

## Renal dysfunction and aortic stiffening in the children with congenital heart diseases

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### Background

Arterial stiffening may decrease impedance mismatch in the proximal arterial system which transmits blood pressure directly to the micro vessels, leading to microvascular damage and renal dysfunction. Renal dysfunction may, in turn, attribute to vascular dysfunction through hypertension, abnormal glucose/lipid metabolism, inflammation, oxidative stress and activation of the renin-angiotensin system. That renal dysfunction correlates with increased arterial stiffness has already been described in adults. We hypothesized that a similar reno-vascular interaction also exists in children with congenital heart disease (CHD).

### Methods and results

During cardiac catheterization, pulse wave velocity (PWV), as a marker of arterial stiffness, was measured during the catheter drawback from ascending aorta to femoral artery in 200 children (age,  $3.4 \pm 4.5$  years) with various CHDs, including functional single ventricle ( $n=117$ ) and repaired/unrepaired biventricular heart ( $n=83$ ). Relationship between PWV and estimated glomerular filtration rate (eGFR:  $112 \pm 27$ ,  $38-180$  ml/min/1.73m<sup>2</sup>) derived from serum level of creatinine ( $0.31 \pm 0.12$ ,  $0.16-0.88$  mg/dl) was then investigated. The PWV [mean  $\pm$  SD] of the proximal and distal aorta were  $601 \pm 222$  and  $442 \pm 142$  cm/sec, respectively. The PWV-proximal aorta but not PWV-distal aorta correlated significantly with eGFR (PWV =  $920 \pm 2.48 * eGFR$ ,  $p < 0.05$ ). Multivariate linear regression analysis confirmed eGFR as an independent determinant of PWV-proximal aorta ( $p=0.028$ ) even after controlling for confounding factors (age, sex, blood pressure, and disease type), whereas age was markedly associated with PWV-distal aorta ( $p=0.031$ ). Interestingly, PWV-distal aorta was positively correlated with serum levels of procollagen type-III peptide even after adjusting for age. Among disease groups, tetralogy of Fallot was also an independent determinant of high PWV ( $p=0.0011$ ).

### Conclusions

This is the first report of reno-vascular interaction even in children with CHD and relatively preserved renal function. Because increased arterial stiffness is an independent risk factor for cardiovascular disease, and because chronic kidney disease is an independent risk factor for cardiovascular morbidity and mortality, these results highlight the importance of close follow-up of reno-vascular function and its interaction with a special consideration of disease specificity in children with CHD. Studies on the effects of reno-vascular protective treatments on prognosis are warranted.