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The influence of right ventricular pressure overload on the expression of pro- and anti-inflammatory cytokines, growth factors and markers of apoptosis in the myocardium of newborn lambs

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Objective: To assess the role of inflammatory mediators, growth factors and apoptosis on myocardial remodeling in a lamb model of moderate pressure overload of the right ventricle (RV).
Methods: 13 newborn lambs (age: 3.3 ± 1.3 days) undergo either pulmonary arterial banding (PAB) (n=6) or were sham operated (n=7). Hemodynamic studies and blood samples taken for determination of cytokine levels were performed prior to and 1, 4 and 12 weeks after surgery. 12 weeks after the operation, RV biopsies were taken to analyse the intramyocardial expression of inflammatory mediators, growth factors and markers of apoptosis. Animals were then euthanised, hearts studied by morphometry, histology and electron microscopy.
Results: In PAB animals a continuous increase of RV Pressure was registered (PA-RV pressure gradient after 12 weeks: 56.67 ± 8.43 mmHg vs. 5.43 ± 1.51 mmHg in controls, $p<0.001$). This was associated with a significant hypertrophy of the RV as well as the LV myocardium. The RTQ-PCR analysis of the biopsies showed a slightly increased intramyocardial expression of all cytokines (TNF-α, IL-1β, IL-6, IL-8, IL-10), growth factors (CT-1, TGF-β, VEGF) and markers of apoptosis (Bcl-Xl, Bak, Fas-l) in PAB lambs vs controls. PAB group showed a significant increase in the intramyocardial expression of CT-1 as well as a systemic increase of IL-1β, IL-10, TGF-β and Bcl-Xl.
Conclusion: Our results show a measurable effect of moderate RV pressure overload on the systemic and intramyocardial expression of pro- and anti-inflammatory cytokines and an even more distinctive effect on growth factors and markers of apoptosis. The connected risk of myocardial remodeling and RV dysfunction should be expected. Systemic liberation of inflammatory mediators and growth factors might be responsible for LV hypertrophy observed in this model.