Association of Albuminuria With Cardiac Dysfunction in USA Hispanic Community

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Abstract

Higher urine albumin-to-creatinine ratio (UACR) has been associated with cardiac dysfunction in the general population. We assessed the association of UACR with cardiac structure and function in the Echocardiographic Study of Latinos (Echo-SOL), an ancillary study of the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) across 4 U.S. sites. Echo-SOL participants underwent standard 2-dimensional echocardiography, including speckle-tracking strain analysis. UACR was categorized as normal and high-normal (based on the midpoint of values below microalbuminuria), microalbuminuria (17 mg/g for men; 25 mg/g for women), and macroalbuminuria (250 mg/g; 355 mg/g). Simultaneous assessments were made of left

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ventricular (LV) mass index and hypertrophy, and measures of LV systolic and diastolic dysfunction. We assessed the association of UACR with subclinical cardiac measures, adjusting for sociodemographic and cardiometabolic factors. Among 1,815 participants (median age 54, female 65%), 42% had normal UACR, 43% high-normal UACR, 13% microalbuminuria, and 2% macroalbuminuria. Prevalence of LV hypertrophy was 13%, LV systolic dysfunction (ejection fraction <50%) 3%, and diastolic dysfunction 53%. After covariate adjustment, both micro- and macroalbuminuria were significantly associated with a two-fold increase in LV hypertrophy. Microalbuminuria but not macroalbuminuria was associated with worse global longitudinal strain. Elevated UACR, even at high-normal levels, was significantly associated with greater diastolic dysfunction. In conclusion, elevated UACR was associated with LV hypertrophy and diastolic dysfunction in the largest known population sample of U.S. Hispanic/Latinos. Screening and detection of even high-normal UACR could be of value to guide CVD prevention efforts among Hispanic/Latino Americans.

Keywords

cardiac dysfunction; echocardiography; kidney; strain

INTRODUCTION

Because U.S. Hispanics/Latinos have a high prevalence of diabetes and obesity,[1] as well as poor health care access and cultural and linguistic barriers that may exacerbate health disparities,[2] they may be particularly prone to heart failure and its complications. However, only limited data are available regarding heart failure and its precursors, which include structural heart disease in the absence of overt symptoms,[3] among Hispanics/Latinos.[4,5] In non-Hispanic populations, the urine albumin-to-creatinine ratio (UACR), a measure of proteinuria and marker of kidney damage, has been associated with cardiovascular disease (CVD) mortality and heart failure,[6,7] as well as subclinical measures of cardiac structure and function.[8] To our knowledge, no studies have examined the association between albuminuria and cardiac dysfunction in U.S. Hispanics/Latinos, despite a disproportionate burden of risk factors leading to chronic kidney disease in some Hispanic groups.[9,10] Using data from the Echocardiographic Study of Latinos (Echo-SOL), we examined the association between UACR and measures of cardiac structure and function among 1,815 Hispanic/Latino individuals who underwent a standardized 2-D echocardiography protocol, including speckle-tracking analysis for measurement of longitudinal strain. We hypothesized that higher UACR would be associated with increased left ventricular (LV) mass and greater systolic and diastolic dysfunction, and that this association would be amplified among participants with impaired kidney function, diabetes mellitus, or hypertension. We also examined associations by sex and by Hispanic/Latino background.

METHODS

The Hispanic Community Health Study (HCHS)/Study of Latinos (SOL) is a community-based cohort study of 16,415 self-identified Hispanic/Latino persons from randomly selected households near 4 U.S. field centers (Bronx, Chicago, Miami, San Diego). The baseline

examination was conducted from February 2008 to July 2011. Sample design and cohort selection have been previously described.[11] Echo-SOL is an ancillary study to the HCHS/SOL designed to characterize cardiac remodeling and systolic and diastolic function in a representative subsample of participants age 45 years who were seen within 36 months of their initial visit.[12] Echo-SOL used stratified random sampling to assure representation of the overall HCHS/SOL population. Echo-SOL participation rates averaged ~80% among those invited, and enrollment occurred from October 2011 through June 2014.

Echo-SOL participants included in this analysis had an interpretable echocardiogram and data available from the baseline HCHS/SOL visit on UACR and other biomarkers. For assessments of diastolic dysfunction, exclusion criteria included current pregnancy, atrial fibrillation identified through electrocardiography, more than mild valvular disease, LV ejection fraction <50%, and LV end-diastolic volume index >97 mL/m^2. Transmitral E/A was not assessed in participants with an absent A wave owing to non-sinus rhythm at echocardiography.

Philips Ultrasound IE-33 or Sonos 5500/7500 was used for echocardiographic measurements at all study sites. This equipment was interfaced with a standard 2.5- to 3.5-MHz phased-array probe, according to American Society of Echocardiography (ASE) recommendations. Standard echocardiographic examination, including M-mode, 2-D, spectral, color-flow and tissue-Doppler study, was performed by experienced sonographers at each center. Speckle-tracking strain (STS) analysis was performed offline using the TomTec Cardiac Performance Analysis package (v1.2.2.7) on acquired 2-D images.[13] A single reader technician and over-reader were used for all studies. Additional details are in the Supplemental Material.

We focused on several echocardiographic parameters of cardiac structure and function. LV mass index (LVMI) was estimated using 2-D guided M-mode measurements and indexed by sex to body surface area.[14] LV hypertrophy was defined by dichotomizing LVMI as >115 g/m^2 for men and >95 g/m^2 for women.[14] Two measures of global LV systolic dysfunction were defined: first, based on an LV ejection fraction <50%, obtained using the bi-plane Simpson method of disks, and second, based on global longitudinal strain (GLS) obtained from STS analysis. GLS is a more sensitive measure of systolic performance than LV ejection fraction, particularly among those with relatively preserved ejection fraction.[15] As previously described,[16] diastolic dysfunction was graded as 0, I, II, or III following an algorithm (Supplemental Figure) that combined ASE guidelines and Redfield criteria using 3 echocardiographic parameters: E/A ratio, E/e' ratio and left atrial volume index (LAVI).[17,18] We dichotomized diastolic dysfunction as grades I–III compared with grade 0, and separately examined LAVI; e', defined as the average of early diastolic annular velocities of the septal and lateral mitral annulus; and E/e' ratio.

UACR was measured in mg/g from spot urine samples at the baseline HCHS/SOL visit. Creatinine was assessed on a Roche Modular P Chemistry Analyzer using a creatinase enzymatic method. Urine albumin was assessed using an immunoturbidimetric method on the ProSpec nephelometric analyzer (Dade Behring, Marburg, Germany). We grouped UACR into 4 categories. More severe categories of kidney dysfunction were based on

established sex-specific thresholds for microalbuminuria (17 and 25 mg/g for men and women, respectively) and macroalbuminuria (250 and 355 mg/g), whereas for the remaining UACR levels we used the midpoint of the distribution below microalbuminuria to create "normal" and "high-normal" levels.[19] We also performed analyses grouping UACR into quartiles after stratification by sex.

Covariates included age, sex, Hispanic/Latino background (Cuban, Dominican, Mexican, Puerto Rican, other), acculturation (U.S.-born, lived in U.S. 10 years, lived in U.S. <10 years), study center, and cardiometabolic traits: body mass index (BMI), systolic blood pressure (SBP), use of antihypertensive medications, diabetes mellitus (including both self-reported physician diagnosis and undiagnosed diabetes mellitus identified through serum glucose 126 mg/dL if fasting >8 hours or 200 mg/dL if fasting 8 hours; post-OGTT glucose 200 mg/dL; or HgA1C 6.5%), smoking, HDL- and LDL-cholesterol levels, use of lipid-lowering medications, and estimated glomerular filtration rate (eGFR). eGFR was considered as a measure of impaired kidney function and determined based on serum cystatin C and creatinine, age, sex, and race.[20]

We examined bivariate relationships between UACR and cardiac outcomes using both categories defined by established cutpoints and sex-specific quartiles. To determine associations with UACR, we developed linear regression models for continuous outcomes and Poisson regression models for dichotomous outcomes to generate prevalence ratios. We adjusted for confounders through serial adjustment, starting first with a model with only UACR as the independent variable; then adding confounders related to demographic characteristics, including age, sex, and Hispanic/Latino background; and finally cardiometabolic risk factors.

We assessed effect modification by sex, eGFR (<60 versus 60 mL/min/1.73 m^2 of body-surface area), diabetes, hypertension status (taking into account self-reported physician diagnosis, measured SBP and DBP, and use of anti-hypertensive medications). On the basis that ancestral or lifestyle differences may modify the role of albuminuria on cardiovascular health,[21] we also examined groups defined by Hispanic/Latino background and level of acculturation. We tested statistical significance of effect modification through use of interaction terms in fully adjusted models, and conducted stratified analyses for interactions significant at the p<0.05 level. No differences were found in sensitivity analyses that excluded participants with pre-existing CVD (i.e., self-reported coronary heart disease, stroke, and heart failure [1% of the study population]), and therefore we report results in the entire group.

Analyses were conducted using R 3.2.0. To address missing data (<3% of values), we implemented multiple imputation using chained equations with the R package mice. All reported effect estimates were weighted to account for the disproportionate selection of the sample and to at least partially adjust for any bias effects due to differential nonresponse in the selected sample at the household and person levels. All participants provided informed consent, and the study was approved by each center's institutional review board.

RESULTS

Demographic and clinical characteristics of the 1,815 study participants are shown in Table 1. Of note, nearly two-thirds of the mostly middle-aged cohort were women. Diagnosed diabetes mellitus was reported by nearly one-fifth, with another 9% having diabetes mellitus identified only through study visit measurements. Almost half had a history of hypertension.

Median UACR was 6.3 mg/g (IQR 4.3, 13.4) among men and 7.7 mg/g (IQR 5.3, 14.3) among women. Using established thresholds, 15% of men and 11% of women met criteria for microalbuminuria, while 3% of men and 1% of women met criteria for macroalbuminuria. Distributions of UACR among participants are shown by clinically defined categories of albuminuria in Table 2 and by quartiles of UACR in Supplemental Table 1.

Median LVMI among men was 87.3 g/m^2 (IQR 74.6, 101.6) and among women 74.4 g/m^2 (64.1, 86.2). Compared with normal UACR levels, macroalbuminuria was associated with a statistically significant 19.2 g/m^2 increase in LVMI in fully adjusted analyses, while microalbuminuria was associated with a significant 5.6 g/m^2 increase (Table 3). High-normal UACR levels did not show a significant association with LVMI as compared with normal levels.

LV hypertrophy was present in 11% of men and 14% of women. Associations of UACR with LV hypertrophy were similar in directionality to associations with LVMI (Table 3). In fully adjusted analyses, macroalbuminuria was significantly associated with a 2.2-fold increase in the prevalence of LV hypertrophy, compared with normal UACR, and microalbuminuria was significantly associated with an almost 2-fold increase. High-normal levels of UACR were associated with LV hypertrophy, but this association did not reach statistical significance.

Regarding LV systolic function, the median LV ejection fraction (LVEF) was 59.3% (IQR 54.9, 62.9) among men and 61.3% (IQR 57.9, 64.2) among women, with LV systolic dysfunction (defined as LVEF <50%) present among 3% of participants. Among men, median GLS was −16.6% (IQR −18.4, −14.8), and among women, it was −18.3% (IQR −20.1, −16.5), with less negative (i.e., more positive) values denoting worse LV function during systole.

In adjusted analyses, both macroalbuminuria and microalbuminuria showed greater systolic dysfunction (LVEF <50%), but these findings were not statistically significant (Table 3). In contrast, there was a significant association between microalbuminuria and less negative GLS (i.e., worse LV systolic function). A similar relationship was seen for macroalbuminuria but was not statistically significant. High-normal UACR was not associated with GLS.

There were 1,628 individuals eligible for analyses of diastolic dysfunction. Some degree of diastolic dysfunction was present in 53%, with grade I dysfunction occurring in 14%, grade II in 37%, and grade III in 2%. We found a graded association between UACR levels and presence of any diastolic dysfunction after adjusting for demographic and cardiometabolic risk factors (Table 3). Those with macroalbuminuria had the highest prevalence of diastolic

dysfunction (61% higher than the normal UACR group), followed by those with microalbuminuria (31% higher). Notably, even participants with high-normal UACR had significantly higher prevalence of diastolic dysfunction compared with participants with normal UACR (by 21%). In analyses evaluating diastolic dysfunction grade as an ordinal variable, there was evidence of a dose-response relationship between levels of albuminuria and diastolic dysfunction (Supplemental Materials).

Analyses of LAVI were conducted in the entire study population. Median LAVI was 22.5 mL/m^2 (IQR 18.3, 27.8) among men and 22.0 mL/m^2 (IQR 18.1, 26.7) among women. Those with microalbuminuria, but not those with milder UACR elevations, had significantly elevated LAVI in fully adjusted analyses. There was suggestion of a stronger association for macroalbuminuria, but this did not attain statistical significance (Table 3).

Analyses of the associations of UACR with e' and E/e' showed similar findings as with diastolic dysfunction defined by grade (Supplemental Table 2) Both e' and E/e' exhibited a significant dose response with albuminuria, even at high-normal UACR levels.

We conducted secondary analyses that categorized UACR into quartiles instead of clinical categories of albuminuria (Supplemental Table 3). In general, we found that measures of diastolic dysfunction were more likely than other study outcomes to have a gradient across the UACR distribution. For example, each higher quartile of UACR was associated with a 12% increase in diastolic dysfunction after full adjustment (p_{trend}<0.0001). In contrast, LVMI and LV hypertrophy were significantly associated only with the highest quartile, and GLS and LAVI showed marginally significant associations for the highest quartile but not the other quartiles.

We explored whether associations of albuminuria with cardiac features were different in those with high-risk disorders. Figure 1 shows stratified associations of measures for which analyses yielded significant (p<0.05) interactions. Associations of UACR with LVMI and LAVI were more pronounced among those with low versus preserved eGFR. The association of UACR with reduced LVEF was stronger among diabetic than non-diabetic participants. By contrast, hypertensive participants showed a diminished association of albuminuria with diastolic dysfunction as compared with normotensive participants.

We also explored potential effect modification of the association between UACR and cardiac dysfunction by sex and by Hispanic background and acculturation. There was evidence of more pronounced associations of UACR with GLS and LAVI among women (p<0.05, Figure 1). While reduced LVEF, GLS, and LV diastolic dysfunction showed significant effect modification by Hispanic background (p<0.05), no one group showed consistently increased strength of associations. We found no evidence of effect modification by time in the U.S.

DISCUSSION

In a broad Hispanic/Latino population largely free of clinical CVD, we found significant associations between albuminuria and several measures of subclinical cardiac structure and function. Our finding with respect to LV mass index is consistent with those from studies in other populations. High-normal UACR was significantly associated with greater LV mass in

the MESA cohort,[19] and LV mass increased with increasing quartiles of UACR in the HyperGEN study.[22] Our results are similar, with the exception that LV mass index was not significantly elevated among those with high-normal as compared with normal UACR levels. This discrepancy may be due to differences in sample size or the younger age of our participants.

For diastolic function measures, even high-normal UACR was associated with greater impairment, suggesting that elevated levels below clinical thresholds for albuminuria may signal cardiac dysfunction and potential future heart failure risk. These findings are consistent with a previously reported dose-response relationship of albuminuria with clinical CVD events.[23] In the present study, the relationship of albuminuria with diastolic dysfunction was of much greater magnitude than associations with LV structure or deformation measures. This observation supports the well-documented clinical usefulness of diastolic function parameters as measures of CVD risk.[24] Indeed, diastolic dysfunction tends to precede the development of LV hypertrophy, and thus represents one of the earliest changes in hypertensive heart disease.[25] A simple measure like UACR, when in the high-normal range, may indicate the presence of cardiac microvascular or endothelial dysfunction. This microvascular dysfunction has been proposed to be central to the development of diastolic dysfunction by leading to diminished NO bioavailability, reduced cGMP/PKG signaling, titin hypophosphorylation, increased stiffness of cardiomyocytes, and decreased LV compliance.[26] Further, endothelial dysfunction may produce microvascular ischemia, resulting in impaired relaxation.

We did not find significant associations of UACR categories with systolic dysfunction defined by reduced LVEF, but participants with microalbuminuria exhibited significantly impaired strain as compared with those having normal UACR levels. There are conflicting findings in the literature with respect to the association between UACR and LV systolic function,[8] likely in part due to the lack of sensitivity of LVEF for mild systolic dysfunction. Our inclusion of strain allowed us to better characterize systolic dysfunction as compared with most existing studies, and we found that microalbuminuria was significantly associated with impaired strain. The only other large study to use this measure to assess the relationship between UACR and systolic dysfunction, of which we are aware, found progressively impaired strain with increasing quartiles of UACR.[27] We found a similar gradient, but it was not as steep and only marginally significant, possibly due a modest number of participants with macroalbuminuria in our study.

There was some evidence of more pronounced associations within higher-risk groups as we hypothesized; the associations of UACR with LV mass index and LAVI were accentuated in subgroups defined by low eGFR, and the association between UACR and reduced LVEF was stronger in diabetic participants. This latter finding could be due in part to relatively low treatment levels for diabetes. In contrast, the relationship of UACR with diastolic dysfunction appeared stronger in normotensive participants, which ran counter to our expectation. Because the observed effect modification was largely driven by the association in the macroalbuminuria subgroup, which had few participants, this finding will require replication in larger studies.

Because Echo-SOL comprised almost two-thirds women, we were able to assess interactions by sex. We detected stronger associations of UACR with strain and LAVI in women. Prior studies have found sex differences in the association of kidney disease with clinical CVD events,[28] but not with LV dysfunction,[15] and additional research is warranted to more fully understand these differences.

A limitation of our study is its cross-sectional design. Also, the number of participants with reduced LVEF was modest, and such reductions mostly fell in the category of mid-range (40% LVEF<50%),[29] precluding separate assessment of more severe LV systolic dysfunction. Despite these limitations, our study is to our knowledge the largest and most comprehensive dataset of echocardiographic parameters focused solely on U.S. Hispanics/Latinos. We used state-of-the-art echocardiographic techniques to gain a more detailed understanding of cardiac function in the context of albuminuria, including GLS, which is a powerful technique for the assessment of early LV systolic dysfunction with distinct advantages over LVEF, including identification of more subtle degrees of dysfunction. Use of a single technician minimized inter-observer variability associated with strain measurements. Finally, we undertook detailed assessment of diastolic dysfunction incorporating transmitral Doppler, tissue Doppler, and LA volume measures, an approach that to our knowledge has been applied in one Chinese study of albuminuria.[30] In summary, our findings support greater attention by providers to albuminuria, even at high-normal levels, as a risk factor for CVD. Interventions to screen for, prevent, and treat albuminuria may be important in Hispanics/Latinos, even in the absence of overt diabetes or hypertension, but this will require further evaluation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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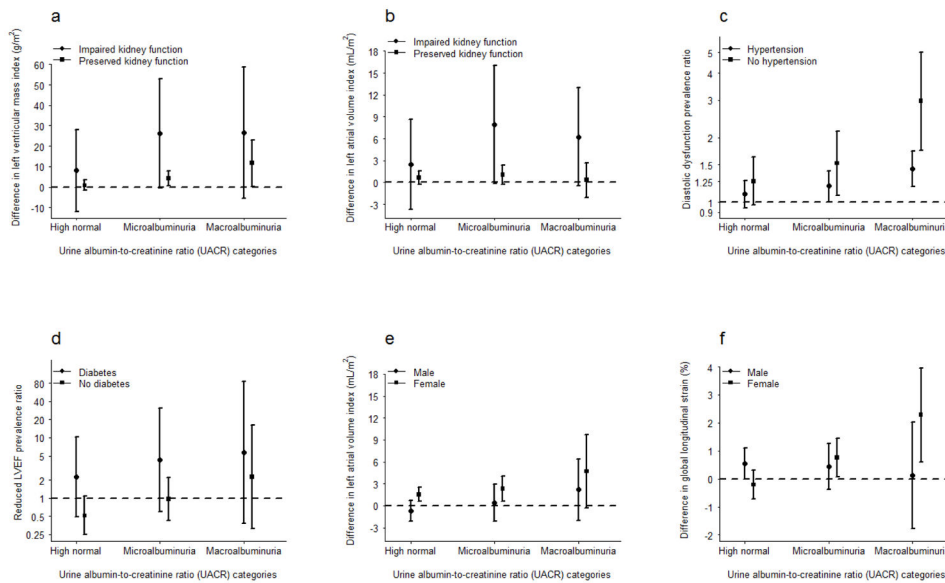
Figure 1. Association of albuminuria with (1a) left ventricular mass index and (1b) left atrial volume index, by eGFR; (1c) diastolic dysfunction, by hypertension status; (1d) reduced left ventricular ejection fraction, by diabetes status; and (1e) left atrial volume index and (1f) global longitudinal strain, by sex

Reference group is normal UACR. Bars represent 95% confidence intervals. For men, high-normal range 5.42–<17 mg/g, microalbuminuria range 17–<250 mg/g, and macroalbuminuria range 250– 3,429 mg/g. For women, high-normal range 6.98–<25 mg/g, microalbuminuria range 25–<355 mg/g, and macroalbuminuria range 355– 11,470 mg/g. Impaired kidney function defined as eGFR <60 mL/min/1.73 m^2 of body surface area.

Table 1

Demographic and clinical characteristics of the Echo-SOL population (N=1,815).

	N	%
Age (median, IQR)	54	49–60
Sex		
Female	1184	65%
Male	631	35%
Field Center		
Bronx	549	30%
Miami	500	28%
San Diego	349	19%
Chicago	417	23%
Ethnicity		
Dominican	326	18%
Central American	176	10%
Cuban	356	20%
Mexican	456	25%
Puerto Rican	347	19%
South American	150	8%
Multiple or other	4	<1%
Acculturation		
U.S.-born	162	9%
Lived in U.S. for 10 years	1291	71%
Lived in U.S. for <10 years	359	20%
Body mass index (kg/m^2) (median, IQR)	29.4	26.3–33.5
Systolic blood pressure (mm Hg) (median, IQR)	135	123–148
Diastolic blood pressure (mm Hg) (median, IQR)	78	71–86
Use of antihypertensive medications	480	26%
History of hypertension	860	47%
Diabetes diagnosis		
Diagnosed diabetic before baseline	336	19%
Undiagnosed diabetic	161	9%
Non-diabetic	1317	73%
Use of anti-diabetes medications	290	16%
Smoking status		
Never	1068	59%
Former	441	24%
Current	304	17%
HDL-cholesterol (mg/dL) (median, IQR)	49	42–58
LDL-cholesterol (mg/dL) (median, IQR)	127	104–151
Use of lipid-lowering medications	356	20%
Estimated glomerular filtration rate (mL/min/1.73 m^2 of body-surface area) (median, IQR)	96.8	84.5–107.2

	N	%
<60	69	4%
60	1726	95%
History of coronary heart disease	5	<1%
History of stroke/transient ischemic attack	9	<1%
History of heart failure	21	1%

N and % presented unless otherwise indicated. IQR = interquartile range.

Missing data: acculturation, N=3; body mass index and diabetes, N=1; systolic blood pressure, N=21; diastolic blood pressure, N=22; use of medications, N=36; smoking and HDL cholesterol, N=2; LDL-cholesterol, N=26; eGFR, N=20.

Table 2

Distribution of urine albumin-to-creatinine ratio (UACR) categories across measures of cardiac structure and function.

	Normal (N=727, 42%)		High-normal (N=733, 43%)		Microalbuminuria (N=222, 13%)		Macroalbuminuria (N=37, 2%)	
	N or mean	% or SD	N or mean	% or SD	N or mean	% or SD	N or mean	% or SD
Cardiac structure								
Left ventricular mass index (mean g/m², SD)	77.9	17.5	81.7	19.0	90.3	24.6	104.4	31.5
Left ventricular hypertrophy (N, %)	56	8%	97	13%	62	28%	13	35%
Systolic function								
Left ventricular ejection fraction (mean %, SD)	60.1%	5.7%	60.4%	5.3%	58.9%	6.0%	60.4%	5.5%
Left ventricular systolic dysfunction (ejection fraction <50%) (N, %)	22	3%	21	3%	12	5%	3	8%
Global longitudinal strain (mean %, SD)	−17.9%	2.7%	−17.6%	2.9%	−16.4%	3.1%	−15.4%	3.7%
Diastolic function								
Diastolic dysfunction * (N, %)								
Normal	364	56%	270	41%	57	31%	3	10%
Grade I	63	10%	99	15%	40	22%	12	41%
Grade II	203	31%	273	42%	84	46%	14	48%
Grade III	20	3%	14	2%	3	2%	0	0%
Grade I–III	286	44%	386	59%	127	69%	26	90%
Left atrial volume index (mean mL/m², SD)	22.6	6.5	23.5	7.5	24.4	9.0	25.9	7.5
Early diastolic annular velocity (e') (mean cm/sec, SD)	8.56	1.99	7.97	2.06	7.42	1.99	6.66	1.82
E/e' ratio (mean, SD)	9.43	2.61	10.19	3.04	10.95	3.55	12.80	4.57

SD = standard deviation.

*
Excluding current pregnancy, atrial fibrillation, more than mild valvular disease, left ventricular ejection fraction <50%, or left ventricular end-diastolic volume index >97 mL/m².

For men, normal UACR range 1.36–<5.42, high normal range 5.42–<17, microalbuminuria range 17–<250, and macroalbuminuria range 250– 3,429. For women, normal UACR range 2.33–<6.98, high normal range 6.98–<25, microalbuminuria range 25–<355, and macroalbuminuria range 355– 11,470. Missing data: Left ventricular mass index and hypertrophy, N=41; left ventricular ejection fraction, N=89; global longitudinal strain and diastolic dysfunction, N=32; left atrial volume index, N=37; e', N=10; E/e' ratio, N=21.

Table 3

Association of urine albumin-to-creatinine ratio (UACR) with measures of cardiac structure and function (N=1,815).

Outcome and level of albuminuria	Model 1			Model 2			Model 3		
Left ventricular mass index	β, g/m²	95% CI	P-value	β, g/m²	95% CI	P-value	β, g/m²	95% CI	P-value
Normal UACR	0.00	Ref.		0.00	Ref.		0.00	Ref.	
High-normal UACR	2.27	−0.60, 5.15	0.12	2.31	−0.31, 4.93	0.08	1.03	−1.48, 3.54	0.42
Microalbuminuria	10.92	6.85, 14.99	<0.0001	8.85	5.03, 12.66	<0.0001	5.57	1.97, 9.18	0.002
Macroalbuminuria	29.10	14.42, 43.78	0.0001	24.42	8.44, 40.40	0.003	19.24	3.57, 34.91	0.02
Left ventricular hypertrophy	PrevR	95% CI	P-value	PrevR	95% CI	P-value	PrevR	95% CI	P-value
Normal UACR	1.00	Ref.		1.00	Ref.		1.00	Ref.	
High-normal UACR	1.17	0.75, 1.82	0.49	1.11	0.70, 1.77	0.66	0.95	0.61, 1.49	0.83
Microalbuminuria	2.82	1.84, 4.31	<0.0001	2.60	1.69, 3.98	<0.0001	1.77	1.18, 2.66	0.01
Macroalbuminuria	3.37	1.68, 6.77	0.0006	3.14	1.55, 6.36	0.001	2.18	1.20, 3.97	0.01
Left ventricular systolic dysfunction (ejection fraction <50%)	PrevR	95% CI	P-value	PrevR	95% CI	P-value	PrevR	95% CI	P-value
Normal UACR	1.00	Ref.		1.00	Ref.		1.00	Ref.	
High-normal UACR	0.73	0.35, 1.53	0.41	0.76	0.37, 1.58	0.47	0.67	0.34, 1.32	0.25
Microalbuminuria	1.69	0.83, 3.45	0.15	1.58	0.77, 3.24	0.22	1.20	0.57, 2.51	0.64
Macroalbuminuria	2.39	0.54, 10.51	0.25	1.69	0.39, 7.26	0.48	1.71	0.43, 6.86	0.45
Global longitudinal strain	β, %	95% CI	P-value	β, %	95% CI	P-value	β, %	95% CI	P-value
Normal UACR	0.00	Ref.		0.00	Ref.		0.00	Ref.	
High-normal UACR	0.21	−0.28, 0.69	0.40	0.22	−0.19, 0.63	0.30	0.12	−0.27, 0.51	0.55
Microalbuminuria	1.49	0.92, 2.05	<0.0001	1.15	0.64, 1.66	<0.0001	0.57	0.07, 1.07	0.02
Macroalbuminuria	1.91	0.56, 3.25	0.01	1.40	−0.14, 2.94	0.07	0.81	−0.63, 2.25	0.27
Diastolic dysfunction (Grade 1 or higher) (N=1,628)	PrevR	95% CI	P-value	PrevR	95% CI	P-value	PrevR	95% CI	P-value
Normal UACR	1.00	Ref.		1.00	Ref.		1.00	Ref.	
High-normal UACR	1.43	1.20, 1.70	0.0001	1.29	1.11, 1.50	0.0007	1.21	1.05, 1.39	0.01
Microalbuminuria	1.65	1.38, 1.98	<0.0001	1.50	1.26, 1.78	<0.0001	1.31	1.11, 1.54	0.001
Macroalbuminuria	2.29	1.97, 2.67	<0.0001	1.98	1.63, 2.39	<0.0001	1.61	1.27, 2.05	0.0001
Left atrial volume index	β, mL/m²	95% CI	P-value	β, mL/m²	95% CI	P-value	β, mL/m²	95% CI	P-value
Normal UACR	0.00	Ref.		0.00	Ref.		0.00	Ref.	
High-normal UACR	0.73	−0.22, 1.67	0.13	0.60	−0.26, 1.45	0.17	0.55	−0.34, 1.44	0.23

Outcome and level of albuminuria	Model 1			Model 2			Model 3		
Left ventricular mass index	β, g/m²	95% CI	P-value	β, g/m²	95% CI	P-value	β, g/m²	95% CI	P-value
Microalbuminuria	1.48	−0.12, 3.07	0.07	1.46	−0.0009, 2.92	0.05	1.48	0.002, 2.96	0.05
Macroalbuminuria	4.36	0.92, 7.79	0.01	4.10	0.57, 7.63	0.02	3.15	−0.003, 6.30	0.05

CI = confidence interval, PrevR = prevalence ratio, UACR = urine albumin-to-creatinine ratio.

Model 1 is unadjusted. Model 2 is adjusted for demographic characteristics (sex, age, Hispanic background, field center). Model 3 is adjusted for demographic characteristics and cardiometabolic risk factors (body mass index, systolic blood pressure, use of antihypertensive medications, diabetes, smoking status, HDL- and LDL-cholesterol, use of lipid-lowering medications, and estimated glomerular filtration rate).