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Distinct patterns of functional right ventricular adaptation to experimental right ventricular pressure vs volume overload

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Introduction: Right ventricular failure due to chronic abnormal loading conditions is a pivotal determinant of prognosis in congenital heart disease. However very little is known about the functional and biomolecular response of the right ventricle (RV) to abnormal pressure- or volume loading and consequently RV-specific treatment is lacking. Our objective was to define the RV response to abnormal loading in terms of systolic and diastolic function and hypertrophy development.
Methods: Wistar rats were subjected to either chronic RV pressure load by pulmonary artery banding (PAB), or chronic RV volume load by aorto-caval shunt (ACS). After 4 weeks, RV pressure-volume measurements were performed.Data are presented as mean±SEM.
Results: PAB resulted in marked pressure load (banding gradient 76±22mmHg) and ACS in marked volume load: cardiac output increased by 54%. All data in the table, see the figure for pressure-volume loops.Though different in nature, the absolute severity of loading appeared equal in both models (Strokework PAB vs ACS=ns). Also, hypertrophy development was equal in PAB and ACS. The classic key genes of hypertrophy regulation (NPPA, NPPB, MCIP) were upregulated in both models, but expression tended to be higher in PAB. The same was true for beta-to-alpha MHC isoform-switch. The haemodynamic responses however were very distinct: Pressure loading led to increased contractility as measured by endsystolic elastance, but insufficient to maintain cardiac output and ejection fraction. Additionally, diastolic function was impaired as indicated by enddiastolic elastance and tau and there was marked dilatation (endsystolic volume).Volume loading resulted in no changes in endsystolic elastance. Diastolic parameters were unchanged whereas the ventricles were significantly dilated.
Conclusions: In this study of experimental RV pressure loading vs volume loading, we show that equal magnitude of loading leads to very different functional responses, which can not be explained by changes in the classic 'LV-hypertrophy-genes'. Further analysis of these models may allow for identification of new RV-hypertrophy-genes, which pose potential targets for RV-specific therapy.

	CON	PAB	ACS
RV wt/bodywt (mg/g)	0.6±0.01	1.2±0.1*	1.1±0.1*
PAB gradient (mmHg)	4±1	76±22*†	7±1
Cardiac output (mL/min)	82±2	70±4*	126±8*$
Strokework (mmHg •mL)	5.2±0.3	15.1±1.8*	13.0±1.0*
Systolic parameters			
ES elastance (mmHg/mL)	59±8	155±27*†	41±4
Ejection Fraction (%)	47±3	27±2*	34±2*
Diastolic parameters			
ED elastance (mmHg/mL)	4±1	9±2*	4±2
Tau (ms)	16±1	21±1*†	16±1
ES Volume (µL)	320±42	648±29*†	839±49*
mRNA/18S expression			
NPPB	1.0±0.3	22.3±6.0*	16.2±4.2*
MCIP	1.0±0.2	7.0±1.2*	5.1±0.9*
bMHC_aMHC_ratio	1.0±0.4	10.9±3.2*	10.3±5.6*

*n=8-10/group: * p<0.05 vs CON, † vs ACS, $ vs PAB*
ES= endsystolic, ED= enddiastolic,NPPA/B= natriuretic propeptide A/B, MCIP=modulatory calcineurin-interacting protein, b/aMHC=beta/alpha myosin heavy chain