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Racial/Ethnic Differences in Left Ventricular Structure and Function in Chronic Kidney Disease: The Chronic Renal Insufficiency Cohort

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BACKGROUND
Chronic kidney disease (CKD) is associated with increased risk of cardiovascular disease (CVD) and it is especially common among Blacks. Left ventricular hypertrophy (LVH) is an important subclinical marker of CVD, but there are limited data on racial variation in left ventricular structure and function among persons with CKD.

METHODS
In a cross-sectional analysis of the Chronic Renal Insufficiency Cohort Study, we compared the prevalence of different types of left ventricular remodeling (concentric hypertrophy, eccentric hypertrophy, and concentric remodeling) by race/ethnicity. We used multinomial logistic regression to test whether race/ethnicity associated with different types of left ventricular remodeling independently of potential confounding factors.

RESULTS
We identified 1,164 non-Hispanic Black and 1,155 non-Hispanic White participants who completed Year 1 visits with echocardiograms that had sufficient data to categorize left ventricular geometry type. Compared to non-Hispanic Whites, non-Hispanic Blacks had higher mean left ventricular mass index (54.7 ± 14.6 vs. 47.4 ± 12.2 g/m$^{2.7}$; $P < 0.0001$) and prevalence of concentric LVH (45.8% vs. 24.9%). In addition to higher systolic blood pressure and treatment with >3 antihypertensive medications, Black race/ethnicity was independently associated with higher odds of concentric LVH compared to White race/ethnicity (odds ratio: 2.73; 95% confidence interval: 2.02, 3.69).

CONCLUSION
In a large, diverse cohort with CKD, we found significant differences in left ventricular mass and hypertrophic morphology between non-Hispanic Blacks and Whites. Future studies will evaluate whether higher prevalence of LVH contribute to racial/ethnic disparities in cardiovascular outcomes among CKD patients.

Keywords: blood pressure; echocardiography; hypertension; left ventricular hypertrophy; race and ethnicity; remodeling; renal insufficiency.

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Chronic kidney disease (CKD) affects over 15 million Americans, and the prevalence has increased significantly over the last 3 decades.[1] CKD increases the risk for a broad range of cardiovascular diseases (CVD) and all-cause mortality.[2–5] Left ventricular hypertrophy (LVH), a subclinical marker of CVD, is associated with shorter cardiovascular event-free survival, higher risk of incident heart failure, and higher risk of death among persons with CKD.[5–8]

Increases in left ventricular mass occur either *via* predominant wall thickening or predominant chamber enlargement that lead to concentric hypertrophy or eccentric hypertrophy. Concentric remodeling is defined as left ventricular wall thickening in the absence of significant increase in left ventricular mass. In contrast to Whites, Blacks may be predisposed to concentric hypertrophy, independently of blood pressure.[9] In the general population, higher prevalence of LVH and concentric hypertrophy among Blacks compared to Whites likely contributes to their increased risk of CVD and death.[9–12]

Studies in nondialysis dependent CKD patients vary with regard to racial/ethnic risk differences for occurrence of CVD events, CVD mortality, and all-cause mortality.[13–19] Several, small studies have examined differences in left ventricular geometry as explanatory factors.[20] We analyzed data from the Chronic Renal Insufficiency Cohort (CRIC) Study—a large, prospective, observational cohort study of men and women (45% non-Hispanic Whites and 46% non-Hispanic Blacks) with mild-to-moderate CKD[21]—to determine whether Blacks have a higher prevalence of concentric hypertrophy than Whites, and if Black race/ethnicity would be associated with increased risk for concentric hypertrophy independent of traditional CVD risk factors.

METHODS

Study design and participants

We conducted cross-sectional analyses among non-Hispanic Black and non-Hispanic White participants in the CRIC study. The design, methods, and baseline characteristics of the CRIC study have been previously published.[21,22] In brief, the CRIC study is an ongoing prospective study of men and women between 21 and 74 years of age with mild-to-moderate CKD, as defined by aged-based estimated glomerular filtration rate (eGFR) entry criteria (range 20–70 ml/min/1.73 m^2). Participants were recruited at 7 centers across the United States between May 2003 and March 2007.[22] Additional Hispanic participants were enrolled from October 2005 to June 2008 at a single CRIC Study site for a total of 3,939 participants (including 1,650 non-Hispanic Black participants and 1,638 non-Hispanic White participants).[23] Our analytic sample included the 2,319 participants (1,164 non-Hispanic Black and 1,155 non-Hispanic White) with echocardiograms performed 1 year after enrollment and whose left ventricular mass index (LVMI) and relative wall thickness (RWT) could be determined. Informed consent was obtained from all participants.

Variables and measurements

We analyzed self-reported sociodemographics, medical history, lifestyle behaviors, and current medication use, blood pressure and anthropometric measurements (height, weight, and waist circumference) at the first annual follow-up visit, the time point at which the echocardiogram was performed. Hypertension was defined as systolic blood pressure (SBP) ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of any antihypertensive medications. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Diabetes was defined as fasting glucose ≥126 mg/dl, random glucose ≥200 mg/dl, or use of insulin or diabetic medication. Glomerular filtration rate was estimated with a study-derived equation.[24]

Transthoracic echocardiography was performed on CRIC participants at the year 1 visit using American Society of Echocardiography established protocols for M-mode, 2-dimensional, and Doppler echocardiography.[25] Left ventricular mass was calculated using 2D images of the left ventricular short axis muscle area and the apical left ventricular length. LVMI was calculated as left ventricular mass in g/height in $m^{2.7}$, a measure thought to be more accurate among persons with CKD.[25,26] Based on prior studies in patients with CKD, we defined LVH as LVMI >50 g/$m^{2.7}$ in males and >47 g/$m^{2.7}$ in females.[23,26–28] RWT was calculated as 2 × posterior wall thickness/left ventricular internal end diastolic diameter. We defined increased RWT as ≥0.45. We used LVMI and RWT to categorize left ventricular geometry as: (1) normal (normal LVMI and RWT), (2) concentric remodeling (normal LVMI and increased RWT), (3) eccentric hypertrophy (increased LVMI and normal RWT), or (4) concentric hypertrophy (increased LVMI and RWT). Left ventricular cavity volumes were calculated using the modified biplane method, and ejection fraction was calculated using Simpson's method of disks.[25] Diastolic function was assessed by mitral inflow E- and A-wave velocities, E-wave deceleration time, and pulmonary venous reverse A-wave duration and categorized as normal or abnormal relaxation (mild, moderately, or severe) using established criteria.[29]

Statistical analysis

We analyzed sociodemographic characteristics, clinical data, and echocardiographic measurements using SAS statistical software (version 9.4; SAS, Cary, NC). For continuous variables, we calculated the mean value and SD or median value and interquartile range. We summarized dichotomous variables as frequencies and proportions. We performed descriptive statistical testing with 2-sample *t* tests, Wilcoxon rank–sum test, and Pearson's Chi squared, and defined significance as $P < 0.05$.

We generated 2 multiple regression models. In the first model, we used multiple linear regression to model LVMI as a continuous outcome measure. In the second, we used multivariable multinomial logistic regression to simultaneously identify correlates of concentric hypertrophy, eccentric hypertrophy, and concentric remodeling vs. normal left ventricular geometry in a single model.

We selected candidate variables based on literature review, input from CRIC investigators, and the results of univariate analyses of left ventricular remodeling. Black race/ethnicity was the primary exposure of interest. Other variables included in the linear regression model were age, sex, history of diabetes, history of myocardial infarction or revascularization, history of peripheral artery disease, history of heart failure, current smoking, SBP, eGFR, hemoglobin, total parathyroid hormone (PTH), fibroblast growth factor 23 (FGF23), and serum phosphate. Due to the small number of measurements of phosphate, PTH, and FGF23 levels at the first follow-up visit, we carried forward the values from participants' baseline visit in our analyses. We also included in the model self-reported use of more than 3 antihypertensive medications as a marker of hypertension severity and 24-hour urinary protein as an additional marker of CKD severity. We did not include hypertension as a categorical variable because the prevalence was approximately 90% in our sample. We did not include BMI in the primary analysis due to collinearity with the LVMI, which is measured in $g/m^{2.7}$. We transformed selected variables to satisfy the assumptions of normality and constant variance. We tested for interactions between race/ethnicity and SBP. For the multinomial logistic regression model, we used the same variables as in the linear regression analyses.

Sensitivity analyses

We conducted 3 sensitivity analyses. First, we restricted the sample of participants to those who did not report a no prior history of heart failure. Second, we restricted the sample of participants to those with a left ventricular ejection fraction >50%. Third, we added BMI as a covariate in the models from the primary analysis to see if it attenuated the association between race/ethnicity and the outcomes of interest.

RESULTS

Characteristics of the 2,319 participants (1,164 non-Hispanic Black and 1,155 non-Hispanic White) who completed year 1 visits with echocardiograms and measured LVMI and RWT are presented in Table 1. Their mean age of the study population was 58.8 ± 10.7 years, and 53.3% were male. Compared to non-Hispanic Whites, non-Hispanic Blacks had higher prevalence of diabetes (51.0% vs. 38.2%; $P < 0.0001$), hypertension (95.3% vs. 81.3%; $P < 0.0001$), pre-existing heart failure (14.6% vs. 7.0%; $P < 0.0001$), and tobacco use (17.8% vs. 8.7%. $P < 0.001$).

Compared to non-Hispanic White participants, non-Hispanic Blacks had higher mean BMI, lower mean eGFR,

Table 1. Sample demographic and clinical characteristics categorized by race/ethnicity

Variables	All (*n* = 2,319)	Non-Hispanic Blacks (*n* = 1,164)	Non-Hispanic Whites (*n* = 1,155)	*P* value (Blacks vs. Whites)
Age, years, mean ± SD	58.8 ± 10.7	58.8 ± 10.3	58.8 ± 11.1	0.94
Sex, female, *n* (%)	1,082 (46.7)	593 (51.0)	489 (42.3)	<0.0001
Systolic blood pressure, mm Hg, mean ± SD	126.4 ± 21.5	132.5 ± 22.7	120.3 ± 18.2	<0.0001
Diastolic blood pressure, mm Hg, mean ± SD	70.3 ± 12.7	72.9 ± 13.5	67.7 ± 11.3	<0.0001
Number of antihypertensive medications, mean ± SD	2.6 ± 1.5	3.0 ± 1.5	2.3 ± 1.5	<0.0001
Body mass index, kg/m^2	31.7 ± 7.5	32.9 ± 8.0	30.6 ± 6.8	<0.0001
Estimated glomerular filtration rate, ml/min/1.73 m^2, mean ± SD	43.4 ± 17.1	41.2 ± 17.0	45.7 ± 16.8	<0.0001
Medical history, *n* (%)				
Diabetes	1,035 (44.6)	594 (51.0)	441 (38.2)	<0.0001
Heart failure	251 (10.8)	170 (14.6)	81 (7.0)	<0.0001
Prior myocardial infarction or coronary revascularization	520 (22.4)	266 (22.9)	254 (22.0)	0.62
Peripheral artery disease	158 (6.8)	87 (7.5)	71 (6.2)	0.20
Hypertension	2,046 (88.3)	1,108 (95.3)	938 (81.3)	<0.0001
Current smoker	307 (13.2)	207 (17.8)	100 (8.7)	<0.0001
Hemoglobin, g/dl, mean ± SD	12.8 ± 1.8	12.3 ± 1.7	13.4 ± 1.6	<0.0001
Serum phosphate*, mg/dl, mean ± SD	3.7 ± 0.6	3.8 ± 0.6	3.6 ± 0.6	<0.0001
Total parathyroid hormone*, pg/ml median(IQR)	52.0 (33.2–84.0)	65.0 (40.0–113.2)	42.2 (30.0–66.0)	<0.0001
Urinary protein, g/24 h, median(IQR)	0.14 (0.07–0.71)	0.24 (0.08–1.11)	0.11 (0.06–0.41)	<0.0001
Glycosylated hemoglobin*, %, mean ± SD	6.6 ± 1.5	6.9 ± 1.7	6.3 ± 1.3	<0.0001
Fibroblast growth factor 23*, RU/ml, median(IQR)	137.8 (91.7–221.9)	145.4 (94.4–240.8)	132.7 (89.1–205.3)	0.0004

*Baseline data instead of year 1 data used.

higher median proteinuria, higher mean hemoglobin A1C, lower hemoglobin, and higher median FGF23 levels (all $P < 0.05$). Non-Hispanic Blacks reported greater use of antihypertensive medications and had higher mean SBP and diastolic blood pressure ($P < 0.0001$).

Left ventricular structure and function differed significantly between non-Hispanic Blacks and non-Hispanic Whites. Non-Hispanic Blacks had higher mean LVMI than Whites (54.7 ± 14.6 vs. 47.4 ± 12.2 g/m$^{2.7}$; $P < 0.0001$) and a higher prevalence of LVH (61.6% vs. 38.7%; $P < 0.0001$) (Table 2). Non-Hispanic Black participants also had higher prevalence of diastolic and systolic dysfunction and larger left ventricular end diastolic volume (P for all comparisons <0.05).

Compared to non-Hispanic Whites, non-Hispanic Blacks had a higher unadjusted prevalence of any type of abnormal left ventricular geometry (87.9% vs. 70.1%; $P < 0.001$). Non-Hispanic Blacks and Whites differed in the distribution of left ventricular geometric patterns ($P < 0.0001$) (Figure 1). Compared to non-Hispanic Whites, non-Hispanic Blacks had a higher prevalence of concentric LVH (45.8% vs. 24.9%) and eccentric LVH (15.8% vs. 13.9%). Non-Hispanic Whites had a higher prevalence of concentric remodeling; however, this was in the setting of a higher prevalence of normal left ventricular geometry and the lower prevalence of LVH.

Multivariable linear and logistic regression analyses

In multivariable linear regression analysis, Black race/ethnicity was associated with higher LVMI (Table 3). Twelve other variables were significantly associated with higher LVMI, including older age, male sex, self-reported use of more than 3 antihypertensive medications, higher SBP, prevalent diabetes, prevalent CVD (peripheral artery disease, prior myocardial infarction or revascularization, heart failure), lower hemoglobin, significant proteinuria, and higher FGF23 and PTH levels.

Table 4 summarizes the multinomial logistic regression analysis of the odds for concentric hypertrophy, eccentric hypertrophy, and concentric remodeling vs. normal left ventricular geometry. Black vs. White race/ethnicity was associated with higher odds for concentric LVH (odds ratio [OR] = 2.73, 95% confidence interval [CI]: 2.02, 3.69). Markers of the hypertension severity—self-reported use of more than 3 antihypertensive medications (OR = 2.10, 95% CI: 1.48, 2.98) and higher SBP (OR = 1.02, 95% CI: 1.01, 1.03)—were also associated with higher odd ratios for concentric hypertrophy; however, these markers of hypertension severity were not associated with a higher odds ratio for concentric remodeling. Other variables associated with higher odds of concentric LVH include older age, absence of diabetes, higher FGF23, lower eGFR, and higher PTH. Black vs. White race/ethnicity was also associated with higher odds for concentric remodeling (OR = 2.16, 95% CI: 1.61, 2.90) and for eccentric hypertrophy (OR = 1.81, 95% CI: 1.27, 2.58).

Sensitivity analyses

In the sensitivity analysis restricted to participants without a history of heart failure, Black race/ethnicity remained independently associated with higher LVMI ($P < 0.001$), and higher odds for concentric hypertrophy (OR = 2.82, 95% CI: 2.05, 3.87), eccentric hypertrophy (OR = 1.65, 95% CI: 1.12, 2.43), and concentric remodeling (OR = 2.13; 95% CI: 1.58, 2.89). In the sensitivity analysis restricted to those with a left ventricular ejection fraction >50% and the analysis that included BMI as a covariate, the association between Black race/ethnicity and higher LVMI and abnormal cardiac remodeling remained significant (data not shown).

DISCUSSION

In a large cohort of men and women with mild-to-moderate CKD, we found that the prevalence of LVH among non-Hispanic Black participants was approximately 1.6 times (61.6% vs. 38.7%) higher than non-Hispanic White participants. Concentric hypertrophy was over 1.8 times (45.8% vs. 24.9%) more prevalent in non-Hispanic Black than non-Hispanic White participants. Non-Hispanic Blacks were significantly more likely to have diastolic and systolic dysfunction and increased left ventricular end diastolic volume than non-Hispanic Whites. In other studies, the prevalence of LVH in CKD patients ranges from 16% to 74%; however, none of these studies directly compared large samples of non-Hispanic Black and non-Hispanic White CKD patients.[6,20,30–34]

Table 2. Echocardiographic characteristics of left ventricular structure and function categorized by race

Variables	Non-Hispanic Blacks (n = 1,164)	Non-Hispanic Whites (n = 1,155)	P value (Blacks vs. Whites)
Left ventricular mass index, g/m$^{2.7}$, mean ± SD	54.7 ± 14.6	47.4 ± 12.2	<0.0001
Presence of left ventricular hypertrophy, n (%)	717 (61.6)	447 (38.7)	<0.0001
Relative wall thickness, mean ± SD	0.54 ± 0.15	0.48 ± 0.11	<0.0001
Left ventricular end diastolic volume, ml, mean ± SD	144.0 ± 48.9	137.4 ± 40.2	0.0003
Diastolic dysfunction, n (%)	804 (76.5)	687 (65.9)	<0.001
Left ventricular ejection fraction by groups, n (%)			
>50%	913 (78.6)	936 (81.2)	0.026
30% to ≤50%	209 (18.0)	197 (17.1)	
≤30%	40 (3.4)	20 (1.7)	

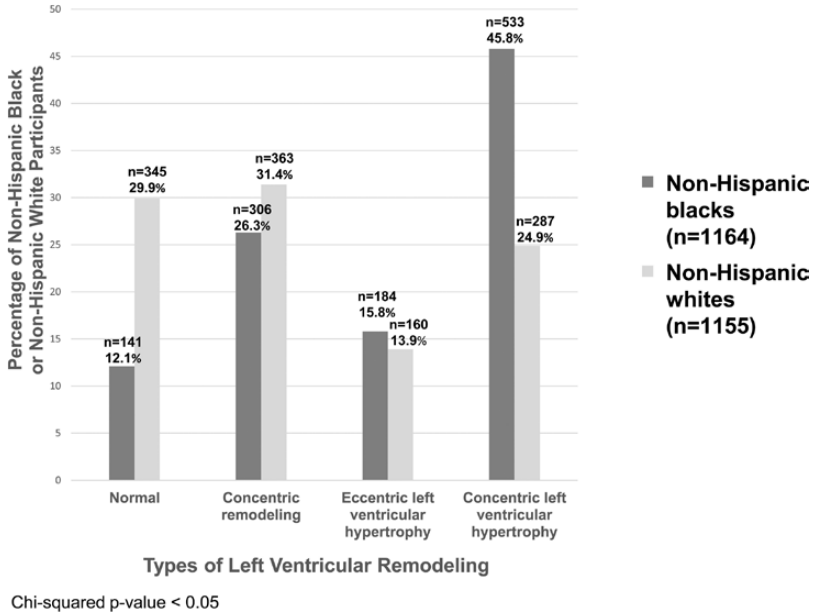

Figure 1. Left ventricular remodeling categorized by race/ethnicity in mild-to-moderate chronic kidney disease. Chi squared *P* value <0.05.

Table 3. Multivariable linear regression model of left ventricular mass index as the dependent variable

Variables	Beta coefficient	SE	*P* value
Black race/ethnicity	**2.53**	**0.57**	**<0.0001**
Female	**−1.50**	**0.56**	**0.008**
Age	**0.06**	**0.03**	**0.04**
Systolic blood pressure	**0.12**	**0.01**	**<0.0001**
More than 3 antihypertensive medications	**5.21**	**0.62**	**<0.0001**
Medical history			
Diabetes	**1.75**	**0.57**	**0.002**
History of myocardial infarction or revascularization	**2.65**	**0.67**	**<0.0001**
Peripheral artery disease	**−2.67**	**1.04**	**0.01**
Current smoker	0.54	0.77	0.49
Heart Failure	**6.01**	**0.90**	**<0.0001**
Per 1 SD lnFGF23	**1.20**	**0.31**	**<0.0001**
Estimated glomerular filtration rate	−0.02	0.02	0.40
Hemoglobin	**−0.64**	**0.18**	**0.0004**
Urinary protein, g/24 h (reference ≤ 0.5)			
0.5–3.5	−0.05	0.70	0.94
>3.5	**3.68**	**1.2**	**0.002**
LnPTH	**1.20**	**0.44**	**0.006**
Phosphate	0.37	0.45	0.42

Variables with *P* value <0.05 are in bold. Abbreviations: FGF23, fibroblast growth factor 23; PTH, parathyroid hormone.

At baseline, CRIC non-Hispanic Black participants with CKD had a greater prevalence of comorbidities and clinical and laboratory markers of CKD severity than non-Hispanic White participants. Many of these characteristics are known to contribute to cardiac hypertrophy. In adjusted analyses, Black race/ethnicity remained independently associated with higher LVMI, 2.7 times higher odds for concentric LVH, and 1.8 higher odds for eccentric hypertrophy, and 2.2 times higher odds for concentric remodeling. The results were qualitatively unchanged when we restricted the analyses to individuals without a prior history of heart failure and with a left ventricular ejection fraction >50%. The persistent association between race/ethnicity and left ventricular remodeling in the adjusted model suggests that other factors beyond cardiovascular risk factors, such as genetic factors, volume load, neurohormonal milieu, extracellular matrix alterations, and other comorbidities,[9] may contribute to the higher prevalence of LVH and difference in type of left ventricular remodeling between Blacks and Whites.

Studies that compared differences in risk for CVD outcomes and death for Blacks and Whites with CKD reported conflicting results.[13–19] A pooled analysis from 4 cohorts found a higher risk of CVD events and death for Blacks than Whites,[13] while a recent CRIC analysis reported a lower risk of death or atherosclerotic event in Blacks than Whites in an adjusted model.[16] Studies in CRIC and in the Multi-Ethnic Study of Atherosclerosis found that the higher risk for heart failure in Blacks than in Whites is largely related to differences in CVD risk factors and socioeconomic status.[16,35] However, these analyses did not examine the relationship between race/ethnicity, left ventricular geometry, and CVD outcomes. In the general population, studies have shown that differences in left ventricular geometry likely contribute to the differences in CVD outcomes between Blacks and Whites.[9–12] Our findings suggest that CVD risk factors alone cannot account for

Table 4. Multinomial logistic model for concentric hypertrophy, eccentric hypertrophy, and concentric remodeling compared to absence of remodeling

	Concentric hypertrophy		Eccentric hypertrophy		Concentric remodeling	
Variables	**Odds ratio (95% CI)**	***P* value**	**Odds ratio (95% CI)**	***P* value**	**Odds ratio (95% CI)**	**P value**
Black race/ethnicity	**2.73 (2.02–3.69)**	**<0.0001**	**1.81 (1.27–2.58)**	**0.001**	**2.16 (1.61–2.90)**	**<0.001**
Female	1.02 (0.76–1.37)	0.90	0.94 (0.66–1.33)	0.72	**0.64 (0.48–0.86)**	**0.003**
Age	**1.04 (1.03–1.06)**	**<0.0001**	**1.02 (1.01–1.04)**	**0.008**	**1.04 (1.03–1.05)**	**<0.0001**
Systolic blood pressure	**1.021 (1.013–1.028)**	**<0.0001**	**1.009 (1.000–1.018)**	**0.04**	0.998 (0.990–1.006)	0.64
More than 3 antihypertensive medications	**2.10 (1.48–2.98)**	**<0.0001**	**2.21 (1.49–3.29)**	**<0.0001**	0.94 (0.65–1.36)	0.73
Medical history						
Diabetes	**0.60 (0.45–0.81)**	**0.001**	**0.69 (0.48–0.98)**	**0.04**	0.81 (0.60–1.09)	0.17
History of myocardial infarction or revascularization	0.71 (0.48–1.03)	0.07	**0.54 (0.35–0.82)**	**0.004**	0.94 (0.63–1.38)	0.74
Peripheral artery disease	1.30 (0.72–2.37)	0.39	1.19 (0.61–2.30)	0.61	0.97 (0.53–1.78)	0.92
Current smoker	0.77 (0.51–1.18)	0.24	1.04 (0.62–1.73)	0.89	0.80 (0.53–1.22)	0.31
Heart failure	1.08 (0.64–1.85)	0.77	0.61 (0.35–1.06)	0.08	**2.36 (1.26–4.42)**	**0.007**
Per 1 SD lnFGF23	**1.26 (1.07–1.49)**	**0.007**	**1.24 (1.02–1.51)**	**0.03**	**1.23 (1.04–1.46)**	**0.01**
Estimated glomerular filtration rate	**0.987 (0.977–0.997)**	**0.02**	0.992 (0.980–1.004)	0.18	0.999 (0.990–1.009)	0.89
Hemoglobin	1.02 (0.93–1.12)	0.69	1.01 (0.90–1.13)	0.90	**1.12 (1.02–1.23)**	**0.02**
Urinary protein, g/24 h (reference ≤ 0.5)						
0.5–3.5	1.13 (0.78–1.65)	0.51	0.91 (0.58–1.42)	0.67	0.95 (0.65–1.38)	0.77
>3.5	1.38 (0.67–2.87)	0.39	2.02 (0.93–4.40)	0.08	1.35 (0.63–2.89)	0.44
LnPTH	**1.37 (1.09–1.73)**	**0.008**	**1.42 (1.08–1.86)**	**0.01**	1.23 (0.98–1.55)	0.08
Phosphate	1.12 (0.88–1.43)	0.37	1.24 (0.93–1.64)	0.14	1.07 (0.84–1.36)	0.60

Odds ratios with *P* value <0.05 are in bold. Abbreviations: CI, confidence interval; FGF23, fibroblast growth factor 23; PTH, parathyroid hormone.

the higher odds concentric hypertrophy, eccentric hypertrophy, and concentric remodeling among Black and Whites in the presence of CKD. Thus, further research in understanding the relationship between race/ethnicity and left ventricular geometry on CVD outcomes in CKD patients is needed.

In support of our results, many of the identified correlates of left ventricular remodeling, such as higher serum FGF23 levels, higher serum phosphate levels, and lower eGFR, are consistent with prior studies of LVH and concentric hypertrophy in the general population and in patients with CKD, including analyses in CRIC.[9,27,36] Our findings also underscore the importance of the relationship between the level of blood pressure and LVH. In our regression models, higher SBP and hypertension severity, measured by use of more than 3 antihypertensive medications, were each positively associated with higher LVMI, eccentric hypertrophy, and concentric hypertrophy.

Our study has a number of strengths. They include a large number of Blacks—a historically underrepresented Black population in large, CKD cohorts—and the consideration of a relatively large number of cardiovascular risk factors. There are also several limitations. Our findings should be interpreted in light of the cross-sectional design, which limits our ability to infer causation. We selected covariates based on literature review, author expertise, and univariate analyses. We used baseline values of phosphate, FGF23, and total PTH measurements in the regression model instead of values from the 1-year follow-up visit due to data availability. The relationship between vitamin D levels, troponin T, N-terminal pro-B-type natriuretic peptide, inflammation, and left ventricular remodeling in CKD patients has been previously investigated in CRIC[28,37–40]; however, these variables were not included in our regression models. Unmeasured variables may have confounded the multivariable models.

This is the first large-scale demonstration of significant differences in left ventricular mass, hypertrophic morphology, and function between non-Hispanic Black and non-Hispanic Whites in a racially balanced, US-based cohort of participants with mild-to-moderate CKD. Future, longitudinal studies will define the impact of differences in cardiac structure and function on risk for adverse cardiovascular event rates, cardiovascular mortality, and all-cause mortality between Black and White CKD patients.

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DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

1. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, Van Lente F, Levey AS. Prevalence of chronic kidney disease in the United States. *JAMA* 2007; 298:2038–2047.
2. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; 351:1296–1305.
3. Muntner P, He J, Hamm L, Loria C, Whelton PK. Renal insufficiency and subsequent death resulting from cardiovascular disease in the United States. *J Am Soc Nephrol* 2002; 13:745–753.
4. Fried LF, Shlipak MG, Crump C, Bleyer AJ, Gottdiener JS, Kronmal RA, Kuller LH, Newman AB. Renal insufficiency as a predictor of cardiovascular outcomes and mortality in elderly individuals. *J Am Coll Cardiol* 2003; 41:1364–1372.
5. Kottgen A, Russell SD, Loehr LR, Crainiceanu CM, Rosamond WD, Chang PP, Chambless LE, Coresh J. Reduced kidney function as a risk factor for incident heart failure: the atherosclerosis risk in communities (ARIC) study. *J Am Soc Nephrol* 2007; 18:1307–1315.
6. Cerasola G, Nardi E, Mulè G, Palermo A, Cusimano P, Guarneri M, Arsena R, Giammarresi G, Carola Foraci A, Cottone S. Left ventricular mass in hypertensive patients with mild-to-moderate reduction of renal function. *Nephrology (Carlton)* 2010; 15:203–210.
7. Eckardt KU, Scherhag A, Macdougall IC, Tsakiris D, Clyne N, Locatelli F, Zaug MF, Burger HU, Drueke TB. Left ventricular geometry predicts cardiovascular outcomes associated with anemia correction in CKD. *J Am Soc Nephrol* 2009; 20:2651–2660.
8. Tsioufis C, Vezali E, Tsiachris D, Dimitriadis K, Taxiarchou E, Chatzis D, Thomopoulos C, Syrseloudis D, Stefanadi E, Mihas C, Katsi V, Papademetriou V, Stefanadis C. Left ventricular hypertrophy versus chronic kidney disease as predictors of cardiovascular events in hypertension: a Greek 6-year-follow-up study. *J Hypertens* 2009; 27:744–752.
9. Drazner MH. The progression of hypertensive heart disease. *Circulation* 2011; 123:327–334.
10. Drazner MH, Dries DL, Peshock RM, Cooper RS, Klassen C, Kazi F, Willett D, Victor RG. Left ventricular hypertrophy is more prevalent in Blacks than Whites in the general population: the Dallas Heart Study. *Hypertension* 2005; 46:124–129.
11. Kizer JR, Arnett DK, Bella JN, Paranicas M, Rao DC, Province MA, Oberman A, Kitzman DW, Hopkins PN, Liu JE, Devereux RB. Differences in left ventricular structure between Black and White hypertensive adults: the Hypertension Genetic Epidemiology Network study. *Hypertension* 2004; 43:1182–1188.
12. Mehta SK, Rame JE, Khera A, Murphy SA, Canham RM, Peshock RM, de Lemos JA, Drazner MH. Left ventricular hypertrophy, subclinical atherosclerosis, and inflammation. *Hypertension* 2007; 49:1385–1391.
13. Weiner DE, Tighiouart H, Amin MG, Stark PC, MacLeod B, Griffith JL, Salem DN, Levey AS, Sarnak MJ. Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies. *J Am Soc Nephrol* 2004; 15:1307–1315.
14. Mehrotra R, Kermah D, Fried L, Adler S, Norris K. Racial differences in mortality among those with CKD. *J Am Soc Nephrol* 2008; 19:1403–1410.
15. Kovesdy CP, Anderson JE, Derose SF, Kalantar-Zadeh K. Outcomes associated with race in males with nondialysis-dependent chronic kidney disease. *Clin J Am Soc Nephrol* 2009; 4:973–978.
16. Lash JP, Ricardo AC, Roy J, Deo R, Fischer M, Flack J, He J, Keane M, Lora C, Ojo A, Rahman M, Steigerwalt S, Tao K, Wolf M, Wright JT Jr, Go AS; CRIC Study Investigators. Race/ethnicity and cardiovascular outcomes in adults with CKD: findings from the CRIC (Chronic Renal Insufficiency Cohort) and Hispanic CRIC studies. *Am J Kidney Dis* 2016; 68:545–553.
17. Derose SF, Rutkowski MP, Levin NW, Liu IL, Shi JM, Jacobsen SJ, Crooks PW. Incidence of end-stage renal disease and death among insured African Americans with chronic kidney disease. *Kidney Int* 2009; 76:629–637.
18. Choi AI, Rodriguez RA, Bacchetti P, Bertenthal D, Hernandez GT, O'Hare AM. White/Black racial differences in risk of end-stage renal disease and death. *Am J Med* 2009; 122:672–678.
19. Kovesdy CP, Quarles LD, Lott EH, Lu JL, Ma JZ, Molnar MZ, Kalantar-Zadeh K. Survival advantage in Black versus White men with CKD: effect of estimated GFR and case mix. *Am J Kidney Dis* 2013; 62:228–235.
20. Cerasola G, Nardi E, Palermo A, Mulè G, Cottone S. Epidemiology and pathophysiology of left ventricular abnormalities in chronic kidney disease: a review. *J Nephrol* 2011; 24:1–10.
21. Feldman HI, Appel LJ, Chertow GM, Cifelli D, Cizman B, Daugirdas J, Fink FC, Franklin-Becker ED, Go AS, Hamm LL, He J, Hostetter T, Hsu CY, Jamerson K, Joffe M, Kusek JW, Landis JR, Lash JP, Miller ER, Mohler ER 3rd, Muntner P, Ojo AO, Rahman M, Townsend RR, Wright JT; Chronic Renal Insufficiency Cohort (CRIC) Study Investigators. The Chronic Renal Insufficiency Cohort (CRIC) Study: Design and Methods. *J Am Soc Nephrol* 2003; 14(7 Suppl 2):S148–S153.
22. Lash JP, Go AS, Appel LJ, He J, Ojo A, Rahman M, Townsend RR, Xie D, Cifelli D, Cohan J, Fink JC, Fischer MJ, Gadegbeku C, Hamm LL, Kusek JW, Landis JR, Narva A, Robinson N, Teal V, Feldman HI; Chronic Renal Insufficiency Cohort (CRIC) Study Group. Chronic Renal Insufficiency Cohort (CRIC) Study: baseline characteristics and associations with kidney function. *Clin J Am Soc Nephrol* 2009; 4:1302–1311.
23. Ricardo AC, Lash JP, Fischer MJ, Lora CM, Budoff M, Keane MG, Kusek JW, Martinez M, Nessel L, Stamos T, Ojo A, Rahman M, Soliman EZ, Yang W, Feldman HI, Go AS; CRIC and HCRIC Investigators. Cardiovascular disease among Hispanics and non-Hispanics in the chronic renal insufficiency cohort (CRIC) study. *Clin J Am Soc Nephrol* 2011; 6:2121–2131.

24. Anderson AH, Yang W, Hsu CY, Joffe MM, Leonard MB, Xie D, Chen J, Greene T, Jaar BG, Kao P, Kusek JW, Landis JR, Lash JP, Townsend RR, Weir MR, Feldman HI; CRIC Study Investigators. Estimating GFR among participants in the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J Kidney Dis* 2012; 60:250–261.
25. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005; 18:1440–1463.
26. Zoccali C, Benedetto FA, Mallamaci F, Tripepi G, Giacone G, Cataliotti A, Seminara G, Stancanelli B, Malatino LS; CREED Investigators. Prognostic impact of the indexation of left ventricular mass in patients undergoing dialysis. *J Am Soc Nephrol* 2001; 12:2768–2774.
27. Bansal N, Keane M, Delafontaine P, Dries D, Foster E, Gadegbeku CA, Go AS, Hamm LL, Kusek JW, Ojo AO, Rahman M, Tao K, Wright JT, Xie D, Hsu CY; CRIC Study Investigators. A longitudinal study of left ventricular function and structure from CKD to ESRD: the CRIC study. *Clin J Am Soc Nephrol* 2013; 8:355–362.
28. Ky B, Shults J, Keane MG, Sutton MS, Wolf M, Feldman HI, Reese PP, Anderson CA, Townsend RR, Deo R, Lo J, Gadegbeku C, Carlow D, Sulik MJ, Leonard MB; CRIC Study Investigators. FGF23 modifies the relationship between vitamin D and cardiac remodeling. *Circ Heart Fail* 2013; 6:817–824.
29. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA, Evangelista A. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr* 2009; 22:107–133.
30. Henry RM, Kamp O, Kostense PJ, Spijkerman AM, Dekker JM, Nijpels G, Heine RJ, Bouter LM, Stehouwer CD. Mild renal insufficiency is associated with increased left ventricular mass in men, but not in women: an arterial stiffness-related phenomenon–the Hoorn Study. *Kidney Int* 2005; 68:673–679.
31. Paoletti E, Bellino D, Cassottana P, Rolla D, Cannella G. Left ventricular hypertrophy in nondiabetic predialysis CKD. *Am J Kidney Dis* 2005; 46:320–327.
32. Peterson GE, de Backer T, Gabriel A, Ilic V, Vagaonescu T, Appel LJ, Contreras G, Kendrick C, Rostand S, Phillips RA; African American Study of Kidney Disease Investigators. Prevalence and correlates of left ventricular hypertrophy in the African American Study of Kidney Disease Cohort Study. *Hypertension* 2007; 50:1033–1039.
33. Stack AG, Saran R. Clinical correlates and mortality impact of left ventricular hypertrophy among new ESRD patients in the United States. *Am J Kidney Dis* 2002; 40:1202–1210.
34. Nardi E, Palermo A, Mulè G, Cusimano P, Cottone S, Cerasola G. Left ventricular hypertrophy and geometry in hypertensive patients with chronic kidney disease. *J Hypertens* 2009; 27:633–641.
35. Bahrami H, Kronmal R, Bluemke DA, Olson J, Shea S, Liu K, Burke GL, Lima JA. Differences in the incidence of congestive heart failure by ethnicity: the multi-ethnic study of atherosclerosis. *Arch Intern Med* 2008; 168:2138–2145.
36. Faul C, Amaral AP, Oskouei B, Hu MC, Sloan A, Isakova T, Gutiérrez OM, Aguillon-Prada R, Lincoln J, Hare JM, Mundel P, Morales A, Scialla J, Fischer M, Soliman EZ, Chen J, Go AS, Rosas SE, Nessel L, Townsend RR, Feldman HI, St John Sutton M, Ojo A, Gadegbeku C, Di Marco GS, Reuter S, Kentrup D, Tiemann K, Brand M, Hill JA, Moe OW, Kuro-O M, Kusek JW, Keane MG, Wolf M. FGF23 induces left ventricular hypertrophy. *J Clin Invest* 2011; 121:4393–4408.
37. Mishra RK, Li Y, DeFilippi C, Fischer MJ, Yang W, Keane M, Chen J, He J, Kallem R, Horwitz EJ, Rafey M, Raj DS, Go AS, Shlipak MG; CRIC Study Investigators. Association of cardiac troponin T with left ventricular structure and function in CKD. *Am J Kidney Dis* 2013; 61:701–709.
38. Smith K, deFilippi C, Isakova T, Gutiérrez OM, Laliberte K, Seliger S, Kelley W, Duh SH, Hise M, Christenson R, Wolf M, Januzzi J. Fibroblast growth factor 23, high-sensitivity cardiac troponin, and left ventricular hypertrophy in CKD. *Am J Kidney Dis* 2013; 61:67–73.
39. Mishra RK, Li Y, Ricardo AC, Yang W, Keane M, Cuevas M, Christenson R, deFilippi C, Chen J, He J, Kallem RR, Raj DS, Schelling JR, Wright J, Go AS, Shlipak MG; Chronic Renal Insufficiency Cohort Investigators. Association of N-terminal pro-B-type natriuretic peptide with left ventricular structure and function in chronic kidney disease (from the Chronic Renal Insufficiency Cohort [CRIC]). *Am J Cardiol* 2013; 111:432–438.
40. Gupta J, Dominic EA, Fink JC, Ojo AO, Barrows IR, Reilly MP, Townsend RR, Joffe MM, Rosas SE, Wolman M, Patel SS, Keane MG, Feldman HI, Kusek JW, Raj DS; CRIC Study Investigators. Association between inflammation and cardiac geometry in chronic kidney disease: findings from the CRIC study. *PLoS One* 2015; 10:e0124772.