)

functional classes were I/II, III and IV in 7, 21 and 15 patients, respectively. Pulmonary haemadynamic data at rest were mean pulmonary artery pressure 50 mm Hg [43: 58], cardiac index 1.88 L/min/m<sup>2</sup> [1.59: 2.21] and pulmonary vascular resistance of 1067 dyn.s.cm<sup>-5</sup> [779: 1394]. All patients were treated according to international guidelines at diagnosis and at follow up visits. Baseline exercise cardiac index was significantly lower in functional class IV (1.99 [1.53: 3.09]) compared to functional class III patients (2.43 [2.03: 2.85]) and in functional class III compared to functional class III patients (3.28 [2.56: 4.41]) (p=0.024). Exercise cardiac index was also significantly lower in patients with a 6-minute walk distance <360 meters (median) (2.09 [1.58: 2.13] versus 2.59 [2.13: 3.34], p=0.041). In a proportional hazard analysis, exercise cardiac index was the best predictor of death with a hazard ratio of 7.5 (95% confidence interval 2.3: 24.3, p=0.001). Exercise cardiac index is a good predictor of exercise capacity. This variable was also the best survival prognostic factor in our group of patients.

### P2301

# Estimation of right ventricular function in highlanders with high altitude pulmonary hypertension and high altitude cor pulmonale

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Tissue Doppler imaging (TDI) is used as additional approach for diagnosis of right ventricular (RV) dysfunction in PH. But RV function obtained by TDI has rarely been investigated in highlanders.

The aim of the study was to evaluate RV functions in highlanders by TDI. **Methods:** Pulmonary haemodynamics and RV functions were evaluated by TDI and Doppler-ECHO in 48 highlanders at altitude of residency (3200-3800 m). All subjects were divided into the three groups: 1st group (n=20) - patients with high altitude pulmonary hypertension (HAPH). 2nd group (n=8) patients with HAPH and RV hypertrophy. 3rd group (n=20) healthy highlanders. All subjects underwent clinical examination, ECG, spirometry. **Results:** 

Right ventricular function in highlanders estimating by TDI

Parameters	Control	Group I	Group II
PAPsyst, mmHg	31.0±3.2	50.1±3.8*	70.2±7.5*
RVD, cm	$1.6 \pm 0.2$	$2.05 \pm 0.4*$	$2.05 \pm 0.4*$
RVAWT, cm	$0.43 \pm 0.03$	$0.44 \pm 0.03$	$0.65 \pm 0.06^{*#}$
Sm, cm s <sup>-1</sup>	17.1±2.5	$16.6 \pm 4.1$	10.3±1.1*
Ea, cm s <sup>-1</sup>	$14.3 \pm 4.0$	13.1±2.2	7.7±1.3*#
Aa, cm s <sup>-1</sup>	12.1±3.0	17.4±3.1*	$13.9 \pm 2.3^{\dagger}$
Ea/Aa	1.2±0.3	$0.8{\pm}0.1$	$0.6{\pm}0.2^{*{\ddagger}}$

RVD, right ventricular dimension; RVAWT, right ventricular anterior wall thickness; PAPsyst, systolic pulmonary arterial pressure; Sm, peak systolic tricuspid annular velocity; Ea, peak early diastolic tricuspid annular velocity; Aa, peak late diastolic tricuspid annular velocity. \*p=0.001 - compare with control; \*p=0.001, \*p=0.002, \*p=0.02 - compare with 1 group.

**Conclusion:** Thus, the evaluation of peak systolic and diastolic tricuspid annular velocity using TDI revealed RV hypertrophic diastolic dysfunction in HAPH patients and RV systolic dysfunction with pseudonormal diastolic dysfunction in patients with HAPH and RV hypotrophy.

### P2302

# Analysis of the cardiac index-PvO2 relationship during vasodilatation challenge as a prognostic factor in pulmonary arterial hypertension

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**Background:** Mixed venous oxygen pressure (PvO2) is a reflection of the tissue oxygenation state. PvO2 is one of the variables associated to survival in patients with pulmonary arterial hypertension (PAH).

**Objectives:** Investigate if the relationship CI – PvO2 during the vasodilatation challenge (VC) is maintained and whether the type of response has any prognostic implication in PAH patients.

**Methods:** We analyzed the hemodynamic and gasometrical variables at baseline and during the response to the acute VC at right heart catheterization of patients with PAH. According to the results, patients were judged to have an appropriate response (AR) (i.e. higher CI=higher PvO2) or not. The midterm survival in both groups was also analyzed.

**Results:** We studied 42 patients with PAH ( $35\pm5$  years); 75% female. For the drug challenge we used adenosine (n=33) and Iloprost (n=9). Patients with AR (n=31) had a significant correlation CI-PvO2 at baseline and during challenge (r=0.67; and 0.52; respectively, p<0.05). In patients with inappropriate response (IR) (n= 11) the correlation was significant at baseline (r=0.59; p< 0.05) but it was lost during challenge (r=0.2; p=NS). The correlation delta CI-delta PvO2 was positive (r=0.44; p<0.05) for those with AR and it was negative for those with IR (r= -0.5; p<0.05). In a preliminary analysis, 5-year mortality appears higher in those with an IR (27.2 versus 15%)

**Conclusions:** Some patients with PAH have an abnormal tissue oxygenation, which may be uncovered by the analysis of the CI-PvO2 relationship. This finding may be of prognostic significance.

# 262. Physiology of human pulmonary hypertension

### P2300

Role of exercise cardiac index to predict NYHA functional class, 6-minute walk test distance and survival in idiopathic, heritable and anorexigen-associated pulmonary arterial hypertension

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None of the established prognostic factors includes measurement of pulmonary haemodynamics during exercise. In a prospective study, we evaluated the prognostic value of exercise pulmonary haemodynamics.

Forty-three patients (22 women) with an age of 55 years (median) [interquartile range (IQR) 46: 68] were included. Right heart catheterization was performed at rest and during an exercise (10-40 W) in the 43 patients. At diagnosis, NYHA

### Diaphragm function in experimental pulmonary hypertension

Emmy Manders<sup>1</sup>, Nico Westerhof<sup>1</sup>, Anton Vonk-Noordegraaf<sup>1</sup>, Frances de Emily Mandets, 1960 Westernor, 2 and a Volkerworkegraal, 1 and og Man<sup>1</sup>, Coen Ottenheigin<sup>2</sup>. <sup>1</sup> Pulmonology, VU University Medical Centre, Amsterdam, Noord-Holland, Netherlands, <sup>2</sup> Physiology, VU University Medical Centre, Amsterdam, Noord-Holland, Netherlands

Introduction: Recently it was suggested that patients with pulmonary hypertension (PH) suffer from diaphragm dysfunction due to increased loading conditions. In the present study the aim is to determine the contractile strength of the diaphragm muscle in PH and control rats. The extensor digitorum longus (EDL) muscle will serve as a control skeletal muscle.

Methods: PH was induced in Wistar rats by a single injection of monocrotaline (60 mg/kg). The diaphragm and EDL (PH n=5; controls n=5) muscle were excised for determination of in vitro contractile properties. Muscle bundles were treated with a relaxing solution (5°C) containing 1% Triton X-100 to permeabilize membranes. Single fibers were mounted on a single fiber apparatus. Maximum force (Fmax), rate constant of force redevelopment (Ktr), as a measure of the cross bridge kinetics, and calcium sensitivity (pCa<sub>50</sub>) were measured in diaphragm and EDL single muscle fibers

Results: In the EDL muscle no significant differences were found in Fmax and pCa<sub>50</sub>. Ktr was significantly higher in PH fibers: 10.86±0.79 vs 15.09±0.74 (p=0.005). The cross sectional area (CSA) of the fibers measured was significantly decreased in PH fibers: 2563±166.7 vs 1961±88.82 µm<sup>2</sup> (p=0.013)

Preliminary data on the diaphragm muscle (n=2), suggest a decrease of Fmax, Ktr, pCa50 and CSA. Fmax: 128.6±4.48 vs 105.5±7.03 mN/mm<sup>2</sup>, Ktr: 8.995±1.39 vs  $7.601 \pm 0.56, pCa_{50}: 5.780 \pm 0.069 \ vs \ 5.720 \pm 0.058, CSA: 2929 \pm 162 \ vs \ 1700 \pm 130$  $\mu m^2$ 

Conclusions: These data suggest a more pronounced effect of PH on the diaphragm muscle compared to EDL. However, more experiments on the diaphragm muscle and fiber type determination is necessary before final conclusions can be drawn.

### P2304

#### A model-based analysis of the effect of hypoxia on regional pulmonary blood flow

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Hypoxic pulmonary vasoconstriction (HPV) diverts blood from hypoxic regions of the lung, optimising ventilation/perfusion (V/Q) matching and gas exchange. In whole lung hypoxia (i.e. high altitude) HPV becomes less effective but still impacts on gas exchange by redirecting blood flow to regions of higher oxygen partial pressure (PO2). The combination of events leading to this response on a regional level is not well understood and is difficult to investigate experimentally, particularly in humans.

In this study we use a structure-based model to investigate the interacting mechanisms that contribute to regional development of HPV under low inspired PO2 (PiO2) to understand its effect on perfusion redistribution in the pulmonary circulation. The mathematical model couples ventilation (V), perfusion (Q), and gas exchange within a patient-specific anatomical structure. Regional alveolar PO2 (PAO2) is simulated for various levels of PiO2. An empirically-derived model of HPV [J Appl Physiol:1988;64(1):68-77] is included in an existing multi-scale model of the pulmonary circulation [doi:10.1152/japplphysiol.00775.2010] and the resultant blood flow predicted.

During hypoxia pulmonary artery pressure and pulmonary vascular resistance increased exponentially with decrements in PiO2. Regions with lower baseline V/Q had lower predicted PAO2 and hence greater vasoconstriction; blood was therefore redistributed preferentially to the gravitationally non-dependent tissue (decreased gravitational flow gradient), in agreement with experimental measurements in animals. Shear stress in the non-dependent region increased proportionately. The resultant decreased blood flow gradient results in a more efficient V/Q matching.

### P2305

### Association of renal dysfunction with cardiac output and right atrial pressure in pulmonary arterial hypertension

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Background: Pulmonary arterial hypertension is disease of the pulmonary vasculature that results in right ventricular (RV) failure and death. Renal insufficiency is recently identified as a key predictor of mortality in PAH patients [1]. Renal dysfunction is associated with decreased cardiac output (CO) in patients with left heart failure. However, little is known about the mechanisms of renal dysfunction and its association with venous congestion in PAH patients with RV dysfunction. Objectives: To investigate the relationship between CO, right atrial pressure (RAP) and estimated glomerular filtration rate (eGFR) in patients with PAH.

Methods: 74 patients underwent baseline right heart catheterization to determine CO and RAP and blood sampling to calculate eGFR. These measurements were repeated in 30 patients after  $12\pm1$  months of follow-up.

**Results:** Mean age was  $52\pm15$  years and 73% of subjects were female. Mean eGFR was  $88\pm24$  ml/min/ $1.73m^2$ , mean CO was  $5.1\pm1.7$  L/min and mean RAP

was 7.0±5 mmHg. Low eGFR at baseline was associated with low CO (R=0.46; p<.0001) and high RAP (R=-0.20; p=0.042). Multivariate regression analysis showed that CO was an independent determinant of eGFR (p=0.01).

After 1 year follow-up, eGFR remained stable, RAP remained unchanged and CO slightly increased (0.9±2.7 L/min; p=0.045). Changes in eGFR were determined by changes in CO (R=0.45; p=0.011) and RAP (R=-0.370; p=0.031). Multivariate analysis revealed that changes in CO were independently related to changes in eGFR (p=0.043).

Conclusions: CO is the main determinant of renal dysfunction in patients with pulmonary arterial hypertension and RV dysfunction.

**References:** 

[1] Benza et al. Circulation 2010.

### P2306

### Novel method for the estimation of PCWP using CINE cardiac MRI in

patients with pulmonary hypertension Andrew Swift<sup>1,2</sup>, Smitha Rajaram<sup>2</sup>, Robin Condliffe<sup>3</sup>, Helen Marshall<sup>2</sup>, Dave Capener<sup>2</sup>, Judith Hurdman<sup>3</sup>, Charlie Elliot<sup>3</sup>, Jim Wild<sup>2</sup>, David Kiely<sup>3</sup>. <sup>1</sup>Cardiovascular Biomedical Research Unit, NIHR, Sheffield, United Kingdom; <sup>2</sup>Academic Unit of Radiology, University of Sheffeild, Sheffield, United Kingdom; <sup>3</sup>Sheffield Pulmonary Vascular Disease Unit, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Introduction: Several studies question the reliability of pulmonary capillary wedge pressure (PCWP) for accurate assessment of left ventricular end-diastolic pressure (LVEDP). Developing markers that can aid the separation of pre and post capillary pulmonary hypertension (PH) is desirable. Due to the elevated ventricular pressure differential in patients with PH the left ventricle becomes deformed. We hypothesise patients with PH owing to left heart disease (PH-LHD) have proportionately less left ventricular (LV) deformation than patients with IPAH due to raised left sided pressures

Methods: 92 patients underwent MRI and RHC within 48 hours; IPAH (n=34), PH-LHD (n=24) and "no PH" (n=34). Short axis CINE images were acquired on a 1.5T whole body MR scanner using a cardiac gated balanced SSFP sequence. LV deformation was defined in all patients using the measured left ventricular systolic eccentricity index (sEI<sup>m</sup>). Linear regression was used to assess the relationship between sEI and mPAP in patients with PCWP ≤15, thus predicted sEI was derived (sEI<sup>p</sup>) and was calculated for all patients.

Results: sEI<sup>p</sup> values were significantly higher than sEI<sup>m</sup> in patients with PH-LHD. No significant difference was demonstrated between sEI<sup>p</sup> and sEI<sup>m</sup> in patients with IPAH. Patients with PH-LHD demonstrated higher sEIP/sEI<sup>m</sup> values than those with IPAH, p<0.0001. A significant correlation was found between sEIP/sEI<sup>m</sup> and PCWP r=0.64, p<0.0001. Good interobserver agreement was demonstrated, k=0.80

Conclusion: Patients with PH-LHD have proportionately less LV deformation than patients with pre-capillary PH. sEIP/sEIm may be a useful marker for differentiating pre from post capillary PH.

#### P2307

### Contrasting cardiopulmonary responses to incremental exercise in patients with schistosomiasis-associated and idiopathic pulmonary arterial hypertension with similar resting hemodynamic impairment

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Schistosomiasis is the most common cause of pulmonary arterial hypertension (PAH) worldwide. It has been reported that schistosomiasis-associated PAH (Sch-PAH) has better hemodynamic profile at diagnosis and a more benign clinical course as compared with idiophatic PAH (IPAH) [Fernandes, C.J.C.S. et al. JACC 2010; 59:715-20]. We hypothesized that Sch-PAH subjects have better physiological responses to incremental cardiopulmonary exercise test (CPET) than IPAH patients, even at similar resting pulmonary hemodynamic impairment. We performed CPET and hemodynamic study in 8 Sch-PAH and 9 IPAH patients. None of them had received any PAH therapy. There were no significant between-group differences on cardiac index (2.1±0.3 vs 2.4±0.7 L/min, p=0.21), pulmonary vascular resistance (p=0.32) and mean pulmonary artery pressure (p=0.48). However, the peak oxygen uptake (V'O<sub>2</sub>) was greater in Sch-PAH (75±21 vs 54±16%pred, p=0.016), as well as the ratio of increases of V'O<sub>2</sub> to work rate  $(8.2\pm1.1 \text{ vs})$  $6.8\pm1.8$  mL/min/W p=0.024). Also, the slope of the ventilatory response as a function of CO2 output was lower in Sch-PAH (41±4 vs 59±18 L<sup>2</sup>/min<sup>2</sup>, p= 0.04), with a shallower heart rate response for a given change in V'O<sub>2</sub> ( $80\pm21$ vs 123±39 beats.ml/min<sup>2</sup>, p=0.02), and a greater peak oxygen pulse (p<0.05). In conclusion. Sch-PAH patients had better physiological responses to exercise than IPAH subjects at similar resting hemodynamic profile. Our data suggest a more preserved hemodynamic response to exercise in Sch-PAH, that might explain its better clinical course as compared with IPAH.

### Nitric oxide metabolite flux during exercise in pulmonary arterial hypertension

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Introduction: Exercise-induced pulmonary arterial hypertension (PAH) is a clinically important stage in the spectrum of PAH. The pathophysiology of abnormal pulmonary vascular responses to exercise is poorly characterized. Endogenous nitric oxide (NO) is an important mediator of vasodilation and accumulating data suggests impaired NO signaling PAH.

Aims: The objective was to test the hypothesis that changes in stable NO metabolites (NOx) in blood during exercise in patients with resting or exercise-induced PAH would differ from NOx in individuals with normal exercise pulmonary arterial pressures. Patients were selected from a population referred to the MGH Cardiopulmonary Exercise Lab for invasive incremental cardiopulmonary exercise testing with pulmonary and radial artery catheters. Simultaneous samples of arterial (a) and mixed venous (mv) blood at rest, peak exercise, and one hour post-exercise were obtained from 10 patients with PAH (VO2max <85% predicted, Qtmax <80% predicted, PAP >30 mmHg, and PVR >80 dyne s cm^5) and 10 controls (VO2max and Qtmax both >80% predicted). These were analyzed for [NOx] using chemiluminescence. Data are median [interquartile ranges]. Comparisons used the Mann-Whitney test.

**Results:** NOx<sub>mv</sub> increased from rest to exercise in controls (45%, [4, 77], p=0.02), but not in PAH (0%, [-27, 15], p=0.97).



NOx<sub>a</sub> increased in both groups (11% [-2, 26] v 7% [-7, 40], p=0.80). NOx flux [Qtmax × (mv – a [NOx])] in controls was greater than PAH (370% [-100, 4869] v -96% [-460, 6], p=0.04).



There were no differences in [NOx] during recovery.

**Conclusions:** Normal pulmonary vasodilation and recruitment during exercise may be dependent on NOx bioavailability in mixed venous blood.

#### P2309

# Comparing cardiac magnetic resonance imaging in group 1 and group 4 pulmonary hypertension

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**Background and aim:** Pulmonary arterial hypertension (PAH, group 1) and chronic thromboembolic PH (CTEPH, group 4) have different pathophysiology. Our study tested the hypothesis that PAH and CTEPH display different characteristics on cardiac magnetic resonance imaging (CMR).

**Methods:** 46 patients (mean age  $54\pm15$  yrs; 22F) entered the study, namely 23 PAH and 23 CTEPH matched for age and sex. They underwent right heart catheterization and cine and phase-contrast CMR (1.5 T scanner, Siemens) with electrocardiographic gating (delay  $\pm48h$ ).

**Results:** PAH and CTEPH had similar body surface area  $(1.7\pm0.2 \text{ vs } 1.8\pm0.2 \text{ m}^2)$  and similar invasive hemodynamics, including mean pulmonary arterial pressure  $(48\pm14 \text{ vs } 47\pm11 \text{ mmHg})$ , pulmonary vascular resistance  $(9\pm4 \text{ vs } 10\pm4 \text{ wu})$  and right atrial pressure  $(7\pm4 \text{ vs } 7\pm5 \text{ mmHg})$  (each p = ns). PAH and CTEPH had similar ventricular morphology and function, especially RV ejection fraction  $(30\pm13 \text{ vs } 30\pm15\%)$ , RV end-diastolic area  $(34\pm8 \text{ vs } 32\pm9 \text{ cm}^2)$ , left ventricular end-diastolic area  $(26\pm5 \text{ vs } 26\pm7 \text{ cm}^2)$  and area ratio  $(1.3\pm0.3 \text{ vs } 1.3\pm0.4)$  (each

p=ns). Pulmonary artery data were similar, namely pulmonary artery trunk diameter (33±4 vs 33±4 mm), pulmonary artery pulsatility (15±8 vs 18±14%), mean pulmonary flow (4.5±1.8 vs 4.1±1.3 L/min), mean flow velocity (9±4 vs 9±3 cm/sec), acceleration time (94±15 vs 101±14 msec) and ejection time (317±34 vs 315±52 msec) (each p=ns).

**Conclusion:** Age- and sex-matched PAH and CTEPH patients displayed similar values of the classical CMR indices. Although these results need to be confirmed on larger samples, it is suggested that the main CMR data may be interpreted without the need to take into account the PAH vs CTEPH etiology.

### P2310

# The indirect Fick method is an unfeasible method for hemodynamic assessment in pulmonary arterial hypertension patients

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The indirect Fick method (Fick<sup>Ind</sup>) is often used for the hemodynamic evaluation in pulmonary arterial hypertension (PAH). As the Fick<sup>Ind</sup> calculates the cardiac output (CO) assuming physiological VO<sub>2</sub> values, this method might be unfeasible for patients with pulmonary vascular diseases. We evaluated the suitability of hemodynamic data obtained by Fick<sup>Ind</sup> in PAH.

Right heart catheterization was performed in 43 PAH patients (age  $61\pm13$  yrs) and 9 controls. 61% of patients suffered from idiopathic PAH, 30% from PAH associated with connective tissue diseases, the remaining 9% from other forms of PAH. Hemodynamic results obtained by Fick<sup>Ind</sup> were compared to data from the thermodilution (TD) method.

Patients and controls did not differ in age and BSA. No significant difference between heart rates during the different techniques was detected in either group. Mean CO determined by Fick<sup>Ind</sup> (CO<sup>Fick</sup>) was 4.3±1.8 and 4.7±1.2 L/min in PAH patients and controls, respectively. In PAH patients CO by TD method (CO<sup>Thermo</sup>) was consistently higher than CO<sup>Fick</sup> (4.9±2.0 L/min) showing a significant difference (Wilcoxor; p<0.001). In controls CO<sup>Thermo</sup> was 5.4±1.4 L/min (not significant to CO<sup>Fick</sup>). Agreement analysis of CO<sup>Thermo</sup> with CO<sup>Fick</sup> revealed a comparable bias between methods in both groups (0.5±1.1 L/min in patients; 0.65±0.82 L/min in controls) with wider limits of agreement for the patient cohort (-1.6 to 2.6 L/min versus -1.0 to 2.3 L/min in controls). Determination of CO by the Fick<sup>Ind</sup> cannot be used in PAH patients as this method

Determination of CO by the Fick<sup>Ind</sup> cannot be used in PAH patients as this method consequently underestimates CO. It can be suggested that the estimated VO<sub>2</sub> values in use for the calculation of the CO are invalid for PAH patients.

#### P2311

### Incapacity to increase pulmonary blood flow determines 6 minutes walking distance in pulmonary hypertension

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Introduction: Pulmonary hypertension (PH) is a disease of elevated pulmonary artery pressure leading to the inability of the overloaded right ventricle to adapt pulmonary blood flow (PBF) and systemic oxygen delivery to peripheral tissue oxygen demand. 6 minutes walk test (6MWT) is a submaximal, well tolerated but strenuous test regularly used for the assessment of PH functional status and is strongly associated to survival.

Aim: To study the adaptation of PBF during a 6MWT.

**Methods:** We measured heart rate (HR) and PBF with a rebreathing device (INNOCOR) before and directly after a 6MWT in 28 patients with chronic thromboembolic pulmonary hypertension and 8 with pulmonary arterial hypertension. The relation between increase (after – before 6MWT) in PBF ( $\Delta$ PBF) in response to 6MWDistance (6MWD) was plotted and different mathematical model applied to describe the relation (Akaike test).

**Results/Discussion:** The best fitting model is a polynomial cubic model, showing a small and constant  $\triangle PBF$  for patients walking less than 300-350 m but more rise in  $\triangle PBF$  is observed with increased distance.



We notice that the rise in  $\triangle$ PBF occurs at comparable 6MWD that is associated with better survival in PH. The stroke volume (PBF/HR) is not increased whatever the distance covered.

**Conclusions:** Ability to substantially increase PBF determines 6MWD and is dependent on chronotropic response in patient with PH.

### A lower resting heart rate may be prognostically favourable in pulmonary arterial hypertension

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**Background:** A resting heart rate (RHR) over 70 bpm is associated with increased mortality in left heart failure. We investigated the prognostic value of RHR in pulmonary arterial hypertension (PAH).

Methods: We related RHR during baseline right heart catheterisation from PAHpatients to their characteristics and outcomes.

**Results:** Data from 126 PAH (84 females, age  $52\pm17y$ , 70 idiopathic, 27 collagen vascular, 12 congenital heart, 13 HIV, 4 portopulmonal) catheterised from 2000 to 2010 were analysed. Patients were in NYHA II/III/IV (18/67/41), mean 6MWD 384±122 m, RHR 82±14 bpm, mPAP 49±17 mmHg, PVR 826±470 dyn\*s\*m-5, the mean follow-up was 46±35 month under optimal medical treatment. Patients with a RHR  $\leq$  70 bpm had a lower PVR 664±384 vs 887±487 dyn\*s\*m-5 but did otherwise not defer from a RHR > 70bpm. 76% of patients with a RHR  $\leq$  70 bpm were alive after 58±37 months compared to 60% with a RHR > 70 bpm.

Survival in Patients with Pulmonary Arterial Hypertension according to their baseline Resting Heart Rate (n=126)







**Conclusion:** In this cohort we found that baseline RHR might be prognostically important in PAH. The role of RHR in PAH and whether reducing RHR in in analogy to left heart failure should be analysed in larger cohorts.

### P2313

### Effect of healthy ageing on alveolar-capillary recruitment during exercise Bryan Taylor, Alex Carlson, Josh O'Malley, Andrew Miller, Bruce Johnson.

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Ageing is associated with deterioration in the structure and function of the pulmonary circulation with a decrease in alveolar-capillary surface area. We asked whether age-related changes in the pulmonary circulation limit alveolar-capillary recruitment and gas exchange during exercise in healthy older adults. 5 old (OLD;  $66\pm 8$  yr, VO<sub>2max</sub> 140±31% age-predicted) and 8 young adults (YNG; 28±2 yr, VO<sub>2max</sub> 131±17% age-predicted) participated. Lung diffusing capacity for carbon monoxide (DLCO), cardiac output (Q), pulmonary capillary blood volume (Vc) and membrane diffusing capacity (Dm) were measured via a rebreathe method at rest and during cycle exercise via pulse oximetry. At rest, DLCO, Vc, and Dm were lower in the OLD vs. the YNG group (22.3 $\pm$ 5.8 vs. 29.6 $\pm$ 4.7 ml/min/mmHg, 70 $\pm$ 26 vs.102 $\pm$ 48 ml, 35.2 $\pm$ 7.9 vs. 46.6 $\pm$ 12.3 ml/min/mmHg, *P*<0.05). However, DLCO increased linearly with exercise intensity in both groups with no plateau or change in slope in DLCO with increasing Q (Fig. 1). Vc and Dm also increased with progressive exercise in both groups (Fig. 1). SaO<sub>2</sub> did not change during exercise in either group.



Figure 1. DLCO, Vc and Dm vs. Q in healthy old (OLD) and young (YNG) adults

These data suggest that the age-associated changes in the pulmonary circulation do not impair alveolar-capillary recruitment and gas exchange during exercise in healthy older adults. NIH HL71478

### P2314

# Right heart volume load response in patients with chronic thromboembolic pulmonary hypertension (CTEPH)

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Aim: To assess the influence of volume load on right heart hemodynamics in pts with moderate and severe CTEPH.

Patients and methods: 20 patients (mean age -  $47\pm11$ , 15 males and 5 females). The 1 group consisted of 9 pts with PAP $\leq$ 30 mm Hg, the 2 group - 11 pts with PAP>30 mm Hg. Right ventricular end-diastolic volume and ejection fraction were evaluated by thermodilution method [Lichtwarck-Aschoff, 2002]. **Results:** Results are summarized in the following table.

	Stages	$PAP \leq 30$	PAP > 30
RVEDVI, ml/m <sup>2</sup>	1	115±15.1	172±18,7
	2	$145 \pm 16.1$	$183 \pm 26,7$
RVEF, %	1	$37.9 \pm 3.75$	20.8±3.15 <sup>a</sup>
	2	37.4±2.75	22.2±3.73ª
CI, 1 min/m <sup>2</sup>	1	$3.00 \pm 0.16$	$2.38 \pm 0.25$
	2	$3.49 \pm 0.24$	$2.40{\pm}0.26^{a}$
PVRI, dyn s sm <sup>-5</sup> /m <sup>2</sup>	1	$113 \pm 18.0$	771±203
	2	158±27.5	$709 \pm 222$
RVEDVI1/2*RVEFI1/2*PAP1/2	1/2	0.80*1.00*0.8	1.01*0.97*0.95
RVSWI1/2	1/2	$0.67 \pm 0.05$	$0.95{\pm}0.05^{a}$

 $\label{eq:stages: 1-before volume load, 2-after rapid infusion of 400 ml of the saline. PVRI-pulmonary vascular resistance index. ^Statistically significance (p<0.05) between groups.$ 

After volume load: The difference in RVEDVI between the groups was not significant. The difference in CI between the groups became significant. This confirmed that there was no increase in CI in group 2. The increase of CI in group 1 was accompanied by PVRI rise. PVRI in group 2 remained high. Right ventricle stroke work dynamic (RVSWI1/2) indicated the presence of diastolic reserves of the RV in moderate CTEPH.

**Conclusion:** There are two main haemodynamic consequences in CTEPH: RV systolic dysfunction due to afterload increase and diastolic impairment as a response to volume load leading to RVEF decrease. The severity of right heart changes could be used in preoperative risk stratification in CTEPH patiens.

# Right ventricular afterload and myocardial oxygen demand during exercise in pulmonary hypertension

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**Background and aim:** In pulmonary hypertension (PH), the increased afterload leads to an increase in right ventricular (RV) myocardial oxygen demand. The RV mean systolic ejection pressure (Pms) and the RV systolic pressure time integral (SPTI) have been proposed as valuable estimates of RV afterload and myocardial oxygen demand, respectively. Our study documented the correlates of Pms and SPTI in PH patients.

Material and methods: Eleven PH patients (mean pulmonary artery pressure mPAP =  $57\pm10$  mmHg) were studied, namely 6 arterial PH and 5 chronic thromboembolic PH. They underwent high-fidelity right heart catheterization at rest and on mild exercise (cycling) while supine. The workload was increased stepwise up to 60W and three-to-six hemodynamic points were obtained. The Pms was calculated as the pulmonary artery pressure (PAP) averaged over the systolic duration, i.e., from end-diastole to dicrotic notch. The SPTI was the Pms times the systolic period product.

**Results:** The full data set consisted of 46 hemodynamic points. The Pms ranged from 60 to 117 mmHg and was related to systolic PAP (sPAP,  $r^2 = 0.99$ ), mPAP ( $r^2 = 0.97$ ) and PA pulse pressure ( $r^2=0.86$ ) (each P < 0.05) but not to systolic duration. The Pms matched 80% sPAP (bias =  $0\pm 2$  mmHg). The SPTI ranged from 15.7 to 32.3 mmHg.sec and was related to PA pulse pressure ( $r^2=0.80$ ), sPAP ( $r^2=0.67$ ), mPAP ( $r^2=0.46$ ) and systolic duration ( $r^2=0.22$ ) (each P < 0.05).

**Conclusion:** In PH patients performing mild exercise, RV afterload (Pms) was related to the steady component of arterial load (mPAP, sPAP) while the RV myocardial oxygen demand (SPTI) was mainly related to the pulsatile component of arterial load (pulse PA pressure).

### P2316

### Effects of interval exercise on cigarette smoke-induced right ventricular dysfunction in mice

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**Background:** Right ventricular heart failure in COPD is thought to be a result of pulmonary hypertension due to increased pulmonary vascular resistance. Exercise, and especially interval training has been shown to be effective in improving left ventricular function, but the same is not shown for right ventricular function in COPD. The goal of this study was to examine the effects of aerobic interval training on cigarette smoke-induced right ventricular heart dysfunction in a mouse model for COPD.

**Methods:** 42 female A/J-OlaHsd mice were exposed to either cigarette smoke (CS) or fresh air (FA), for 14 weeks, 6 hours/day, 5 days/week. For the next four weeks they were either kept sedate (Se) or put through interval treadmill running (IT) for 1 hour/day, 5 days/week. After this period the mice were sedated with light isoflurane anaesthesia and the heart function was evaluated with echocardiography. Tricuspid annular plane systolic excursion (TAPSE) was used as a measurement of right ventricular function. **Results:** 

	Mean VO2max (mL/kg <sup>0,75</sup> /min)	Mean TAPSE (mm)
FA-Se	32,1	0,71
FA-IT	40,5	0,82
CS-Se	32,9	0,46
CS-IT	41,6	0,75

Maximal oxygen uptake was higher for the IT groups compared to the Se groups (p<0,05). TAPSE was reduced for the CS-Se group compared to all other groups (p<0,001). There were no significant difference between the CS-IT group and the FA-Se group (p=0,35). The FA-IT group had significantly increased TAPSE compared to the FA-Se group (p<0,05), but not the CS-IT group (p=0,2).

**Conclusion:** Smoke exposure of A/J-OlaHsd mice causes a significant reduction in right ventricular function measured by echocardiographic TAPSE. This reduction seems to be normalized by intensive interval training.

#### P2317 Right ventricular diastolic stiffness in idiopathic pulmonary arterial hypertension

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Introduction: Idiopathic pulmonary arterial hypertension (iPAH) is a fatal disease with grim prognosis due to subsequent development of right heart failure (RHF). Findings in experimental pulmonary hypertension models suggest RHF is associated with increased diastolic stiffness.

**Objective:** This study investigates whether right ventricle (RV) diastolic stiffness is increased in iPAH patients.

**Methods:** Right heart catheterization (RHC) and MRI were performed in 28 patients suspected with iPAH. Based on pulmonary artery pressure, patients were divided into controls (7) and iPAH (21). Diastolic elastance (diastolic stiffness), was quantified by the slope of diastolic pressure-volume relation, constructed by plotting RV end-systolic volumes and begin-diastolic pressures against RV end-diastolic ressures. Subsequently, we investigated whether diastolic elastance was associated with disease severity by comparing patients with lower RV stoke volumes (RVSV) and patients with higher RVSV.

**Results:** Diastolic elastance was significantly altered in iPAH (iPAH  $0.25\pm0.04$  vs. Con  $0.07\pm0.006$ , p=0.024). In addition, patients with lower RVSV had significantly higher diastolic elastance (LowSV $0.38\pm0.05$  vs HighSV  $0.114\pm0.02$ ).



**Conclusion:** This study demonstrates that RV diastolic stiffness is increased in iPAH-patients and is associated with disease severity. In future studies we will investigate the prognostic relevance of these changes.

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