

Remodeling in Experimental Right Ventricular Volume Overload: a Systematic Review

Bossers G.P.L. (1,2), Hagdorn Q.A.J.(1,2), Ploegstra M.J.(1), Borgdorff M.A.J.(1), Silljé H.H.J.(2), Berger R.M.F.(1), Bartelds B.(1,2)

Department of Pediatrics, Center for Congenital Heart Diseases, University of Groningen, University Medical Center Groningen, The Netherlands (1); Department of Experimental Cardiology, University of Groningen, University Medical Center Groningen, The Netherlands (2)

Introduction: The improved treatment options for children with congenital heart disease (CHD) leads to a growing group of survivors with longstanding residual lesions. The most prevalent is increased right ventricular (RV) volume load, e.g. after correction for Tetralogy of Fallot. Increased volume loading plays a significant role in the development of RV failure in patients with CHD. It is unclear how to recognize, treat or prevent failure in the volume loaded RV.

Objective: The purpose of this systematic review is to evaluate the pathophysiological and hemodynamic adaptation mechanisms involved in the development of RV failure after volume loading investigated in animal models.

Methods and results: Using a pre-specified search strategy, a priori published on the online platform CAMARADES, we identified 1221 unique citations. 102 were eligible for full text review, after which we identified 18 relevant studies. We found two models for RV volume loading in five species: 1) shunt or 2) regurgitation. After data-extraction and meta-analysis, we confirmed effective volume loading, as RV end diastolic volume/area significantly increased in all studies ($p < 0.001$). Cardiac output (CO) increased significantly only in shunt models (shunt: $p < 0.001$; regurgitation: $p = 0.737$). Increased RV end diastolic pressure in combination with stable systolic parameters (dP/dt max, TAPSE) suggests diastolic dysfunction. Initial increase of preload recruitable stroke work implies a positive adaptation mechanism of the RV, which declines over time ($p = 0.012$). Direct measurement of diastolic function is lacking. Patterns in structural and molecular changes show that fibrosis is a long-term effect in the volume loaded RV, in contrast to hypertrophy, which showed to be unrelated to volume load duration. Systematic analysis of other pathways is lacking, thus specific patterns cannot be discerned from the included studies.

Conclusions: This first systematic review of experimental RV volume load showed a consistent pattern of RV dilatation and diastolic dysfunction rather than systolic failure. In the absence of systolic dysfunction, RV dysfunction is most likely due to diastolic failure, which can be related to the development of fibrosis. Standardized volume load quantification and identification of involved molecular pathways is mandatory to refine the characterization of the volume loaded RV.