The relationship between right ventricle-arterial coupling and cardiac metabolism in pulmonary arterial hypertension - multimodal study.

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Background
Right ventricular (RV) function is a major determinant of survival in patients with pulmonary arterial hypertension (PAH). The concept of coupling mainly refers to the relationship between ventricular contractility and afterload. In advanced PAH, to maintain cardiac output, RV dilates and the uncoupling occurs with wall stress and increased metabolic demand. We previously confirmed that impaired RV function is associated with increased glucose uptake of RV myocytes estimated by PET, which marks patients with worse prognosis.

Purpose
Whether echocardiographic approach of coupling parameters in PAH patients has relationship with RV metabolic alterations.

Methods
Twenty-six stable PAH patients (mean age 49.92±15.94 years) and sixteen healthy subjects (control group) were enrolled into the study. The TAPSE, reflecting RV contractility, was obtained by mono-dimensional echo in standard technique. The echo estimation of the sPAP was reflecting RV afterload. Ventricular-arterial coupling was evaluated by the ratio between those two parameters. All PAH patients had also right heart catheterization (RHC) and PET performed during baseline visit. Heart glucose metabolism was assessed with fluorodeoxyglucose (FDG) as a tracer in PET. Its uptake was quantified as mean standardized uptake value (SUV) for both left ventricle (LV) and RV. Mean follow-up time of this study was 16.6±7.5 months and the clinical end-point (CEP) was defined as death or clinical deterioration.

Results
Most of enrolled patients were in the WHO functional Class III (61%, 16). There were significant correlations between echo-derived hemodynamic parameters and RHC-derived values e.g. emPAP vs mPAP (RHC), r=0.86, p<0.001. Echo-estimated RV ventricular-arterial coupling parameter (TAPSE/sPAP) was 0.35±0.20 in PAH group and 1.51±0.22 in control group, p<0.001. Mean SUV RV/LV ratio was 1.03±0.68 in PAH group and 0.19±0.08 in controls, p<0.005. Echo-derived TAPSE/sPAP significantly correlated with hemodynamic parameters from RHC – cardiac output and pulmonary vascular resistance. Interestingly, we also observed significant correlations of TAPSE/sPAP with glucose uptake in PET - SUV RV as well as with SUV RV/LV (r=-0.63, p=0.0006; r=-0.50, p=0.0009), confirming higher metabolic demand in uncoupled heart in case of PAH. Furthermore, patients who reached CEP (n = 15, 57%) had a significantly lower TAPSE/esPAP ratio (0.29±0.17 vs 0.43±0.21, p=0.04) and higher SUV RV/LV (1.39±0.79 vs 0.55±0.45, p=0.01). ROC analysis revealed significant cut-off value of TAPSE/esPAP in predicting CEP (AUC 0.72 (95% CI 0.52-0.92), p=0.03). Patients with TAPSE/esPAP lower than 0.25 mm/mmHg had worse prognosis, log-rank test, p=0.001 (Figure 1).

Conclusions
Simple echocardiographic parameter reflecting RV coupling (TAPSE/esPAP) related to altered myocardium metabolism in PAH may predict outcome in patients with PAH.
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