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Title: The proANP increase during exercise may predict the PAP increase in connective tissue disease patients at risk of PAH

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Body: Background: Natriuretic peptides (brain natriuretic peptide (BNP) and atrial natriuretic peptide (ANP)) are produced in cardiomyocytes of different myocardial regions. In case of dilation of the heart, BNP and ANP are excessivly released into the circulation. BNP is used as a biomarker in patients with chronic heart failure and pulmonary hypertension (PH). ANP is a marker of acute cardiac stress and may reflect actual hemodynamic changes during exercise. In connective tissue disease (CTD) an excessive increase of pulmonary pressure may represent an early stage of pulmonary vascular disease and may be clinically relevant. Patients and Methods: We investigated plasma levels of proANP and NTproBNP during right heart catheterization at rest and exercise in patients with CTD without PH. The levels at rest and during exercise were compared by Wilcoxon signed rank test. The correlations between the changes of meanPAP and NTproBNP as well as meanPAP and proANP were calculated by Spearman's test. Results: N=47 patients (resting meanPAP: 16±3 mmHg, meanPAP at maximal exercise: 37±8 mmHg) were included. NTproBNP and proANP significantly increased from rest to exercise (NTproBNP rest: 91±102 pg/mL, max. exercise: 96±96 pg/mL, $p<0.001$; proANP rest: 2.43 ±1.22 pg/mL, maximal exercise: 2.92±1.33 pg/mL, $p<0.001$). The increase in proANP levels between rest and maximal exercise significantly correlated with the increase in meanPAP ($p= 0.007$, $r= 0.404$), but there was no significant correlation for NTproBNP ($p=0.606$). Conclusion: Our results suggest that the exercise induced increase of proANP in patients with connective tissue disease may indicate the exercise-induced increase in PAP.