Mid-region pro-adrenomedullin (MR-proADM) and cardiac measures in children and adolescents with chronic kidney disease.

Chee Teck Koh, Teng Hiang Heng, Chloe Xiaoyun Chan, Yiong Huak Chan, Sharon Sher Leen Teo, Kar Hui Ng, Perry Lau, U Mya Than, Swee Chye Quek, Lieng Hsi Ling, Lingli Gong, Ching Kit Chen, Hui Kim Yap, Isaac Desheng Liu

Department of Paediatrics, KTP-National University Children's Medical Institute, National University Hospital

Introduction

- Cardiac dysfunction is prevalent in paediatric patients with chronic kidney disease (CKD), resulting in increased risk of morbidity and mortality. [1]
- Diastolic dysfunction is usually an early finding and frequently precedes systolic dysfunction. Tissue doppler imaging (TDI) provides a sensitive means of assessing early diastolic dysfunction. Robust biomarkers for cardiovascular risk stratification are lacking in paediatric CKD. [2,3]
- This study aims to determine the association between diastolic dysfunction with a circulating biomarker, mid-region pro-adrenomedullin (MR-proADM) in paediatric patients with chronic kidney disease.

Method

- Cross-sectional analysis of baseline parameters was carried out in a cohort of 63 (36 male, median age 13.6 [IQR 10.5] years) patients with chronic kidney disease.
- Diastolic dysfunction was evaluated by measuring the peak of early diastolic flow velocities (E), the peak of late diastolic flow velocities (A) of mitral inflow on M-mode, the ratio E to A (E/A) as well as Tissue Doppler Imaging (TDI) E', TDI E'/A' and Mitral E/ Septal E'.
- MR-proADM was measured along with routine biochemical parameters including haemoglobin and intact parathyroid hormone as well as cardiovascular risk factors such as dyslipidemia and obesity.
- Univariate and multivariate linear regression was performed to investigate the association between abnormal echocardiographic parameters and MR-proADM, and receiver operating characteristic (ROC) analysis was used to determine discriminatory performance of MR-proADM for cardiac diastolic dysfunction.

Characteristic	Frequency	Percentage (%)
CKD stage		
Stage G2-4	29	46.0
Stage G5D	34	54.0
Gender		
Male	36	57.1
Female	27	42.9
Race		
Chinese	33	52.4
Others	30	47.6
Kidney etiology		
Glomerular	20	68.3
Non-glomerular	43	31.7
	Median	Interquartile range (IQR)
Age at diagnosis, years	0.7	5.51
Duration of disease, years	8.9	8.93

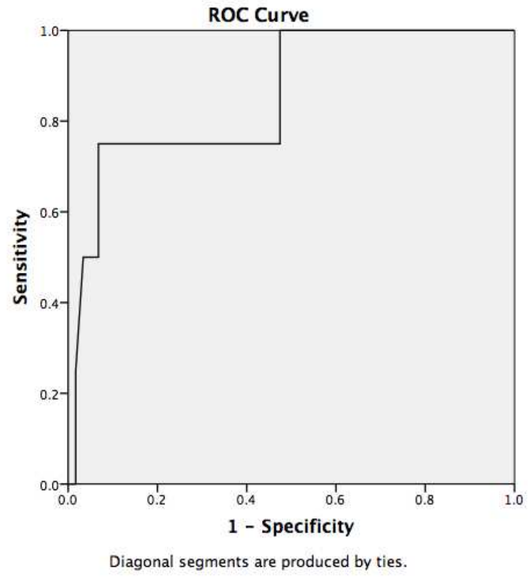
Table 1. Sociodemographic characteristics of the patients.

Variable	Total patients (n=63)	Patients at CKD Stage G2-4 (n=29)	Patients at CKD Stage G5D (n=34)	p-value
LV structure	Median (IQR)			
IVSD	0.65 (0.16)	0.63 (0.15)	0.67 (0.22)	0.486
LVEDD	4.11 (0.97)	4.17 (0.77)	4.09 (1.04)	0.751
LVPWD	0.70 (0.19)	0.70 (0.14)	0.72 (0.21)	0.741
LVMI, g/m2.7	30.53 (10.62)	30.39 (8.69)	31.10 (15.44)	0.465
LV geometry	N (%)			
Normal	55 (87.30)	27 (42.84)	28 (44.44)	
Concentric remodelling	2 (3.20)	1 (1.59)	1 (1.59)	
Concentric LVH	2 (3.20)	0	2 (3.17)	
Eccentric LVH	4 (6.30)	1 (1.59)	3 (4.76)	

Table 2. Echocardiographic characteristics and left ventricular structure and geometry.

Results

- Overall prevalence of diastolic dysfunction was 15.9% (10 patients).
- On univariate regression analysis, we observed a significant inverse association between MR-proADM and M-mode mitral inflow (B = -0.36, 95%CI -0.50 to -0.22; p<0.001), TDI septal E'/A' (B = -0.22, 95%CI -0.34 to -0.10; p<0.001) and TDI lateral E'/A' (B = -0.40, 95%CI -0.56 to -0.23; p<0.001) respectively.
- There was also a significant association between MR-proADM and diastolic dysfunction as defined by TDI E' < 8cm/s.
- We also observed that baseline MR-proADM was predictive of abnormal diastolic function parameters at 1 year's follow up.
- Using a multivariate linear regression model, MR-proADM remained independently associated with M-mode mitral inflow (B = -0.33, 95%CI -0.56 to -0.11; p=0.004) and TDI septal E'/A' (B = -0.20, 95%CI -0.36 to -0.04; p=0.016) respectively.
- A cut-off of MR-proADM >2.84 nmol/L (AUC 85.4%; p=0.019) had a sensitivity of 75% and a specificity of 93.3% for diastolic dysfunction defined as mitral inflow E/A ratio <1.



Conclusion

MR-proADM is associated with diastolic dysfunction and may be useful for prognosticating early cardiac dysfunction in children and adolescents with chronic kidney disease.

References

1. Mitsnefes, M. M. Cardiovascular disease in children with chronic kidney disease. *J Am Soc Nephrol* **23**, 578-585, doi:10.1681/asn.2011111115 (2012).
2. Mencarelli, F. *et al.* Left ventricular mass and cardiac function in a population of children with chronic kidney disease. *Pediatr Nephrol* **29**, 893-900, doi:10.1007/s00467-013-2710-6 (2014).
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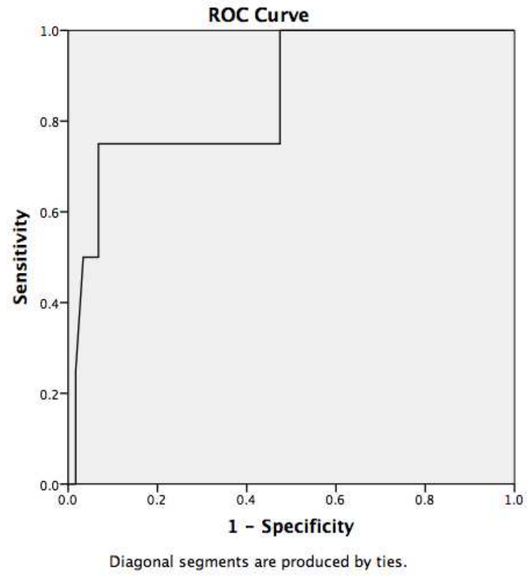

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