physiological index of myocardial reserve and thus at inefficient ratios, may predispose to reduced exercise capacity.

Methods Using RV conductance catheterisation and contemporaneous incremental cardiopulmonary exercise testing, we evaluated Ees/Ea against peak VO_2 in twenty patients with pulmonary vascular disease. Ees/Ea was compared with haemodynamic predictors of exercise capacity obtained from standard right heart catheterisation.

Results Resting Ees/Ea, absolute peak VO_2 and predicted peak VO_2 were 0.86 ± 0.40 , $19.6 \pm 6.7 \text{ ml/Kg/min}$ and $88 \pm 23\%$ respectively. Univariable predictors of absolute peak VO_2 were patient gender, NYHA class, mean right atrial pressure, mean pulmonary artery pressure, cardiac index, conductance RV stroke volume and Ees/Ea (all $p < 0.10$). On bivariate analysis, the predictive value of Ees/Ea improved following adjustment for RV stroke volume ($p = 0.03$) but not for mean RA pressure ($p = 0.21$). Only Ees/Ea related linearly to percent predicted VO_2 ($R^2 = 0.32$, $p = 0.01$). RV diastolic decay ($-dP/dt_{\min}$) showed good correlation with O_2 pulse evolution ($r = 0.62$, $p < 0.01$) although no single haemodynamic parameter differentiated absolute peak VO_2 above and below its median value.

Discussion VA coupling is a marker of RV energetic efficiency and adds to the debate on the multifactorial determinants of exercise capacity in PH. Ees/Ea was comparable to other predictive haemodynamic parameters of exercise capacity and may represent the 'recruitable' myocardial reserve, important for maintaining cardiac output at increased metabolic demand. Ees/Ea may be a potential therapeutic target given the unclear relationship between pulmonary haemodynamics and patient symptoms.

Abstract S48 Table 1. Univariate predictors of exercise capacity expressed by absolute and predicted VO_2 .

	Univariable analysis		Univariable analysis	
	Peak VO_2 ml/Kg/min		Peak VO_2 % predicted	
		P Value		P Value
<i>Clinical</i>				
Age	-0.16	0.50	0.22	0.34
Gender	0.53	0.02	-0.25	0.29
BSA	-0.33	0.16	-0.25	0.30
NYHA Class	-0.62	<0.01	-0.18	0.44
<i>Swan Ganz</i>				
Mean RAP (mmHg)	-0.42	0.06	-0.30	0.21
mPAP (mmHg)	-0.56	0.01	-0.38	0.10
Cardiac Index (L/min/m ²)	0.60	<0.01	0.21	0.38
<i>Conductance</i>				
RVSW	-0.12	0.61	-0.37	0.11
SV	0.39	0.09	-0.08	0.74
Ees (mmHg/ml)	0.06	0.79	-0.18	0.45
Ea (mmHg/ml)	-0.29	0.22	-0.34	0.14
Ca (ml/mmHg)	0.33	0.16	0.14	0.54
Ees/Ea	0.45	0.04	0.56	0.01

values represent standardised Beta coefficients

S49 THE DIAGNOSTIC VALUE OF MEASURING AAG DURING EXERCISE IN PATIENTS WITH PULMONARY HYPERTENSION

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The exercise response in pulmonary hypertension (PH) has characteristic features, including decreased peak oxygen consumption (VO_2 -peak), increased ventilatory inefficiency (VE/VCO₂ slope) and widened alveolar-arterial oxygen-gradient (AaG). We wished to evaluate if the AaG at peak exercise predicted those patients likely to have PH who would subsequently require catheter studies.

Methods We performed a retrospective analysis of patients referred to Hammersmith Hospital between Feb 2008 and Feb 2012 for investigation of Pulmonary Hypertension (PH) who underwent cardiopulmonary exercise testing (CPX) with testing of AaG using arterial blood gas analysis at peak exercise. Patients found to have alternative cardiac or respiratory diagnoses were excluded. Patients given diagnoses of Pulmonary Arterial Hypertension or Pulmonary Hypertension due to Left Heart Disease and with temporally coincident data from CPX and RHC (within 3 months) were included. Patients without cardiorespiratory diagnoses were healthy controls. The VE/VCO₂ slope and AaG were compared to the diagnosis of PH and the trans-pulmonary pressure gradient (TPG), (the difference between mean pulmonary artery pressure (mPAP) and pulmonary capillary wedge pressure (PCWP) or left ventricular end diastolic pressure (LVEDP) where available).

Results Using logistic regression to predict a diagnosis of PH, AaG had an odds ratios of 2.98 ($p < 0.01$) and receiver operating characteristic curve for sensitivity and specificity had area under the curve (ROC-AUC) of 0.92. An AaG cut-off of 2.5kPa had 90% sensitivity and 80% specificity. Similarly, VE/VCO₂ had an odds ratio of 1.21 ($p < 0.01$) and ROC-AUC 0.85 for predicting PH. Combining AaG and VE/VCO₂ had ROC-AUC of 0.94 for diagnosing PH without significant interaction between AaG and VE/VCO₂. For predicting a TPG >12mmHg, AaG had an odds ratios of 4.54 ($p < 0.01$) and ROC-AUC of 0.95. VE/VCO₂ had an odds ratio of 1.10 ($p < 0.01$) and ROC-AUC 0.74 for predicting TPG >12mmHg.

Conclusion CPX has become part of the diagnostic workup of patients with PH. AaG measured at peak exercise has a high sensitivity and specificity in predicting patients with PH, which may help determining which patients will require invasive catheter studies. The AaG provides independent information than VE/VCO₂ alone in predicting PH and may be useful in the investigation of PH.

S50 HYPERSENSITIVITY PNEUMONITIS COMPLICATED BY PULMONARY HYPERTENSION; PATIENT CHARACTERISTICS AND RESPONSE TO TARGETED THERAPY

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Background Hypersensitivity pneumonitis (HP) results from repeated exposure to a sensitizing antigen, normally an organic particle. It can be acute, sub-acute or chronic (1). There is very little literature describing the association of pulmonary hypertension (PH) with HP (2). We aimed to summarize the clinical characteristics and outcomes including responses to targeted therapy in patients with HP and PH in a tertiary referral centre.

Methods Cases diagnosed between 1992 and 2008 were identified through a central database. PH was defined as mean pulmonary artery pressure $\geq 25 \text{ mmHg}$ on right heart catheter or right ventricular systolic pressure of $\geq 50 \text{ mmHg}$ on echocardiogram. Data was collected through case note and electronic record review. Analysis was performed using Graphpad prism.

Abstract S50 Table 1. Demographics of patients with PH and HP.

	n = 19
Age at diagnosis	54 (42, 62) years
Female	14
Duration of disease prior to onset of PH	6 (2, 9) years
Alive	7
Time of onset of PH until time of death	8 (2.8, 20) months
BNP at diagnosis	35 (10.75, 152) pmol/L
RHC	
mPAP	36 (31.25, 44.25) mmHg
PVR	8 (5.3, 11.7) WU
CO	3 (3.1, 5.7) L/min
PCWP/LVEDP	8 (5.2, 13) mmHg
Echo	
RVSP	71 (53, 87) mmHg
TR vel	372 (350, 439) cm/s
PacT	72 (67, 101) ms
PFTs	
FEV1 % predicted	53 (42, 73) %
FVC % predicted	54 (43, 80) %
TLCoc % predicted	25 (18, 27) %
KCOc % predicted	47(31, 63) %
Treatment	
Sildenafil	7
Sildenafil and endothelin antagonist	3

Results Nineteen consecutive patients with PH and HP were identified. Fifteen had chronic HP as evidenced by fibrosis on HRCT, whilst 4 had sub-acute disease. Demographic and baseline findings are listed in table 1. Right ventricular (RV) dysfunction was found in 14 patients. Ten were treated with targeted therapy (sildenafil +/- endothelin receptor antagonist), of these 7 had evidence of RV dysfunction. Median BNP fell between pre and first post sildenafil measurement from 80 to 27 pmol/L but failed to reach statistical significance ($p = 0.11$). RV function improved in 2 of 6 patients with available follow up echocardiogram at a median of 4 months. There was no consistent change in RVSP, TR velocity or pulmonary acceleration time with treatment. Twelve patients died, a median of 8 months (0.2 - 46) from diagnosis of PH. Although not reaching statistical significance, the median arterial pO_2 was higher in survivors (7.25 versus 5.85 kPa; $p = 0.11$).

Conclusion Chronic and sub-acute HP can be complicated by PH. Mortality in this group was extremely high despite targeted therapy. PO_2 was generally lower in those who died. The diagnosis of PH in HP patients may well be a pre-terminal event. Further work is needed to understand which patients may respond to advanced therapies.

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Mechanisms of muscle wasting

S51 KLOTHO IS ASSOCIATED WITH SKELETAL MUSCLE DYSFUNCTION AND OXIDATIVE STRESS IN COPD

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Introduction Klotho is a transmembrane protein; klotho null mice develop sarcopenia and emphysema. We have previously found serum soluble klotho levels to be lower in COPD patients (ATS 2013). We hypothesised that klotho protects against muscle dysfunction by reducing oxidative stress which is a known feature of skeletal muscle dysfunction in COPD.

Aims

1. To relate quadriceps klotho levels to protein carbonylation and muscle strength in COPD patients.
2. To determine the effect of smoking cessation on *vastus lateralis* protein carbonylation and klotho.

Methods In 47 COPD patients (mean FEV₁ 53 (23)%pred), we measured fat-free mass index (FFMI) and quadriceps strength (as QMVC/BMI). Klotho and protein carbonylation were assessed in *vastus lateralis* protein extracts. 7 current smokers (3 with COPD) had measurements before and after successful smoking cessation. Differences were assessed by Mann-Whitney and

Abstract S51 Figure 1. Vastus lateralis Protein carbonylation (left panel) and klotho levels (right panel) in COPD patients A) with (n=12) or without (n=35 reduced FFMI), B) with (n=24) or without (n=23) reduced QMVC/BMI and C) with (n=6) or without (41 reduced FFMI and QMVC/BMI).