Cardiovascular Disease and Subsequent Kidney Disease

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Background: Chronic kidney disease is a risk factor for cardiovascular disease (CVD); however, it is uncertain if CVD is a risk factor for progression or development of kidney disease.

Methods: Individual patient data were pooled from 2 longitudinal, community-based, limited-access studies, the Atherosclerosis Risk in Communities Study and the Cardiovascular Health Study. Baseline CVD was defined by stroke, angina, claudication, transient ischemic attack, coronary angioplasty or bypass, and recognized or silent myocardial infarction. Study outcomes included kidney function decline, defined by an increase in serum creatinine level of at least 0.4 mg/dL (≥35.4 µmol/L), and development of kidney disease, defined by an increase in serum creatinine level of at least 0.4 mg/dL (≥35.4 µmol/L) in which the baseline serum creatinine level was less than 1.4 mg/dL (<123.8 µmol/L) in men and less than 1.2 mg/dL (<106.1 µmol/L) in women and the final serum creatinine levels exceeded these levels. Secondarily, kidney function decline was defined by an estimated glomerular filtration rate (eGFR) reduction of at least 15 mL/min per 1.73 m², and development of kidney disease was defined by an eGFR reduction of at least 15 mL/min per 1.73 m² in which the baseline eGFR was at least 60 mL/min per 1.73 m² and the final eGFR was below these levels. Multivariate logistic regression analysis was used to determine the association between CVD and outcomes.

Results: Among 13,826 individuals, the mean±SD baseline serum creatinine level was 0.9±0.2 mg/dL (79.6±17.7 µmol/L), and the mean±SD baseline eGFR was 89.8±20.1 mL/min per 1.73 m². In serum creatinine level–based models, 520 individuals (3.8%) experienced kidney function decline, and 314 individuals (2.3%) developed kidney disease during a mean±SD of 9.3±0.9 years of follow-up. Baseline CVD, present in 1,787 individuals (12.9%), was associated with an increased risk of all outcomes (odds ratio, 1.70; 95% confidence interval, 1.36-2.13), an odds ratio of 1.75 (95% confidence interval, 1.32-2.32) for serum creatinine level, and odds ratios of 1.28 (95% confidence interval, 1.13-1.45) and 1.54 (95% confidence interval, 1.26-1.89) for eGFR for kidney function decline and development of kidney disease, respectively.

Conclusion: Cardiovascular disease is independently associated with kidney function decline and with the development of kidney disease.

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Chronic kidney disease is an independent risk factor for cardiovascular disease (CVD), however, it is unknown if the opposite is true, namely, is CVD associated with kidney function decline and the development of kidney disease? Previous studies of risk factors for kidney function decline have evaluated hypertension, diabetes mellitus (DM), and nontraditional CVD risk factors, including inflammation and endothelial dysfunction. Most of these studies have demonstrated independent associations between CVD risk factors and worsening kidney function.

The relationship between CKD and CVD may be bidirectional, with impaired kidney function increasing the risk of CVD and with CVD increasing the risk of development and progression of CKD. Accordingly, the goal of the present study was to assess if the presence of CVD is associated with kidney function decline and development of CKD in a community-based population.
STUDY POPULATION

Individual patient data were pooled from the following 2 longitudinal, community-based, limited-access data sets—the Atherosclerosis Risk in Communities (ARIC) Study14 and the Cardiovascular Health Study (CHS).13 Pooling data from these cohorts provides a large sample that allows multivariate adjustment for risk factors and enhances generalizability. From 1987 to 1989, the ARIC Study recruited 15 792 subjects between the ages of 45 and 64 years from 4 communities. From 1989 to 1990, the CHS recruited 5201 subjects 65 years and older who were randomly selected from Medicare eligibility files in 4 communities. In both studies, follow-up occurred at approximate 3-year intervals. Although an additional 687 African American participants were recruited in the CHS from 1992 to 1993, they were not evaluated for the present study because of the limited follow-up time. The final serum creatinine level measurement occurred at visit 4 in the ARIC Study (1996-1998) and at visit 3 in the CHS (1996-1997). Details of recruitment and follow-up for the studies are described elsewhere.14,15

KIDNEY FUNCTION

The baseline serum creatinine level was assessed in 15 582 subjects (98.7%) in the ARIC Study and in 5716 subjects (97.1%) in the CHS. Because serum creatinine level assays vary across laboratories, we indirectly calibrated the mean individual study serum creatinine values from the ARIC Study and the CHS to the mean Third National Health and Nutrition Examination Survey values for a given age, sex, and race, resulting in adjustments of −0.29 mg/dL (−2.12 µmol/L) in the ARIC Study and −0.11 mg/dL (−0.97 µmol/L) in the CHS.5 The baseline serum creatinine values for the pooled cohort were determined by subtracting these adjustments from measured serum creatinine values. It is also essential to adjust for changes in laboratory measurements over time. We used previously published calibration factors to account for this laboratory drift16,17, in the ARIC Study, 0.18 mg/dL (15.9 µmol/L) was added to the visit 4 measurements in the ARIC Study, while 0.11 mg/dL (9.7 µmol/L) was subtracted from the visit 3 measurements in the CHS.

BASELINE VARIABLES

Baseline CVD was defined by (1) prior recognized or silent myocardial infarction defined by self-reported history of a physician-diagnosed event or by characteristic changes on the baseline electrocardiogram, (2) angina based on the Rose questionnaire, (3) stroke and transient ischemic attack defined by consensus committees within the CHS and the ARIC Study based on patient recall and medical records, (4) intermittent claudication based on the Rose questionnaire, and (5) prior coronary angioplasty or bypass procedures. The CHS definitions of CVD were designed to mirror those of the ARIC Study.14,15 Other baseline characteristics included medication use, medical history (DM or hypertension), lifestyle characteristics (smoking and alcohol intake), demographics (age, sex, race, and educational achievement), physical examination findings (height, weight, electrocardiogram results, and systolic and diastolic blood pressure), and laboratory variables (hematocrit and glucose, albumin, total cholesterol, and high-density lipoprotein cholesterol levels). Race was defined as white or as African American. Education level was dichotomized according to high school graduation status. Cigarette smoking and alcohol intake were dichotomized as current users and as nonusers. The presence of DM was defined by insulin or oral hypoglycemic medication use or as a fasting glucose level of at least 126 mg/dL (≥7.0 mmol/L). Hypertension was defined as a systolic blood pressure of at least 140 mm Hg, a diastolic blood pressure of at least 90 mm Hg, or antihypertensive medication use. Body mass index was calculated as weight in kilograms divided by height in meters squared.2 The estimated glomerular filtration rate (eGFR) was calculated using the 4-variable Modification of Diet in Renal Disease study equation.1

STUDY OUTCOMES

The study outcomes of kidney function decline and development of kidney disease were investigated using a serum creatinine level–based definition and an eGFR-based definition. In serum creatinine level–based models, kidney function decline was defined by a serum creatinine level increase between the first and last visits of at least 0.4 mg/dL (≥35.4 µmol/L), as this value was above that which could be explained by chance (used previously in the ARIC Study16) and was above that used previously in the CHS18 to define a decline in kidney function. Development of kidney disease was defined by a serum creatinine level increase of at least 0.4 mg/dL (≥35.4 µmol/L) in which the baseline serum creatinine level was less than 1.4 mg/dL (≤123.8 µmol/L) in men and less than 1.2 mg/dL (≤106.1 µmol/L) in women and the final serum creatinine levels exceeded these levels.19,20 In eGFR-based models, kidney function decline was defined by an eGFR decrease of at least 15 mL/min per 1.73 m², as an eGFR decline of at least 15 mL/min per 1.73 m² exceeds by greater than 50% the upper limit of normal age–related decline (approximately 1 mL/min per 1.73 m² per year) expected in 9 to 10 years of follow-up.1 Development of kidney disease was defined by an eGFR decrease of at least 15 mL/min per 1.73 m² in participants with a baseline eGFR of at least 60 mL/min per 1.73 m² and a final eGFR below this threshold.1

STUDY SAMPLE

From a pooled sample of 20 993 individuals, we excluded 350 individuals with missing age, sex, race, or baseline serum creatinine level data and 27 individuals with a baseline eGFR of less than 15 mL/min per 1.73 m² to avoid misclassification and confounding by imminent kidney failure with subsequent hemodialysis, peritoneal dialysis, or kidney transplantation. Of the remaining 20 616 individuals, 6348 did not have a final serum creatinine value, with 2276 (35.9%) of the latter individuals dying before their scheduled final study visit, and 442 were missing data on other covariates, yielding a final population of 13 826 individuals. To assess possible biases, we compared individuals with missing data with the final cohort using χ² tests and analysis of variance.

STATISTICAL ANALYSIS

Baseline characteristics were compared using χ² tests and analysis of variance wherever appropriate. Odds ratios associated with baseline CVD for the study outcomes were determined using multivariate logistic regression models that adjusted for a priori identified clinically relevant covariates (age, sex, race, educational achievement, study of origin, DM, smoking, alcohol use, history of hypertension, body mass index, systolic blood pressure, hematocrit, albumin level, total and high-density lipoprotein cholesterol levels, and baseline kidney function [serum creatinine level or eGFR]).

To graphically present these findings, we calculated the predicted probability of the study outcomes using multivariate logistic regression models for subjects who had and those who did not have baseline CVD, varying the level of baseline kidney function while fixing the values of the other covariates in

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Sensitivity Analysis

All sensitivity analyses were based on models defining kidney function decline by a serum creatinine level rise of at least 0.4 mg/dL (≥35.4 μmol/L). To evaluate the effect of competing outcomes between kidney function decline and all-cause mortality, we used a Cox proportional hazards model to assess whether baseline CVD affected the composite outcome of a serum creatinine level increase of at least 0.4 mg/dL (≥35.4 μmol/L) and time to death after adjustment for the covariates already listed. Time to kidney disease was defined by the duration between the initial and final serum creatinine measurements.

To evaluate for possible bias by study, we analyzed the ARIC Study and the CHS data separately. Because heart failure may be an important factor mediating kidney function decline in individuals with CVD, we also performed a subgroup analysis among individuals from the CHS after excluding those with baseline heart failure (heart failure at baseline was not defined in the ARIC Study). Also, because we did not have data on baseline angiotensin-converting enzyme (ACE) inhibitor use in the ARIC Study, we analyzed the CHS cohort with adjustment for ACE inhibitor use. Finally, we examined the relationship between prior coronary disease, defined by only myocardial infarction or coronary revascularization, and kidney function decline. All analyses were performed using SAS version 9.1 software (SAS Institute, Cary, NC).

RESULTS

There were 13,826 individuals included in this study, with a mean age of 57.6±9.1 years. Among 1787 individuals (12.9%) with baseline CVD, 960 had a history of myocardial infarction, angioplasty, or bypass; 886 had baseline angina; 549 had prior stroke; and 106 had claudication. The mean baseline serum creatinine level was 0.9±0.2 mg/dL (79.6±17.7 μmol/L) in individuals who had and those who did not have CVD; however, given the sample size and rounding, this represented a statistically significant higher serum creatinine level in those with baseline CVD. The mean ± SD baseline eGFR was 89.8±20.1 mL/min per 1.73 m², with the baseline eGFR being significantly lower in those with prevalent CVD (Table 1).

SERUM CREATININE LEVEL–BASED ANALYSES

During a mean ± SD follow-up of 9.3±0.9 years, 520 individuals (3.8%) developed kidney function decline, defined by a serum creatinine level increase of at least 0.4 mg/dL (≥35.4 μmol/L). Among 1787 individuals with baseline CVD, 128 (7.2%) had a decline in kidney function, while among 12,039 individuals without baseline CVD, 392 (3.3%) had a decline in kidney function (P<.001). Individuals with a decline in kidney function had significantly higher baseline serum creatinine levels and were more likely to be older, have hypertension and DM, and be of African American race (Table 2). In multivariate regression models, individuals with baseline CVD were at significantly increased risk of kidney function decline (odds ratio [OR], 1.70; 95% confidence interval [CI], 1.36-2.13) (Figure 1). After excluding individuals with an elevated baseline serum creatinine level, 314 individuals (2.3%) had a rise in serum creatinine level of at least 0.4 mg/dL (≥35.4 μmol/L) and a final serum creatinine level greater than 1.4 mg/dL (123.8 μmol/L) in men and greater than 1.2 mg/dL (106.1 μmol/L) in women (Table 3). Among these individuals, baseline CVD was associated with a significantly increased risk of developing kidney disease (OR, 1.75; 95% CI, 1.32-2.32) (Table 4 and Figure 2).

eGFR-BASED ANALYSES

There were 4516 individuals with a decrease in eGFR of at least 15 mL/min per 1.73 m² (Table 2). Among 1787 individuals with baseline CVD, 607 (34.0%) had a decline in kidney function, while among 12,039 individuals without baseline CVD, 3909 (32.5%) had a decline in kidney function (P=.22). Baseline CVD was independently associated with an eGFR decline during the follow-up period (OR, 1.28; 95% CI, 1.13-1.45). Of 729 individuals (5.6%) who developed kidney disease, 155 (21.3%) had baseline
CVD, while among 12,342 individuals (94.4%) who did not develop kidney disease, 1,452 (11.8%) had CVD (P < .001) (Table 3). In multivariate analyses, baseline CVD was independently associated with development of kidney disease (OR, 1.54; 95% CI, 1.26-1.89) (Table 4).

SENSITIVITY ANALYSES

There were 2,276 deaths (16.5%) before the final visit. Individuals with baseline CVD were at significantly increased risk of the composite outcome that included mortality and a decline in kidney function between the first and last visits (hazard ratio, 1.84; 95% CI, 1.69-2.00). When analyses were stratified by the study of origin, individuals in the ARIC Study and the CHS were at increased risk of the primary study outcome of kidney function decline (OR, 1.71; 95% CI, 1.30-2.25; and OR, 1.82; 95% CI, 1.20-2.76, respectively). In models evaluating the CHS cohort after individuals with heart failure were excluded, this association remained statistically significant (OR, 1.72; 95% CI, 1.12-2.62). When baseline ACE inhibitor use was evaluated in the CHS cohort, CVD was independently associated with kidney function decline (OR, 1.82; 95% CI, 1.20-2.76), and ACE inhibitor use was protective (OR, 0.30; 95% CI, 0.10-0.87). Finally, when defining CVD as only history of myocardial infarction or a cardiac procedure, CVD remained associated with kidney function decline (OR, 1.93; 95% CI, 1.45-2.59).

MISSING DATA

When evaluating the primary study outcome, almost 77.5% of the individuals completed, on average, more than 9 years of follow-up. Among 3,928 (22.1%) of the 17,754 individuals alive at the time of the final study visit who did not have a final serum creatinine level documented, 934 had demographic and clinical data but no phlebotomy performed; these individuals were predominantly from the CHS (91.1%) and had demographic and clinical data but no phlebotomy performed; these individuals were predominantly from the CHS (91.1%) and had a higher prevalence of baseline CVD (22.0% vs 18.0%, P < .001) and CVD risk factors (including DM) (12.5% vs 8.8%, P = .008) than individuals from the CHS who completed the study. Individuals missing data from their final visit altogether (n = 2,994) were predomi-

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Table 2. Distribution of Risk Factors Among 13,826 Subjects Stratified by Kidney Function Decline*

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Kidney Function Decline (n = 13,306)</th>
<th>Kidney Function Decline (n = 520)</th>
<th>No Kidney Function Decline (n = 9,309)</th>
<th>Kidney Function Decline (n = 4,516)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>57.5 ± 9.1</td>
<td>60.8 ± 9.5</td>
<td>58.3 ± 9.4</td>
<td>56.2 ± 8.3</td>
</tr>
<tr>
<td>Female sex</td>
<td>56.9</td>
<td>45.2</td>
<td>52.9</td>
<td>63.7</td>
</tr>
<tr>
<td>African American race</td>
<td>18.1</td>
<td>31.0</td>
<td>15.9</td>
<td>24.1</td>
</tr>
<tr>
<td>High school graduate</td>
<td>80.7</td>
<td>69.8</td>
<td>80.8†</td>
<td>79.2</td>
</tr>
<tr>
<td>ARIC Study origin</td>
<td>79.7</td>
<td>74.4</td>
<td>75.8</td>
<td>87.0</td>
</tr>
<tr>
<td>Lifestyle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>19.3‡</td>
<td>20.6</td>
<td>17.7</td>
<td>22.6</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>58.3</td>
<td>46.7</td>
<td>59.2</td>
<td>55.2</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>12.5</td>
<td>24.6</td>
<td>12.7§</td>
<td>13.4</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6.1</td>
<td>21.2</td>
<td>5.6</td>
<td>8.9</td>
</tr>
<tr>
<td>Hypertension</td>
<td>39.3</td>
<td>66.7</td>
<td>40.0§</td>
<td>41.0</td>
</tr>
<tr>
<td>Physical characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>122.0 ± 18.6</td>
<td>134.1 ± 22.5</td>
<td>122.1 ± 18.4</td>
<td>123.2 ± 19.8</td>
</tr>
<tr>
<td>Body mass index [1]</td>
<td>27.2 ± 4.9</td>
<td>28.5 ± 5.1</td>
<td>27.3 ± 4.9§</td>
<td>27.2 ± 5.0</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>1.5</td>
<td>5.4</td>
<td>1.6§</td>
<td>1.8</td>
</tr>
<tr>
<td>Baseline laboratory values</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Albumin level, g/dL</td>
<td>3.9 ± 0.3</td>
<td>3.9 ± 0.3</td>
<td>3.9 ± 0.3</td>
<td>3.9 ± 0.3</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>41.7 ± 3.8§</td>
<td>41.7 ± 4.2</td>
<td>42.1 ± 3.1</td>
<td>41.1 ± 3.8§</td>
</tr>
<tr>
<td>Serum creatinine level, mg/dL</td>
<td>0.9 ± 0.2</td>
<td>1.0 ± 0.3</td>
<td>0.9 ± 0.2</td>
<td>0.8 ± 0.2</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate, mL/min per 1.73 m²</td>
<td>89.9 ± 19.8</td>
<td>87.0 ± 26.1</td>
<td>83.8 ± 17.4</td>
<td>101.9 ± 19.7</td>
</tr>
<tr>
<td>Cholesterol levels, mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>213.8 ± 40.3</td>
<td>217.0 ± 45.5</td>
<td>214.0 ± 39.9§</td>
<td>213.8 ± 41.7</td>
</tr>
<tr>
<td>High-density lipoprotein</td>
<td>52.8 ± 16.8</td>
<td>48.4 ± 15.9</td>
<td>52.1 ± 16.5</td>
<td>53.6 ± 17.2</td>
</tr>
</tbody>
</table>

Abbreviation: ARIC, Atherosclerosis Risk in Communities.
SI conversion factors: To convert serum creatinine to micromoles per liter, multiply by 88.4; cholesterol to millimoles per liter, multiply by 0.0259.
*Data are given as mean ± SD or as percentages. Unless otherwise indicated, P < .01 for all comparisons between groups. The subpopulation values do not total 13,826 because a person from the Cardiovascular Heart Study was missing at the last visit, and thus we could not estimate the glomerular filtration rate from the Modification Diet in Renal Disease equation; however, we did have this person’s serum creatinine level.
†P < .05.
‡P < .10.
§P > .20.
Calculated as weight in kilograms divided by height in meters squared.
nantly from the ARIC Study (92.3%), were disproportionately of African American race (35.1%), and had a higher prevalence of baseline CVD and CVD risk factors than individuals who completed the study.

**COMMENT**

Our study demonstrates that CVD is associated with subsequent kidney function decline and development of kidney disease. This association persisted after adjusting for demographic and clinical characteristics and remained robust in multiple analyses using serum creatinine level and eGFR to assess kidney function. Although several studies have evaluated epidemiological risk factors for progression of kidney disease, to our knowledge, this is the first community-based study that has demonstrated that CVD is independently associated with kidney function decline and with development of kidney disease.

Previous studies demonstrated an association between baseline CKD and development of CVD, and ongoing research is exploring mechanisms underlying this association. However, there have been fewer investigations into potential associations between CVD and progression of kidney disease. In the ARIC Study, O'Hare et al demonstrated an association between low ankle brachial index and rise in serum creatinine level. Other studies examining the relationship between CVD and kidney function found an association of heart failure and carotid intima-media thickness with an increase in serum creatinine level over time. Investigators from the Framingham Heart...
Study\textsuperscript{12} demonstrated that DM, hypertension, and other traditional CVD risk factors predicted development of CKD, while Levin et al\textsuperscript{24} found that CVD was an independent risk factor for progression to kidney replacement therapy in a cohort of 313 patients followed up in nephrology clinics.

There are several possible explanations for the increased risk of kidney function decline and development of kidney disease in individuals with CVD. First, the presence of baseline CVD may identify individuals with greater duration and severity of shared CVD and kidney disease risk factors, particularly DM and hypertension. Second, atherosclerotic disease may also affect the renal vasculature, causing disease of small or large vessels and resulting in CKD. Third, the presence of baseline CVD may identify individuals who will eventually develop heart failure, and these individuals may develop kidney function decline due to decreased kidney perfusion. Fourth, CVD predisposes individuals to cardiac procedures, including cardiac catheterization, which may result in kidney damage from intravenous contrast or atheroemboli.

Our study has many strengths. The pooled population is a large and diverse population with 9 years of follow-up and is likely generalizable to a wide age range. In addition, as studies designed to evaluate CVD, the ARIC Study and the CHS devoted considerable effort to identifying CVD and CVD risk factors at study enrollment. Despite using multiple sensitivity analyses, our results remain robust.

Our study has some limitations as well. One limitation is that there is no accepted definition of kidney function decline. We a priori chose to define kidney function decline as a fixed rise in serum creatinine level of at least 0.4 mg/dL (\(\geq 35.4 \mu mol/L\)), as it likely exceeds the threshold of serum creatinine level increase that could be due to chance.\textsuperscript{16} The use of this outcome as a surrogate for kidney function decline is supported by consistent associations seen in our study between kidney function decline and previously described risk factors for development or progression of CKD, including DM, hypertension, older age, and African American race.\textsuperscript{12,25,26}

Furthermore, we used an eGFR-based definition of kidney function decline. The number of individuals with kidney function decline based on eGFR far exceeded that seen with serum creatinine level–based models. It is likely that many individuals are misclassified as having kidney function decline based on changes in eGFR extrapolated from minimal serum creatinine level changes at lower baseline serum creatinine levels, and this is consistent with the known decreased precision of the Modification of Diet in Renal Disease study equation at the highest eGFR. This imprecision is attenuated in the development of the kidney disease model, which examines changes occurring at a lower eGFR (in the range of 60 mL/min per 1.73 m\(^2\)). Other limitations include the lack of ACE inhibitor use data in the ARIC Study population and the absence of baseline proteinuria data. Initial enrollment in these studies predated widespread use of angiotensin blockade in kidney disease; therefore, the present study may more accurately reflect the natural course of the disease.

Despite a high rate of follow-up, a sizable number of individuals who survived for the duration of the study were missing final serum creatinine levels. Individuals with complete data but no phlebotomy performed at the final study

### Table 4. Unadjusted and Adjusted Relationships Between Baseline Cardiovascular Disease and Study Outcomes

<table>
<thead>
<tr>
<th>Method</th>
<th>Kidney Function Decline Outcome</th>
<th>Development of CKD Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Serum creatinine level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated GFR</td>
<td>1.08 (0.97-1.19)*</td>
<td>1.28 (1.13-1.45)</td>
</tr>
</tbody>
</table>

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate. *\(P=.20\), \(P<.001\) for all others.
visit were predominantly from the CHS, and we suspect that comorbid illness in most of these older individuals may have prevented phlebotomy. Given their higher prevalence of baseline CVD and risk factors for development and progression of kidney disease, we suspect that their exclusion biases the results toward the null hypothesis. Individuals missing all data from their final visit were predominantly from the ARIC Study and were disproportionately of African American race, again with higher prevalence of DM and hypertension. Therefore, we suspect that their loss also biases the results toward the null hypothesis.

In summary, the present study demonstrates that CVD is independently associated with kidney function decline and with development of kidney disease. Further studies using other markers for kidney damage, such as proteinuria level, will be needed to confirm this association. This study identifies a population that may benefit from (1) increased CVD risk factor surveillance and intervention, (2) heightened awareness of the risk factors associated with kidney disease, and (3) greater attention to and treatment for sequelae of kidney disease. Because these patients are mainly under the care of primary care physicians and cardiologists, it is important to draw attention to the increased risk of kidney disease in this population, with goals of preventing further progression, managing sequelae of kidney disease as they arise, and adequately preparing individuals for kidney failure with timely nephrology referrals. Only with recognition of risk factors for kidney disease can this happen.

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Disclaimer: The views expressed in this article do not necessarily reflect the opinions of the National Heart, Lung, and Blood Institute.

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REFERENCES