Asthma phenotyping and biomarkers

P66   CAN WE IDENTIFY ASTHMA AND COPD OVERLAP
SYNDROME (ACOS) FROM A SEVERE DIFFICULT
ASTHMA CLINIC PATIENT COHORT?

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Introduction Asthma-COPD Overlap Syndrome (ACOS) is characterised by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD, which can be difficult to define. In response to the document produced by GINA and GOLD (2014) there is a need for further studies to identify the proportion of ACOS patients within treatment centres. Patients with features of ACOS are reported between 15–55% and have outcomes that are far worse than COPD or asthma alone.[1]

Objectives To locally identify the proportion and current management of ACOS patients within a tertiary treatment centre.

Method The study was carried out retrospectively reviewing patient data over a 6 month period from electronically documented clinic letters, discharge summaries, pathology and lung function results. Patients included were identified from a severe difficult asthma clinic list at a large tertiary centre in London.

Results 101 patients were reviewed with a mean age of 49.1 years. Table 1 identifies patients with chronic airflow limitation with a cohort of 6.9% (n = 7) diagnosed as asthma and COPD; showing fixed airway obstruction (n = 6), mean age 54.6 years. There are no patients receiving LABA mono therapy, however 7.9% patients have no ICS in their treatment plan.

Abstract P66 Table 1

		Patient Cohort (n = 101)	Mean
FEV1/FVC	≤ 70%	50.5% (n = 51)	67.6%
	>70%	49.5% (n = 50)	
Blood Eosinophil	<0.5 (×10^9/L)	63.4% (n = 64)	0.5
	≥0.5 (×10^9/L)	27.7% (n = 28)	
Blood Neutrophil	<7.0 (×10^9/L)	70.3% (n = 71)	5.5
	≥7.0 (×10^9/L)	20.8% (n = 21)	
Total IgE	<81	18.9% (n = 19)	357
	≥81	43.6% (n = 44)	
Smoking History	Non Smoker	54.5% (n = 55)	
	Ex Smoker	22.8% (n = 23)	
	Smoker	9.9% (n = 10)	
BTS/SIGN STEP 4–5		39.6% (n = 40)	
BDP equivalence range		400–4000	1705
Doctor diagnosed as Asthma and COPD		6.9% (n = 7)	
Current Treatment	SAMA Monotherapy	2.0% (n = 2)	
	LAMA Monotherapy	3.0% (n = 3)	
	ICS Monotherapy	4.0% (n = 4)	
	ICS/LABA	77.2% (n = 78)	
	Omalizumab	11.9% (n = 12)	
	Non - ICS	7.9% (n = 8)	

ACOS can potentially be identified in 10 patients with a raised IgE and eosinophil count, FEV1/FVC ≤ 70% showing fixed airway obstruction who are listed as non-smokers; these patients are currently on ICS/LABA treatment.

Conclusion This review of severe difficult asthma clinic patients highlights the challenge in identifying ACOS patients. Spirometry results documented are of limited value in diagnosis between asthma, COPD and ACOS; reversibility testing would be more indicative for future work. Interestingly we have a relatively young patient population on high BDP doses and some potentially at risk due to no ICS treatment. Further prospective studies in the form of patient questionnaires is required in order to identify detailed clinical history to aid earlier diagnosis and management.

REFERENCE
1   Diagnosis of Diseases of Chronic Airflow Limitation: Asthma, COPD, and Asthma – COPD Overlap Syndrome (ACOS). GINA and GOLD, 2014

P67   BRONCHIECTASIS IN SEVERE UNCONTROLLED ASTHMA

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Introduction and objectives Bronchiectasis can contribute to severe and difficult to control asthma. It is important to recognise bronchiectasis in asthmatics and treat them accordingly. In order to estimate the presence of bronchiectasis in severe asthma, and the relation with the clinical and functional parameters we studied 40 patients with severe uncontrolled asthma, in a stable condition.

Methods The symptoms, the duration of asthma diagnosis, the number of exacerbations/year, cycles of corticosteroids and antibiotic treatment/year, spirometry, and bronchial colonisation were estimated. High resolution computed tomography (HRCT) was performed to evaluate the presence and extent of bronchiectasis. HRCT were studied by an expert thoracic radiologist, according to Smith scale for bronchiectasis (score 0–24), taking a score≥3 as radiologically significant.

Results Forty patients were studied, 28 women, mean age (±SD) 57.9 years (±12.4), 32 non smokers. Mean ACT score was 14.2 (±4.9).

The main symptoms were: cough (92%), wheezing (95%), dyspnea (92%), sputum production (72%) of which mucoid (52%), mucopurulent and purulent (48%). Mean duration of asthma diagnosis was 16.5(±11.5) years, exacerbations: 4.4 (±2.7)/year, corticosteroid per os cycles/year: 4.4 (±3.1), antibiotic cycles/year: 2.8(±2.2).

In 27 patients (67,5%) bronchiectasis was diagnosed: Smith score: 5.2(±4.2).

The mean FEV_1 was 72.6% (±21.1) of predicted, FVC 79.1% (±19.4), FEV_1/FVC ratio 67.3 (±9.7). Nine patients (22.5%) were colonised with pathogens, 6 of whom with Pseudomonas Aeruginosa. Patients with sputum production had a higher Smith score compared to those without expectoration (6.3 ± 4.2 vs 2.3 ± 2.2 respectively Z = 2.8, p = 0.005). In addition, patients with pathogens in sputum cultures had a higher Smith score compared to those with normal flora (10 ± 4.2 vs 3.8 ± 3 respectively, Z = 3.5, p < 0.0001) (Figure 1).
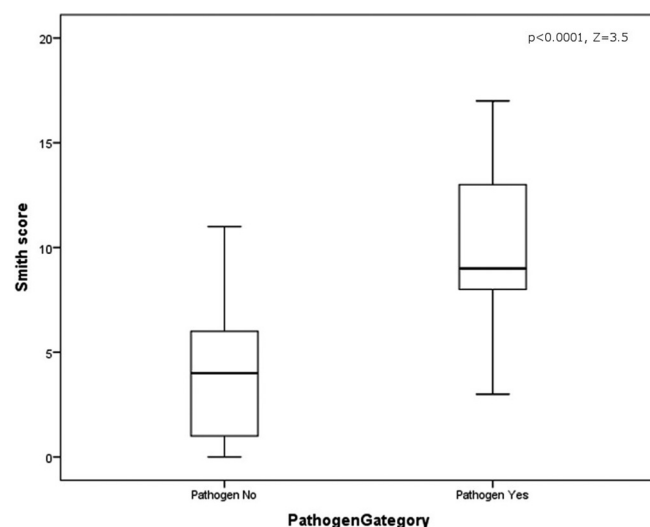
Abstract P67 Figure 1 Smith score in patients with pathogens in sputum cultures and in patients with normal flora

No correlation was found between the extent of bronchiectasis and the lung function parameters. The severity of bronchiectasis (Smith score) was correlated to the number of antibiotic cycles/year (p = 0.002, r = 0.48). In addition, a lower ACT score was related with a higher asthma exacerbation rate (r = -0.52, p = 0.001).

Conclusion The evidence of bronchiectasis on HRCT is common in patients with severe uncontrolled asthma. Sputum production and pathogen isolation in sputum culture may indicate the presence of this comorbidity and the need of antibiotics as an additional treatment.

P68   PHENOTYPING INFECTION ASSOCIATED ASTHMA: A CASE-CONTROL STUDY

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Introduction and objectives Asthmatics experiencing recurrent infective exacerbations, resembling a bacterial bronchitis, are often started on prophylactic antibiotics but this phenotype of asthma is not well understood. We sought to: a) compare asthmatics with and without recurrent infections using a case-control approach and b) phenotype asthmatics with recurrent infections to evaluate the heterogeneity within this population.

Methods We reviewed Leicester difficult asthma clinic letters within two calendar years (01/01/2013–31/12/2014) and utilised an asthma database to identify matched (age, sex, BMI and GINA treatment step) controls. Case definition: a clinician diagnosis of asthma and ≥2 respiratory tract infections/preceding year requiring oral antibiotics or on prophylactic antibiotics. Control definition: a clinician diagnosis of asthma, no evidence of recurrent infections and not prescribed prophylactic antibiotics. A 1:1 case-control ratio was used. 71 cases and 71 controls were identified. The antibiotic use, physiology, CT imaging, immunoglobulins and pneumococcal serotype meta-data were evaluated. Model based cluster analysis was performed to phenotype the cases with no *a priori* assumption made on the number of clusters. Age, sex, age of onset, sputum eosinophil count and

Juniper Asthma Control Score were used as the input variables (Am J Respir Crit Care Med.2008 Aug 1;178(3):218–24).

Results The cases were predominately female (69%), obese with recurrent infections (mean:4.25/preceding year) and had an impaired asthma-related quality life compared to controls (p = 0.0285). Cluster analysis identified three groups. Cluster 1: male, eosinophilic, on oral corticosteroids with a low IgM, had poor lung function and bronchial wall thickening and bronchiectasis on CT. Cluster 2: female with a blood neutrophilia and preserved lung function. Cluster 3: female, non-atopic with impaired asthma control, a low IgG and air trapping on CT. 63.3% of patients on prophylactic antibiotics (n = 49) had a reduction in infective exacerbation frequency. The proportion of patients on antibiotics within each cluster and response was similar.

Conclusion Three subphenotypes of asthma with recurrent infections have been identified. Further immunpathological studies to evaluate the mechanism of infection in each subphenotype, the host microbiome and response to antimicrobials are required.

P69   AN EXPLORATORY STUDY TO INVESTIGATE THE RELATIONSHIP BETWEEN FRACTION OF EXHALED NITRIC OXIDE (FENO) HOME MONITORING AND EOSINOPHILIC AIRWAY INFLAMMATION IN ADULTS WITH SEVERE ASTHMA

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Introduction FeNO is a non-invasive surrogate marker of corticosteroid-responsive airway inflammation that may be measured using small portable devices. We aimed to determine (i) the reliability and feasibility of twice-daily FeNO home monitoring in adults with severe asthma, as well as (ii) to explore the relationship between serial FeNO measurements and gold standard markers of eosinophilic airway inflammation.

Methods Ten patients with severe asthma (BTS treatment steps 4/5) were recruited from the Difficult Asthma Clinic at Glenfield Hospital. Patients were provided with portable FeNO monitors (NOBreath, Bedfont Scientific Ltd., Maidstone, UK) for a period of eight weeks, and asked to record twice-daily FeNO (at a flow rate of 50 ml/s) and PEF readings, as well as daily visual analogue scores for cough, breathlessness and wheeze, using paper diaries. They attended fortnightly visits during the study period, at which they underwent sputum induction and full blood count.

Results Nine patients completed the study. The median (range) intraclass correlation coefficient of triplicate FeNO measurements was 0.83 (0.78 – 0.92) for morning measurements and 0.82 (0.71 – 0.97) for evening measurements. There was a median of 7.1% missing data (range 2.7 – 14.3%). FeNO measurements correlated strongly with sputum and blood eosinophil counts, with the strongest correlations observed with a 9-day FeNO moving average, and a lag time of -1 day for sputum eosinophils (r = 0.571, p < 0.001) and -2 days for blood eosinophil counts (r = 0.691, p < 0.0001), suggesting that changes in sputum and blood eosinophil counts tended to precede changes in FeNO by 1 and 2 days respectively. In contrast there were no consistent relationships seen between FeNO and either PEF or visual analogue scores.

Conclusion Home monitoring of FeNO is feasible and the measurements are repeatable. Daily FeNO measurements correlate