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Title: The sPAP/VO2 ratio during cardiopulmonary exercise testing as predictor of manifest pulmonary hypertension

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Body: Background: Pulmonary hypertension (PH) is characterised by an inappropriate increase of pulmonary artery pressure (PAP) compared to cardiac output. We evaluated the systolic PAP (sPAP) during cardiopulmonary exercise test (CPET) in relation to maximum oxygen uptake (VO2max) as surrogate for cardiac output. Patients and Methods: We evaluated the sPAP/VO2max ratio in respect to presence or absence of PH. We retrospectively analysed right heart catheters studies (RHC) during CPET in 387 patients referred for workup of PH. We prospectively validated the ratio in 52 patients with normal echocardiography at rest, who underwent echocardiography during CPET followed by RHC. Results: In the retrospective study, a manifest PH was found in 97 patients (69 precapillary PH, 28 postcapillary PH). The sPAP/VO2max ratio was mean 2,13 (SD 1,29) in both groups. In 204 patients an exercise induced pulmonary hypertension (eiPH, mPAP > 30 mm Hg at maximum exercise) was diagnosed (96 precapillary eiPH, 108 postcapillary eiPH). The sPAP/VO2 max ratio was 1,25 (0,80) in both groups. In 86 patients with normal pulmonary circulation at rest and during exercise the sPAP/VO2max ratio was 0,97 (0,67). ANOVA revealed highly significant differences of sPAP/VO2max ratio between the groups. The ROC analysis revealed a cut-off value of 0,61 with a sensitivity of 0,94 and specificity of 0,28 to detect manifest PH. Prospectively, in 52 patients a sPAP/VO2max ratio < 0,61 at echocardiography during CPET could exclude manifest PH with a sensitivity of 100%. Conclusion: A sPAP/VO2max can be measured by echocardiography during CPET. A ratio < 0.61 excludes manifest PH with a negative predictive value of

100%.