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Risk Factors for Rapid Kidney Function Decline Among African Americans: The Jackson Heart Study (JHS)

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Abstract

Background—Racial differences in rapid kidney function decline exist, but less is known regarding factors associated with rapid decline among African Americans. A greater understanding of potentially modifiable risk factors for early kidney function loss may help reduce the burden of kidney failure in this high-risk population.

Study Design—Prospective cohort study.

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Contributions: Research idea and study design: BAY, RK, EB, BK, IHdB, WW, TF, NB, CR-C, MG, NNP, JH, AC; data acquisition: BAY, RK, AC; data analysis/interpretation: BAY, RK, EB, BK, IHdB, WW, TF, NB, CR-C, MG, NNP, JH, AC; statistical analysis: RK; supervision or mentorship: JH, AC, NNP. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. BAY takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Setting & Participants—3653 African-American participants enrolled in the Jackson Heart Study (JHS) with kidney function data from two of three examinations (2000-2004 and 2009-2013). Estimated glomerular filtration rate (eGFR) was calculated from serum creatinine using the CKD-EPI creatinine equation.

Predictors—Demographics, socioeconomic status, lifestyle, clinical risk factors for kidney failure.

Outcomes—Rapid decline was defined as a ≥ 30% decline in eGFR during follow-up. We quantified the association of risk factors with rapid decline in multivariable models.

Measurements—Clinical (systolic blood pressure, albuminuria [albumin-creatinine ratio]) and modifiable risk factors.

Results—Mean age was 54 ± 12 (SD) years, 37% were male, average body mass index was 31.8 ± 7.1 kg/m_2, 19% had diabetes mellitus (DM) and mean eGFR was 96.0 ±20 ml/min/1.73m_2 with an annual rate of decline of 1.27 ml/min/1.73m_2. Those with rapid decline (11.5%) were older, more likely to be of low/middle income, had higher systolic blood pressure, and greater DM than those with non-rapid decline. Factors associated with ≥30% decline were older age (adjusted OR per 10 years older, 1.51; 95% CI, 1.34-1.71); cardiovascular disease (adjusted OR, 1.53; 95% CI, 1.12-2.10), higher systolic blood pressure (adjusted OR per 17 mm Hg greater, 1.22; 95% CI, 1.06-1.41); DM (adjusted OR, 2.63; 95% CI, 2.02-3.41), smoking (adjusted OR, 1.60; 95% CI, 1.10-2.31), and albumin-creatinine ratio > 30 mg/g (adjusted OR, 1.55; 95% CI, 1.08-1.21). Conversely, results did not support associations of waist circumference, C-reactive protein, and physical activity with rapid decline.

Limitations—No mid study creatinine measurement at examination 2 (2005-2008).

Conclusions—Rapid decline heterogeneity existed among African Americans in JHS. Interventions targeting potentially modifiable factors may help reduce the incidence of kidney failure.

Keywords

chronic kidney disease (CKD); African American; ethnic differences; kidney disease progression; disease trajectory; rapid kidney function decline; estimated glomerular filtration rate (eGFR); risk factor; renal failure; Jackson Heart Study (JHS)

Chronic kidney disease (CKD) is a growing public health concern that disproportionately affects African Americans.[1,2] African Americans are 2- to 4-fold more likely to develop end stage renal disease (ESRD) than whites[3], which is thought to be due to increased prevalence of known risk factors among African Americans, such as diabetes mellitus (DM)[4], hypertension[5] and genetic polymorphisms such as apolipoprotein L1 (*APOL1),* and sickle cell trait.[6,7,3] Even with adequate treatment of hypertension, greater than 50% of African Americans with CKD progressed to ESRD when evaluated prospectively in a randomized controlled trial with adequate blood pressure control.[8,9] Variation in the rate of kidney function decline was reported, and proteinuria was found to be the most predictive variable associated with kidney function progression. However, given these findings, less is known regarding risk factors for rapid kidney function decline among African Americans in the

general population with normal kidney function at baseline. Data from the Coronary Artery Risk Development in Young Adults (CARDIA) study showed that blacks had earlier onset and faster rates of decline of kidney function than whites, but intra-racial characteristics of blacks with rapid kidney function decline were not reported.[10] Most other published studies have had small numbers and have not evaluated potential heterogeneity in the incidence and progression of CKD among African Americans.

The Jackson Heart Study (JHS) is one of the largest ongoing prospective population-based cohort studies of African Americans developed to evaluate risk factors for the development and progression of cardiovascular diseases (CVDs). In this study, we evaluate the association of known and novel risk factors for rapid kidney function decline in a large African-American cohort.

METHODS

Study Population

Subjects from the JHS[11,12] were recruited from the tri-county region (Hinds, Madison, and Rankin) of metropolitan Jackson, MS. Recruitment and data collection protocols and survey instruments have been described previously.[13] Briefly, participants were originally recruited from 2000-2004 as part of the Atherosclerosis Risk in Communities (ARIC) study (ages 35-85 years). Additional younger and older participants were recruited as part of the JHS family study, such that ages of the 5301 subjects recruited at baseline ranged from 21-94. Participants were recruited and followed up for three examinations: examination 1 (2000-2004), examination 2 (2005-2008), and examination 3 (2009-2013). Creatinine was obtained during examinations 1 and 3 only. Participants without serum creatinine measured at examinations 1 or 3 (those on dialysis (self report) at examination 1, those who died prior to examination 3, and those who were lost to follow-up were excluded from analyses (n=1648). Initial analyses were conducted on the full population, while sensitivity analyses were conducted on a subset of subjects for whom urine albumin values were available at baseline (n=2382) and for whom albuminuria was imputed using sex and age as imputation factors (n=1271) (Figure 1). The original JHS protocol was approved by the institutional review boards of the University of Mississippi Medical Center, Jackson State University, and Tougaloo College (UMMC protocol #1998-6004; approval #FWA00003630) and each participant gave written informed consent. For the current study, additional site approval was obtained through the University of Washington Human Subjects Division (Institutional Review Board #43773**).**

Definition of Rapid Kidney Function Decline

Serum creatinine was measured using a multipoint enzymatic spectrophotometric assay at the baseline study visit initially using the Vitros Ortho-Clinical Diagnostics Analyzer (Raritan, NJ).[14] Serum creatinine was re-measured in 2006 for 206 participants using the enzymatic method on a Roche Chemistry analyzer (Roche Diagnostics Corp, Indianapolis IN). To harmonize serum creatinine measurements across time, we calibrated all examination 1 serum creatinine measurements to those at examination 3, using the isotope-dilution mass spectrometry (IDMS)-traceable method. [15] We then estimated glomerular

filtration rate (eGFR) from serum-calibrated creatinine using the CKD-EPI creatinine equation,[16] which was derived from a series of pooled cohorts that used the iothalomate clearance as the criterion standard.

Percentage of rapid kidney function decline (rapid decline) was defined as a decline of 30% or more within the 10-year time frame of longitudinal follow-up (n=420).[17,18] Similar outcomes were obtained when rapid decline was defined as an absolute annual loss of 3 mL/min/1.73 m2 or more (n=551) (table S1, available as online supplementary material). Results are reported using ≥30% decline unless otherwise specified. The trajectory of kidney function decline was based on 2 time points available from serum creatinine tests available from examinations 1 and 3. We modeled the relative decline in eGFR by estimating the subject-specific slope between time and natural log-transformed eGFR. The natural logarithim of the relative change in eGFR over time was then used as the outcome in regression analyses dichotomized at ≥30%.

$$\frac{(eGFR_1 - eGFR_3)}{eGFR_3} * 100\% \approx ln\,(eGFR_1) - ln\,(eGFR_3)$$

Definition of Potential Exposures

Potential exposures of interest included the following: age in years; sex; income (low, lower-middle, upper-middle, and affluent); education (<high school, high school graduate, ≥ General Education Development (GED) test but less than a college degree, and college degree); body mass index (BMI) in kg/m^2; systolic blood pressure (SBP) and diastolic blood pressure (DBP) are the average of two blood pressure readings (mmHg); hypertension defined as blood pressure > 140/90 mmHg or the use of blood pressure medications; DM defined as having a blood sugar > 126mg/dL, hemoglobin A1c ≥ 6.5% or receiving insulin or other hypoglycemic agents 2 weeks prior to baseline visit. Other exposures of interest included high-sensitivity C-reactive protein (mg/dL); fasting low-density lipoprotein (LDL) cholesterol (mg/dL); fasting high-density lipoprotein (HDL) cholesterol (mg/dL); physical activity (self-report); general health (self report); current smoking; prevalent CVD (history of coronary artery disease, stroke, or angiogioplasty); and waist circumference (cm).. The American Heart Association categorization for physical activity (Poor health =0, Intermediate health =1, ideal health =2) and nutrition categorization (Poor health =0, Intermediate health =1, ideal health =2) are based on the Association's “Life Simple 7” scale and include the following definitions. Physical Activity: (Poor Health is defined as 0 min. of moderate physical activity and 0 min. of vigorous physical activity; Intermediate Health is >0-<150 min. of moderate physical activity or >0-<75 min. of vigorous physical activity or >0-<150 min. of combined moderate and vigorous physical activity < 150; Ideal Health is ≥150 min. of moderate physical activity or ≥ 75 min. of vigorous physical activity or ≥150 min. of combined moderate and vigorous physical activity) and Nutritional health (Poor Health was defined as 0-1 components; Intermediate Health, as 2-3 components; and Ideal Health, as 4-5 components of the following: [based on 2000-kcal diet]: Fruits and vegetables: ≥ 4.5 cups/day; Fish: > 3.5 ounces, twice per week; Sodium: < 1500 mg/d; Sugary beverages: < 450 kcal/wk; or whole grains: ≥ 3 servings/day).

All participants were requested to collect a 24-hour urine sample. Starting October 2002, random spot urine samples were collected for baseline participants. Urinary albumin was therefore measured by two different methods at examination 1: a random spot morning urine collection (n=1589) or a timed 24-hour urine collection (n= 570).[14] A subset of participants (n=223) collected urine samples using both methods. Urine albumin-creatinine ratio (ACR; mg/g) was calculated for both sample types. Urine ACR from spot urine samples correlated highly with ACR from timed urine samples (r=0.965) (Figure S1). No subjects had more than one spot urine albumin. For participants with no examination 1 urine sample, multiple imputation employing chained equations was conducted for ACR (n=1271), using sex and age as the main predictor variables.

Statistical Analysis

We compared the characteristics of those with and without rapid decline in kidney function. We evaluated change in eGFR between examinations 1 and 3 by mean, median, and rapid decline defined as percentage change (log slope) ≥30% in the entire cohort and by stage of eGFR category (≥90, 60-89, and <60 ml/min/1.73m^2). In addition we evaluate absolute decline in eGFR >3ml/min/1.73m^2 per year with and without adjustment for baseline eGFR, and further evaluated absolute decline in kidney function in linear regression models (tables S2-S3).

The prevalence of risk factors by rapid decline was evaluated for those included in the cohort. Because only two fixed time points were available for kidney function determination, univariate and multivariable associations of risk factors with percent decline ≥30%, or absolute decline were conducted with logistic regression and presented as odds ratios (ORs). Initial models, based on *a priori* risk factor inclusion and those factors significant in univariate analyses, included adjustment for age, education, sex, prevalent CVD, SBP, DM, smoking, and general health as well as lipid levels (total, LDL, and HDL cholesterol) and high-sensitivity C-reactive protein. Analyses were performed using SPSS 22 (Released 2013. Armonk, NY: IBM Corp). Sensitivity analyses were conducted with and without imputation of urinary albumin at baseline to determine potential effects of albuminuria on the primary outcome. Data were complete for all covariates, except income (14.8%), education (0.2%), private insurance (0.5%), physical activity (0.1%), nutrition status (9.2%), diabetes (0.1%), smoking (0.9%), and ACR (34.8%). We used multivariate multiple imputation with 5 imputations and assumed the data were completely missing at random. The fully conditional approach [19] was used since it is a more flexible method that does not rely on the assumption of multivariate normality. The final analysis was conducted with imputed urinary albumin using multivariable logistic regression and presented as adjusted ORs.

RESULTS

Participant Characteristics

Of the 5301 participants recruited for examination 1, there were 1648 excluded for the original analyses (91 were missing creatinine in examination 1, 978 were missing creatinine in examination 3, 548 died prior to examination 3, 10 were receiving dialysis at baseline

(self-report), and 21 were lost to follow-up), leaving 3653 participants for the primary analyses (table S4). Excluded participants were slightly older, had lower income, less than high school education, more DM (29% vs. 19%), hypertension (68% vs. 59%), had eGFR <60 ml/min/1.73m^2 (12% vs. 4%), and had ACR >30 mg/g among those for whom albuminuria was measured (20% vs. 10%). Among the 3653 participants included in our analyses, the mean duration of follow up was 8.04 ±0.86 (standard deviation) years.

Primary Outcome

The annual linear rate of decline of kidney function was 1.27 ± 1.97 ml/min/1.73m^2 and the mean change in eGFR between examinations 1 and 3 was 10.41%±17.30% (median change, 8.22%; interquartile range, 0.00%-18.83%).

Rapid decline occurred among 420 (11.5%) participants over 10-12 years of follow-up. Those with rapid decline were older, had lower income, less education, higher SBP, lower eGFR, and slightly higher ACR at baseline; in addition, they were less likely to have private insurance, and more likely to have prevalent diabetes and hypertension, (Table 1). Similar patterns were seen when rapid decline was defined as eGFR > 3ml/min/1.73m^2 per year (Table S1). Characteristics of subjects grouped by baseline eGFR (≥90, 60-89, <60 ml/min/1.73m^2) showed that those with eGFR<60ml/min/1.73m^2 were older; less likely to be male and have private insurance; had less income and education; had higher BMI, waist circumference, and SBP; were more likely to have hypertension; and were receiving more antihypertensive medications (Table 2). Rapid decline was more likely to occur among those with eGFR <60ml/min/m^2 (33.8%), compared to those with eGFR of 60-89 ml/min/m^2 (11.9%) or eGFR ≥90ml/min/m^2 (9.9%) (Table 3). The average mean change in eGFR was greatest for those with eGFR < 60 ml/min/1.73m^2 at 17.93±29.95 mL/min/1.73 m2.

As shown in Table 4, baseline factors associated with rapid kidney function decline included older age (OR per 10 years older, 1.90; 95% CI, 1.57-2.30), greater SBP (OR per 17 mm Hg [equivalent to 1 standard deviation] greater, 1.32; 95% CI, 1.12-1.57), greater ACR (OR per doubling, 1.27; 95% CI, 1.16-1.40), or ACR >30 mg/g (OR, 2.95; 95% CI, 1.89-4.62) (in a separate model). With affluent income as the reference category, low, lower-middle, and middle-affluent income categories were all associated with increased odds of rapid decline compared; however, private insurance status was not associated with rapid decline. Physical activity, diet, BMI, waist circumference, male sex, prevalent CVD, and lipid levels (LDL cholesterol, HDL cholesterol, and triglycerides) were not independently associated with rapid decline. Further sensitivity analyses to determine risk factors associated with >20% rapid kidney function (instead of 30% decline) showed similar results (Table S2). We also found similar results when evaluating rapid absolute kidney function decline (defined as eGFR >3 ml/min/1.73m^2 per year) with and without adjustment for baseline eGFR (Table S3) or when evaluating absolute decline as a continuous variable (Table S4). As shown in Table 5, when stratifying results by eGFR ≥ 60 and <60 ml/min/1.73m^2, age, prevalent CVD, SBP, DM, smoking, and ACR remained risk factors for progression in the higher-eGFR category; however, for those with eGFR <60 ml/min/1.73m^2, only diabetes remained associated with rapid kidney function decline (adjusted OR, 4.22; 95% CI, 1.35-13.22).

Composite Outcome

Evaluation of a composite outcome of 30% kidney function decline or death in the JHS as a sensitivity analysis was conducted to determine if death was a significant competing risk of poor outcomes. Subjects included in the prior analyses (n=3653) and those who died prior to examination 3 (n=460) were included for this analysis. The composite outcome of death or 30% kidney function decline occurred in 883 subjects. Those who died prior to follow up examination 3 had lower education and eGFR, were less likely to have private insurance, and more likely to have diabetes and hypertension, compared with those who had creatinine measured at examination 3 (Table S5). The adjusted odds of the composite outcome of death or 30% decline in kidney function was found to be associated with age (adjusted OR per 10-year older, 1.88; 95% CI, 1.70-2.08), income, prevalent CVD (adjusted OR, 1.77; 95% CI, 1.40-2.25), SBP (adjusted OR per 17-mm Hg greater, 1.16; 95% CI, 1.03-1.31), DM (adjusted OR, 2.41; 95% CI, 1.90-3.05), smoking, triglycerides, high-sensitivity C-reactive protein, and ACR >30 mg/g (Table 6).

DISCUSSION

Amongst one of the largest African American population-based cohort studies, we found that some traditional risk factors (age, diabetes, SBP, education, smoking, and albuminuria) were associated with rapid kidney function decline. In contrast, some risk factors for rapid decline identified in other cohorts, such as BMI, C-reactive protein, LDL and triglycerides, were not associated with rapid decline in this population. Kidney function decline was most rapid amongst those with CKD defined by eGFR <60 ml/min/1.73 m^2 compared to those with eGFR ≥ 60ml/min/1.73 m^2. Education remained a strong predictor and income trended towards association with rapid decline. This study is strengthened by the fact it is one of the largest prospective cohort studies in African Americans conducted in a general population and had over 8-10 years of follow up for most participants.

Socioeconomic status has long been associated with development of ESRD as well as increased morbidity and morality amongst those with CKD, particularly among African Americans and other minority populations.[20,21] Even if access to health care is available, African Americans from lower incomes and poorer neighborhoods are more likely to have prevalent CKD,[20,22] progression of CKD, and more severe albuminuria[23] than those who have higher incomes or who reside in more affluent neighborhoods. Furthermore, among African Americans, those with lower socioeconomic status are more likely to have prevalent CKD.[24] Mediators of low cosioeconomic status and CKD prevalence appear to be related to modifiable risk factors such as smoking, alcohol use, diet, and physical activity, which are reported to contribute 20% of risk variance, while comorbid conditions contribute 30%, and access to care 11%.[25] The current study found that education was a potent predicator of rapid kidney function decline, while income and access to care trended towards an association.

Obesity is prevalent and a national health care problem that disproportionately affects African Americans and other minority group[26] and has been shown to be a risk factor for development of ESRD,[27] Controversy, however, exists regarding obesity and rapid decline and incident CKD. Fox and colleagues showed in the Framingham study that predominately

white adults had 23% greater risk of CKD for every 1-standard deviation increase in BMI. In addition, Cardiovascular Health Study De Boer and colleagues showed that BMI is associated with rapid kidney function decline (defined as >3 ml/min/1.73 m2 per year).[28] Race was adjusted for, but not presented separately. Furthermore, Malkina and colleagues found obesity is associated with rapid decline, defined as >5 ml/min/m2 per year, when using creatinine estimates of glomerular function but not cystatin C estimates; however, they reported that incident CKD is not associated with obesity. Race and ethnicity were adjusted for, but not reported separately in this analysis. [29] Conversely, in the CARDIA STudy Grubbs et al reported obesity is associated with incident CKD.[30] Waist circumference and BMI were not associated with rapid decline in this evaluation of the JHS population; however, most subjects had an elevated BMI at baseline. Additional analyses stratified by sex and comparisons to non-minority populations may be in order to further evaluate risk of BMI, abdominal obesity, and progression of CKD in African American populations.

Diabetes is a well-known risk factor for development of CKD and ESRD, particularly among African Americans.[4,31] In general, African Americans are known to have worse diabetes control and more likely to have albuminuria and proteinuria than whites, even in populations with similar access to care.[32,33] Results from the current analysis confirm that diabetes remained a potent risk factor for rapid decline in African Americans, the risk of which was attenuated by adjustment for albuminuria. Diabetes and treatment of albuminuria remain modifiable risk factors that may alter the course of kidney function decline in African Americans.

The association of smoking with progression of kidney disease has been controversial.[34] Smoking is potentially an additional modifiable risk factor that has been shown to be associated with CKD and kidney function decline in other populations.[35,36] Smoking has been shown to increase the risk of diabetic kidney disease as well as non-diabetic kidney disease.[37] Potential mechanisms for the association of smoking with kidney disease include increased oxidative stress, lipid accumulation and advanced glycation end products in those with diabetes as well as lower nitric oxide production, all of which can contribute to worsening kidney disease. In cross-sectional studies, those with CKD awareness were 82% more likely to report tobacco avoidance than those who were unaware of their CKD status,[38] and in a very small trial, smoking cessation was found to be associated with less rapid decline in subjects with progressive CKD.[39] Thus, smoking cessation is another potentially modifiable risk factor that could substantially lower risk of rapid decline in this population.

Hypertension is another well-known risk factor for development of CKD and for CKD progression. Hypertension is most likely a bidirectional risk factor in that it is both a cause and consequence of kidney disease. However, among African Americans, CKD progression still occurs in over 50% of those with well-treated hypertension, as shown in African American Study of Kidney Disease and Hypertension (AASK).[9] In the current study, for every standard deviation (17 mmHg) increment in SBP, the risk of rapid decline increased by 32%. Guidelines for blood pressure control remain controversial, particularly for those with CKD.[40] Even after adjustment for hypertensive medications, SBP was a factor associated with rapid decline. Further studies regarding risk of progression with various targets of

blood pressure are needed to help further develop blood pressure guidelines specifically for African Americans.

Serum creatinine was available at only two time points, ten years apart, which did not allow for accurate assessment of annual rate of decline of kidney function. Three time points would allow better precision to determine the trajectory of kidney function decline and would also allow us to evaluate additional outcomes based on the early trajectory of rapid decline. In addition, GFR was not directly measured, and was estimated from serum creatinine rather than serum cystatin C; however, creatinine-based eGFR has been validated against gold-standard standards and found to be accurate.[41] Finally, since the study is not linked to the US Renal Data System, we were not able to ascertain validated incident ESRD. Linkage of JHS with the US Renal Data System is a future activity that will improve analyses for ESRD outcomes.

In summary, this study of JHS enrollees is to our knowledge the first longitudinal evaluation of a large general population-based African American cohort study that determined risk factors for rapid kidney function decline. Heterogeneity of rapid decline has been postulated, but sample sizes in other cohorts have limited the evaluation of these variables in a cohort with normal or mildly and severely decreased kidney function at baseline. This initial analysis will allow for future analyses of JHS cohort and will allow further evaluation of novel risk factors that might be unique to this population. Older age remains a potent factor for rapid decline, as does baseline level of kidney disease and albuminuria. Modifiable risk factors such as diabetes, hypertension, and smoking are important risk factors for progression of CKD as is education, while obesity and inflammation were not shown in this population to be as significant. Interventional studies targeting these modifiable risk factors at various levels of kidney function are needed to evaluate if ESRD is preventable in this high-risk population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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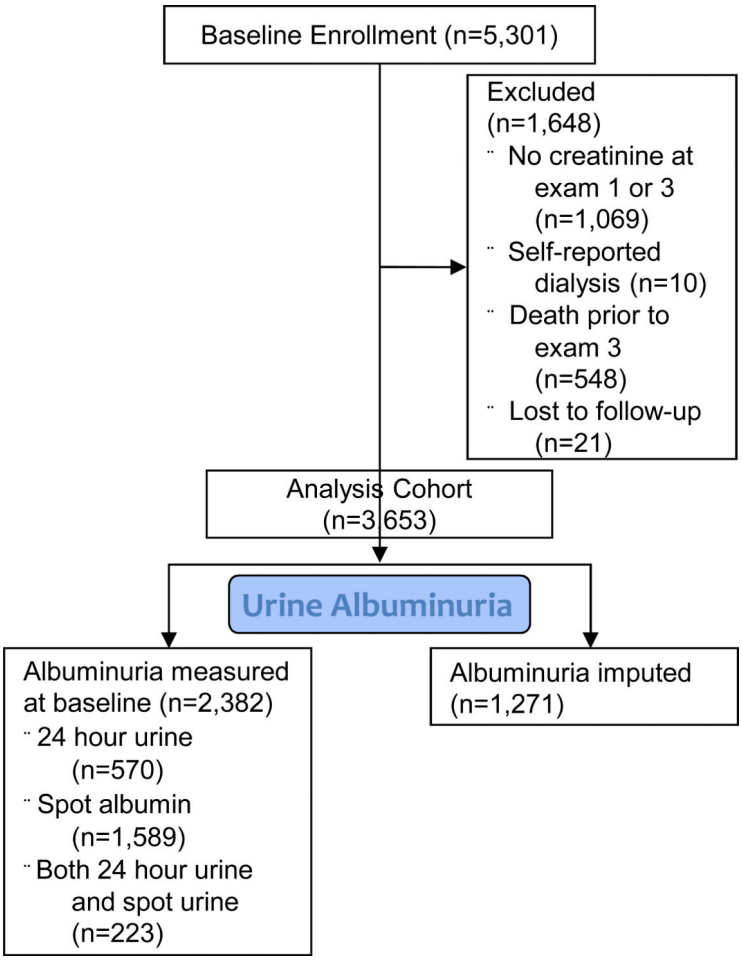

Figure 1.
Jackson Heart Study flow diagram.

Table 1

Baseline characteristics of participants of the Jackson Heart Study cohort

Characteristics	Analysis Cohort (N=3653)	Non-Rapid Decline (n=3233 [89%])	Rapid Decline* (n=420 [11%])
Age, y	54 (12)	53 (12)	61 (11)
Male sex	1339 (37%)	1202 (37%)	137 (33%)
Income	3112	2760	352
Poor	372 (12%)	317 (12%)	55 (16%)
Lower-middle	698 (22%)	588 (21%)	110 (31%)
Upper-middle	959 (31%)	867 (31%)	92 (26%)
Affluent	1083 (35%)	988 (36%)	95 (27%)
Education	3646	3227	419
< HS	596 (16%)	486 (15%)	110 (26%)
HS graduate	625 (17%)	546 (17%)	79 (19%)
GED - <college degree	816 (22%)	734 (23%)	82 (20%)
College degree	1609 (44%)	1461 (45%)	148 (35%)
Private insurance	2580 (71%)	2328 (72%)	252 (60%)
BMI, kg/m^2	31.8 (7.1)	31.7 (7.1)	32.5 (7.0)
Waist circumference, cm	100.5 (16.0)	100.0 (16.0)	103.8 (15.9)
SBP, mmHg	126 (17)	125 (17)	133 (20)
DBP, mmHg	79 (10)	79 (10)	78 (11)
DM	685 (19%)	512 (16%)	173 (41%)
HTN	2138 (59%)	1797 (56%)	341 (81%)
HTN medications	1747 (59%)	1453 (56%)	294 (77%)
β Blockers	338 (11%)	273 (11%)	65 (17%)
Calcium Channel Blockers	657 (22%)	527 (20%)	130 (34%)
Diuretics	1123 (38%)	931 (36%)	192 (50%)
ACE inhibitors	537 (15%)	434 (13%)	103 (25%)
ARBs	284 (8%)	235 (7%)	49 (12%)
Creatinine, mg/dL	0.96 (0.24)	0.90 (0.21)	0.95 (0.36)
eGFR, ml/min/1.73m^2	96 (20)	97 (19)	89 (23)
eGFR < 60 ml/min/1.73m^2	142 (4%)	94 (3%)	48 (11%)
ACR, mg/g	5.7 [3.8-10.5]	6.0 [3.7-12.2]	9.7 [4.8-30.3]
Imputed ACR >30mg/g	447 (12%)	344 (11%)	103 (25%)
Cholesterol			
Total, mg/dL	199 (39)	199 (39)	205 (44)
LDL mg/dL	127 (36)	127 (36)	128 (38)
HDL mg/dL	52 (14)	52 (14)	53 (15)
Hemoglobin A1c, %	5.89 (1.17)	5.80 (1.01)	6.60 (1.87)
hs-CRP, mg/L	2.61 [1.06-5.60]	2.53 [1.02-5.48]	3.37 [1.49-6.33]

Note: Values for categorical variables are given as number (percentage); values for continuous variables, as mean ± standard deviation or median [interquartile range]. Conversion factors for units: cholesterol in mg/dL to mmol/L, ×0.02586; creatinine in mg/dL to μmol/L, ×88.4.

GED = General Education Development, BMI= body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, DM, diabetes mellitus; HTN = hypertension, ACE = angiotensin-converting enzyme, ARBs = angiotensin receptor blockers, eGFR = estimated glomerular filtration rate, ACR = albumin-creatinine ratio, LDL= low-density lipoprotein, HDL = high-density lipoprotein, HS, high school; hs-CRP = high-sensitivity C-reactive protein.

* Rapid kidney function decline defined as ≥ 30% decline in eGFR within the 10-year time frame of longitudinal follow-up.

Table 2

Baseline characteristics of Jackson Heart Study participants in analysis cohort, by baseline eGFR

Characteristics	eGFR ≥ 90 (n=2314)	eGFR 60 – 89 (n=1197)	eGFR < 60 (n=142)
Age, y	51 (11)	60 (11)	66 (10)
Malesex	820 (35%)	487 (41%)	32 (23%)
Income			
Poor	240 (12%)	109 (11%)	23 (20%)
Lower-middle	410 (21%)	256 (25%)	32 (28%)
Upper-middle	636 (32%)	291 (28%)	32 (28%)
Affluent	677 (35%)	380 (37%)	26 (23%)
Education			
< HS	298 (13%)	253 (21%)	45 (32%)
HS graduate	396 (17%)	204(17%)	25 (18%)
GED - <college degree	581 (25%)	208 (17%)	27 (19%)
College degree	1035 (45%)	530 (44%)	44 (31%)
Private insurance	1695 (74%)	808 (68%)	77 (55%)
BMI, kg/m^2	32.0 (7.6)	31.5 (6.3)	32.2 (6.2)
Waist circumference, cm	100.2 (17.0)	100.6 (14.1)	103.4 (14.6)
SBP, mm Hg	124 (16)	129 (18)	131 (22)
DBP, mmHg	79 (10)	79 (11)	76 (13)
DM	405 (18%)	231 (19%)	49 (35%)
HTN	1183 (51%)	825 (69%)	130 (92%)
HTN medications	931(52%)	693 (67%)	123 (92%)
β Blockers	162 (9%)	147 (14%)	29 (22%)
Calcium Channel Blockers	367 (20%)	240 (23%)	50 (37%)
Diuretics	578 (32%)	453 (56%)	92 (69%)
ACE inhibitors	275 (12%)	217 (18%)	45 (32%)
ARBs	160 (7%)	97 (8%)	27 (19%)
Creatinine, mg/dL	0.86 (0.15)	1.09 (0.16)	1.55 (0.49)
eGFR ml/min/1.73m^2	108 (12)	79 (8)	49 (10)
ACR, mg/g	5.7 [3.9-9.9]	5.6 [3.7-10.7]	11.0 [5.5-45.3]
ACR>30mg/g	131 (8%)	76 (10%)	28 (32%)
Cholesterol			
Total, mg/dL	196 (39)	204 (39)	213 (51)
LDL, mg/dL	125 (35)	130 (36)	135 (46)
HDL, mg/dL (SD)	52 (14)	52 (15)	52 (14)
Hemoglobin A1c, %	5.85 (1.23)	5.92 (1.03)	6.28 (1.19)
hs-CRP, mg/L	2.61 [1.04-5.54]	2.42 [1.06-5.26]	4.27 [1.57-9.05]

Note: Values for categorical variables are given as number (percentage); values for continuous variables, as mean ± standard deviation or median [interquartile range]. eGFRs expressed in mL/min/1.73 m2. Conversion factors for units: cholesterol in mg/dL to mmol/L, ×0.02586; creatinine in mg/dL to μmol/L, ×88.4.

GED= General Education Development, BMI= body mass index, CVD=cardiovascular disease, HTN= hypertension, SBP= systolic blood pressure, DBP=diastolic blood pressure, LDL=low-density lipoprotein, HDL = high-density lipoprotein, HS, high school; hs-CRP= high-sensitivity C-reactive protein, and ACR=albumin-creatinine ratio, eGFR = estimated glomerular filtration rate

Table 3

Change in eGFR between examinations 1 and 3 and by baseline eGFR status in the Jackson Heart Study.

	All	Baseline eGFR			p-value
		≥ 90 ml/min/1.73m^2	60—89 ml/min/1.73m^2	< 60 ml/min/1.73m^2	
Percent change*					
Mean ±SD	10.41 ±17.30	10.58 ±14.93	9.17 ±19.22	17.93 ±29.95	<0.001
Median [IQR]	8.22 [0.00 to 18.83]	7.91 [0.00 to 17.72]	8.56 [−2.24 to 19.42]	16.67 [1.73 to 34.57]	0.005
Rapid decline*	420 (11.5%)	230 (9.9%)	142 (11.9%)	48 (33.8%)	<0.001

Note: Change expressed in mL/min/1,73 m2.

SD= standard deviation, IQR=interquartile range, eGFR=estimated glomerular filtration rate,

* Log slope.

** Rapid kidney function decline; ΔeGFR ≥30%.

Table 4

Association of risk factors with Rapid Decline in Kidney Function in the Jackson Heart Study

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Further Adjusted^ OR (95% CI)
Age, per 10-y older	1.75 (1.59, 1.92)	1.51 (1.34, 1.71)	1.47 (1.28, 1.68)
Income			
Low	1.89 (1.36, 2.63)	1.30 * (0.82, 2.06)	1.29 (0.82, 2.05)
Lower-middle	1.81 (1.37, 2.39)	1.20 (0.84, 1.71)	1.20 (0.84, 1.71)
Upper-middle	1.14 (0.86, 1.52)	1.03 (0.75, 1.43)	1.03 (0.74, 1.42)
Affluent	1.00 (reference)	1.00 (reference)	1.00 (reference)
Education			
< HS	2.24 (1.72, 2.93)	1.06 (0.75, 1.50)	1.06 (0.75, 1.50)
HS graduate	1.43 (1.07, 1.92)	1.04 (0.73, 1.49)	1.04 (0.73, 1.49)
GED - <college degree	1.11 (0.83, 1.47)	1.04 (0.73, 1.49)	1.03 (0.72, 1.48)
College degree	1.00 (reference)	1.00 (reference)	1.00 (reference)
Private insurance	0.58 (0.47, 0.71)	1.00 (0.77, 1.31)	1.00 (0.77, 1.31)
AHA physical activity category			
Ideal health	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate health	1.04 (0.76, 1.42)	0.81 (0.57, 1.16)	0.81 (0.57, 1.16)
Poor health	1.48 (1.12, 1.96)	0.87 (0.63, 1.19)	0.87 (0.63, 1.19)
AHA nutrition category			
Ideal health	1.00 (reference)	1.00 (reference)	1.00 (reference)
Intermediate health	0.69 (0.27, 1.79)	1.00 (0.37, 2.72)	1.01 (0.37, 2.73)
Poor health	0.91 (0.34, 2.39)	1.01 (0.38, 2.72)	1.02 (0.37, 2.73)
Waist circumference, per 16.2 cm greater#	1.25 (1.14, 1.38)	1.11 (0.91, 1.35)	1.11 (0.91, 1.36)
BMI, per 7.0 kg/m2 greater#	1.13 (1.02, 1.25)	0.95 (0.77, 1.16)	0.94 (0.77, 1.16)
BMI category			
Normal: < 25 kg/m2	1.00 (reference)	1.00 (reference)	1.00 (reference)
Overweight: 25 – 29 kg/m2	1.00 (0.71, 1.42)	0.77 (0.51, 1.14)	0.76 (0.51, 1.13)
Obese: ≥ 30 kg/m2	1.36 (0.98, 1.88)	0.83 (0.52, 1.32)	0.82 (0.51, 1.31)
Male sex	0.82 (0.66, 1.02)	0.86 (0.66, 1.12)	0.96 (0.66, 1.11)
Prevalent CVD	2.71 (2.04, 3.62)	1.53 (1.12, 2.10)	1.51 (1.10, 2.08)
SBP, per 17-mm Hg greater#	1.50 (1.34, 1.68)	1.22 (1.06, 1.41)	1.22 (1.06, 1.40)
Diabetes	3.74 (3.01, 4.64)	2.63 (2.02, 3.41)	2.65 (2.04, 3.44)
Current smoker	1.37 (1.02, 1.83)	1.60 (1.10, 2.31)	1.62 (1.12, 2.35)
LDL cholesterol, per 36 mg/dL greater#	0.99 (0.87, 1.14)	0.95 (0.83, 1.09)	0.95 (0.83, 1.09)
Triglyceride, per doubling	1.51 (1.31, 1.74)	1.19 (1.01, 1.40)	1.18 (1.00, 1.39)
hs-CRP, per doubling	1.13 (1.06, 1.20)	1.06 (0.98, 1.14)	1.06 (0.98, 1.14)
ACR, per doubling	1.24 (1.14, 1.35)	1.15 (1.08, 1.21)	1.14 (1.08, 1.21)

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Further Adjusted^ OR (95% CI)
ACR > 30 mg/g imputed*	2.06 (1.12, 3.75)	1.55 (1.17, 2.06)	1.55 (1.18, 2.05)
eGFR, per 2 mL/min/1.73 m2 lower#	1.50 (1.35, 1.68)	---	1.07 (0.93, 1.24)

Note: All models were adjusted for age, income, education, insurance, AHA physical categories, AHA nutritional categories, waist circumference, BMI (continuous, BMI categories was a separate model), sex, prevalent CVD, SBP, diabetes, smoking, LDL cholesterol, triglycerides, hs-CRP, ACR (doubling and >30 mg/g imputed in separate models), and eGFR. Rapid kidney function decline defined as ≥ 30% decline in eGFR within the 10-year time frame of longitudinal follow-up. Conversion factor for cholesterol in mg/dL to mmol/L, ×0.02586.

CI, confidence interval; GED= General Education Development, AHA= American Heart Association, BMI= body mass index, CVD=cardiovascular disease, HTN= hypertension, SBP= systolic blood pressure, DBP=diastolic blood pressure, LDL=low-density lipoprotein, HDL = high-density lipoprotein, HS, high school; hs-CRP= high-sensitivity C-reactive protein, and ACR=albumin-creatinine ratio, eGFR = estimated glomerular filtration rate, OR, odds ratio

^For baseline eGFR.

*p=0.02 for trend

**Model of ACR per doubling separate from ACR > 30 mg/g imputed.

#Increment equivalent to 1 standard deviation.

Table 5

Association of risk factors with rapid decline in Kidney Function in the Jackson Heart Study, Stratified by baseline eGFR

Characteristics	Baseline eGFR ≥ 60 ml/min/1.73 m^2 (n=3511)	Baseline eGFR < 60 mls/min/1.73m^2 (n=142)
Age, per 10-y older	1.57 (1.38, 1.79)	0.64 (0.34, 1.22)
Income		
Low	1.40 (0.88, 2.22)	0.74 (0.11, 4.81)
Lower-middle	1.32 (0.92, 1.92)	0.47 (0.10, 2.25)
Upper-middle	1.03 (0.73, 1.45)	0.57 (0.12, 2.67)
Affluent	1.00 (reference)	1.00 (reference)
Education		
< HS	1.04 (0.72, 1.51)	3.08 (0.57, 16.78)
HS graduate	1.16 (0.80, 1.69)	0.23 (0.04, 1.35)
GED-<college degree	1.06 (0.72, 1.54)	2.06 (0.46, 9.19)
College degree	1.00 (reference)	1.00 (reference)
Private insurance	0.96 (0.73, 1.28)	1.14 (0.39, 3.39)
AHA physical activity category		
Ideal health	1.00 (reference)	1.00 (reference)
Intermediate health	1.13 (0.38, 3.37)	0.23 (0.05, 1.11)
Poor health	1.05 (0.35, 3.18)	0.72 (0.18, 2.95)
AHA nutrition category		
Ideal health	1.00 (reference)	1.00 (reference)
Intermediate health	1.05 (0.35, 3.18)	1.35 (0.02, 80.13)
Poor health	1.13 (0.38, 3.37)	2.31 (0.05, 114.15)
Waist circumference, per 16.2 cm greater[#]	1.13 (0.91, 1.39)	0.84 (0.18, 3.90)
BMI, per 7.0 kg/m2 greater[#]	0.94 (0.75, 1.16)	1.27 (0.21, 7.62)
Male sex	0.97 (0.66, 1.15)	1.12 (0.34, 3.68)
Prevalent CVD	1.84 (1.32, 2.57)	0.25 (0.07, 0.83)
SBP, per 17 mm Hg greater[#]	1.23 (1.06, 1.42)	1.27 (0.21, 7.62)
Diabetes	2.59 (1.98, 3.39)	4.22 (1.35, 13.22)
Current smoker	1.66 (1.15, 2.39)	1.40 (0.16, 12.31)
LDL cholesterol, per 36 mg/dL greater[#]	0.93 (0.79, 1.09)	0.94 (0.54, 1.62)
Triglyceride, per doubling	1.14 (0.95, 1.36)	1.95 (0.60, 6.33)
hs-CRP, per doubling	1.05 (0.97, 1.13)	0.82 (0.61, 1.10)
ACR, per doubling	1.13 (1.07, 1.20)	1.06 (0.82, 1.37)
ACR > 30 mg/g imputed[**]	1.49 (1.13, 1.98)	1.29 (0.35, 4.74)

Note: Associations are given as adjusted odds ratio (95% confidence interval). All models were adjusted for age, income, education, insurance, AHA physical categories, AHA nutritional categories, waist circumference, BMI (continuous, BMI categories was a separate model), sex, prevalent CVD, SBP, diabetes, smoking, LDL cholesterol, triglycerides, hs-CRP, ACR (doubling and >30 mg/g imputed in separate models), and eGFR.

Rapid kidney function decline defined as ≥ 30% decline in eGFR within the 10-year time frame of longitudinal follow-up. Conversion factor for cholesterol in mg/dL to mmol/L, ×0.02586.

GED= General Education Development, AHA= American Heart Association, BMI= body mass index, CVD=cardiovascular disease, HTN= hypertension, SBP= systolic blood pressure, DBP=diastolic blood pressure, LDL=low-density lipoprotein, HDL = high-density lipoprotein, HS, high school; hs-CRP= high-sensitivity C-reactive protein, and ACR=albumin-creatinine ratio, eGFR = estimated glomerular filtration rate,

** Model of ACR per doubling separate from ACR > 30 imputed.

Increment equivalent to 1 standard deviation.

Table 6

Association of risk factors with composite outcome of ≥30% Kidney Function decline or death in the Jackson Health Study

Characteristics	Adjusted* OR (95% CI)
Age, per 10-y older	1.88 (1.70, 2.08)
Income	
Low	1.77 (1.19, 2.62)
Lower-middle	1.36 (1.02, 1.79)
Upper-middle	1.16 (0.87, 1.54)
Affluent	1.00 (reference)
Education	
< HS	1.08 (0.83, 1.42)
HS graduate	1.06 (0.80, 1.39)
GED-<college degree	1.02 (0.77, 1.35)
College degree	1.00 (reference)
Private insurance	0.73 (0.59, 0.90)
AHA physical activity category	
Ideal health	1.00 (reference)
Intermediate health	0.80 (0.59, 1.07)
Poor health	0.86 (0.67, 1.11)
AHA nutrition category	
Ideal health	1.00 (reference)
Intermediate health	1.09 (0.48, 2.47)
Poor health	1.12 (0.51, 2.47)
Waist circumference, per 16.2 cm greater#	1.07 (0.89, 1.29)
BMI, per 7.0 kg/m2 greater#	0.94 (0.78, 1.13)
Male sex	1.14 (0.93, 1.41)
Prevalent CVD	1.77 (1.40, 2.25)
SBP, per 17 mm Hg greater#	1.16 (1.03, 1.31)
Diabetes	2.41 (1.90, 3.05)
Current smoker	2.00 (1.45, 2.76)
LDL cholesterol, per 36 mg/dL greater#	1.00 (0.90, 1.12)
Triglyceride, per doubling	1.18 (1.03, 1.34)
hs-CRP, per doubling	1.06 (1.00, 1.12)
ACR > 30 mg/g imputed	1.66 (1.27, 2.18)

Note: All variables adjusted for each other; dichotomous ACR in model (N=4125: composite outcome = 883; n=462 deaths). Conversion factor for cholesterol in mg/dL to mmol/L, ×0.02586.

CI, confidence interval; GED= General Education Development, AHA= American Heart Association, BMI= body mass index, CVD=cardiovascular disease, HTN= hypertension, SBP= systolic blood pressure, DBP=diastolic blood pressure, LDL=low-density lipoprotein,

HDL = high-density lipoprotein, HS, high school; hs-CRP= high-sensitivity C-reactive protein, and ACR=albumin-creatinine ratio, eGFR = estimated glomerular filtration rate OR, odds ratio

*All models were adjusted for age, income, education, insurance, AHA physical categories, AHA nutritional categories, waist circumference, BMI (continuous), sex, prevalent CVD, SBP, diabetes, smoking, LDL, triglycerides, hs-CRP, and ACR (>30 mg/g imputed).

#Increment equivalent to 1 standard deviation.