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Title: End-tidal CO2 pressure may facilitate differential diagnostics between PH patients with chronic heart or lung disease and CTEPH

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Body: Background: End-tidal CO₂ pressure (PETCO₂) is a simple parameter, which may be assessed at rest or during exercise during cardiopulmonary exercise testing (CPET). PETCO2 changes have been described in patients with cardiac failure and acute pulmonary embolism, as well as in pulmonary hypertension (PH), but it is not known if PETCO2 may be helpful in differentiating between PH subgroups. Patients and Methods: We retrospectively investigated PETCO₂ data of patients with a meanPAP >25 mmHg at rest, due to chronic left heart (LH-PH), and pulmonary disease (Lu-PH) or CTEPH. PETCO2 was measured at rest and during maximal exercise. Mean values were compared by ANOVA and multiple comparisons were performed with Scheffé equation as post hoc test. Results: N= 46 patients were included (LH-PH: n= 14, mean PAP 40±11 mmHg, PVR 327±188 dyn s cm⁻⁵, PAWP 21±5 mmHg; Lu-PH: n=15, meanPAP 34±8 mmHg, PVR 441±266 dyn s cm⁻⁵, FEV1%pred. 63±27; CTEPH: n=17, meanPAP 46±11mmHg, PVR 732±308 dyn s cm⁻⁵). PETCO₂ at rest was 4.97±1.04 mmHg, 4.70±1.19 mmHg, and 3.55±0.71 mmHg in LH-PH, Lu-PH and CTEPH patients. The PETCO2 difference between LH-PH and CTEPH was 1.38 (CI 95% 0.48 to 2.29 p=0.001), and between Lu-PH and CTEPH 1.14 (CI 95% 0.24 to 2.04 p=0.007). Comperable similar results were obtained with PETCO₂ during maximal exercise. Conclusion: PH caused by CTEPH is characterized by lowered PETCO₂ as compared to PH due to chronic heart or lung disease.