

Online Data Supplement

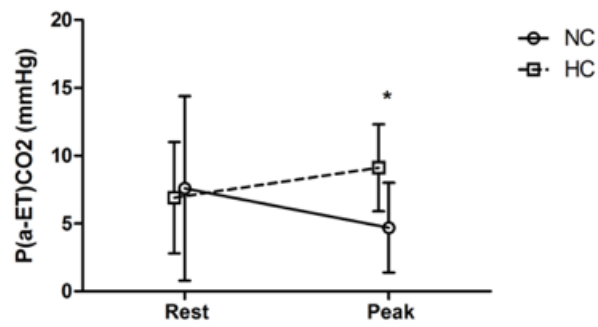
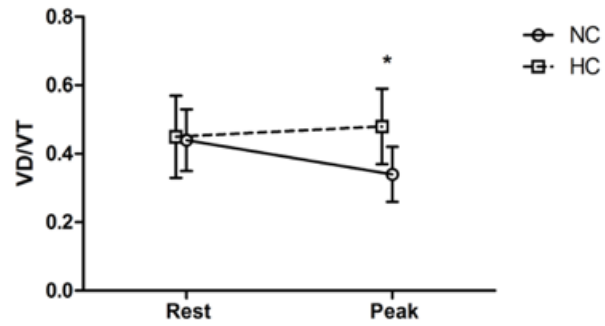
Supplemental Table 1 – Clinical characteristics and gas exchange variables according to aetiology of pulmonary hypertension

	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 ²)	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 ²)	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 _L CO (%pred)	73±15	73±12	31±3	<0.01
V _E /V _{CO₂} slope	44 (37-50)	68 (55-79)	52 (47-54)	<0.01

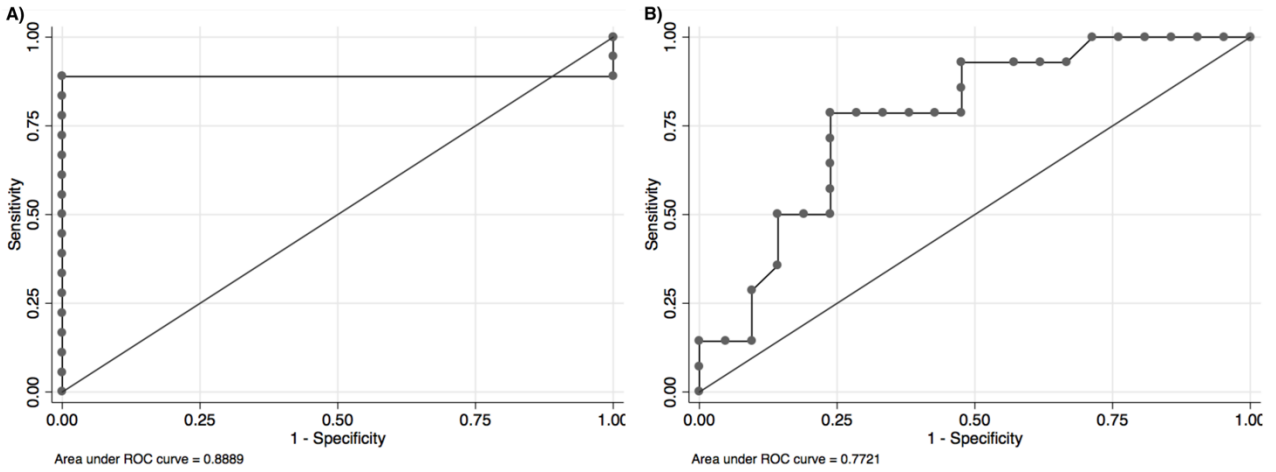
V'O ₂ peak (mL/kg/min)	19.2±4.4	14.8±3.8	15.2±0.4	<0.01
VO ₂ peak (%pred)	60.3±14.5	58.4±19.8	33±4.3	<0.01
PaO ₂ rest	83.5±11.2	69.0±8.8	71.6±7.9	<0.01
PaO ₂ peak	78.0±14.4	61.9±10.8	43.1±3.8	<0.01
PaCO ₂ rest	32.9±4.1	30.6±3.5	30.1±2.2	NS
PaCO ₂ peak	30.5±3.8	29.0±4.5	26.6±2.9	NS
V _D /V _T rest	0.40±0.09	0.50±0.11	0.54±0.07	<0.01
V _D /V _T peak	0.35±0.09	0.54±0.08	0.50±0.06	<0.01
P _(a-ET) CO ₂ rest	6.0±5.7	9.5±3.8	6.1±3.4	0.048
P _(a-ET) CO ₂ peak	5.4±2.9	11.0±3.0	8.7±1.9	<0.01
P _{ET} CO ₂ max	30.6±4.9	22.2±5.5	23.8±2.7	<0.01

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_LCO/V_A – diffusion capacity for carbon monoxide adjusted for alveolar volume; Hg – haemoglobin; V_E/V'CO₂ – minute ventilation/carbon dioxide output; V'O₂ peak – oxygen consumption at peak exercise; V_D/V_T – physiologic dead space fraction; P_(a-ET)CO₂ – arterial-end-tidal PCO₂ difference; P_(ET-a)O₂ – end-tidal-arterial PO₂ difference; P_{ET}CO₂ max – end-tidal PCO₂ maximal value.

Supplemental Figure 1 - Rest to Peak VD/VT and Rest-to-Peak P(a-ET)CO₂ according to resting PaCO₂. VD/VT and P(a-ET)CO₂ 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)CO₂ increases in HC patients, whereas VD/VT and P(a-ET)CO₂ 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).

