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Association of urine albumin excretion with incident heart failure hospitalization in community-dwelling adults

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Abstract

Objectives—To examine the association of urinary albumin excretion with incident heart failure (HF) hospitalization.

Background—Excess urinary albumin excretion is more strongly associated with incident stroke and coronary heart disease risk in black than in white individuals. Whether similar associations extend to HF is unclear.

Methods—In 24,433 Reasons for Geographic and Racial Differences in Stroke (REGARDS) study participants free of suspected HF at baseline, we examined the associations of urinary albumin to creatinine ratio (ACR) with expert-adjudicated incident hospitalization for HF overall, and stratified by race and HF subtype (preserved vs. reduced ejection fraction). Models were adjusted for socio-demographic, clinical and laboratory variables including estimated glomerular filtration rate, and multiple imputation was used to account for missing covariate data.

Results—After a median 9.2 years of follow-up, 881 incident HF events (332 preserved ejection fraction, 447 reduced ejection fraction, 102 unspecified) were observed. Compared to the lowest ACR category (< 10 mg/g), the risk of incident HF increased with increasing ACR categories

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(10-29 mg/g, hazard ratio [HR] 1.49, 95%CI 1.26,1.78; 30-300 mg/g, HR 2.32, 95%CI 1.93, 2.78; >300 mg/g, HR 4.42 95% CI 3.36,5.83) in the fully-adjusted model. Results did not differ by race. The magnitude of the association of ACR with HF with preserved ejection fraction was greater than with HF with reduced ejection fraction (HR comparing highest vs. lowest ACR category 6.20, 95%CI 4.15,9.26 vs. 4.37,95%CI 3.00,6.25, $P=0.05$).

Conclusions—Higher ACR was associated with greater risk of incident HF hospitalization in community-dwelling black and white adults.

INTRODUCTION

Black adults are at substantially higher risk of developing heart failure (HF) than white adults (1). The reasons for this disparity are unclear. Excess urinary albumin excretion is an important marker of kidney injury, is more common in black individuals than white individuals, and is associated with a higher risk for cardiovascular disease events and death (2–4). We have previously shown that higher urinary albumin excretion was associated with a greater risk of incident stroke and coronary heart disease (CHD) in participants of the Reasons for Geographic and Racial Differences in Strokes (REGARDS) study (5,6). In addition, we showed that the magnitude and strength of these associations were greater in black individuals than in white individuals in multivariable adjusted analyses. Whether similar racial differences exist in the relationship between urinary albumin excretion and HF is unclear. Most prior studies examining the relationship between urinary albumin excretion and HF outcomes in general population-based cohorts had relatively low representation of black individuals (7–19), limiting their ability to determine if there is racial heterogeneity in the association of urinary albumin excretion with HF. Further, only a few studies assessed the association of urine albumin excretion with HF by different HF subtypes (preserved vs. reduced ejection fraction) (10,11,15). In the current study, we examined the association of urinary albumin excretion with incident hospitalization for HF in participants of the REGARDS study. In addition, we examined whether these associations differed by HF subtype and by race.

METHODS

Study Participants

The REGARDS study is a population-based investigation of stroke incidence in black and white US adults ≥45 years of age. Details of the study design have been described elsewhere (20). Briefly, the study was designed to provide approximately equal representation of men and women, and oversampled black individuals and persons living in the “stroke belt” of the US. Potential participants were identified from commercially available lists of residents and recruited through an initial mailing followed by telephone contacts. Trained interviewers conducted computer-assisted telephone interviews to obtain information including participants’ sociodemographics, cardiovascular risk factors, cigarette smoking, physical activity, and use of medications. Following this call, certified health professionals conducted an in-home study visit that included an electrocardiogram recording and inventory of medications. In addition, fasting blood and urine samples were collected during the in-home visit and shipped to the University of Vermont Central Laboratory using

standardized procedures. Overall, 30,239 black and white adults were enrolled between January 2003 and October 2007. The REGARDS study protocol was approved by the Institutional Review Boards governing research in human subjects at the participating centers and all participants provided informed consent.

Primary Exposure of Interest

The exposure of interest was baseline urine albumin to creatinine ratio (ACR). Urine albumin was measured by nephelometry using the BNII ProSpec nephelometer (Now Siemens AG), and urine creatinine was measured by the rate Jaffe method using the Modular-P chemistry analyzer (Roche/Hitachi, Basel, Switzerland).

Ascertainment of Outcomes

The outcomes of interest were incident HF hospitalizations, detected via telephone follow-up with participants every 6 months through December 31st, 2015. Adjudication of HF hospitalizations was performed independently by two clinician investigators with disagreements resolved by discussion. If agreement fell below 80%, adjudicators were retrained. Heart failure events were based on signs and symptoms, laboratory studies (troponin-I, troponin-T, creatinine kinase-MB fraction, B-type natriuretic peptide), electrocardiogram, chest x-ray, and assessments of left ventricular function. Signs and symptoms of HF included paroxysmal nocturnal dyspnea, orthopnea, abnormal jugular vein distension, pulmonary rales, cardiomegaly, central venous pressure >16 mm Hg, edema, nocturnal cough, exertional dyspnea, hepatomegaly, pleural effusion, heart rate >120/minute, and 4.5 kilogram weight loss in 5 days with diuresis. Heart failure with reduced ejection fraction (HFrEF) was defined as EF <50% or qualitative report of reduced EF. Heart failure with preserved ejection fraction (HFpEF) was defined as EF ≥ 50% or qualitative report of preserved EF. Heart failure events that were not able to be categorized as reduced or preserved ejection fraction were classified as unspecified.

In order to focus on incident HF hospitalizations, we excluded individuals with suspected HF at baseline, determined by current use of HF-related medications at the baseline visit. Heart failure-related medications included use of carvedilol, any loop diuretic, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers plus beta blockers in the absence of hypertension, or digoxin in the absence of atrial fibrillation.

Covariates of Interest

Age, sex, smoking history, annual family income, and educational attainment were determined by self-report. Systolic blood pressure was defined as the average of two seated measures taken after a 3 minute rest. History of CHD was defined as having any of the following: evidence of myocardial infarction on the baseline electrocardiogram, self-report of a prior history of a cardiac procedure (coronary artery bypass surgery or percutaneous angioplasty), or self-reported history of myocardial infarction. Diabetes was defined as self-reported use of insulin or oral hypoglycemic agents, fasting serum glucose concentration of 126 mg/dL or higher, or a non-fasting serum glucose concentration of 200 mg/dL or higher. Using height and weight measured during the in-home study visit, body mass index (BMI) was calculated. Use of lipid-lowering and anti-hypertensive medications was based on self-

report and pill bottle review during the home visit. Serum concentrations of total cholesterol, high-density lipoprotein cholesterol (HDL-C), and high-sensitivity c-reactive protein (hsCRP) were measured using established assays, and estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease (CKD) Epidemiology Collaboration formula (21).

Statistical Analyses

Baseline characteristics of participants were compared across categories of ACR (< 10 mg/g, 10-29 mg/g, 30-300 mg/g, > 300 mg/g) using descriptive statistics. The Kaplan-Meier method was used to calculate the cumulative incidence of HF hospitalization by strata of ACR. Age- and sex- adjusted incidence rates for incident HF hospitalization were calculated by strata of ACR. Cox proportional hazards models were used to estimate the hazard ratio of incident HF hospitalization as a function of ACR in sequential, multivariable-adjusted models. Models included established HF risk factors and factors that had a plausible biologic link to both ACR and HF. Model 1 adjusted for age, sex and race. Model 2 adjusted for variables in model 1 plus systolic blood pressure, diastolic blood pressure, BMI, annual family income (< vs. \$20,000/year), educational achievement (< vs. high school diploma), diabetes status (yes vs. no), current smoking (yes vs. no), history of CHD (yes vs. no), history of atrial fibrillation by self-report or electrocardiogram (yes vs. no), left ventricular hypertrophy (by electrocardiogram criteria; yes vs. no), use of lipid lowering medications (yes vs. no), and use of renin-angiotensin-aldosterone inhibitors (yes vs. no). Model 3 further adjusted for laboratory factors (HDL-C, total cholesterol, triglycerides, eGFR, and natural log-transformed hsCRP). All Cox models were fitted using imputed data to account for missing covariate data. Missing data were imputed using multivariable multiple imputation by fully conditional specification with ten datasets. In all models, urinary ACR was analyzed as a categorical variable, with the lowest category (< 10 mg/g) serving as the referent group.

Given our prior findings that the relationship between ACR and incident stroke and CHD differs by race, we repeated the analyses stratified by race. Although the decision to stratify all analyses by race was made *a priori*, we also formally examined for effect modification by race by testing the statistical significance of ACR category $\times$ race interaction terms in multivariable-adjusted Cox models using a post-estimation Wald test to obtain an omnibus *P*-value for interaction between ACR categories and race. In secondary analyses, we examined the association of ACR with HFrEF and HFpEF, separately, using an identical modeling strategy as described above. To evaluate whether the association of ACR with incident HF hospitalization varied by HF subtype, we tested for heterogeneity in the association of ACR with HF subtypes (preserved, reduced, unknown) using the likelihood ratio test as described by Wang *et al.* (22). A two-tailed *P*value < 0.05 was considered statistically significant. All analyses were conducted using SAS software version 9.4 (SAS Institute, Cary, NC).

RESULTS

Study Population

After excluding 531 participants missing follow-up data, 3938 participants with suspected HF or missing data on HF at baseline, 1159 participants missing ACR data, and 221 participants receiving dialysis or missing data on dialysis history at baseline, a total of 24,433 were included in the analyzed sample (Supplemental Figure 1). The characteristics of the study sample are summarized in Table 1. In general, higher urinary ACR values were associated with older age, black race, male sex, lower education and income, current smoking, higher blood pressure, higher BMI, current use of statins or anti-hypertensive medications, higher hsCRP, lower eGFR and a history of diabetes and CHD.

Urine ACR and incident HF hospitalization

After a median 9.2 years of follow-up (interquartile range 6.4-10.9), a total of 881 incident HF hospitalizations occurred. Higher categories of urinary ACR were associated with higher cumulative incidence of HF hospitalization (Supplemental Figure 2). Similarly, age- and sex-adjusted incidence rates of HF per 1000 person-years of follow-up increased with increasing categories of ACR (Table 2) in the study population overall, and in black and white participants, separately.

The adjusted hazard ratios (HRs) of incident HF hospitalization by categories of urinary ACR overall and stratified by race are shown in Table 2. Higher categories of baseline urinary ACR were associated with higher risk of incident HF hospitalization in models adjusted for age, sex and race (ACR < 10 mg/g, ref; 10-29 mg/g, HR 1.89, 95%CI 1.60,2.25; 30-300 mg/g, HR 3.61, 95%CI 3.03,4.32; > 300 mg/g, HR 10.46, 95%CI 8.24,13.28). Following adjustment for sociodemographic, clinical and laboratory factors, higher categories of urinary ACR remained associated with higher risk of incident HF hospitalization, such that in the fully adjusted model, participants with an ACR greater than 300 mg/g had an over 4-fold greater risk of incident HF hospitalization as compared to participants with an ACR less than 10 mg/g (HR 4.42, 95%CI 3.36,5.83). Adjustment for socio-demographic and clinical factors appeared to play the largest role in attenuating effect estimates in sequential models (Supplemental Table 1). The magnitude and strength of these associations did not differ by race ($P_{\text{interaction}}=0.93$).

The Figure shows age- and sex-adjusted incidence rates per 1000 person-years of follow-up according to baseline urine ACR and eGFR categories. In general, the risk of incident HF hospitalization increased with increasing categories of ACR within each eGFR stratum. Table 3 depicts fully-adjusted HRs of incident HF hospitalization according to baseline urine ACR and eGFR categories, with an eGFR greater than or equal to 60 ml/min/1.73m² and an ACR < 10 mg/g serving as the referent group. The risk of incident HF hospitalization increased with increasing categories of ACR and decreasing categories of eGFR, with individuals with an eGFR < 30 ml/min/1.73m² and an ACR > 300 mg/g having a nearly 9-fold greater risk of incident HF hospitalization as compared to the referent group. Adjustment for socio-demographic and clinical factors appeared to play the largest role in attenuating effect estimates in sequential models (Supplemental Table 2).

Urine ACR and incident HF subtype

Table 4 depicts the association of urine ACR categories with incident HF hospitalization stratified by HF subtype (preserved, reduced, unspecified). Of the 881 incident HF hospitalization events, 332 were classified as HFpEF, 447 as HFrEF, and 102 as unspecified subtype. Analogous to the results of the primary outcome analyses, higher ACR categories were associated with higher risk of incident HF hospitalization in multivariable-adjusted models irrespective of HF subtype. The magnitude of the association of ACR with incident HF hospitalization was greater for HFpEF than HFrEF, though this was of borderline statistical significance (P -value for overall likelihood ratio test=0.05). Results were similar when HFrEF was defined as an ejection fraction <40% (Supplemental Table 3).

DISCUSSION

In participants of the REGARDS study, higher ACR was associated with a greater risk of incident HF hospitalization independently of established risk factors for HF including baseline eGFR.

Prior studies have examined the association of urine ACR with HF outcomes and in general, have shown that higher urine ACR is an independent risk factor for HF in general population-based cohorts (7–19). However, these studies had low representation of black individuals or relatively few HF events, limiting their ability to determine whether the association of ACR with HF differed by race. The current study addresses this knowledge gap by showing that the association of urine ACR with incident HF hospitalization does not appreciably vary by black vs. white race. This is in contrast to what we previously observed in two prior studies in REGARDS (5,6), in which higher ACR was a stronger risk factor for incident stroke and CHD in black vs. white participants. There may be several reasons for the discrepancies in these findings. High urine albumin excretion is thought to represent an integrated marker of kidney injury as well as a general marker of systemic microvascular injury. The link between ACR and HF may be more strongly related to underlying kidney injury, which is a powerful risk factor for HF irrespective of race. In contrast, higher urine ACR may be more strongly related to CHD risk factors, CHD and stroke as a marker of systemic microvascular injury, which may differentially impact individuals by race (23). Adults with HF tend to have a high prevalence of CHD and CHD risk factors (hypertension, diabetes, smoking, etc.), all of which associate with microvascular injury. Understanding whether microvascular injury specific to the glomerulus underlies the link between ACR and HF may help to identify novel targets for reducing the incidence of heart failure and mitigating its severity in high risk populations.

The results of this study also reinforce the notion that ACR is a strong risk factor for HF outcomes independent of baseline eGFR. Across strata of eGFR, age- and sex-adjusted incidence rates of HF hospitalization increased in parallel with increasing categories of ACR, even for mildly elevated ACR (> 10 mg/g), suggesting that ACR confers important prognostic information irrespective of underlying kidney function. This has important clinical applications as therapies directly aimed at reducing ACR such as RAAS inhibition may be under-utilized for the prevention of HF in individuals at high risk for the development of albuminuria (such as those with diabetes or hypertension), particularly if

they have normal eGFR. Indeed, the percentage of individuals in the highest ACR category taking RAAS inhibitors at baseline in this study was relatively low given the degree of their albuminuria (55%, Table 1). This may highlight a key area for improvement in efforts to reduce the risk of developing HF, particularly in high risk groups such as those with diabetes. Further, clinicians may be wary of starting or increasing RAAS inhibition in individuals with reduced eGFR for fear of worsening underlying kidney function. However, as shown in Table 3, individuals in the highest risk categories for ACR (>300 mg/g) and eGFR (<30 ml/min/1.73m²) had a nearly 9-fold increased risk of incident HF hospitalization as compared to those in the lowest risk category for both, supporting the potential importance of RAAS inhibitors in reducing HF risk in those with severe kidney disease and albuminuria.

Few studies examined the association of urine ACR with HF subtypes, and the results that do exist have been conflicting. One study showed that urine ACR was more strongly associated with HFpEF (10), another to HFrEF (15), whereas a third (11) showed no appreciable differences by subtype in community-based populations. Importantly, most of these studies had relatively few events, limiting their statistical power to detect potentially modest associations. The results of the current study show that the magnitude of the association of ACR with HFpEF was greater than with HFrEF, though this difference was of borderline statistical significance ($P=0.05$). Nevertheless, the monotonic increase in risk with increasing categories of ACR was striking for both HFpEF and HFrEF, indicating that excess urinary albumin excretion is a strong risk factor for HF no matter the subtype. Further, the relative risk difference comparing the highest vs. lowest ACR category was higher in our study than has been reported in other studies, underscoring the importance of examining the association of ACR with HF outcomes in contemporary cohorts such as REGARDS.

Our study had limitations. We only had a single measurement of ACR, which may have led to exposure misclassification for some study participants. This would bias our results to the null so our findings could underestimate true associations. Next, some ACR categories had relatively few events, particularly in the HF subtype analyses, which may have reduced power to detect significant associations with HF outcomes in these categories or to detect differences in the associations by HF subtype. Furthermore, we had limited information with respect to disease progression over time, which may play a role in racial differences in these outcomes. While we attempted to exclude individuals with HF at baseline, we used surrogate measures to detect suspected HF at baseline and did not have information on the diagnosis of HF by a clinician at the baseline visit (24). Finally, the inclusion of only black or white participants may limit the generalizability of these results to other races/ethnicities in the US.

In summary, higher ACR was a strong and independent risk factor for incident hospitalization for HF in the REGARDS study. This relationship did not appear to differ by race and was strong irrespective of HF subtype, underscoring the importance of ACR as a biomarker of cardiovascular risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

HF	Heart Failure
CHD	coronary heart disease
REGARDS	Reasons for Geographic and Racial Differences in Stroke
ACR	albumin to creatinine ratio
eGFR	estimated glomerular filtration rate
hsCRP	high-sensitivity C-reactive protein
HFpEF	heart failure with preserved ejection fraction
HFrfEF	heart failure with reduced ejection fraction
BMI	body mass index
HDL-C	high density lipoprotein cholesterol

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CLINICAL RELEVANCE

The finding that higher urinary albumin to creatinine ratio was associated with higher risk of incident heart failure hospitalization underscores the importance of urinary albumin excretion as a risk factor for heart failure in community-dwelling adults. This has important clinical applications as therapies directly aimed at reducing urinary albumin excretion, such as inhibition of the renin-angiotensin-aldosterone system, may be underutilized for the prevention of heart failure in high-risk groups like individuals with diabetes or hypertension. The results of these study support the use of these therapies in high-risk groups, particularly in individuals with reduced estimated glomerular filtration rate.

TRANSLATIONAL OUTLOOK

Increased urinary albumin excretion is a marker of both glomerular kidney injury and systemic microvascular injury. A number of factors have been shown to influence vascular health, but which factors are most relevant in explaining the strong, independent association of urinary albumin excretion with heart failure is unclear. Understanding the extent to which cellular and molecular mechanisms underlying microvascular injury—whether specific to the glomerulus or more systemic—underlie the link between urinary albumin excretion and heart failure may help to identify novel targets for reducing the incidence and severity of heart failure.

Figure.

Age- and sex-adjusted incidence rate of heart failure hospitalization per 1000 person-years of follow-up as a function of urine albumin to creatinine ratio and estimated glomerular filtration rate categories

Table 1.

Baseline characteristics overall and by urine albumin to creatinine ratio categories in participants without a history of heart failure at baseline.

	Full sample	Urine albumin to creatinine ratio categories			
		< 10 mg/g	10-29 mg/g	30-300 mg/g	> 300 mg/g
N	24 433	15 646	5532	2745	510
Age, years, mean (SD)	64 (9)	63 (9)	66 (10)	67 (10)	66 (9)
Black, N(%)	9674 (39)	5826 (37)	2173 (39)	1327 (48)	348 (64)
Male, N(%)	11 218 (46)	7343 (47)	2217 (39)	1350 (38)	308 (57)
<high school diploma, N(%)	2774 (11)	1487 (9)	704 (13)	484 (17)	99 (18)
<\$20,000/year income, N(%)	4039 (16)	2196 (14)	1032 (19)	660 (24)	151 (28)
BMI, kg/m ² , mean (SD)	28.9 (5.9)	28.7 (5.6)	29.0 (6.2)	29.7 (6.4)	29.9 (6.5)
SBP, mmHg, mean (SD)	127 (16)	125 (15)	130 (17)	134 (18)	141 (20)
DBP, mmHg, mean (SD)	77 (10)	75 (9)	77 (10)	79 (11)	81 (11)
Lifestyle Habits					
Current smoking, N(%)	3596 (15)	2104 (13)	827 (15)	527 (19)	138 (26)
Exercise (none), N(%)	7775 (32)	4596 (30)	1900 (35)	1035 (38)	244 (46)
Co-morbidities					
Diabetes, N(%)	4451 (18)	1965 (13)	1261 (23)	926 (33)	299 (56)
CHD, N(%)	3618 (15)	1917 (12)	946 (17)	582 (21)	173 (33)
Hypertension, N (%)	13 896 (57)	7912 (51)	3529 (64)	2024 (74)	431 (85)
Medication use					
Statins, N(%)	7238 (29)	4346 (28)	1740 (31)	938 (34)	214 (39)
Antihypertensive, N(%)	13 470 (55)	7795 (50)	3338 (60)	1903 (68)	434 (80)
RAAS inhibitors, N(%)	7953 (32)	4468 (28)	1993 (36)	1193 (43)	299 (55)
eGFR, ml/min/1.73 ² , mean (SD)	86.4 (18.9)	87.9 (16.9)	86.4 (18.9)	81.8 (23.2)	64.3 (30.7)
hsCRP, mg/L, median [IQR]	2.1 [0.9,4.8]	1.9 [0.9,4.3]	2.3 [0.9,5.1]	2.9 [1.2,6.4]	3.5 [1.3,7.7]

Abbreviations: SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHD, coronary heart disease; RAAS, renin angiotensin aldosterone system; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitivity C-reactive protein.

Table 2.

Incidence rates (95% confidence interval) per 1000 person-years of follow-up and hazard ratios (95% confidence interval) of incident heart failure hospitalization according to baseline urine albumin to creatinine ratio categories overall and stratified by race.

	Urine albumin to creatinine ratio categories			
	< 10 mg/g	10-29 mg/g	30-300 mg/g	> 300 mg/g
Overall				
N, events/at risk	324/15 646	241/5532	221/2745	95/510
IR	2.22 (1.97,2.48)	4.18 (3.49,4.65)	7.87 (6.82,9.08)	22.31 (18.15,27.41)
HR Model 1	ref	1.89 (1.60,2.25)	3.61 (3.03,4.32)	10.46 (8.24,13.28)
HR Model 2	ref	1.52 (1.28,1.79)	2.52 (2.09,3.03)	5.46 (4.20,7.09)
HR Model 3	ref	1.49 (1.26,1.78)	2.32 (1.93,2.78)	4.42 (3.36,5.83)
Black				
N, events/at risk	110/5844	84/2165	91/1311	54/326
IR	2.26 (1.87,2.73)	4.48 (3.39,5.58)	8.36 (6.75,10.35)	23.32 (17.79,30.55)
HR Model 1	ref	1.98 (1.49,2.64)	3.73 (2.82,4.94)	10.57 (7.58,14.72)
HR Model 2	ref	1.59 (1.19,2.14)	2.55 (1.92,3.40)	5.43 (3.74,7.88)
HR Model 3	ref	1.59 (1.19,2.13)	2.41 (1.80,3.21)	4.69 (3.12,7.04)
White				
N, events/at risk	214/9802	157/3367	130/1434	41/184
IR	2.13 (1.85,2.46)	3.83 (3.22,4.56)	7.24 (5.96,8.79)	20.64 (14.99,28.39)
HR Model 1	ref	1.81 (1.47,2.24)	3.46 (2.75,4.35)	10.05 (7.07,14.29)
HR Model 2	ref	1.44 (1.17,1.78)	2.44 (1.92,3.09)	5.06 (3.46,7.40)
HR Model 3	ref	1.42 (1.14,1.75)	2.18 (1.71,2.78)	4.05 (2.76,5.94)

Abbreviations: IR, incidence rate; HR, hazard ratio

Model 1 is adjusted for age, sex and race (in analyses not stratified by race)

Model 2 is adjusted for factors in Model 1 plus systolic blood pressure, diastolic blood pressure, body mass index, annual family income (< vs. \$20,000/year), educational achievement (< vs. high school diploma), diabetes status (yes vs. no), current smoking (yes vs. no), history of coronary heart disease (yes vs. no), history of atrial fibrillation by self-report (yes vs. no), left ventricular hypertrophy (yes vs. no), use of lipid lowering medications (yes vs. no), and use of renin-angiotensin-aldosterone inhibitors (yes vs. no)

Model 3 is adjusted for factors in Model 2 plus high-density lipoprotein cholesterol, total cholesterol, triglycerides, estimated glomerular filtration rate, and natural log-transformed C-reactive protein

Table 3.

Hazard ratios (95% confidence interval) of incident heart failure hospitalization according to baseline urine albumin to creatinine ratio and estimated glomerular filtration rate categories.

		Urine albumin to creatinine ratio categories			
		< 10 mg/g	10-29 mg/g	30-300 mg/g	> 300 mg/g
eGFR ≥ 60	ref		1.45 (1.19,1.76)	2.39 (1.93,2.94)	5.14 (3.67,7.23)
eGFR 30 – 59	1.71 (1.25,2.33)		2.45 (1.78,3.37)	3.39 (2.49,4.61)	5.29 (3.47,8.06)
eGFR < 30	3.37 (0.86,13.28)		2.71 (0.77,9.53)	4.08 (1.75,9.49)	8.83 (4.80,16.22)

Abbreviations: eGFR, estimated glomerular filtration rate in ml/min/1.73m²

The model is adjusted for age, sex, race, systolic blood pressure, diastolic blood pressure, body mass index, annual family income (< vs. \$20,000/year), educational achievement (< vs. high school diploma), diabetes status (yes vs. no), current smoking (yes vs. no), history of coronary heart disease (yes vs. no), history of atrial fibrillation by self-report (yes vs. no), left ventricular hypertrophy (yes vs. no), use of lipid lowering medications (yes vs. no), use of renin-angiotensin-aldosterone inhibitors (yes vs. no), high-density lipoprotein cholesterol, total cholesterol, triglycerides, estimated glomerular filtration rate, and natural log-transformed C-reactive protein.

Table 4.

Hazard ratios (95% confidence interval) of incident heart failure hospitalization according to baseline urine albumin to creatinine ratio categories, stratified by heart failure subtype

		Urine albumin to creatinine ratio categories			
		< 10 mg/g	10-29 mg/g	30-300 mg/g	> 300 mg/g
Preserved					
N		119	96	79	38
HR Model 1	ref		1.97 (1.49,2.59)	3.50 (2.61,4.69)	11.62 (7.92,17.03)
HR Model 2	ref		1.57 (1.19,2.07)	2.43 (1.79,3.29)	6.09 (4.05,9.17)
HR Model 3	ref		1.56 (1.18,2.05)	2.32 (1.71,3.14)	6.20 (4.15,9.26)
Reduced					
N		173	118	111	45
HR Model 1	ref		1.85 (1.46,2.35)	3.49 (2.72,4.47)	9.19 (6.58,12.83)
HR Model 2	ref		1.46 (1.15,1.86)	2.42 (1.87,3.12)	4.64 (3.20,6.72)
HR Model 3	ref		1.44 (1.13,1.83)	2.29 (1.78,2.96)	4.37 (3.00,6.35)
Unspecified					
N		32	27	31	12
HR Model 1	ref		1.90 (1.13,3.22)	4.68 (2.80,7.83)	13.05 (6.64,25.65)
HR Model 2	ref		1.58 (0.92,2.70)	3.45 (2.02,5.86)	8.02 (3.84,16.75)
HR Model 3	ref		1.52 (0.89,2.60)	3.27 (1.92,5.58)	6.75 (3.19,14.32)

Abbreviations: HR, hazard ratio

Model 1 is adjusted for age, sex and race

Model 2 is adjusted for factors in Model 1 plus systolic blood pressure, diastolic blood pressure, body mass index, annual family income (< vs. \$20,000/year), educational achievement (< vs. high school diploma), diabetes status (yes vs. no), current smoking (yes vs. no), history of coronary heart disease (yes vs. no), history of atrial fibrillation by self-report (yes vs. no), left ventricular hypertrophy (yes vs. no), use of lipid lowering medications (yes vs. no), and use of renin-angiotensin-aldosterone inhibitors (yes vs. no)

Model 3 is adjusted for factors in Model 2 plus high-density lipoprotein cholesterol, total cholesterol, triglycerides, estimated glomerular filtration rate, and natural log-transformed C-reactive protein