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Title: Pulmonary vascular reactivity in pulmonary hypertension due to left heart disease

Dr. Christian 32759 Gerges christian.gerges@meduniwien.ac.at MD ¹, Dr. Mario 32760 Gerges mario.gerges@meduniwien.ac.at MD ¹, Ms. Marie 32761 Lang langm2@univie.ac.at ¹, Prof. Dr Julia 32762 Mascherbauer julia.mascherbauer@meduniwien.ac.at MD ¹ and Prof. Dr Irene 32763 Lang irene.lang@meduniwien.ac.at MD ¹. ¹ Department of Internal Medicine II, Division of Cardiology, Medical University of Vienna, Vienna, Austria, 1090 .

Body: **PURPOSE:** Pulmonary hypertension (PH) due to left heart disease (LHD) is the most common subset of PH. It is defined by an increase of mean pulmonary artery pressure (mPAP) ≥ 25 mmHg in the presence of a mean pulmonary capillary wedge pressure (mPCWP) > 15 mmHg. In the current guidelines PH due to LHD with a TPG > 12 mmHg is labeled as “out-of-proportion” PH, as opposed to what is labeled as “passive” PH. Recent data have shown that patients with “out-of-proportion” PH and a diastolic pulmonary vascular pressure gradient (DPG) ≥ 7 mmHg have an increased mortality and significant pulmonary vascular disease. We hypothesize that these patients may benefit from vasodilator treatment. The aim of this study was to compare the degree of acute vasoreactivity to inhaled nitric oxide (NO) in “out-of-proportion” PH with a DPG ≥ 7 mmHg to that of “passive” PH and “out-of-proportion” PH with a DPG < 7 mmHg. **METHODS:** A prospective data set of 94 patients with PH due to LHD undergoing first diagnostic right heart catheterizations at rest and after inhalation of 40 ppm NO was analyzed. 31 patients were classified as “passive” PH, 28 as “out-of-proportion” PH with a DPG < 7 mmHg and 35 as “out-of-proportion” PH with a DPG ≥ 7 mmHg. **RESULTS:** The strongest decrease of mPAP was observed in patients with “out-of-proportion” PH and a DPG ≥ 7 mmHg (-5.1 ± 4.7 mmHg, $p < 0.001$). In contrast there was no significant change in mPAP in patients with “out-of-proportion” PH and a DPG < 7 mmHg (-2.2 ± 5.9 mmHg, $p = 0.075$). In “passive” PH mPAP did not change upon NO inhalation. **CONCLUSION:** DPG identifies patients with “out-of-proportion” PH who have significant pulmonary vascular disease that is reactive to inhaled NO.