Abstract S47 Table 1. Median treatment effects on PVR and CI

	PVR, dyn·sec/cm^5 (relative benefit* to placebo expressed in %)				CI, L/min/m^2			
	Macitentan 3mg	p-value	Macitentan 10mg	p-value	Macitentan 3mg	p-value	Macitentan 10mg	p-value
All	-28.7 (-32.2,-19.2)	<0.0001	-37.4 (-46.3,-26.6)	<0.0001	0.5 (0.3,0.8)	<0.0001	0.6 (0.4,0.9)	<0.0001
Treatment Naïve	-19.9 (-34.2,0.8)	0.06	-40.3 (-52.0,-22.3)	0.0002	0.4 (0.1,0.8)	0.01	0.6 (0.2,1.0)	0.004
Treated	-34.4 (-45.6,-22.3)	<0.0001	-33.3 (-45.6,-20.7)	0.0001	0.6 (0.4,1.0)	<0.0001	0.6 (0.2,1.0)	0.005
FC I/II	-35.2 (-49.2,-21.6)	<0.0001	-46.0 (-57.2,-28.8)	<0.0001	0.5 (0.2,0.9)	0.002	0.7 (0.2,1.1)	0.005
FC III/IV	-21.8 (-37.8,-9.2)	0.002	-29.0 (-43.8,-16.6)	0.0003	0.5 (0.3,0.9)	0.0001	0.6 (0.3,1.0)	0.001

Median (95% CL) placebo-corrected change from baseline and Wilcoxon test p-values; *based on the log of Month 6/baseline values

only chance of cure. Data on the long term survival after PEA are limited.

Method All patients who have undergone a PEA for CTEPH at Papworth hospital were included between January 1997 and November 2012. Patients who had a re-do operation were excluded. Pre- and post-operative data on haemodynamics, exercise capacity, functional class and targeted PAH therapies taken were obtained from our PH database and from other UK PH centres. The long-term survival of patients who returned for follow-up at 3 months post PEA was determined using the NHS spine summary care record tracking system. Overseas patients were censored when last seen.

Results 880 patients underwent PEA over the 15 year period. The mean age was 57 (range 15–84) and 53% were male. The majority (89%) were in WHO functional class 3 or 4 prior to surgery with an average mean pulmonary artery pressure (mPAP) of 47 mmHg and PVR of 795 dynes. 65% of patients were taking at least 1 targeted therapy as a "bridge to surgery". Post surgery the majority of patients (86%) were in WHO functional class 1 or 2 at the 12 month follow-up with only 17% taking targeted therapy. There was a reduction in the average mPAP to 27 mmHg and PVR to 308 dynes by 12 months. The 10 year conditional survival post PEA of the first 314 patients from the cohort (Freed *et al*. J Thorac Cardiovasc Surg, 2011;141:383–7) was 74%.

Conclusion The conditional survival of a subset of the cohort at 10 years was 74%. There was a significant functional and haemodynamic improvement in the majority of patients at 12 months post surgery. Only 17% of patients at 12 months post surgery were being treated with targeted therapy.

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S47 EFFECT OF MACITENTAN ON HAEMODYNAMICS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION: RESULTS FROM THE LONG-TERM, RANDOMISED, PLACEBO-CONTROLLED SERAPHIN TRIAL

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Introduction and objectives Macitentan, a novel dual endothelin receptor antagonist (ERA), significantly reduced morbidity and mortality in pulmonary arterial hypertension (PAH) patients in the SERAPHIN trial (NCT00660179), the first event-driven outcomes trial in PAH. A substudy in SERAPHIN investigated the effect of macitentan on patients' cardiac haemodynamics.

Methods 742 PAH patients were randomised to placebo, macitentan 3 mg, or macitentan 10 mg once-daily. Stable background PAH therapy, except injectable prostanoids and other ERAs, were allowed. At selected centres, patients underwent right heart catheterisation at randomisation and Month 6. Changes from baseline to Month 6 for mean right atrial pressure (mRAP), mean pulmonary arterial pressure (mPAP), pulmonary vascular resistance (PVR), cardiac index (CI) and mixed venous oxygen saturation (SvO_2) were calculated for all patients and stratified in an exploratory analysis for background PAH therapy and baseline WHO functional class I/II vs III/IV. Median treatment effects (95% CL) between placebo and macitentan are reported.

Results 187 patients participated in the substudy (51% were treatment-naïve and 56% in WHO FC III/IV). Baseline median values for all patients on placebo (n = 68), macitentan 3 mg (n = 62) and 10 mg (n = 57) were: mRAP 7.0, 8.0, 7.0 mmHg; mPAP 52.0, 54.0, 52.3 mmHg; PVR 800, 785, 789 dyn·sec/cm^5; CI 2.49, 2.23, 2.47 L/min/m^2; and SvO_2 66.0, 64.5, 66.5%, respectively. Overall, haemodynamic parameters improved at Month 6 with macitentan and worsened with placebo. Beneficial treatment effects with macitentan were statistically significant ($P < 0.05$) for PVR and CI for both subgroups, except for PVR in treatment naïve patients treated with macitentan 3mg (Table).

Conclusions Macitentan significantly improved cardio-pulmonary haemodynamics in PAH patients. Improvements in PVR and CI were consistent irrespective of background PAH therapy and baseline WHO FC.

S48 INEFFICIENT VENTRICULO-ARTERIAL COUPLING CONTRIBUTES TO REDUCED EXERCISE CAPACITY IN PULMONARY HYPERTENSION

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Introduction Ventriculo-arterial (VA) coupling (Ees/Ea) in the right heart is defined by RV end-systolic elastance (Ees) and pulmonary arterial effective elastance (Ea) with Ees/Ea representing the mechanical efficiency of forward flow from the RV. Ees/Ea may influence exercise capacity in pulmonary hypertension (PH) because patients exhibit cardiac limitation at peak oxygen uptake (peak VO_2) and suffer impaired exercise cardiac output adaptation. We hypothesised that Ees/Ea in the RV represents a

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 ± 6.7ml/Kg/min and 88 ± 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
Clinical				
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
Swan Ganz				
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/m2)	0.60	<0.01	0.21	0.38
Conductance				
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 (VO2-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 ≥25mmHg on right heart catheter or right ventricular systolic pressure of ≥50 mmHg on echocardiogram. Data was collected through case note and electronic record review. Analysis was performed using Graphpad prism.