ORIGINAL RESEARCH

# Kidney Disease Measures and Left Ventricular Structure and Function: The Atherosclerosis Risk in Communities Study

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***Background*—**Heart failure is one of the most important complications of chronic kidney disease (CKD). However, few studies comprehensively investigated left ventricular (LV) structure and function in relation to 2 key CKD measures, estimated glomerular filtration rate (eGFR) and urine albumin/creatinine ratio (ACR).

***Methods and Results*—**Among 4175 ARIC (Atherosclerosis Risk in Communities) participants (aged 66–90 years during 2011–2013), we quantified the association of eGFR and ACR with echocardiogram parameters of LV mass, size, systolic function, and diastolic function. Adjusting for demographic variables, both CKD measures were significantly associated with most echocardiogram parameters. Additionally accounting for other potential confounders, we observed significantly higher LV mass index according to reduced eGFR (82.3 [95% confidence interval (CI), 77.6–87.0] g/m$^2$ for eGFR <30 mL/min per 1.73 m$^2$, 80.9 [95% CI, 77.3–84.6] g/m$^2$ for eGFR 30–44 mL/min per 1.73 m$^2$, and 80.1 [95% CI, 76.7–83.5] g/m$^2$ for eGFR 45–59 mL/min per 1.73 m$^2$ compared with 78.7 [95% CI, 75.3–82.1] g/m$^2$ for eGFR 75–89 mL/min per 1.73 m$^2$; trend $P$<0.001). Regarding LV size and function, significant differences were observed for some parameters, particularly at eGFR <30 mL/min per 1.73 m$^2$. For ACR, the associations remained significant for most parameters (eg, LV mass index, 91.5 [95% CI, 86.6–96.5] g/m$^2$ for ACR ≥300 mg/g and 82.9 [95% CI, 79.4–86.3] g/m$^2$ for ACR 30–299 mg/g compared with 77.7 [95% CI, 74.4–81.1] g/m$^2$ for ACR <10 mg/g [trend $P$<0.001]; left arterial volume index, 24.9 [95% CI, 22.9–26.8] and 24.7 [95% CI, 23.4–26.1] mL/m$^2$ compared with 23.4 [95% CI, 22.1–24.7] mL/m$^2$, respectively [trend $P$=0.010]). Dichotomizing echo parameters with clinical thresholds, the stronger relationships of ACR over eGFR were further evident.

***Conclusions*—**LV mass was related to both CKD measures, whereas LV size and function were robustly associated with albuminuria. These results have implications for pathophysiological processes behind cardiorenal syndrome and targeted cardiac assessment in patients with CKD. **(*J Am Heart Assoc*. 2017;6:e006259. DOI: 10.1161/JAHA.117.006259.)**

**Key Words:** albuminuria • cardiac function • cardiac structure • epidemiology • glomerular filtration rate

Chronic kidney disease (CKD), defined as reduced glomerular filtration rate (GFR) or elevated albuminuria, is a major global public health problem.[1,2] CKD affects >10% of adults in the world[3–6] and is an independent predictor of cardiovascular disease.[7,8] Indeed, individuals with CKD are more likely to die because of cardiovascular disease before they reach end-stage renal disease.[9] Although CKD has been shown to relate to various cardiovascular outcomes, a recent international meta-analysis demonstrated that CKD was more strongly associated with the risk of heart failure than of coronary heart disease and stroke.[10]

In this connection, several studies have investigated the association between CKD measures and cardiac structure and function.[11–20] However, most of these studies mainly assessed left ventricular (LV) mass or hypertrophy as a parameter of cardiac structure but did not necessarily evaluate measures of LV size. Also, LV function (both systolic and diastolic) was less often studied compared with cardiac structure. Moreover, only a limited number of studies simultaneously evaluated 2 key measures of CKD, estimated GFR (eGFR) and albuminuria, in this context. Thus, the relationship of any specific cardiac functional or structural phenotypes with either or both of reduced eGFR and elevated

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Accompanying Tables S1, S2 and Figures S1 through S5 are available at http://jaha.ahajournals.org/content/6/9/e006259/DC1/embed/inline-supplementary-material-1.pdf

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## Clinical Perspective

### What Is New?

- This study examined the associations of estimated glomerular filtration rate and albuminuria with left ventricular structure and systolic and diastolic function in a large community-based cohort.
- Left ventricular mass was related to both chronic kidney disease measures, whereas left ventricular size and function were robustly associated with albuminuria.
- The associations with estimated glomerular filtration rate tended to become evident at the severely reduced level of <30 mL/min per 1.73 $m^2$, whereas even a high normal albumin/creatinine ratio of 10 to 29 mg/g demonstrated significant associations with some cardiac structural and functional abnormalities.

### What Are the Clinical Implications?

- Our data suggest individuals with elevated albuminuria and possibly those with severely reduced estimated glomerular filtration rate (<30 mL/min per 1.73 $m^2$) are potential candidates for targeted cardiac assessment.
- Our results also have implications for pathophysiological processes behind cardiorenal syndrome.

albuminuria is not certain. This information will help us better understand the pathophysiological characteristics behind cardiac abnormalities related to CKD and contemplate who with CKD may require cardiac assessment. Therefore, the objective of this study is to comprehensively examine the associations of eGFR and albuminuria with LV structure and systolic and diastolic function in a large community-based cohort, the ARIC (Atherosclerosis Risk in Communities) study.

## Methods

### Study Participants

The ARIC study enrolled 15 792 participants aged 45 to 64 years at visit 1 from 1987 to 1989 from 4 communities in the United States: Washington County, Maryland; suburban Minneapolis, Minnesota; Forsyth County, North Carolina; and Jackson, Mississippi.[21] Three triennial follow-up visits were subsequently performed (visit 2 during 1990–1992, visit 3 during 1993–1995, and visit 4 during 1996–1998), and the latest visit (visit 5) was conducted from 2011 to 2013. ARIC study participants provided information on demographic and behavioral variables and medical history to a trained interviewer at each visit. Physical assessment and blood sample collection were performed according to standardized procedures.[22]

Cardiac echo was planned in the overall study population only at visit 5 in the ARIC study. Of 6538 participants at visit 5, we excluded those who reported race other than white or black (n=18 [0.3%]) or had missing values of kidney measures (n=820 [12.5%]), cardiac echo parameters (n=1073 [16.4%]), or covariates of interest (n=452 [6.9%]), leaving a final study population of 4175 participants. Participants who were excluded from the study demonstrated poorer status for some clinical conditions (eg, higher prevalence of diabetes mellitus and cardiovascular disease) than those who were included in the analysis. However, most echo parameters were similar between the 2 groups (Table S1). All participants gave informed consent, and the study was approved by the institutional review boards of all participating institutions.

### Kidney Measures

Our primary exposures were eGFR and albuminuria at visit 5, although we used these CKD measures at prior visits for a sensitivity analysis, as described subsequently. We primarily used the CKD-EPI equation with both creatinine and cystatin C, currently considered best, for estimating GFR.[23] We repeated the analysis using eGFR based on the CKD-EPI creatinine equation,[24,25] because kidney function is often assessed by serum creatinine as a sole filtration marker in clinical practice. At ARIC visit 5, serum creatinine concentration was measured using a creatinase enzymatic method on a Roche Modular P Chemistry Analyzer standardized to isotope dilution mass spectrometry.[26] Cystatin C was measured by a turbidometric method standardized against the international calibrator standard.[26] As recommended in clinical guidelines,[27] urinary albumin/creatinine ratio (ACR) from a random urine sample was used as a measure of albuminuria. Albumin in urine was measured using an immunoturbidometric method on the ProSpec nephelometric analyzer, whereas urine creatinine was measured using the aforementioned creatinase enzymatic method.[26] Details about the methods used for assessing serum creatinine, cystatin C, and ACR at prior visits were published previously.[28,29]

### Echocardiogram Assessment

Details about the protocol of the ARIC visit 5 echocardiographic evaluation were previously described.[30] Briefly, all imaging data were acquired on a Philips iE33 instrument by trained sonographers, according to the study-specific protocol, including 2-dimensional, Doppler, and tissue Doppler imaging (TDI). All the reading was centrally performed by echocardiographers at the Brigham and Women's Hospital (Boston, MA) echo core laboratory. The current analysis focused on parameters of LV mass/thickness (interventricular septal wall thickness at diastole, posterior wall thickness at diastole, LV mass index, and relative wall thickness), size (LV end-diastolic diameter, LV end-systolic diameter, LV end-

diastolic volume index, and LV end-systolic volume index), LV systolic function (ejection fraction [EF], TDI S', and global longitudinal strain [GLS] derived from speckle-tracking assessment), and LV diastolic function (left atrial volume index, early mitral inflow peak velocity, early mitral annulus TDI velocity, and early mitral inflow peak velocity/early mitral annulus TDI velocity). We observed similar results for indexing to both body surface area and height ($m^{2.7}$) and, thus, show results for echo parameters indexed to body surface area when appropriate. Empirically, we a priori determined the following as the primary echo parameter for each key element of cardiac structure and function: LV mass index for LV mass, LV end-diastolic volume index for LV size, LV EF for systolic function, and left atrial volume index for diastolic dysfunction.

## Covariates

Demographic (age, sex, and race) and lifestyle (smoking status, alcohol intake, and physical activity) variables were based on self-report. Smoking status and alcohol intake were dichotomized as current versus former/never. Physical activity was categorized into 5 categories (much less, less, the same, more, and much more) based on self-reported leisure time activity relative to others with the same age. Certified technicians measured blood pressure 3 times with participants in the sitting position after 5 minutes of rest using a validated automatic sphygmomanometer (the OMRON HEM-907 XL). The average of the last 2 readings was recorded. Participants were asked to bring all medications, including antihypertensive and antidiabetic drugs, which were coded by trained personnel. Diabetes mellitus was defined as a fasting glucose level ≥7.0 mmol/L, a nonfasting glucose level ≥11.1 mmol/L, self-reported physician diagnosis of diabetes mellitus, or use of glucose-lowering medications. Total cholesterol and high-density lipoprotein cholesterol levels were determined using enzymatic methods meeting the National Cholesterol Education Program's accuracy performance criteria. Prevalent coronary heart disease and stroke were defined as self-reported history at visit 1 or clinical events from visit 1 through 5. Hospitalization for heart failure, physician diagnosis of heart failure, and self-reported treatment for heart failure between visits 1 and 5 were considered prevalent heart failure.

## Statistical Analysis

Baseline characteristics were demonstrated across groups based on categories of eGFR (≥90, 75–89, 60–74, 45–59, 30–44, and <30 mL/min per 1.73 $m^2$) and ACR (<10, 10–29, 30–299, and ≥300 mg/g).[8,27] Differences in variables across the categories were assessed by ANOVA or $\chi^2$ test, as appropriate. Subsequently, using linear regression models, we assessed whether cardiac echo parameters differ across those kidney categories independently of potential confounders. Potential confounders included age, race, sex, center, smoking status, alcohol intake, physical activity, body mass index, diabetes mellitus, antihypertensive drugs, systolic and diastolic blood pressures, history of coronary disease, stroke, and heart failure, total and high-density lipoprotein cholesterol levels, and the other kidney measures (namely, ACR for eGFR analysis and eGFR for ACR analysis). We implemented 2 models, demographically adjusted (age, race, sex, and center) and fully adjusted (all potential[31] confounders listed above). Because we were interested in the independent associations of CKD measures with LV structure and function, we mainly present data from fully adjusted models. *P* value for trend was based on models with the category median for each CKD measure as a continuous variable.[32,33] The trend analysis for eGFR was restricted to eGFR <90 mL/min per 1.73 $m^2$, given the J-shaped relationships often seen in higher eGFR, as shown in Results.

For the prespecified primary echo parameters, we characterized continuous associations according to both kidney measures with their linear spline terms using linear regression models (knots at aforementioned thresholds for both eGFR and ACR). Subsequently, to provide a more clinical perspective, we ran logistic regression with echo parameters dichotomized at clinical thresholds as dependent variables and kidney measure categories as independent variables. For this analysis, eGFR 75 to 89 mL/min per 1.73 $m^2$ and ACR <10 mg/g were treated as references based on number of individuals in our study, clinical guidelines,[27] and previous literature for older adults.[34] All analyses were conducted in Stata 13, and $P<0.05$ was considered statistically significant.

## Results

Of 4175 participants, 23.5% (n=979) were black and 43.0% (n=1796) were men. Of those participants, 36.5% (n=1525) had reduced eGFR <60 mL/min per 1.73 $m^2$ and 18.4% (n=768) had high ACR ≥30 mg/g (9.9% [n=413] had both). We observed a weak correlation between eGFR and ACR ($r=-0.17$). In general, those with lower eGFR and higher ACR had a worse cardiovascular risk profile (eg, older age and higher likelihood of having diabetes mellitus, hypertension, and history of cardiovascular disease) compared with those with preserved eGFR and lower ACR (Table S2 and Table 1).

When we adjusted for demographic variables, both eGFR and ACR were associated with the prespecified primary echo parameters (LV mass index, LV end-diastolic volume index, LV EF, and left atrial volume index; Figure). For all 4 parameters, the associations were weak or largely flat at eGFR >45 mL/min per 1.73 $m^2$ and became steep lower than this range (<30 mL/min per 1.73 $m^2$ for left atrial volume index). In

**Table 1.** Demographic and Clinical Characteristics According to ACR Categories

| Characteristics | ACR Categories, mg/g | | | |
|---|---|---|---|---|
| | <10 (n=2036) | 10–29 (n=1371) | 30–299 (n=658) | ≥300 (n=110) |
| Age, y | 75 (5) | 76 (5) | 77 (5) | 77 (5) |
| Center, n (%) | | | | |
| Forsyth County, NC | 463 (22.7) | 301 (22.0) | 148 (22.5) | 18 (16.4) |
| Jackson, MS | 420 (20.6) | 269 (19.6) | 157 (23.9) | 46 (41.8) |
| Suburban Minneapolis, MN | 619 (30.4) | 416 (30.3) | 178 (27.0) | 20 (18.2) |
| Washington County, MD | 534 (26.2) | 385 (28.1) | 175 (26.6) | 26 (23.6) |
| Black race, n (%) | 455 (22.3) | 295 (21.5) | 182 (27.7) | 47 (42.7) |
| Male sex, n (%) | 930 (45.7) | 488 (35.6) | 319 (48.5) | 59 (53.6) |
| Current smoking, n (%) | 96 (4.7) | 89 (6.5) | 55 (8.4) | 4 (3.6) |
| Current drinking, n (%) | 1037 (50.9) | 669 (48.8) | 293 (44.5) | 47 (42.7) |
| Physical activity in relation to peers, n (%) | | | | |
| Much less | 62 (3.0) | 45 (3.3) | 37 (5.6) | 8 (7.3) |
| Less | 228 (11.2) | 199 (14.5) | 112 (17.0) | 23 (20.9) |
| Same | 667 (32.8) | 478 (34.9) | 223 (33.9) | 44 (40.0) |
| More | 755 (37.1) | 475 (34.6) | 199 (30.2) | 27 (24.6) |
| Much more | 324 (15.9) | 174 (12.7) | 87 (13.2) | 8 (7.3) |
| BMI, kg/m$^2$ | 29 (5) | 28 (6) | 29 (6) | 30 (6) |
| Diabetes mellitus, n (%) | 589 (28.9) | 460 (33.5) | 309 (47.0) | 70 (63.6) |
| Antihypertensive drugs, n (%) | 1451 (71.3) | 1010 (73.7) | 527 (83.1) | 105 (95.4) |
| Systolic BP, mm Hg | 127 (16) | 132 (18) | 137 (20) | 147 (20) |
| Diastolic BP, mm Hg | 66 (10) | 66 (11) | 67 (11) | 68 (12) |
| History of stroke, n (%) | 52 (2.6) | 51 (3.7) | 36 (5.5) | 9 (8.2) |
| History of CHD, n (%) | 263 (12.9) | 191 (13.9) | 114 (17.3) | 31 (28.2) |
| History of heart failure, n (%) | 245 (12.0) | 205 (15.0) | 115 (17.5) | 40 (36.4) |
| Total cholesterol, mmol/L | 4.7 (1.0) | 4.8 (1.1) | 4.6 (1.1) | 4.5 (0.9) |
| HDL cholesterol, mmol/L | 1.3 (0.3) | 1.4 (0.4) | 1.3 (0.4) | 1.3 (0.4) |
| eGFR, mL/min per 1.73 m$^2$ | 71 (16) | 71 (17) | 65 (20) | 49 (23) |
| ACR, median (interquartile interval), mg/g | 6 (5–8) | 15 (12–20) | 57 (40–102) | 611 (399–1384) |

Values are mean (SD) unless otherwise specified. ACR indicates urine albumin/creatinine ratio; BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; eGFR, estimated glomerular filtration rate; and HDL, high-density lipoprotein.

contrast, ACR demonstrated monotonic dose-response relationships to all the 4 primary echo parameters.

When we further accounted for other potential confounders, the associations of eGFR with LV mass, size, and function were attenuated, but remained significant, for several parameters (Figure S1 and Table 2). In these fully adjusted models, the significant association was most consistently seen across different parameters for LV mass/hypertrophy (Table 2), followed by those of LV size and diastolic dysfunction. The association was least evident for LV systolic function parameters, although there was a significant association with EF. Statistically significant results with eGFR 75 to 89 mL/min per 1.73 m$^2$ as the reference were most commonly observed in individuals with severely reduced eGFR (<30 mL/min per 1.73 m$^2$; ie, posterior wall thickness at diastole, relative wall thickness, LV end-diastolic volume index, LV end-systolic volume index, LV end-systolic diameter, and EF). Participants with eGFR ≥90 mL/min per 1.73 m$^2$ also demonstrated significant alterations of some parameters of LV mass and size.

The attenuation by the adjustment for the other potential confounders was not that evident for ACR (Figure S1 and

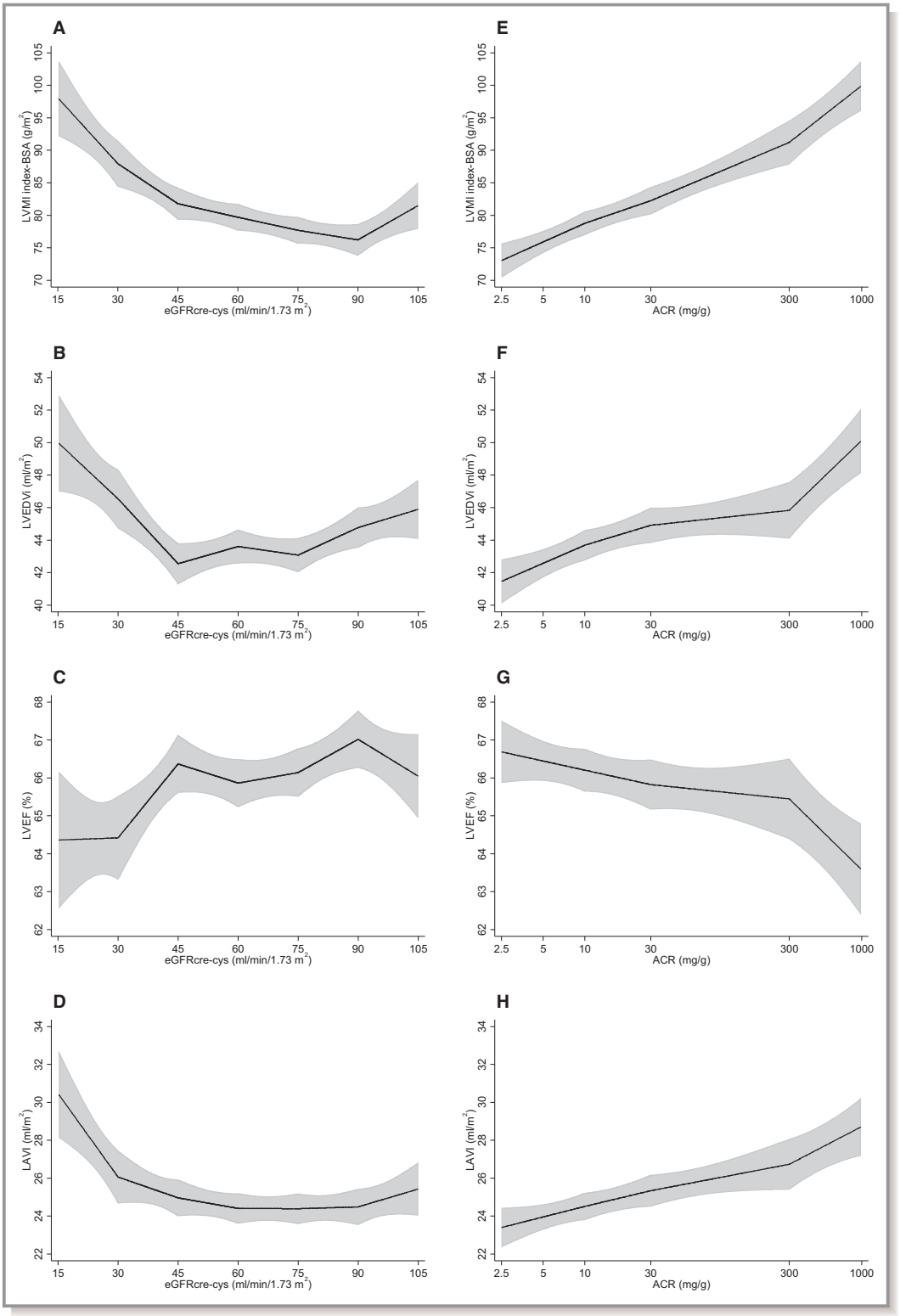


**Figure.** Demographically adjusted values of the primary echo parameters representing left ventricular (LV) mass (A & E), size (B & F), systolic function (C & G), and diastolic function (D & H), according to estimated glomerular filtration rate (eGFR) (A-D) and albumin/creatinine ratio (ACR) (E-H), based on linear regression models. Values were adjusted for age, race, sex, and center. Solid lines represent point estimates, and shaded areas indicate 95% confidence intervals. Cre-cys indicates creatinine and cystatin C; EF, ejection fraction; LAVI, left atrial volume index; LVEDVI, LV end-diastolic volume index; and LVMI, LV mass index.

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**Table 2.** Fully Adjusted Predicted Values (95% Confidence Intervals) of Echo Parameters Representing LV Mass, Size, Systolic Function, and Diastolic Function According to eGFR Categories Based on Linear Regression Models

| Echo Parameters | eGFR Categories, mL/min per 1.73 $m^2$ | | | | | | |
|---|---|---|---|---|---|---|---|
| | ≥90 (n=348) | 75–89 (n=983) | 60–74 (n=1319) | 45–59 (n=972) | 30–44 (n=443) | <30 (n=110) | *P* Value for Trend |
| LV mass related | | | | | | | |
| LVMI (g/$m^2$) | 81.1 (77.3–84.9)* | 78.7 (75.3–82.1) | 79.8 (76.4–83.1) | 80.1 (76.7–83.5) | 80.9 (77.3–84.6)* | 82.3 (77.6–87.0) | <0.001 |
| IVSd (cm) | 1.06 (1.03–1.09)* | 1.04 (1.01–1.07) | 1.05 (1.02–1.07) | 1.06 (1.03–1.08)* | 1.06 (1.03–1.09) | 1.06 (1.02–1.09) | <0.001 |
| PWTd (cm) | 0.91 (0.88–0.93) | 0.90 (0.88–0.92) | 0.91 (0.88–0.93) | 0.91 (0.89–0.94)* | 0.91 (0.88–0.94) | 0.95 (0.91–0.98)* | <0.001 |
| RWT | 0.41 (0.40–0.43) | 0.41 (0.40–0.42) | 0.41 (0.40–0.42) | 0.42 (0.40–0.43) | 0.41 (0.40–0.42) | 0.43 (0.41–0.45)* | 0.03 |
| LV size | | | | | | | |
| LVEDVI (mL/$m^2$) | 45.0 (43.0–47.0)* | 43.2 (41.4–45.0) | 43.3 (41.6–45.1) | 42.7 (40.9–44.4) | 43.1 (41.2–45.0) | 45.3 (42.8–47.7)* | 0.15 |
| LVESVI (mL/$m^2$) | 15.5 (14.3–16.7)* | 14.6 (13.5–15.7) | 15.0 (13.9–16.1) | 14.8 (13.7–15.9) | 15.0 (13.8–16.1) | 16.5 (14.9–18.0)* | <0.001 |
| LVEDD (cm) | 4.47 (4.38–4.56) | 4.43 (4.35–4.51) | 4.46 (4.38–4.54) | 4.44 (4.36–4.52) | 4.47 (4.39–4.56) | 4.46 (4.35–4.57) | 0.07 |
| LVESD (cm) | 2.57 (2.48–2.66) | 2.52 (2.44–2.61) | 2.57 (2.48–2.65)* | 2.57 (2.49–2.65)* | 2.61 (2.52–2.69)* | 2.65 (2.54–2.77)* | <0.001 |
| LV systolic function | | | | | | | |
| EF (%) | 66.3 (65.1–67.6) | 66.7 (65.5–67.8) | 66.1 (65.0–67.2)* | 66.2 (65.1–67.3) | 66.3 (65.1–67.5) | 64.8 (63.3–66.3)* | <0.001 |
| TDI S' lateral (cm/s) | 6.17 (5.94–6.40) | 6.20 (5.99–6.41) | 6.15 (5.94–6.36) | 6.12 (5.91–6.32) | 6.16 (5.93–6.38) | 6.25 (5.96–6.54) | 0.30 |
| TDI S' septal (cm/s) | 6.86 (6.53–7.19) | 6.99 (6.69–7.29) | 6.99 (6.69–7.28) | 6.97 (6.68–7.26) | 6.89 (6.57–7.21) | 7.07 (6.66–7.47) | 0.39 |
| Longitudinal strain (%) | −17.8 (−18.2 to −17.3) | −17.9 (−18.3 to −17.5) | −18.0 (−18.4 to −17.6) | −17.9 (−18.3 to −17.4) | −17.9 (−18.4 to −17.5) | −17.8 (−18.4 to −17.2) | 0.12 |
| LV diastolic function | | | | | | | |
| LAVI (mL/$m^2$) | 24.5 (23.0–26.0) | 23.7 (22.4–25.1) | 23.9 (22.5–25.2) | 23.4 (22.0–24.7) | 23.7 (22.3–25.2) | 24.8 (23.0–26.7) | 0.36 |
| E/e′ lateral | 11.3 (10.6–12.1) | 11.5 (10.8–12.1) | 11.5 (10.9–12.2) | 11.5 (10.8–12.1) | 11.5 (10.8–12.3) | 12.2 (11.2–13.1) | 0.11 |
| E/e′ septal | 13.7 (12.8–14.5) | 13.4 (12.6–14.2) | 13.6 (12.8–14.3) | 13.6 (12.8–14.3) | 13.9 (13.1–14.7) | 14.0 (13.0–15.1) | <0.001 |
| e′ Lateral (cm/s) | 6.73 (6.36–7.10) | 6.72 (6.38–7.06) | 6.65 (6.32–6.98) | 6.68 (6.35–7.02) | 6.71 (6.36–7.07) | 6.86 (6.40–7.32) | 0.54 |
| e′ Septal (cm/s) | 5.47 (5.21–5.73) | 5.62 (5.39–5.86) | 5.53 (5.30–5.76) | 5.49 (5.26–5.72)* | 5.51 (5.27–5.76) | 5.69 (5.36–6.01) | 0.01 |
| E/A | 0.90 (0.85–0.96) | 0.90 (0.85–0.95) | 0.89 (0.84–0.94) | 0.88 (0.83–0.93) | 0.90 (0.85–0.95) | 0.95 (0.88–1.02) | 0.87 |

Values were adjusted to mean values of age, race, sex, center, smoking status, alcohol intake, physical activity, body mass index, diabetes mellitus, antihypertensive medication, systolic and diastolic blood pressures, total and high-density lipoprotein cholesterol levels, prevalent stroke, coronary heart disease, heart failure, and albumin/creatinine ratio. *P* value for trend was based on a model implementing a median value of each eGFR category <90 mL/min per 1.73 $m^2$ as a continuous variable. E indicates early mitral inflow peak velocity; e′, early mitral annulus TDI velocity; E/A, peak velocity flow in early to late diastole; EF, ejection fraction; eGFR, estimated glomerular filtration rate; IVSd, interventricular septal wall thickness at diastole; LAVI, left atrial volume index; LV, left ventricular; LVEDD, LV end-diastolic diameter; LVEDVI, LV end-diastolic volume index; LVESD, LV end-systolic diameter; LVESVI, LV end-systolic volume index; LVMI, LV mass index; PWTd, posterior wall thickness at diastole; RWT, relative wall thickness; and TDI, tissue Doppler imaging.
*Indicates significant difference compared with eGFR 75 to 89 mL/min per 1.73 $m^2$.

**Table 3.** Fully Adjusted Predicted Values (95% Confidence Intervals) of Echo Parameters Representing LV Mass, Size, Systolic Function, and Diastolic Function According to ACR Categories Based on Linear Regression Models

| Echo Parameters | ACR Categories, mg/g | | | | *P* Value for Trend |
|---|---|---|---|---|---|
| | <10 (n=2036) | 10–29 (n=1371) | 30–299 (n=658) | ≥300 (n=110) | |
| LV mass related | | | | | |
| LVMI (g/m$^2$) | 77.7 (74.4–81.1) | 80.4 (77.1–83.8)* | 82.9 (79.4–86.3)* | 91.5 (86.6–96.5)* | <0.001 |
| IVSd (cm) | 1.04 (1.01–1.07) | 1.06 (1.03–1.08)* | 1.06 (1.04–1.09)* | 1.11 (1.07–1.15)* | <0.001 |
| PWTd (cm) | 0.90 (0.88–0.92) | 0.91 (0.89–0.94)* | 0.93 (0.90–0.95)* | 0.96 (0.93–1.00)* | <0.001 |
| RWT | 0.41 (0.40–0.42) | 0.41 (0.40–0.43) | 0.42 (0.40–0.43)* | 0.42 (0.40–0.44) | 0.03 |
| LV size | | | | | |
| LVEDVI (mL/m$^2$) | 42.5 (40.8–44.3) | 43.6 (41.9–45.4)* | 44.5 (42.7–46.3)* | 46.9 (44.3–49.4)* | <0.001 |
| LVESVI (mL/m$^2$) | 14.5 (13.4–15.6) | 15.0 (14.0–16.1)* | 15.6 (14.5–16.8)* | 17.5 (15.9–19.1)* | <0.001 |
| LVEDD (cm) | 4.42 (4.34–4.50) | 4.46 (4.38–4.54)* | 4.48 (4.39–4.56)* | 4.62 (4.50–4.74)* | <0.001 |
| LVESD (cm) | 2.54 (2.46–2.62) | 2.57 (2.48–2.65) | 2.60 (2.52–2.69)* | 2.69 (2.57–2.81)* | <0.001 |
| LV systolic function | | | | | |
| EF (%) | 66.6 (65.5–67.7) | 66.2 (65.1–67.3) | 65.8 (64.6–66.8)* | 64.6 (63.0–66.2)* | <0.001 |
| TDI S' lateral (cm/s) | 6.16 (5.96–6.37) | 6.21 (6.01–6.42) | 6.11 (5.90–6.33) | 5.90 (5.59–6.20)* | 0.07 |
| TDI S' septal (cm/s) | 7.01 (6.72–7.30) | 6.94 (6.65–7.23) | 6.92 (6.62–7.22) | 6.93 (6.50–7.35) | 0.66 |
| Longitudinal strain (%) | −18.1 (−18.5 to −17.7) | −17.9 (−18.3 to −17.5)* | −17.7 (−18.1 to −17.2)* | −17.0 (−17.6 to −16.4)* | <0.001 |
| LV diastolic function | | | | | |
| LAVI (mL/m$^2$) | 23.4 (22.1–24.7) | 23.8 (22.5–25.1) | 24.7 (23.4–26.1)* | 24.9 (22.9–26.8) | 0.01 |
| E/e′ lateral | 11.4 (10.7–12.0) | 11.5 (10.8–12.1) | 11.9 (11.2–12.6)* | 12.2 (11.3–13.2)* | <0.001 |
| E/e′ septal | 13.3 (12.5–14.0) | 13.4 (12.7–14.2) | 14.2 (13.4–15.0)* | 15.6 (14.5–16.7)* | <0.001 |
| e′ Lateral (cm/s) | 6.80 (6.48–7.13) | 6.69 (6.36–7.02) | 6.52 (6.18–6.86)* | 6.20 (5.72–6.68)* | <0.001 |
| e′ Septal (cm/s) | 5.66 (5.44–5.89) | 5.56 (5.33–5.79)* | 5.34 (5.10–5.58)* | 4.91 (4.57–5.24)* | <0.001 |
| E/A | 0.90 (0.85–0.95) | 0.89 (0.84–0.94) | 0.89 (0.84–0.94) | 0.87 (0.80–0.95) | 0.50 |

Values were adjusted to mean values of age, race, sex, center, smoking status, alcohol intake, physical activity, body mass index, diabetes mellitus, antihypertensive medication, systolic and diastolic blood pressures, total and high-density lipoprotein cholesterol levels, prevalent stroke, coronary heart disease, heart failure, and estimated glomerular filtration rate. *P* value for trend was based on a model implementing a median value of each ACR category as a continuous variable. ACR indicates albumin/creatinine ratio; E, early mitral inflow peak velocity; e′, early mitral annulus TDI velocity; E/A, peak velocity flow in early to late diastole; EF, ejection fraction; IVSd, interventricular septal wall thickness at diastole; LAVI, left atrial volume index; LV, left ventricular; LVEDD, LV end-diastolic diameter; LVEDVI, LV end-diastolic volume index; LVESD, LV end-systolic diameter; LVESVI, LV end-systolic volume index; LVMI, LV mass index; PWTd, posterior wall thickness at diastole; RWT, relative wall thickness; and TDI, tissue Doppler imaging.
*Indicates significant difference compared with ACR <10 mg/g.

Table 3); overall, the independent associations were more robust and more consistently seen in various echo parameters compared with eGFR. Specifically, both ACR categories of macroalbuminuria (≥300 mg/g) and microalbuminuria (30–299 mg/g) were significantly associated with almost all parameters representing LV mass, size, and diastolic function. Even high normal ACR (10–29 mg/g) was significantly associated with several LV measures. Regarding LV systolic function, higher ACR categories were significantly associated with lower EF and GLS but not necessarily with lateral and septal TDI S'.

Subsequently, we ran logistic regression models to evaluate whether these kidney measures contribute to alterations of those echo parameters exceeding clinical thresholds. For eGFR, we only observed significant associations sporadically (Table 4). In contrast, both macroalbuminuria and microalbuminuria were significantly associated with various parameters of abnormal LV structure and function compared with the reference of ACR <10 mg/g (Table 5). We observed significantly higher odds of LV hypertrophy and systolic dysfunction based on GLS, even in high normal ACR of 10 to 29 mg/g.

In terms of sensitivity analyses, we observed similar associations when creatinine-based eGFR was investigated (Figure S2). When we excluded those with a history of coronary heart disease or heart failure, the associations of eGFR with LV structure and function were considerably attenuated, whereas the associations of ACR remained similar (Figure S3). This attenuation for eGFR was driven by the exclusion of those with prevalent heart failure but not by the

**Table 4.** Fully Adjusted ORs (95% Confidence Intervals) of Having Abnormal Echo Parameters Representing LV Mass, Size, Systolic Function, and Diastolic Function According to eGFR Categories Based on Logistic Regression Models

| | eGFR Categories, mL/min per 1.73 $m^2$ | | | | | |
|---|---|---|---|---|---|---|
| Echo Parameters | ≥90 (n=348) | 75–89 (n=983) | 60–74 (n=1319) | 45–59 (n=972) | 30–44 (n=443) | <30 (n=110) |
| LV mass related | | | | | | |
| LVMI (≥115 g/$m^2$ for men and ≥95 g/$m^2$ for women) | | | | | | |
| Abnormal cases, n (%) | 26 (7) | 68 (7) | 130 (10) | 113 (12) | 71 (16) | 33 (30) |
| OR (95% CI) | 1.09 (0.67–1.77) | Ref | 1.30 (0.94–1.79) | 1.17 (0.83–1.64) | 1.18 (0.79–1.75) | 1.53 (0.87–2.66) |
| RWT (>0.42) | | | | | | |
| Abnormal cases, n (%) | 140 (40) | 416 (42) | 598 (45) | 482 (50) | 206 (46) | 65 (59) |
| OR (95% CI) | 0.88 (0.68–1.14) | Ref | 1.07 (0.90–1.27) | 1.18 (0.98–1.43) | 0.92 (0.72–1.18) | 1.44 (0.93–2.22) |
| LV size | | | | | | |
| LVEDVI (≥76 mL/$m^2$) | | | | | | |
| Abnormal cases, n (%) | 5 (1.4) | 5 (0.5) | 12 (0.9) | 17 (1.7) | 8 (1.8) | 7 (6.4) |
| OR (95% CI) | 3.10 (0.84–11.4) | Ref | 2.12 (0.70–6.37) | 3.21 (1.08–9.49) | 2.73 (0.77–9.72) | 3.94 (0.91–17.0) |
| LVESVI (≥31 mL/$m^2$) | | | | | | |
| Abnormal cases, n (%) | 10 (2.9) | 10 (1.0) | 30 (2.3) | 26 (2.7) | 15 (3.4) | 7 (6.4) |
| OR (95% CI) | 2.85 (1.12–7.25) | Ref | 2.15 (1.01–4.57) | 1.93 (0.88–4.26) | 1.91 (0.77–4.76) | 1.55 (0.47–5.11) |
| LV systolic function | | | | | | |
| EF (<55%) | | | | | | |
| Abnormal cases, n (%) | 13 (3.7) | 22 (2.2) | 54 (4.1) | 39 (4.0) | 24 (5.4) | 10 (9.1) |
| OR (95% CI) | 1.71 (0.83–3.54) | Ref | 1.75 (1.04–2.96) | 1.42 (0.80–2.50) | 1.59 (0.82–3.07) | 1.94 (0.79–4.77) |
| Longitudinal strain (>−14%) | | | | | | |
| Abnormal cases, n (%) | 18 (5.2) | 42 (4.3) | 75 (5.7) | 58 (6.0) | 31 (7.0) | 10 (9.1) |
| OR (95% CI) | 1.17 (0.65–2.10) | Ref | 1.30 (0.87–1.95) | 1.13 (0.73–1.75) | 0.97 (0.57–1.66) | 0.68 (0.29–1.56) |
| LV diastolic function | | | | | | |
| LAVI (≥34 mL/$m^2$) | | | | | | |
| Abnormal cases, n (%) | 45 (13) | 107 (11) | 144 (11) | 140 (14) | 81 (18) | 29 (26) |
| OR (95% CI) | 1.27 (0.86–1.88) | Ref | 0.92 (0.70–1.21) | 1.04 (0.78–1.40) | 1.11 (0.78–1.58) | 1.20 (0.69–2.07) |
| E/e′ septal (≥15) | | | | | | |
| Abnormal cases, n (%) | 59 (17) | 156 (16) | 256 (19) | 250 (26) | 142 (32) | 47 (43) |
| OR (95% CI) | 1.10 (0.78–1.56) | Ref | 1.11 (0.88–1.40) | 1.31 (1.03–1.68) | 1.40 (1.04–1.89) | 1.52 (0.94–2.45) |

Adjusted for age, race, sex, center, smoking status, alcohol intake, physical activity, body mass index, diabetes mellitus, antihypertensive medication, systolic and diastolic blood pressures, total and high-density lipoprotein cholesterol levels, prevalent stroke, coronary heart disease, heart failure, and albumin/creatinine ratio. CI indicates confidence interval; E, early mitral inflow peak velocity; e′, early mitral annulus tissue Doppler imaging velocity; EF, ejection fraction; eGFR, estimated glomerular filtration rate; LAVI, left atrial volume index; LV, left ventricular; LVEDVI, LV end-diastolic volume index; LVESVI, LV end-systolic volume index; LVMI, LV mass index; OR, odds ratio; Ref, reference; and RWT, relative wall thickness.

exclusion of prevalent coronary disease cases (Figure S4). In this population without a history of cardiac disease, the associations of eGFR with LV structure and function were weak, even when we tested average eGFR across ARIC visits 2, 4, and 5 over ≈20 years (Figure S5).

## Discussion

In our study, both lower eGFR and higher albuminuria were independently associated with LV mass, size, and systolic and diastolic function. Of these LV measures, high LV mass was most consistently associated with both CKD measures, followed by LV dilation and diastolic dysfunction. Their associations with systolic dysfunction tended to be weaker than the other LV measures, but higher ACR demonstrated a consistent association with systolic dysfunction, particularly when assessed by reduced GLS. Comparing 2 CKD measures, more robust and consistent associations were observed for ACR over eGFR. The associations with eGFR tended to become evident at the severely reduced level of <30 mL/min

**Table 5.** Fully Adjusted ORs (95% Confidence Intervals) of Having Abnormal Echo Parameters Representing LV Mass, Size, Systolic Function, and Diastolic Function According to ACR Categories Based on Logistic Regression Models

| Echo Parameters | ACR Categories, mg/g | | | |
|---|---|---|---|---|
| | <10 (n=2036) | 10–29 (n=1371) | 30–299 (n=658) | ≥300 (n=110) |
| LV mass related | | | | |
| LVMI (≥115 g/m$^2$ for men and ≥95 g/m$^2$ for women) | | | | |
| Abnormal cases, n (%) | 137 (7) | 158 (12) | 107 (16) | 39 (36) |
| OR (95% CI) | Ref | 1.51 (1.18–1.95) | 1.92 (1.43–2.58) | 3.49 (2.10–5.79) |
| RWT (>0.42) | | | | |
| Abnormal cases, n (%) | 872 (43) | 631 (46) | 338 (51) | 66 (60) |
| OR (95% CI) | Ref | 1.05 (0.91–1.22) | 1.19 (0.98–1.43) | 1.41 (0.91–2.17) |
| LV size | | | | |
| LVEDVI (≥76 mL/m$^2$) | | | | |
| Abnormal cases, n (%) | 20 (1) | 11 (1) | 17 (3) | 6 (5) |
| OR (95% CI) | Ref | 0.87 (0.40–1.90) | 2.15 (1.02–4.53) | 2.87 (0.83–9.95) |
| LVESVI (≥31 mL/m$^2$) | | | | |
| Abnormal cases, n (%) | 36 (2) | 29 (2) | 27 (4) | 6 (5) |
| OR (95% CI) | Ref | 1.33 (0.79–2.26) | 2.15 (1.22–3.81) | 1.52 (0.50–4.60) |
| LV systolic function | | | | |
| EF (<55%) | | | | |
| Abnormal cases, n (%) | 73 (4) | 49 (4) | 33 (5) | 7 (6) |
| OR (95% CI) | Ref | 0.99 (0.67–1.46) | 1.25 (0.79–2.00) | 1.03 (0.40–2.65) |
| Longitudinal strain (>−14%) | | | | |
| Abnormal cases, n (%) | 80 (4) | 81 (6) | 54 (8) | 19 (17) |
| OR (95% CI) | Ref | 1.52 (1.09–2.11) | 1.81 (1.23–2.66) | 2.93 (1.53–5.61) |
| LV diastolic function | | | | |
| LAVI (≥34 mL/m$^2$) | | | | |
| Abnormal cases, n (%) | 221 (11) | 177 (13) | 123 (19) | 25 (23) |
| OR (95% CI) | Ref | 1.14 (0.91–1.42) | 1.48 (1.13–1.93) | 1.15 (0.66–2.00) |
| E/e′ septal (≥15) | | | | |
| Abnormal cases, n (%) | 363 (18) | 298 (22) | 196 (30) | 53 (48) |
| OR (95% CI) | Ref | 1.04 (0.87–1.25) | 1.34 (1.07–1.68) | 2.04 (1.29–3.23) |

Adjusted for age, race, sex, center, smoking status, alcohol intake, physical activity, body mass index, diabetes mellitus, antihypertensive medication, systolic and diastolic blood pressures, total and high-density lipoprotein cholesterol levels, prevalent stroke, coronary heart disease, heart failure, and estimated glomerular filtration rate. ACR indicates albumin/creatinine ratio; CI, confidence interval; E, early mitral inflow peak velocity; e′, early mitral annulus tissue Doppler imaging velocity; EF, ejection fraction; LAVI, left atrial volume index; LV, left ventricular; LVEDVI, LV end-diastolic volume index; LVESVI, LV end-systolic volume index; LVMI, LV mass index; OR, odds ratio; Ref, reference; and RWT, relative wall thickness.

per 1.73 m$^2$, whereas even a high normal ACR of 10 to 29 mg/g demonstrated significant associations with some cardiac structural and functional abnormalities.

To our knowledge, only 1 previous study comprehensively evaluated all aspects of LV mass, size, and systolic and diastolic function and both CKD measures, eGFR and albuminuria, in the same study population.[15] Our study is unique in various aspects. The current study has a much larger sample size (4157 versus 540 participants) and investigated a community-based sample instead of a clinical population with hypertension and diastolic dysfunction.[15] Also, we incorporated state-of-the-art systolic function parameters, GLS, and the best equation for eGFR to date with both serum creatinine and cystatin C.[23] All of these factors probably contributed to detecting important signals for the associations of both low eGFR and high ACR with LV structure and function.

Our study highlights LV hypertrophy as a key cardiac pathophysiological feature in CKD, which is in line with the fact that this cardiac property has been most intensively

studied in the context of CKD.[35] This is also consistent with an observation by Dr. Richard Bright in 1836, "It is observable, that the hypertrophy of the heart seems, in some degree, to have kept pace with the advance of disease in the kidneys."[36] There are several plausible mechanisms behind the positive association of CKD and LV mass, such as volume overload, activated renin-angiotensin system, anemia, and uremic toxins.[35] Indeed, a few studies demonstrate reduction in LV mass after the correction of anemia, use of diuretics, and frequent hemodialysis.[35] Also, renin-angiotensin system inhibitors are known to prevent CKD progression, reduce albuminuria, and regress increased LV mass.[27,37]

It is of importance that high ACR was associated with all of LV mass, size, systolic function, and diastolic function in our study and demonstrated more robust associations than eGFR. This observation is in agreement with a recent international collaborative study showing a similar pattern for clinical risk of heart failure.[10] Although exact mechanisms behind the close link between albuminuria and altered LV structure and function are not clear, this may reflect the property of albuminuria as an indicator of systemic vascular damage, endothelial dysfunction, and microvascular injury.[38] Indeed, microvascular injury is considered to play an important role in the development of heart failure.[39] Also, albumin in the urine can damage the kidney and stimulate production of inflammatory molecules,[40] which may also contribute to alteration of cardiac structure and function.[41]

The association of LV structure and function with eGFR tended to be apparent at <30 mL/min per 1.73 $m^2$. This GFR level is where the risk of the accumulation of uremic toxins starts to increase.[27] In our study, the associations of eGFR and LV structure and function were considerably attenuated after excluding those with a history of heart failure. There are a few possible explanations for this attenuation. First, we might be simply losing important information by excluding those with extreme cardiac abnormalities. Second, it is possible that given our cross-sectional design, the significant associations between lower eGFR and LV structure and function in the entire study sample may also reflect lower eGFR as a consequence of clinical heart failure because the association between the kidney and the heart is known to be bidirectional.[42] This attenuation may also reflect that those with both reduced eGFR and cardiac abnormality may be prone to develop clinical signs and symptoms, increasing the chance of a heart failure diagnosis. To fully dissect these possibilities, a prospective investigation with frequently repeated cardiac echo examinations would be needed.

To our knowledge, there are no established guidelines for cardiac screening in patients with CKD (except for those initiating dialysis[43]). In this context, our data suggest individuals with elevated albuminuria and possibly those with severely reduced GFR (<30 mL/min per 1.73 $m^2$) are potential candidates for targeted cardiac assessment. Various cardiac echo parameters (LV mass, systolic function, and diastolic function) have been shown to predict adverse health outcomes in individuals with CKD.[35] Nonetheless, the cost-effectiveness of such a targeted cardiac assessment among CKD patients with elevated albuminuria and possibly those with severely reduced GFR should be evaluated in future studies.

There are several limitations in our study to be taken into account. First, the lack of baseline echo data in the ARIC study does not allow us to evaluate the association of CKD with longitudinal changes in cardiac structure and function. Second, the study population consisted of older whites and blacks and, thus, the extrapolation to other age categories or racial/ethnic groups needs to be done carefully. Finally, as true for any observational studies, we cannot rule out the possibility of residual confounding, despite our rigorous statistical adjustment.

In conclusion, both lower eGFR and higher albuminuria were independently associated with echo parameters of LV structure and function. Among these LV parameters tested, higher LV mass was most consistently associated with CKD. The association with LV size, systolic function, and diastolic function was observed robustly for albuminuria. These results have implications for pathophysiological processes linking CKD to heart failure and targeted cardiac assessment in CKD patients.

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## Disclosures

None.

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Supplemental Material

Table S1. Characteristics between participants who were excluded vs. included in the current analysis

| Variables | mean(SD) or n(%) excluded | mean(SD) or n(%) included | N excluded | N included |
|---|---|---|---|---|
| Age | 77 (6) | 76 (5) | 2363 | 4175 |
| Center | | | | |
| Forsyth County, NC | 514 (21.8%) | 930 (22.3%) | 2363 | 4175 |
| Jackson, MS | 525 (22.2%) | 892 (21.4%) | 2363 | 4175 |
| Suburban Minneapolis, MN | 675 (28.6%) | 1233 (29.5%) | 2363 | 4175 |
| Washington County, MD | 649 (27.5%) | 1120 (26.8%) | 2363 | 4175 |
| Race (Black) | 565 (24.1%) | 979 (23.4%) | 2345 | 4175 |
| Sex (Male) | 897 (38.0%) | 1796 (43.0%) | 2363 | 4175 |
| Current smoker | 119 (6.1%) | 244 (5.8%) | 1937 | 4175 |
| Current drinker | 934 (48.3%) | 2046 (49.0%) | 1933 | 4175 |
| Physical activity | | | | |
| Much less | 103 (5.6%) | 152 (3.6%) | 1831 | 4175 |
| Less | 302 (16.5%) | 562 (13.5%) | 1831 | 4175 |
| Same | 619 (33.8%) | 1412 (33.8%) | 1831 | 4175 |
| More | 582 (31.8%) | 1456 (34.9%) | 1831 | 4175 |
| Much more | 225 (12.3%) | 593 (14.2%) | 1831 | 4175 |
| BMI | 29 (6) | 29 (6) | 2094 | 4175 |
| Diabetes | 823 (42.7%) | 1428 (34.2%) | 1929 | 4175 |
| Anti-HTN use | 1834 (78.1%) | 3113 (74.6%) | 2348 | 4175 |
| SBP | 130 (20) | 131 (18) | 2328 | 4175 |
| DBP | 66 (11) | 66 (11) | 2328 | 4175 |
| prevalent stroke | 121 (5.1%) | 153 (3.7%) | 2352 | 4175 |
| prevalent CHD | 377 (16.7%) | 604 (14.5%) | 2252 | 4175 |
| prevalent HF | 518 (21.9%) | 596 (14.3%) | 2363 | 4175 |
| Total cholesterol | 4.7 (1.1) | 4.7 (1.1) | 2250 | 4175 |
| HDL cholesterol | 1.4 (0.4) | 1.3 (0.4) | 2250 | 4175 |
| eGFRcre-cys | 63 (19) | 66 (18) | 2262 | 4175 |
| ACR | 80 (326) | 55 (328) | 1584 | 4175 |
| Echo variables | | | | |
| LVMI index-BSA | 81.1 (22.7) | 79.7 (20.5) | 1885 | 4175 |
| IVSd | 1.04 (0.17) | 1.05 (0.17) | 1897 | 4175 |
| PWTd | 0.94 (0.15) | 0.93 (0.14) | 1907 | 4175 |
| RWT | 0.43 (0.08) | 0.43 (0.08) | 1894 | 4175 |
| LVEDVi | 43.6 (12.1) | 44.4 (11.1) | 1713 | 4175 |
| LVESVi | 16.0 (7.8) | 15.7 (6.7) | 1713 | 4175 |
| LVEDD | 4.43 (0.55) | 4.41 (0.51) | 1894 | 4175 |
| LVESD | 2.68 (0.56) | 2.63 (0.50) | 1901 | 4175 |
| LVEF | 64.2 (7.8) | 65.4 (6.4) | 1744 | 4175 |
| TDI S' lateral | 6.31 (1.35) | 6.55 (1.27) | 1929 | 4175 |
| TDI S' septal | 7.22 (1.75) | 7.42 (1.67) | 1914 | 4175 |
| Longitudinal strain | -17.6 (3.0) | -18.0 (2.4) | 1523 | 4175 |
| LAVI | 27.6 (12.2) | 25.7 (7.9) | 1870 | 4175 |
| E/e' lateral | 10.3 (4.2) | 10.3 (4.0) | 1905 | 4175 |
| E/e' septal | 12.8 (5.1) | 12.5 (4.6) | 1915 | 4175 |
| e' lateral | 7.34 (2.38) | 6.92 (1.91) | 1915 | 4175 |
| e' septal | 5.85 (1.74) | 5.59 (1.36) | 1925 | 4175 |
| E/A | 0.86 (0.29) | 0.86 (0.29) | 1654 | 4175 |

Table S2. Demographic and clinical characteristics according to eGFR categories

| n (%), mean(SD) | 90+ n=348 | 75-89 n=983 | 60-74 n=1,319 | 45-59 n=972 | 30-44 n=443 | <30 n=110 |
|---|---|---|---|---|---|---|
| Age, year | 73 (4) | 74 (4) | 76 (5) | 77 (5) | 78 (5) | 78 (5) |
| Center, % | | | | | | |
| Forsyth County, NC | 70 (20.1) | 231 (23.5) | 297 (22.5) | 221 (22.7) | 86 (19.4) | 25 (22.7) |
| Jackson, MS | 142 (40.8) | 219 (22.3) | 240 (18.2) | 170 (17.5) | 87 (19.6) | 34 (30.9) |
| Suburban Minneapolis, MN | 79 (22.7) | 299 (30.4) | 420 (31.8) | 293 (30.1) | 123 (27.8) | 19 (17.2) |
| Washington County, MD | 57 (16.4) | 234 (23.8) | 362 (27.4 | 288 (29.6) | 147 (33.2) | 32 (29.1) |
| Race (Black), % | 157 (45.1) | 240 (24.4) | 260 (19.7) | 191 (19.7) | 93 (21.0) | 38 (34.5) |
| Sex (Male), % | 139 (39.9) | 449 (45.7) | 574 (43.5) | 401 (41.3) | 177 (40.0) | 56 (50.9) |
| Current smoking, % | 20 (5.8) | 56 (5.7) | 92 (7.0) | 54 (5.6) | 17 (3.8) | 5 (4.5) |
| Current drinking, % | 175 (50.3) | 550 (56.0) | 649 (49.2) | 448 (46.1) | 182 (41.1) | 42 (38.2) |
| Physical activity, % | | | | | | |
| Much less | 10 (2.9) | 25 (2.5) | 38 (2.9) | 42 (4.3) | 24 (5.4) | 13 (11.8) |
| less | 46 (13.2) | 124 (12.6) | 150 (11.4) | 137 (14.1) | 83 (18.7) | 22 (20.0) |
| Same | 117 (33.6) | 292 (29.7) | 437 (33.1) | 352 (36.2) | 170 (38.4) | 44 (40.0) |
| More | 123 (35.3) | 379 (38.6) | 492 (37.3) | 313 (32.2) | 123 (27.8) | 26 (23.6) |
| Much more | 52 (14.9) | 163 (16.6) | 202 (15.3) | 128 (13.2) | 43 (9.7) | 5 (4.6) |
| BMI | 28 (6) | 28 (6) | 29 (5) | 29 (5) | 30 (6) | 29 (6) |
| Diabetes, % | 120 (34.5) | 284 (28.9) | 410 (31.1) | 352 (36.2) | 205 (46.3) | 57 (51.8) |
| Antihypertensive drugs, % | 216 (62.1) | 662 (67.3) | 938 (71.1) | 774 (79.6) | 419 (94.6) | 104 (94.5) |
| Systolic BP, mmHg | 130 (17) | 131 (17) | 131 (17) | 131 (19) | 131 (19) | 135 (25) |
| Diastolic BP, mmHg | 67 (10) | 68 (10) | 67 (10) | 65 (11) | 63 (11) | 62 (12) |
| History of stroke, % | 8 (2.3) | 25 (2.5) | 40 (3.0) | 34 (3.5) | 31 (7.0) | 10 (9.1) |
| History of CHD, % | 24 (6.9) | 96 (9.8) | 177 (13.4) | 162 (16.7) | 100 (22.6) | 40 (36.4) |
| History of heart failure, % | 40 (11.5) | 95 (9.7) | 144 (10.9) | 166 (17.1) | 114 (25.7) | 46 (41.8) |
| Total cholesterol, mmol/L | 4.8 (1.1) | 4.7 (1.1) | 4.7 (1.1) | 4.6 (1.0) | 4.5 (1.1) | 4.5 (1.3) |
| HDL cholesterol, mmol/L | 1.5 (0.4) | 1.4 (0.4) | 1.3 (0.4) | 1.3 (0.3) | 1.2 (0.3) | 1.2 (0.4) |
| ACR, mg/g | 10 (7, 17) | 10 (6, 18) | 9 (6, 18) | 11 (6, 24) | 16 (8, 42) | 75 (16, 445) |
| eGFR, ml/min/1.73m$^2$ | 97(6) | 82 (4) | 68 (4) | 53 (4) | 39 (4) | 23 (7) |

Values are mean (SD), n (%), or median (interquartile interval). BMI: body mass index, BP: blood pressure, CHD: coronary heart disease, HDL: high density lipoprotein, eGFR: estimated glomerular filtration rate, ACR: urine albumin-to-creatinine ratio

Figure S1. Adjusted values of the primary echo parameters representing LV mass, size, systolic function, and diastolic function according to eGFR and ACR based on linear regression models. Values were adjusted for age, race, sex, center, smoking status, alcohol intake, physical activity, BMI, diabetes, anti-hypertensive medication, systolic and diastolic blood pressures, total and HDL cholesterols, prevalent stoke, CHD and HF, and each kidney measure.

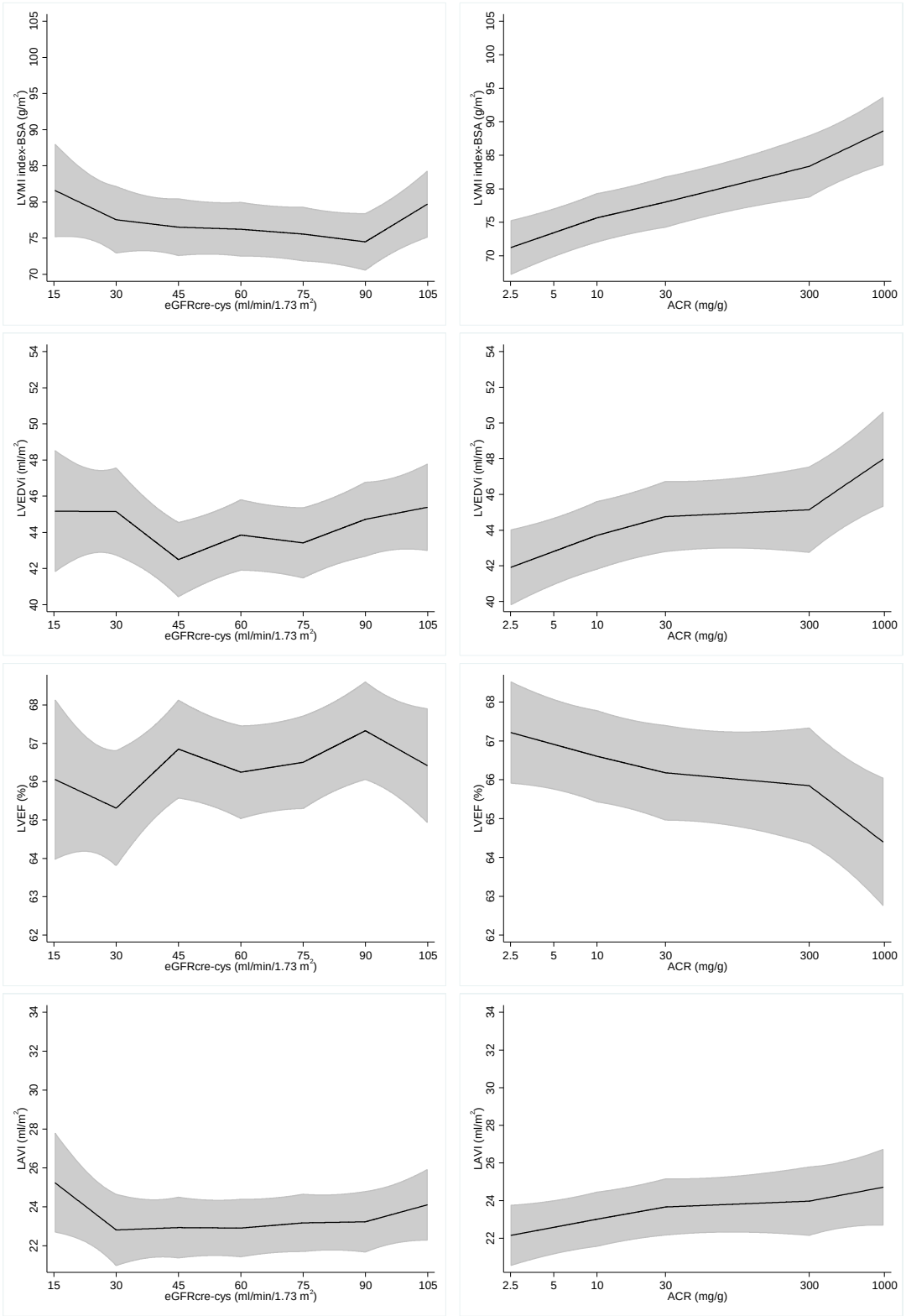
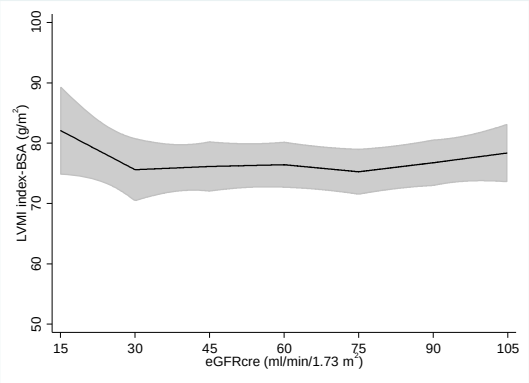
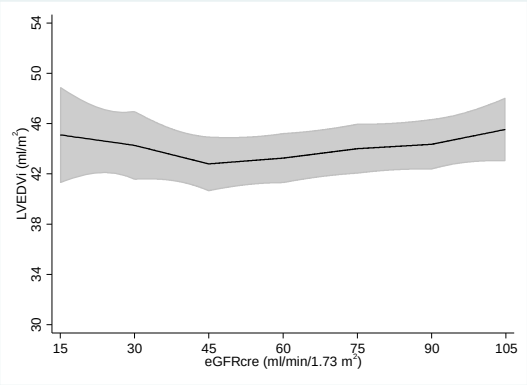
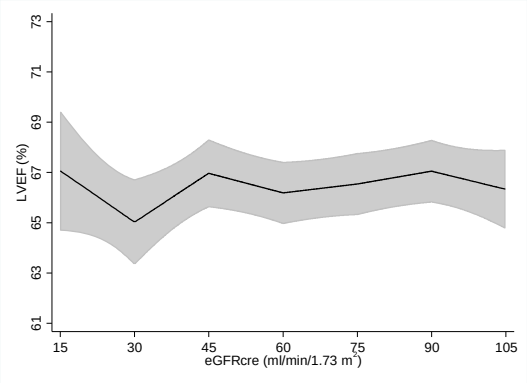


Figure S2. Adjusted values of the primary echo parameters according to eGFR based on creatinine-based equation using linear regression models. Values were adjusted for age, race, sex, center, smoking status, alcohol intake, physical activity, BMI, diabetes, anti-hypertensive medication, systolic and diastolic blood pressures, total and HDL cholesterols, prevalent stoke, CHD and HF, and each kidney measure.



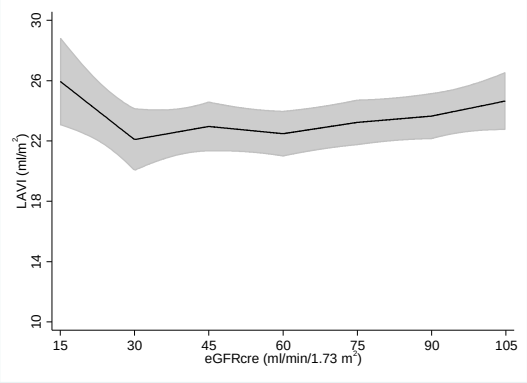



Figure S3. Fully adjusted values of the primary echo parameters representing LV thickness, size, systolic function, and diastolic function according to eGFR and ACR among those without history of CHD or HF at baseline (n=3,227) based on linear regression models.

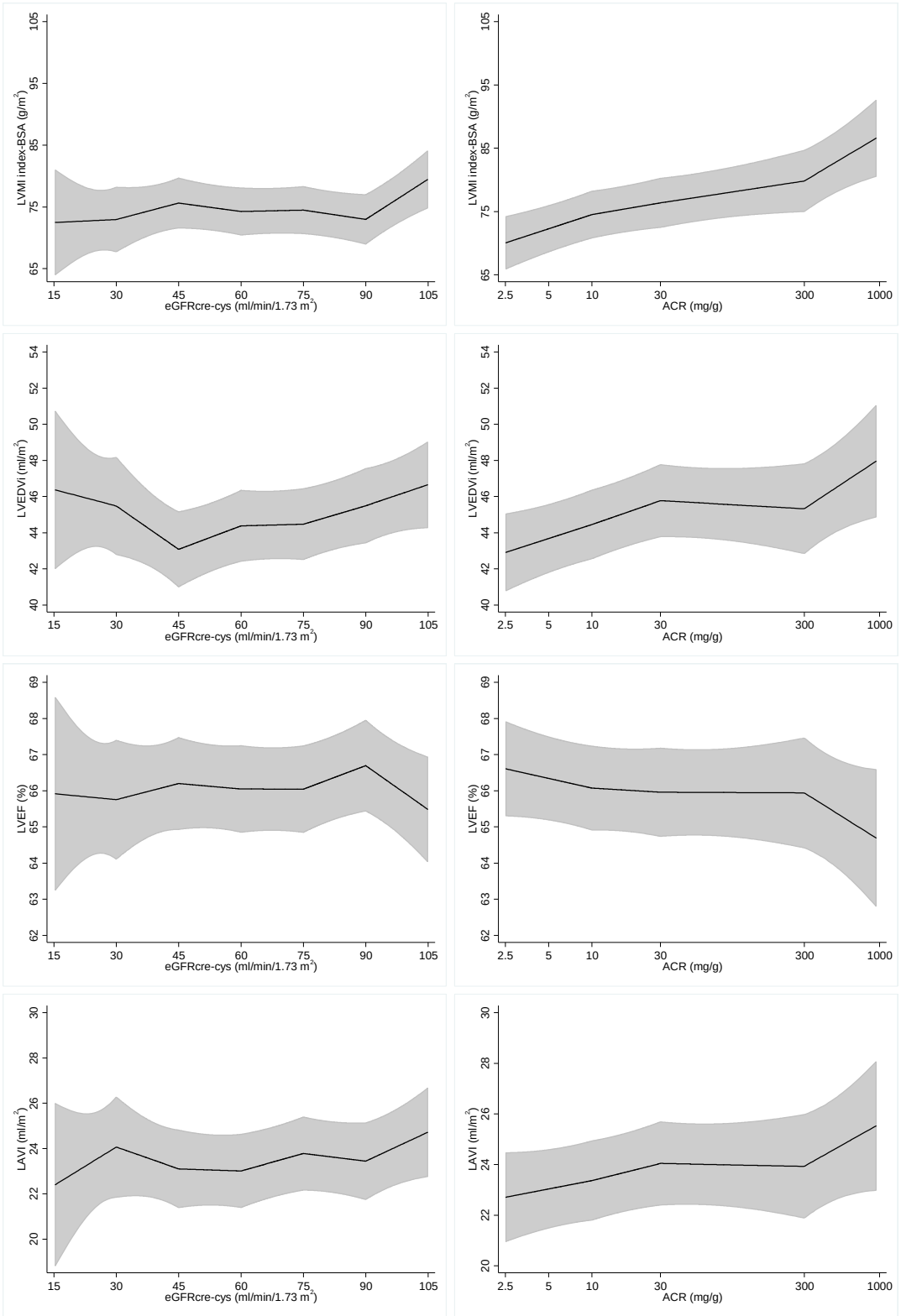


Figure S4. Fully adjusted values of the primary echo parameters representing LV thickness, size, systolic function, and diastolic function according to eGFR among those without history of CHD (left) and those without HF at baseline (n=3,576 and 3,570, respectively) based on linear regression models.

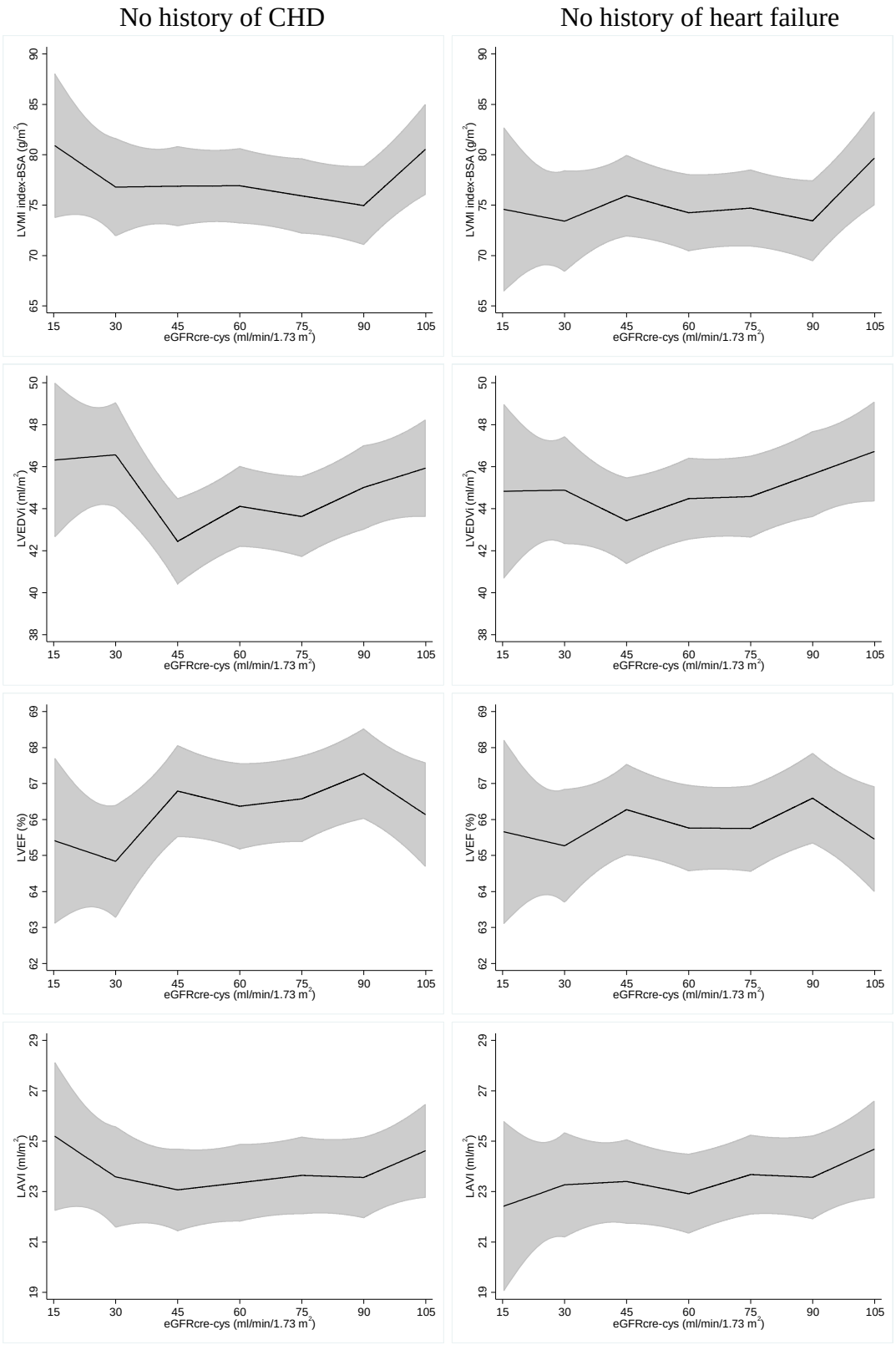


Figure S5. Fully adjusted values of the primary echo parameters representing LV thickness, size, systolic function, and diastolic function according to average eGFR across visits 2, 4, and 5 and average ACR between visits 4 and 5 among those without prevalent CHD or HF at visit 5 (n=3,227) based on linear regression models