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Title: Systemic inflammation in older adults with asthma-COPD overlap syndrome

Ms. Juan Juan 22182 Fu juanjuan.fu@uon.edu.au^{1,3,4}, Dr. Vanessa M. 22183 McDonald Vanessa.McDonald@hnehealth.nsw.gov.au^{1,2,3,4}, Prof. Dr Peter G. 22184 Gibson Peter.Gibson@hnehealth.nsw.gov.au MD^{1,3,4,5} and Dr. Jodie L 22185 Simpson jodie.simpson@hnehealth.nsw.gov.au^{1,3,4}. ¹ Priority Research Centre for Asthma and Respiratory Diseases, University of Newcastle, NSW, Australia, NSW2308 ; ² School of Nursing and Midwifery, Faculty of Health, University of Newcastle, NSW, Australia, NSW2308 ; ³ Department of Respiratory and Sleep Medicine, John Hunter Hospital, New Lambton, Newcastle, NSW, Australia, NSW2305 ; ⁴ Respiratory Medicine, Hunter Medical Research Institute, Newcastle, NSW, Australia, NSW2305 and ⁵ Respiratory Medicine, Woolcock Institute of Medical Research, Sydney, NSW, Australia, NSW2037 .

Body: Background: The overlap of asthma and COPD is common in older people with obstructive airway disease (OAD). Systemic inflammation is associated with adverse clinical outcomes and co-morbidities in COPD, but its role on asthma-COPD overlap syndrome is unknown. This study aimed to examine systemic inflammation in asthma-COPD overlap, and the potential clinical relevance with OAD. Method: Serum high sensitivity C-reactive protein (hsCRP), Interleukin 6 (IL-6) and serum amyloid A (SAA) were measured in 108 adults older than 55 years comprising healthy controls (n=27), asthma (n=7), COPD (n=29) and asthma-COPD overlap (n=45). Spirometry, induced sputum, quality of life, co-morbidities and medications were assessed. Levels of systemic inflammatory mediators were compared, and the associations with clinical characteristics were tested in multivariate regression model. Results: Patients with asthma-COPD overlap had significantly elevated IL-6 levels. SAA level was raised in both the COPD and asthma-COPD overlap groups. CRP level was significantly increased in COPD. The disease groups had different patterns of systemic inflammation. CRP was positively associated with BMI, whereas IL-6 was predicted by age, FEV1%predicted, and cardiovascular disease. SAA level was associated with co-morbidity, and females had higher SAA level than males. Systemic markers were not associated with airway inflammation. Conclusion: Systemic inflammation is a common and important component of the asthma-COPD overlap. The pattern of systemic inflammation in asthma-COPD overlap is differing from COPD characterized as an elevated IL-6 and SAA levels. It is not related to airway inflammation, and may be an independent treatment target.