

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

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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

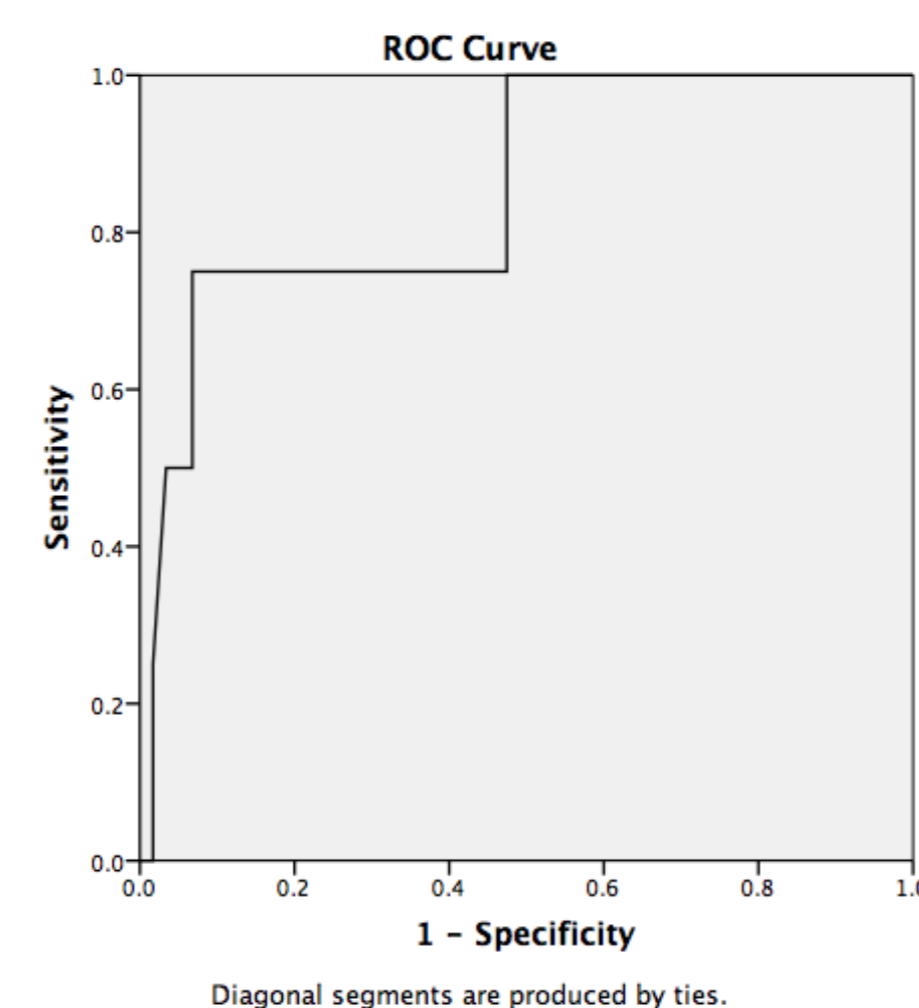
Table 1. Sociodemographic characteristics of the patients.

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/m ^{2.7}	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

- Mitsnefes, M. M. Cardiovascular disease in children with chronic kidney disease. *J Am Soc Nephrol* **23**, 578-585, doi:10.1681/asn.2011111115 (2012).
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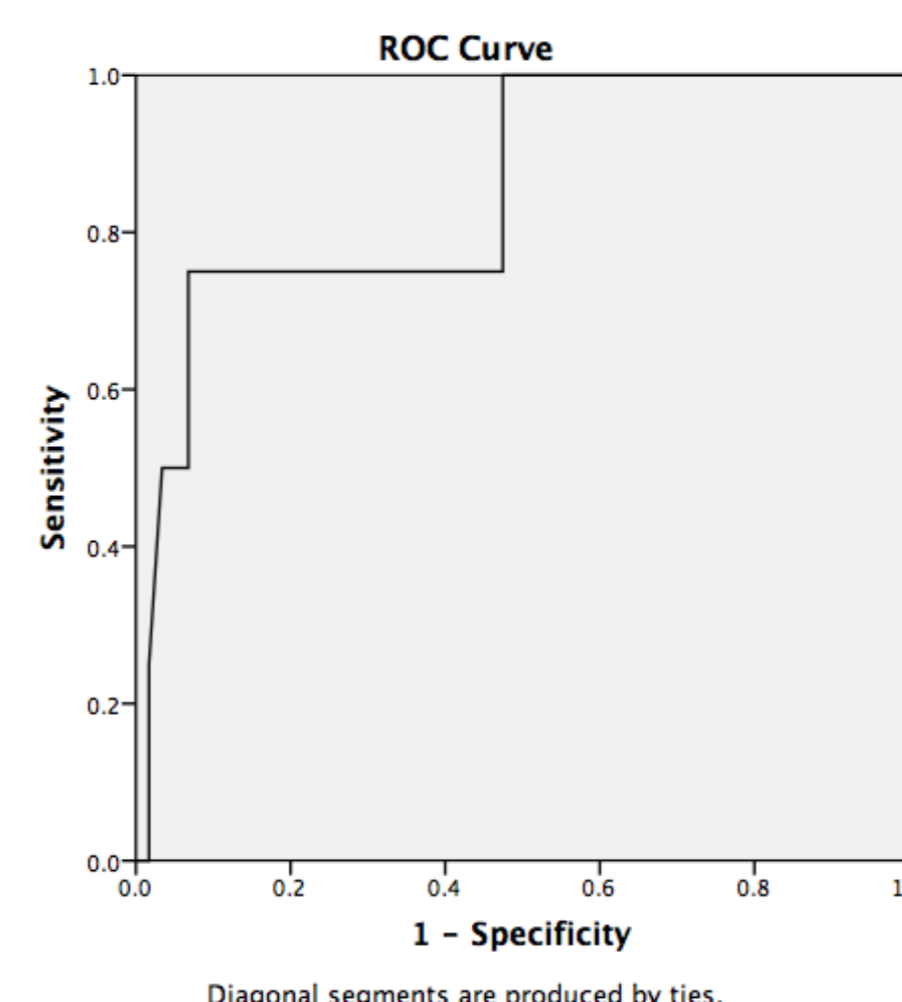
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