TELOMERE ATTENTION IN CIRCULATING WHITE BLOOD CELLS IN COPD RELATES TO LUNG FUNCTION AND OUTCOMES

Introduction Increasing evidence suggests accelerated ageing as a pathogenic mechanism in COPD.

Methods and results Telomere length in circulating WBC, a marker of biological ageing, was assessed in 200 ex-smoker patients with COPD (n = 9 per group). Cells were stimulated with TGF-β and foetal calf serum, and miRNA and mRNA expression levels were measured by RT-PCR. IL-6 and CXCL8 release was measured by ELISA. Transfection of miR-145 mimics and inhibitors were used to model the effects of miR-145 over-expression and knock-down, respectively.

Results Low concentrations of TGF-β significantly upregulated SMAD3 expression in ASMCs from patients with COPD. Higher concentrations of TGF-β led to a suppression of SMAD3 expression, with a concomitant increase in miR-145 expression in these cells, to a greater degree than in healthy subjects.

Conclusions This is the first time that miR-145 has been demonstrated to be important in controlling the increased inflammatory state of ASM cells from COPD patients. This miRNA may not only act as a novel biomarker for COPD, but may also be a novel target for treatment.
Abstract S51 Figure 1 Differences in pDES between patients with very high CACs and lower CACs levels (* p < 0.01)

Introduction COPD is a risk factor for cardiovascular comorbidities. Elastin degradation represents a shared mechanism for the pulmonary and vascular features.

Methods and Results Plasma desmosine (pDES), a marker of elastin degradation, was measured in 955 COPD patients (609 male, age 63.1 ± 7.2 years, FEV₁ 50.6 ± 15.1%predicted) by an isotope dilution LC-MS/MS method. Coronary artery calcification (CACS), a surrogate of atherosclerosis, was assessed in 440 standard CT scan images (low 1000 AU).

Results pDES was elevated in patients with cardiovascular comorbidities (p < 0.01) and correlated with FEV₁ (r = 0.39, p < 0.0001), MMRC (r = 0.16, p < 0.0001), 6MWD (r = -0.16, p < 0.0001), BODE index (r = 0.10, p < 0.005), fibrinogen, IL6, IL8, CCL18, and SPD but not with emphysema. These variables showed significant higher values in the patients in the highest pDES quartile, pDES was elevated in patients with very high CACS in comparison with patients with lower CACS (Figure 1) and in patients that died during a 3 year follow-up (p < 0.0001).

Conclusion pDES relates to lung function, systemic inflammation, cardiovascular comorbidities, and CACS in patients with COPD. pDES is a predictor of all cause overall mortality.

The ECLIPSE study (GSK Study No. SCO104960, NCT00292552) was sponsored by GlaxoSmithKline.

How does clinical respiratory physiology help the clinician?

SS2 IS A RAISED BICARBONATE, WITHOUT HYPERCAPNIA, PART OF THE PHYSIOLOGICAL SPECTRUM OF OBESITY-RELATED HYPOVENTILATION?

Introduction Obesity Hypoventilation Syndrome (OHS) is conventionally defined by the combination of obesity (BMI >30 kg/m²) and daytime hypercapnia (PaCO₂ >6 kPa, with no other explanation) and sleep-disordered breathing may or may not be included. OHS patients have a higher morbidity, mortality, and health care utilisation compared with non-hypercapnic obese subjects. We hypothesised that in obese patients, even in the absence of a raised daytime PaCO₂, the presence of a raised plasma standard bicarbonate, or base excess (BE, as a biomarker of whole body acid-base balance) would be associated with some well-recognised features of OHS (reduced ventilatory drives to hypoxia and hypercapnia, and nocturnal hypoventilation), thus suggesting they represent ‘early’ OHS.

Methods Obese subjects (BMI >30 kg/m²) were identified from a variety of sources, and divided into those with: 1) normal arterial blood gases and normal acid-base balance, 2) an isolated raised BE (≥2 mmol/L), and 3) awake arterial hypercapnia (>6 kPa, i.e. established OHS). Two-point ventilatory responses to hypoxia (15 min poikilocapnic response to 15% O₂) and hypercapnia (15 min response to 5%CO₂ in O₂) were performed. Derivatives included the fall in SaO₂ and respiratory rate and sleep studies. For nearly all the ventilatory response and sleep study derivatives, group 2 (with only an isolated raised BE) represented a middling group, and for some of the measures this middle group was more similar to group 3, with established OHS, rather than group 1.

Conclusion This study shows that obese individuals with raised BE, but without awake hypercapnia, probably represent an intermediary stage towards overt obesity-hypoventilation syndrome. Further studies will be required to establish if early intervention for this group is beneficial.

SS3 NEURAL RESPIRATORY DRIVE AND SYMPTOMS LIMITING EXERCISE CAPACITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Introduction Obstructive pulmonary disease (COPD) is typically characterized by obstruction and hyperinflation of the lungs, which impair gas exchange and lead to symptoms such as dyspnea and reduced exercise capacity. The neural respiratory drive is a critical factor in determining exercise capacity. Understanding the neural mechanisms that limit exercise in COPD is essential for developing effective therapeutic strategies.

Methods and Results We performed a comprehensive study that included clinical assessments, pulmonary function tests, exercise testing, and polysomnography in a group of patients with stable COPD. The primary outcome was the exercise capacity measured by 6-minute walking distance (6MWD) and the secondary outcomes were respiratory muscle strength, ventilatory drive, and sleep architecture.

Results In patients with COPD, we observed a significant reduction in 6MWD compared to healthy controls. The respiratory muscle strength was also reduced, indicating impaired inspiratory muscle function. Furthermore, we found a decreased ventilatory drive, measured as the slope of the ventilatory response to hypoxic challenge. Polysomnography showed increased sleep disordered breathing (SDB) in this group, with higher apnea-hypopnea index (AHI) scores compared to controls.

Conclusion Our findings suggest that impaired respiratory muscle function and reduced ventilatory drive contribute to the reduced exercise capacity in patients with COPD. Targeted interventions to improve respiratory muscle strength and ventilatory drive may be beneficial in enhancing exercise capacity and quality of life in these patients.

SS4 COMBINED RESPIRATORY AND VASCULAR COME FROM THE SAME SOURCE

Introduction Obesity hypoventilation syndrome (OHS) is a condition characterized by respiratory failure, often due to obstructive sleep apnea, and associated with obesity. However, a significant proportion of patients with OHS do not have sleep apnea, suggesting a possible vascular component.

Methods and Results We conducted a retrospective review of patients with OHS and investigated the association between obesity, arterial elastin degradation, and vascular calcification. We measured plasma desmosine (pDES), a biomarker of elastin degradation, and coronary artery calcium score (CACS), a measure of vascular calcification.

Results We found a significant correlation between pDES and CACS, indicating that obesity and elastin degradation are related to vascular calcification. Furthermore, patients with higher CACS levels had higher pDES levels, suggesting a common underlying mechanism.

Conclusion Our study highlights the importance of considering vascular health in the management of OHS, as interventions targeting vascular disease may improve respiratory outcomes in these patients.