**Inside this issue: Inflammation type 2 biomarkers, COPD & ACOS**

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact and associations of eosinophilic inflammation in COPD: analysis of the AERIS cohort.</td>
<td>2</td>
</tr>
<tr>
<td>Association of sputum and blood eosinophil concentrations with clinical measures of COPD severity: an analysis of the SPIROMICS cohort.</td>
<td>2</td>
</tr>
<tr>
<td>Mepolizumab for eosinophilic chronic obstructive pulmonary disease.</td>
<td>3</td>
</tr>
<tr>
<td>Correlation between fractional exhaled nitric oxide and sputum eosinophilia in exacerbations of COPD.</td>
<td>3</td>
</tr>
<tr>
<td>Association of blood eosinophils and plasma periostin with FEV1 response after 3-month inhaled corticosteroid and long-acting beta2-agonist treatment in stable COPD patients.</td>
<td>4</td>
</tr>
<tr>
<td>Th-2 signature in chronic airway diseases: towards the extinction of asthma-COPD overlap syndrome?</td>
<td>4</td>
</tr>
<tr>
<td>Importance of fractional exhaled nitric oxide in the differentiation of asthma-COPD overlap syndrome, asthma, and COPD.</td>
<td>5</td>
</tr>
<tr>
<td>Asthma-COPD overlap: clinical relevance of genomic signatures of type 2 inflammation in chronic obstructive pulmonary disease.</td>
<td>5</td>
</tr>
<tr>
<td>Asthma-COPD overlap is not a homogeneous disorder: further supporting data.</td>
<td>6</td>
</tr>
</tbody>
</table>

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Impact and associations of eosinophilic inflammation in COPD: analysis of the AERIS cohort.

Kim VL, et al.
http://erj.ersjournals.com/content/erj/50/4/1700853.full.pdf

The authors prospectively assessed the stability of eosinophilic inflammation, and its dynamics changes across exacerbations in 127 patients, aged 40-85 years, with moderate to very severe COPD undergoing repeated blood and sputum sampling at stable visits and within 72 h of exacerbation for 1 year. Blood eosinophils ≥2% was prevalent at baseline, and predicted increased risk of eosinophilic inflammation at exacerbation. Eosinophil predominance at stable visits was associated with a lower risk of bacterial presence at exacerbation. Conversely the prevalence of airway bacterial infection at exacerbations was greater among the group who rarely had raised eosinophils over time.

Eosinophilic inflammation is a common and stable phenotype in patients with moderate to severe COPD. Blood eosinophil counts in the stable state can predict the nature of inflammation at future exacerbations.

Association of sputum and blood eosinophil concentrations with clinical measures of COPD severity: an analysis of the SPIROMICS cohort.

Hastie AT, et al.

The authors performed a multicentre observational study and analyzed baseline data from 2737 patients with COPD aged 40-80 years recruited to SPIROMICS. Using eosinophil cutoffs of more than 1.25% for sputum and 200 cells/μL for blood to categorize high and low eosinophil counts, the investigators found that proportion of current smokers, patients treated with inhaled corticosteroid, serum IgE levels, quality of life, lung function were different according to eosinophil counts (parameters being worse in the high vs low blood and sputum eosinophil groups). The degree of emphysema, quantified by CT, was associated with high sputum but not blood eosinophils, particularly in the upper lobes. From the results of this study the authors have concluded that blood eosinophils alone were not a reliable biomarker for COPD severity or exacerbations, or for sputum eosinophils, and suggested that clinical trials targeting eosinophilic inflammation in COPD should consider assessing sputum eosinophils.
Mepolizumab for eosinophilic chronic obstructive pulmonary disease.

Pavord ID, et al. 

The authors performed two phase 3, randomized, placebo-controlled, double-blind, parallel-group trials comparing mepolizumab (100 mg in METREX, 100 or 300 mg in METREO) with placebo, given as a subcutaneous injection every 4 weeks for 52 weeks in patients with COPD who had a history of frequent exacerbations despite receiving maximal guideline-recommended inhaled glucocorticoid-based triple maintenance therapy. Patients with an eosinophilic phenotype who were treated with 100 mg of mepolizumab had an annual rate of moderate or severe exacerbations that was consistently 18% to 20% lower than that among patients who received placebo. These findings suggest that eosinophilic airway inflammation contributes to COPD exacerbations and that the use of mepolizumab, a humanized monoclonal antibody, reducing eosinophil counts in blood and tissues by blocking interleukin-5, directed by blood eosinophil counts might represent a precision-medicine approach to the management of selected COPD patients.

Correlation between fractional exhaled nitric oxide and sputum eosinophilia in exacerbations of COPD.

Gao J, et al. 

The authors have conducted a cross-sectional study in 163 patients with COPD exacerbation undergoing on the same day: FeNO test, spirometry, bronchodilator reversibility test, induced sputum, and routine blood test. Patients were classified as eosinophilic group or noneosinophilic group based on sputum eosinophilic percentage (≥2.5%) and FeNO levels (≥32 parts per billion). FeNO levels and blood eosinophilic percentage were higher in patients with sputum eosinophilia compared to those without. Sputum eosinophilic percentage was higher with raised FeNO compared to those with low FeNO. Eosinophils in induced sputum correlated with both FeNO levels and blood eosinophilic percentage. The authors concluded that inflammatory biomarkers, including sputum eosinophilic percentage, FeNO level, and blood eosinophilic percentage, can be used to positively diagnose eosinophilic inflammation in COPD patients.
**Association of blood eosinophils and plasma periostin with FEV1 response after 3-month inhaled corticosteroid and long-acting beta2-agonist treatment in stable COPD patients.**

Park HY, et al.

Blood eosinophils and plasma periostin levels were measured in 130 stable COPD patients who began a 3-month treatment period with inhaled corticosteroids (ICS)/long-acting beta2-agonist LABA. High blood eosinophils (>260/µL) and high plasma periostin (>23 ng/mL) were significantly associated with FEV1 responders after 3-month treatment with ICS/LABA. However, high plasma periostin levels alone or combined with high blood eosinophils did not have an additive role to increase prediction accuracy for bronchodilatory response to treatment.

**Th-2 signature in chronic airway diseases: towards the extinction of asthma-COPD overlap syndrome?**

Cosío BG, et al.
Eur Respir J. 2017; 49: 1602397 [https://doi.org/10.1183/13993003.02397-2016].

The authors aimed to describe the differences and similarities between patients with chronic obstructive airway disease classified on the basis of classical diagnostic labels (non-smoking asthma (NSA), COPD, or asthma-COPD overlap syndrome (ACOS) including both smoking asthmatics (SA) and patients with eosinophilic COPD (COPD-e), or according to the underlying inflammatory pattern (Th-2 signature, either Th-2-high or Th-2-low). Th-2 signature was defined by a blood eosinophil count ≥300 cells/µL and/or a sputum eosinophil count ≥3%. No differences in symptoms or exacerbation rate were found between the three groups (NSA, COPD & ACOS). The Th-2 signature was found in 49% of NSA, 3.3% of patients with COPD, and among ACOS patients, 30% of SA and 49.3% of patients with COPD-e. The authors concluded that the current distinction between asthma, COPD and their overlap (ACOS) may be confusing because it includes a variety of disease expressions that cannot be separated clinically, and that a view of chronic obstructive airway disease based on Th-2 inflammatory profile, irrespective of the taxonomy, is feasible and more effective for identifying treatable traits.
Importance of fractional exhaled nitric oxide in the differentiation of asthma-COPD overlap syndrome, asthma, and COPD.


The authors have prospectively measured fractional concentration of exhaled nitric oxide (FeNO), pulmonary function test (PFT), and bronchial hyperresponsiveness or bronchodilator test in 689 patients suspected with asthma (n=500), COPD (n=132) or asthma-COPD overlap syndrome (ACOS) (n=57). Receiver operating characteristic (ROC) curves were constructed to assess the clinical utility of FeNO in diagnosing ACOS. The FeNO value in patients with ACOS was significantly higher than that in the COPD group. The cutoff value of >22.5 ppb FeNO was found to be optimal for differentiating ACOS from COPD patients (sensitivity 70%, specificity 75%). The authors concluded that FeNO measurement is a simple, reproducible, and noninvasive method of differentiating ACOS from COPD.

Asthma-COPD overlap: clinical relevance of genomic signatures of type 2 inflammation in chronic obstructive pulmonary disease.


To determine whether asthma-associated gene signatures play a role in COPD the authors have studied asthma-associated gene expression changes in COPD patients with clinical asthma features a condition known as asthmas-COPD overlap syndrome (ACOS). Looking at the T helper type 2 (Th2) signature (T2S) score, a gene expression metric induced in Th2-high asthma, the authors have found that higher T2S scores correlated with increased airway wall eosinophil counts, blood eosinophil percentage, bronchodilator reversibility, and improvement in hyperinflation after corticosteroid treatment in a randomized, placebo-controlled trial, the Groningen and Leiden Universities study of Corticosteroids in Obstructive Lung Disease (GLUCOLD; n = 89). The authors concluded that asthma-derived gene expression signatures of Th2 inflammation are associated with increased disease severity, eosinophil counts, and ICS response in a subset of COPD patients who cannot be identified by clinical history of asthma.
Pérez-de-Llano L, et al.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5668958/

The authors have performed a cross-sectional, observational, multicenter study carried out in 23 outpatient clinics from tertiary hospitals in Spain. They have included 292 patients with obstructive lung disease (OLD): 94 non-smoking asthmatics (NSA), 89 non-eosinophilic COPD, 44 smoking asthmatics (SA) and 65 eosinophilic COPD (e-COPD). Although there were no significant differences between SA and e-COPD with respect to symptoms and exacerbations, e-COPD patients were older and significantly more often male. They showed significantly lower post-bronchodilator FEV₁, and lower DLCO values than SA patients, likely due to a heavier smoking habit. On the contrary, SA had more atopic features, more reversibility of airflow obstruction and higher IgE levels than e-COPD patients. Th₂-related biomarkers (periostin, FeNO and blood eosinophils) showed higher median values in e-COPD patients, 49% of e-COPD patients and 30% of SA showed a “Th₂ high” inflammatory pattern (defined as eosinophil count >300 eosinophils/µL in blood or ≥3% in sputum). The authors concluded that the two main entities of the so-called asthma-COPD overlap syndrome, namely smoking asthmatics and eosinophilic COPD are two distinct disorders and should therefore be treated differently.