

23. Pressure unloading therapy improves vascular reactivity in a rat model of aortic constriction induced arterial hypertension

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Background In the long term, uncontrolled arterial high blood pressure adversely affects the entire circulatory system, as it leads to the manifestation of left ventricular hypertrophy (LVH) and to direct damage to the blood vessel walls. On the contrary, recent studies have demonstrated that the termination of the pathological stimulus of high blood pressure is able to evoke the regression of the pre-established LVH, a phenomenon called reverse remodeling. However, it is still debated whether the reverse remodeling process also occurs in the vasculature or not. Therefore, we investigated the effects of pressure unloading therapy on the vascular structural and functional alterations induced by pressure overload in a rat model.

Methods Aortic morphometry was studied in hematoxylin&eosin stained sections and vascular function was investigated in an organ bath system 6- or 12 weeks after abdominal aortic banding (AB) (AB 6-week or AB 12-week), respectively. Sham-operated animals served as controls (Sham 6- or sham 12-week). Abdominal aortic debanding (DB) procedure was performed after the 6th experimental week (AB+DB 12-week).

Results Intima-media thickness and intima-media cross-section area normalized to body weight were significantly higher in the AB 12-week group compared to the sham 12-week group, and similar in the AB+DB 12-week and sham 12-week groups. In vitro functional experiments showed impaired maximal endothelium dependent vasorelaxation (R_{max}) to acetylcholine (Sham 12-week 83 ± 1 vs AB 12-week 66 ± 2 vs AB+DB 12-week $78 \pm 2\%$, $p < 0.05$) and significant shift of the sodium nitroprusside concentration–response curves to the right without any alterations in the R_{max} comparing the 12-week AB group to the 12-week sham group, which were reversed by debanding. Nevertheless, there were no significant changes in these parameters between AB 6- and AB 12-week groups. Additionally, even though the AB 12-week group showed significantly greater maximum contraction to phenylephrine, debanding of the aortic constriction significantly reduced vasoconstrictive response to phenylephrine compared to sham 12-week group (Sham 12-week 3.1 ± 0.2 vs AB 12-week 4.1 ± 0.1 vs AB+DB 12-week $2.6 \pm 0.1g$, $p < 0.05$).

Conclusions Our results suggest that vascular structural and functional changes induced by pressure overload in rats were regressed by mechanical unloading therapy. Exploring the molecular pathways involved in pressure unloading induced prevention would generate effective treatments.