Title: Cardiac MRI demonstrates findings of subclinical HFpEF in patients with CKD Stage 3-4

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Introduction: Heart failure with preserved ejection fraction (HFpEF) is a major manifestation of cardiovascular disease in chronic kidney disease (CKD). Early identification of individuals with CKD at risk for clinical HFpEF is important to understanding the pathogenesis of HFpEF and identifying potential therapies. Cardiac magnetic resonance imaging (CMR) provides precise measurements of cardiac structure and may potentially identify subclinical cardiac abnormalities in patients with pre-dialysis CKD.

Hypothesis: Compared to healthy volunteers, patients with CKD without clinical heart failure will have evidence of early HFpEF, suggested by an increase in left atrial (LA) volume, left ventricular (LV) hypertrophy, and an abnormal mitral inflow pattern on CMR.

Methods: Our cross-sectional study included 141 individuals with CKD stage 3-4 (eGFR 20-45 ml/min per 1.73m^2) without clinical HF enrolled in the COMBINE (CKD Optimal Management with Binders and NicotinamidE) multicenter clinical trial, and 24 healthy age- and sex-matched volunteers. Baseline CMR findings were compared between the two groups and adjusted for age, body mass index (BMI) and systolic blood pressure (SBP).

Results: Individuals with CKD were older and had higher SBP and BMI. Both groups had similar ejection fraction. In unadjusted models, individuals with CKD demonstrated significantly greater LV mass index, higher LA end-systolic volume index, and lower mitral valve E/A ratio (Table 1). After adjustment for covariates, individuals with CKD had significantly lower mitral valve E/A ratio compared to healthy volunteers (β -0.12; 95% confidence interval -0.24, -0.01; p = 0.03).

Conclusions: CKD status in individuals without clinical HF is associated with a lower mitral valve E/A ratio, an early marker of impaired LV filling during diastole and subclinical HFpEF. Understanding mechanisms of HFpEF development in CKD is necessary to identify targeted therapies for the CKD population.

Table 1. Baseline characteristics and CMR parameters of participants

	CKD Participants N = 141	**Healthy Volunteers N = 24**	***p* - value**
Age, years	64.8 ± 11.9	60.4 ± 7.3	**0.02**
Female, %	52 (36.9)	9 (37.5)	0.95
Black, %	41 (29.1)	2 (8.3)	**0.04**
BMI, kg/m^2	31.7 ± 6.8	26.5 ± 4.0	**<.001**
SBP, mmHg	128.5 ± 16.9	118.5 ± 11.5	**<.001**
eGFR, ml/min/1.73m^2	33.2 ± 7.2	85.9 ± 16.0	**<.001**
MRI Parameters			
Left ventricular mass index, g/m$^{2.7}$	29.5 ± 8.5	23.4 ± 4.0	**<.001**
Left ventricular end diastolic volume index, mL/m$^{2.7}$	33.1 ± 9.8	33.7 ± 6.9	0.79
Left atrial end systolic volume index, mL/m$^{2.7}$	12.8 ± 7.0	10.6 ± 3.2	**0.02**
Left atrial end diastolic volume index, mL/m$^{2.7}$	21.0 ± 8.2	20.8 ± 6.4	0.89
Ejection fraction, %	62.4 ± 9.6	61.7 ± 4.0	0.56
Mitral Valve E velocity (cm/s)	45.5 ± 15.3	47.5 ± 12.5	0.56
Mitral Valve A velocity (cm/s)	56.7 ± 15.1	46.9 ± 12.0	**0.003**
Mitral Valve EA ratio	0.8 ± 0.3	1.0 ± 0.2	**0.002**