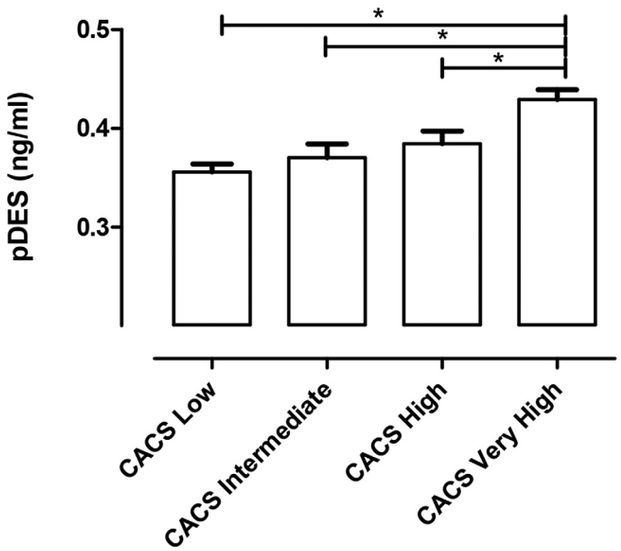

Abstract S51 Figure 1 Differences in pDES between patients with very high CACS and lower CACS levels (* $p < 0.01$)

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, FEV_1 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 FEV_1 ($r = 0.39$, $p < 0.0001$), 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.

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How does clinical respiratory physiology help the clinician?

S52 IS A RAISED BICARBONATE, WITHOUT HYPERCAPNIA, PART OF THE PHYSIOLOGICAL SPECTRUM OF OBESITY-RELATED HYPOVENTILATION?

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Introduction Obesity Hypoventilation Syndrome (OHS) is conventionally defined by the combination of obesity (BMI >30 kg/m^2) and daytime hypercapnia ($PaCO_2$ >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 $PaCO_2$, 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.

Abstract S52 Table 1

Mean and SDs. Ventilatory data averaged over last 5 minutes of each 15 minute challenge	Group 1 Normal $PaCO_2$ and Normal BE (n = 33)	Group 2 Normal $PaCO_2$ and Elevated BE (n = 22)	Group 3 Elevated $PaCO_2$ (OHS) (n = 16)	ANOVA p-value
BMI (kg/m^2)	45.2(9.1)	46.5(7.9)	51.6(11.7)	0.056
$PaCO_2$ (kPa)	5.15(0.47)[a]	5.42(0.32)[a]	6.62(0.91)[b]	<0.001
Base excess (mmol/l)	+0.12(1.38)[a]	+3.01(0.98)[b]	+4.78(2.10)[c]	<0.001
Hypoxic Ventilatory Response Test				
Decrease in $\%SpO_2$	2.50 (1.64)[a]	3.68 (2.07)[b]	5.01 (0.40)[b]	**0.002**
Ventilatory response (l/min/$\%SpO_2$)	2.42(4.48)	0.40(0.41)	0.66(1.20)	0.058
Hypercapnic Ventilatory Response Test				
Rise in end-tidal CO_2 (kPa)	0.73(0.33)	0.65(0.39)	0.80(0.46)	0.14
Ventilatory response to CO_2 (l/min/kPa)	1.57(0.91)	0.87(0.69)	0.70(0.59)	0.50
Sleep Data				
=4% oxygen desaturation index (ODI, events/h)	40.6(26.3)	53.9(44.5)	55.7(40.8)	0.28
Percentage of time spent with $\%SpO_2$<90%	17.3 (19.3)[a]	27.7(28.7)[b]	42.3(34.7)[b]	**0.012**

[a, b, c] grouping of data determined by ANOVA and Duncan's post hoc comparison.

Methods Obese subjects (BMI >30 kgs/m^2) 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 arterial 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% O_2) and hypercapnia (15 min response to 5%CO_2 in O_2) were performed. Derivatives included the fall in SaO_2 and rise in end-tidal CO_2 when stable, and conventional ventilatory drive calculations. Polygraphic sleep studies were done with the derivatives of intermittent (oxygen desaturation index) and prolonged hypoxia (time below 90% SaO_2) reported here.

Results 71 subjects (BMI 47.2, SD 9.8; age 52.1, SD 8.8) were recruited into the above three groups (33, 22, and 16 respectively). The table shows the BMI, $PaCO_2$ and BE for the three groups, along with the selected derivatives of the ventilatory drive measurements 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.

S53 NEURAL RESPIRATORY DRIVE AND SYMPTOMS LIMITING EXERCISE CAPACITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction Exercise capacity in chronic obstructive pulmonary disease (COPD) is limited both by abnormal pulmonary mechanics, reported as breathlessness, and by leg muscle fatigue. To improve functional capacity it is important to understand the primary physiological constraint. Neural respiratory drive (NRD), measured using the diaphragm electromyogram expressed as a proportion of maximum (EMG_{di}%max), quantifies the load on the respiratory muscles imposed by abnormal pulmonary mechanics, and relates closely to breathlessness. We hypothesised that end-exercise EMG_{di}%max would be higher in patients stopping because of breathlessness than in those stopping because of leg fatigue.
Methods EMG_{di}, ventilation (V_E), oxygen consumption (VO_2) and ventilatory reserve (V_E/MVV%) were measured in 23 COPD patients (median (IQR) FEV_1 39 (30.0 to 56.8)%predicted) during exhaustive cycle ergometry. Differences in physiological variables between groups of patients stopping because of breathlessness, leg fatigue or both were examined using 1-way ANOVA.
Results EMG_{di}%max was higher in patients stopping because of breathlessness (n = 12, EMG_{di}%max 75.7 (69.5 to 77.1)%) than in those stopping because of leg fatigue (n = 8, EMG_{di}% max 44.1 (39.4 to 63.3)%, $p < 0.05$). There were no significant differences in end-exercise V_E or VO_2. V_E/MVV% tended to higher levels in the breathless group.
Discussion These results suggest that patients limited by breathlessness due to ventilatory constraints can be identified as those reaching near-maximal levels of NRD during exercise. Measurement of EMG_{di}%max during exercise could prove useful in identifying patients whose functional performance would be best optimised by improving pulmonary mechanics rather than interventions to train peripheral muscle groups.

S54 NEURAL RESPIRATORY DRIVE MEASURED USING PARASTERNAL INTERCOSTAL MUSCLE ELECTROMYOGRAPHY IN PATIENTS WITH INTERSTITIAL LUNG DISEASE

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Introduction Forced vital capacity (FVC) and gas transfer (TLCO) are often used to assess disease severity and monitor progression in patients with interstitial lung disease (ILD). Difficulty in performing the required manoeuvres, particularly in severe disease, and inherent measurement variability makes detection of clinically important changes difficult using these parameters. There is, therefore, a need for new biomarkers in this patient group. Neural respiratory drive (NRD) reflects the load on the respiratory system and the capacity of the respiratory muscles. Parasternal intercostal muscle electromyography (EMGpara) provides a non-invasive measure of NRD which relates to disease severity and breathlessness in obstructive lung diseases. Measurements of EMGpara in ILD could potentially quantify overall disease severity.
Aim The aim of the study was to investigate the relationships between EMGpara, lung function, breathlessness, functional status and quality of life (QoL) in ILD.
Method EMGpara was measured in 45 patients with a range of fibrotic lung diseases using surface electrodes placed in the second intercostal spaces bilaterally. Mean peak root mean square EMGpara per breath was calculated and expressed as a percentage of maximum EMGpara (EMGpara%max). The neural respiratory drive index (NRDI) was derived by multiplying EMGpara%max by the respiratory rate. Spirometry and lung gas transfer were performed and the composite physiologic index (CPI) calculated. Six minute walk test (6MWT) and 4 metre gait speed (4MGS) were used to determine functional status. Health-related quality of life was assessed with the King's Brief Interstitial Lung Disease (K-BILD) and the St George's Respiratory Questionnaires (SGRQ). The Baseline Dyspnea Index (BDI) was used to grade breathlessness.
Results NRDI correlated significantly with VC%predicted (r = -0.36, p = 0.018) and the CPI (r = 0.40, p = 0.01) No significant correlations were found between EMGpara or NRDI and breathlessness, QoL or functional status.
Conclusion EMGpara is a feasible measure in ILD. EMGpara correlates with prognostic markers suggesting potential value as a biomarker integrating important pathophysiological changes in lung mechanics in fibrotic ILDs. The lack of association with QoL measures and BDI requires further investigation.

Abstract S54 Table 1 Patient characteristics, EMGpara%max, NRDI, lung function and functional status in forty-five patients with ILD. Correlation coefficients for the relationship between NRDI and individual variables given (* $p < 0.05$)

Parameter	Median	Range	Correlation with NRDI (r=)
Age (years)	65	35–85	-
BMI	27.5	20.6–40.7	-
FEV_1%predicted	82.5	41 -148	-0.38*
FVC%predicted	83	43–137	-0.36*
TLCO%predicted	48	21–78	-0.25
EMGpara%max (%)	8.1	3.4–20.2	-
NRDI a.u.	148	61–514	-
K-BILD	65	21–100	-0.007
SGRQ	37	2.3–80	-0.74
BDI	6	–11	-0.004
CPI	44	9.8–64	0.40*
6MWD (%predicted)	58	18–130	-0.15
4MGS (m/s)	0.88	0.46–1.95	-0.21

S55 NEURAL RESPIRATORY DRIVE USING PARASTERNAL ELECTROMYOGRAPHY IN CLINICALLY STABLE CYSTIC FIBROSIS PATIENTS: A PHYSIOLOGICAL MARKER OF LUNG DISEASE SEVERITY AND EXERCISE CAPACITY

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Introduction Measurement of neural respiratory drive, using parasternal intercostal muscle electromyography (EMGpara), has previously been shown to relate to pulmonary function impairment and exercise-induced breathlessness in advanced cystic fibrosis (CF). This measure reflects the load on the respiratory system and the capacity of the respiratory muscles and therefore may provide a composite measure of overall lung disease severity. In order to utilise EMGpara clinically in CF, its relationship to standard physiological outcome measures requires further investigation across a broad range of disease severities. Aim: To investigate the relationships between EMGpara and standard measures of pulmonary function and exercise performance in patients with CF.
Methods Thirty patients with clinically stable CF were recruited. EMGpara was recorded during five minutes of tidal breathing using electrodes positioned in the second intercostal space directly lateral to the sternum. Peak EMGpara per breath was averaged over the final minute of the recording and expressed as a percentage of EMGpara recorded during a maximal inspiratory manoeuvre (EMGpara%max). Spirometry, lung volumes by body