enables discrimination of chronic obstructive pulmonary disease and asthma. Am J Respir Crit Care Med *2009;180*:1076-1082.
11. Fens N *et al*. External validation of exhaled breath profiling using an electronic nose in the discrimination of asthma with fixed airways obstruction and COPD. Clin Exp Allergy 2011;41:1371-1378.
12. Fens N *et al*. Exhaled air molecular profiling in relation to inflammatory subtype and activity in COPD. Eur Respir J 2011;38:1301-1309.

STRUCTURAL CHANGES: IMAGING IN COPD

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Lung cancer screening trials provide an opportunity to study the natural history of emphysema by using CT lung density as a surrogate parameter. In the Danish Lung Cancer Screening Trial, 4,104 participants were randomized to *either* annual screening with low dose CT for 5 years (2005-2009) *or* no screening (control group). Participants were 50-70 years of age, current or ex-smoker with minimum 20 pack-years, and FEV_1 of at least 30% of predicted normal at baseline. Ex-smokers had to have quit after the age of 50 years and less than 10 years before inclusion. In addition, measurements from individuals who changed their smoking habit during the study, where excluded from the current analysis from the date of change of smoking habit. At screening rounds, smoking habits were recorded and spirometry was performed. CT lung density was measured as the volume-adjusted 15^{th} percentile density (PD15). Almost half (47%) had airflow obstruction (AFO) at study entry. The influences of age, sex, height, BMI, smoking and AFO on FEV_1 and PD15 were analyzed in mixed effects multiple regression models. A progressive decline in FEV_1 has been widely accepted as the hallmark of COPD. However, recent evidence indicates that the rate of FEV_1 decline is higher in mild to moderate COPD than in severe COPD. Usually changes in FEV_1 are measured in ml that is *absolute*, however, changes can also be measured *relative* as a percentage of the actual FEV_1. In absolute terms those with the best FEV_1 consistently showed the steepest decline, whereas in relative terms most fast decliners were found among those with low FEV_1, which seems more intuitive. Furthermore, relative measurements implied statistically significant acceleration of decline with advancing age, smoking (pack-years) and severity of AFO. Female sex and current smoking increased PD15 at baseline, and both increased the annual decline in PD15. The presence and severity of AFO was a strong predictor of low PD15 at baseline and of increased annual decline in PD15. In conclusion, relative measurements lead to a better understanding of changes in FEV_1, and PD15 as a measure of structural changes in COPD seems to be are more sensitive indicator of progression of disease.

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