

## Online Data Supplement

Supplemental Table 1 – Clinical characteristics and gas exchange variables according to aetiology of pulmonary hypertension

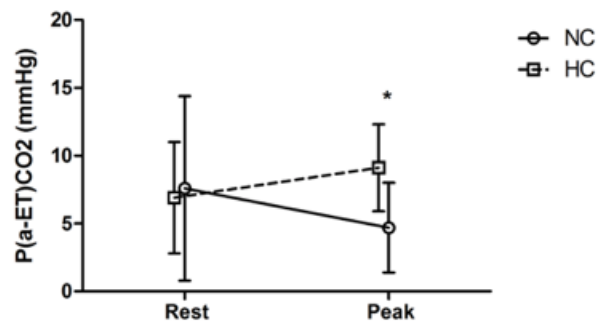
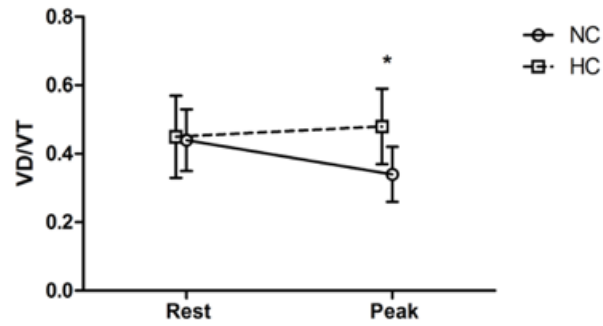
	PAH (n=34)	CTEPH (n=19)	PVOD (n=6)	p- value
Age (y)	39 (29-45)	63 (48-70)	23 (23-26)	0.001
Female Sex	21 (62%)	11 (58%)	1 (17%)	NS
BMI (kg/m <sup>2</sup> )	24 (21.6-28)	25 (24-28.1)	20.5 (20-21)	0.002
NYHA				
I	12 (35%)	2 (11%)	0 (0%)	0.03
II	17 (50%)	9 (47%)	2 (33%)	
III	5 (15%)	7 (37%)	4 (67%)	
6MWT (m)	553±97	439±93	521±80	0.01
mPAP (mmHg)	49±14	47±12	43±8	NS
PAWP (mmHg)	9±3	9±4	8±3	NS
CI (L/min/m <sup>2</sup> )	3.7±0.7	2.6±0.5	3.3±2	<0.01
PVR (Wood units)	6.5±2.7	8.5±3.6	5.7±1.2	<0.01
D <sub>L</sub> CO (%pred)	73±15	73±12	31±3	<0.01
V <sub>E</sub> /V <sub>CO<sub>2</sub></sub> slope	44 (37-50)	68 (55-79)	52 (47-54)	<0.01

V'O <sub>2</sub> peak (mL/kg/min)	19.2±4.4	14.8±3.8	15.2±0.4	<0.01
VO <sub>2</sub> peak (%pred)	60.3±14.5	58.4±19.8	33±4.3	<0.01
PaO <sub>2</sub> rest	83.5±11.2	69.0±8.8	71.6±7.9	<0.01
PaO <sub>2</sub> peak	78.0±14.4	61.9±10.8	43.1±3.8	<0.01
PaCO <sub>2</sub> rest	32.9±4.1	30.6±3.5	30.1±2.2	NS
PaCO <sub>2</sub> peak	30.5±3.8	29.0±4.5	26.6±2.9	NS
V <sub>D</sub> /V <sub>T</sub> rest	0.40±0.09	0.50±0.11	0.54±0.07	<0.01
V <sub>D</sub> /V <sub>T</sub> peak	0.35±0.09	0.54±0.08	0.50±0.06	<0.01
P <sub>(a-ET)</sub> CO <sub>2</sub> rest	6.0±5.7	9.5±3.8	6.1±3.4	0.048
P <sub>(a-ET)</sub> CO <sub>2</sub> peak	5.4±2.9	11.0±3.0	8.7±1.9	<0.01
P <sub>ET</sub> CO <sub>2</sub> max	30.6±4.9	22.2±5.5	23.8±2.7	<0.01

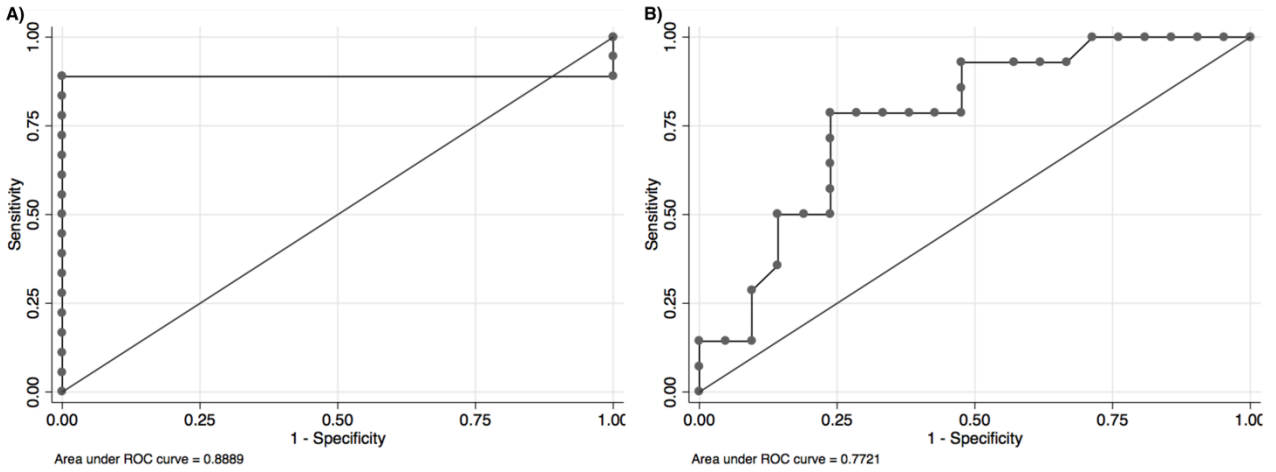
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Abbreviations: BMI – body mass index; PAH – pulmonary arterial hypertension; CTEPH – chronic thromboembolic pulmonary hypertension; PVOD – pulmonary veno-occlusive disease; NYHA – New York Heart Association functional class; 6MWT – 6-minute walk test distance; mPAP – mean pulmonary arterial pressure; PAWP – pulmonary artery wedge pressure; CI – cardiac index; PVR – pulmonary vascular resistance; D<sub>L</sub>CO/V<sub>A</sub> – diffusion capacity for carbon monoxide adjusted for alveolar volume; Hg – haemoglobin; V<sub>E</sub>/V<sub>CO<sub>2</sub></sub> – minute ventilation/carbon dioxide output; V'O<sub>2</sub> peak – oxygen consumption at peak exercise; V<sub>D</sub>/V<sub>T</sub> – physiologic dead space fraction; P<sub>(a-ET)</sub>CO<sub>2</sub> – arterial-end-tidal PCO<sub>2</sub> difference; P<sub>(ET-a)</sub>O<sub>2</sub> – end-tidal-arterial PO<sub>2</sub> difference; P<sub>ET</sub>CO<sub>2</sub> max – end-tidal PCO<sub>2</sub> maximal value.

Supplemental Figure 1 - Rest to Peak VD/VT and Rest-to-Peak P(a-ET)CO<sub>2</sub> according to resting PaCO<sub>2</sub>. VD/VT and P(a-ET)CO<sub>2</sub> are similar at rest in patients with resting hypocapnia (HC) and normocapnia at rest (NC). At peak exercise, VD/VT does not change and P(a-ET)CO<sub>2</sub> increases in HC patients, whereas VD/VT and P(a-ET)CO<sub>2</sub> decrease in NC patients. \*p<0.05 HC vs NC.



Supplemental Figure 2 - Receiver operating characteristic curves for detecting a peak  $\dot{V}O_2$  value  $>15$  mL/kg/min according to maximal  $P_{ET}CO_2$  in A) patients who were normocapnic at rest ( $PaCO_2$  35-45 mmHg) and B) patients who were hypocapnic at rest ( $PaCO_2 \leq 34$  mmHg).



Supplemental Figure 3 - Peak exercise work rate versus  $V_D/V_T$  at peak exercise,  $P_{(a-ET)CO_2}$  at peak exercise and maximal  $P_{ETCO_2}$  ( $P_{ETCO_2}$  Max) in patients with resting hypocapnia (HC) and resting normocapnia (NC).

