European Respiratory Society
Annual Congress 2012

Abstract Number: 7086

Publication Number: 344

Abstract Group: 5.3. Allergy and Immunology

Keyword 1: Asthma - mechanism **Keyword 2:** Airway smooth muscle **Keyword 3:** Airway management

Title: Asthma phenotypes associated with vocal cord/laryngeal dysfunction

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Body: Aim: To identify asthma phenotypes in patients with refractory and non-refractory asthma in whom inappropriate vocal cord closure and laryngeal dysfunction (LD) may occur (Low et al, AJRCCM, 2011). Methods: We evaluated 57 patients with mild to moderate non-refractory asthma (N=31) or refractory asthma (N=26). Dynamic 320 slice computerised tomography (CT) of larynx was done and a validated algorithm was used to accurately measure vocal cord lateral diameter during inspiration and expiration. Excessive narrowing of the airways was diagnosed if a predetermined lower limit of normal was exceeded. The asthma groups were compared by semi-supervised cluster analysis to identify asthma phenotypes associated with laryngeal dysfunction. Results: Overall vocal cord diameter was reduced below the lower limit of normal in 26 of 57 cases (46%). There was no relationship with asthma severity (LD) in refractory asthma: 12/26 (46%) versus non-refractory 14/31 (45%). Laryngeal dysfunction was associated with increased age ($P < 0.034$) bronchodilator (BD) responses <12% ($P < 0.009$) and difficult speech when breathless ($P<0.019$). There were 3 unique phenotype clusters associated with abnormal vocal cord narrowing and determinants of cluster membership were: 1. age > 40 years, female, bronchodilator response < 12%, difficulty speaking when breathless; 2. age > 40 years, bronchodilator response < 12%, BMI > 30kgs / m^2; 3. female, bronchodilator response < 12%, BMI > 30kgs / m^2. Conclusion: Our results indicate that vocal cord behaviour is abnormal in asthma, irrespective of severity. However, laryngeal dysfunction may often be associated with particular patient phenotypes and contribute to their overall symptomatic burden of disease.