Association of Chronic Kidney Disease With Atrial Fibrillation Among Adults in the United States
REasons for Geographic and Racial Differences in Stroke (REGARDS) Study

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Background—Atrial fibrillation (AF) is common among patients with end-stage renal disease, but few data are available on its prevalence among adults with chronic kidney disease (CKD) of lesser severity.

Methods and Results—We evaluated the association of CKD with ECG-detected AF among 26 917 participants in the REGARDS study, a population-based cohort of African-American and white US adults 45 years of age. Estimated glomerular filtration rate (eGFR) was calculated using the abbreviated Modification of Diet in Renal Disease study equation and albuminuria was defined as a urinary albumin to creatinine ratio ≥30 mg/g. Participants were categorized by renal function: no CKD (eGFR ≥60 mL/min/1.73 m² without albuminuria, n=21 081), stage 1 to 2 CKD (eGFR ≥60 mL/min/1.73 m² with albuminuria n=2938), stage 3 CKD (eGFR 30 to 59 mL/min/1.73 m², n=2683) and stage 4 to 5 CKD (eGFR <30 mL/min/1.73 m², n=215). The prevalence of AF among participants without CKD, and with stage 1 to 2, stage 3, and stage 4 to 5 CKD was 1.0%, 2.8%, 2.7% and 4.2%, respectively. Compared with participants without CKD, the age-, race-, and sex-adjusted odds ratios for prevalent AF were 2.67 (95% confidence interval, 2.04 to 3.48), 1.68 (95% confidence interval, 1.26 to 2.24) and 3.52 (95% confidence interval, 1.73 to 7.15) among those with stage 1 to 2, stage 3, and stage 4 to 5 CKD. The association between CKD and prevalent AF remained statistically significant after further multivariable adjustment and was consistent across numerous subgroups.

Conclusions—Regardless of severity, CKD is associated with an increased prevalence of AF among US adults. (Circ Arrhythm Electrophysiol. 2011;4:26-32.)

Key Words: chronic kidney disease ♦ atrial fibrillation ♦ electrocardiography

Atrial fibrillation (AF) is a frequent cardiac arrhythmia and confers a 2- to 3-fold increased risk of ischemic stroke and mortality.1–3 AF increases in prevalence with age, approaching 10% among adults ≥80 years old.4 Renal disease and AF share several risk factors, including hypertension, diabetes mellitus, and coronary artery disease (CAD).5–7 A high prevalence of AF has been reported among patients with end-stage renal disease on dialysis.8,9 Patients with end-stage renal disease, however, represent a small fraction of individuals with chronic kidney disease (CKD), and the burden of AF among adults with less severe CKD has not been well investigated. Therefore, the goal of the current study was to evaluate the burden of AF in relation to renal function among US adults not on dialysis. Additionally, we determined demographic and clinical correlates of AF by CKD severity. To do so, we analyzed data from participants enrolled in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study.

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Methods

Study Participants
The REGARDS study is a population-based, longitudinal study of African-American and white US adults age ≥45 years of age, enrolled between January 2003 and October 2007.10 The study was designed to oversample African-Americans and to provide approxi-
mate equal representation of men and women; the final cohort included 26% African-American women, 16% African-American men, 29% white women, and 29% white men. By design, 56% (goal, 50%) of the sample was recruited from the eight Southern United States (North Carolina, South Carolina, Georgia, Alabama, Mississippi, Tennessee, Arkansas, and Louisiana), commonly referred to as the “stroke belt,” with the remaining 44% of the sample recruited from the other 40 contiguous US states. Individuals were identified from commercially available lists of residents and recruited through an initial mailing followed by telephone contacts. Overall, 30,239 individuals were enrolled in the REGARDS study. After excluding participants receiving hemodialysis (n = 117), missing serum creatinine measurements (n = 1092), with implanted pacemakers or poor-quality ECG recordings (n = 846), and without urinary albumin and creatinine measurements (n = 1243) data from 26,917 participants were included in the present analysis. The REGARDS protocol was approved by the institutional review boards governing research in human subjects at the participating centers and all participants provided verbal consent before the telephone interview and written consent before study examinations.

Data Collection
Baseline demographic and clinical data were collected through telephone interviews, self-administered questionnaires, and in-home examinations. After obtaining consent, trained interviewers conducted computer-assisted telephone interviews to obtain participants’ demographic information, cigarette smoking status, and self-reports of a prior diagnosis of major comorbid conditions (diabetes, hypertension, myocardial infarction, stroke, coronary revascularization, and AF). A self-reported history of AF was defined as an affirmative response to the question: “Has a physician or a health professional ever told you that you had atrial fibrillation?”

Trained staff then conducted in-home study visits 3 to 4 weeks after the interview, in which prescription and over-the-counter medications were documented via pill bottle review, a physical examination was performed, blood and urine samples were collected, and a resting ECG was recorded.

Systolic and diastolic blood pressure was estimated as the average of 2 measurements. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure as ≥90 mm Hg, or the use of antihypertensive medication. Height and weight were measured during the study visit, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Diabetes was defined as a serum glucose level ≥126 mg/dL for participants who had fasted ≥8 hours before sampling, serum glucose ≥200 mg/dL for those who had not fasted, or self-report of a prior diagnosis of diabetes with current use of insulin or oral hypoglycemic medications. Of REGARDS study participants included in the current analysis, 87% had fasted more than 8 hours before their blood draw.

The first 8459 REGARDS participants underwent 7-lead ECG recording acquired by applying the standard 4 limb electrodes and a midstandard electrode, whereas the rest of REGARDS participants underwent standard 12-lead ECG recording. The ECGs were read and coded at a central reading center by electrocardiographers blinded to the other REGARDS study data.

Left ventricular hypertrophy (LVH) was defined on the basis of the sex-specific Cornell voltage criteria in the 12-lead ECGs, whereas a modified Cornell voltage criteria was used in the 7-lead ECGs.

Symptoms of heart failure were defined as being present if participants reported having to sleep on 2 or more pillows to help breathing and awakening caused by difficulty breathing. These criteria were associated with a specificity of approximately 83% for the detection of heart failure among community-dwelling adults. Prevalent CAD at baseline was defined based on a self-reported history of myocardial infarction or coronary revascularization (coronary angioplasty or bypass surgery). Hypercholesterolemia was defined as an LDL-cholesterol ≥160 mg/dL for those who fasted 8 or more hours before sampling, total serum cholesterol ≥240 mg/dL for those who had not fasted, or current lipid-lowering medication use. High-sensitivity C-reactive protein (CRP) ≥3 mg/L was defined as elevated.

Using isotope-dilution mass spectrometry traceable serum creatinine, estimated GFR (eGFR) was calculated using the abbreviated Modification of Diet in Renal Disease study equation. All analyses were repeated using the CKD-EPI equation with similar results (data not shown). Albuminuria was defined as a urinary albumin-to-creatinine ratio ≥30 mg/g. CKD stages were defined using the recommendations of the National Kidney Foundation: no CKD (eGFR ≥60 mL/min/1.73 m² without albuminuria), stage 1 to 2 CKD (eGFR ≥60 mL/min/1.73 m² with albuminuria), stage 3 CKD (eGFR of 30 to 59 mL/min/1.73 m²), and stage 4 to 5 CKD (eGFR <30 mL/min/1.73 m²). Individuals with stage 1 and 2 CKD were grouped together to represent the presence of albuminuria with preserved GFR, and participants with stage 4 and 5 CKD were grouped together to provide an adequate sample size for stable estimates.

Statistical Analysis
The primary outcome was prevalent ECG-detected AF. Participant characteristics and the prevalence of ECG-detected AF were calculated by CKD stage. The statistical significance of linear trends for participant characteristics across CKD stages was tested by linear and logistic regression for continuous and dichotomous variables, respectively. The odds ratios (ORs) for prevalent AF associated with stage 1 to 2, 3, and 4 to 5 CKD versus no CKD were calculated using logistic regression. An initial model included adjustment for age, race, and sex. A subsequent model included additional adjustment for other potential confounders, including geographic region of residence (inside or outside the stroke belt), current smoking, BMI, hypertension, diabetes, coronary disease, symptoms of heart failure, LVH, hypercholesterolemia, statin use, renin-angiotensin system inhibitor use, and elevated CRP. To assess the consistency of the associations, the multivariable-adjusted ORs for prevalent AF associated with CKD stage were calculated using logistic regression within participant subgroups. For the subgroup analyses, participants with stage 3, 4, or 5 CKD were combined because of the limited number of participants with stage 4 or 5 CKD. To assess the statistical significance of differences in the association of stage 1 to 2 and stage 3 to 5 CKD with AF across subgroup, interaction terms (eg, stage 1 to 2 CKD*female sex and stage 3 to 5 CKD*women) were incorporated into the multivariable models.

Next, the age-, race-, and sex-adjusted ORs for prevalent AF associated with demographics and clinical risk factors were calculated for each CKD group (no CKD, stage 1 to 2 CKD, and stage 3 to 5 CKD) separately. Variables significantly associated with AF in age-, race-, and sex-adjusted analyses were included in multivariable-adjusted models. Additionally, the OR for prevalent AF associated with albuminuria among participants with stage 3 to 5 CKD was calculated in a separate multivariable-adjusted model. For secondary analyses, the prevalence and ORs for AF, defined on the basis of self-report or ECG, were calculated by CKD stage. All analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC).

Results
Patient Characteristics
REGARDS participants with more advanced CKD were older and more likely to be African-American (Table 1). Diabetes, hypertension, CAD, symptoms of heart failure, LVH, and elevated CRP were more frequent, and BMI and serum cholesterol levels were higher among individuals with more advanced CKD. Additionally, statin and renin-angiotensin system inhibitor drug use were more common among participants with progressively worsening renal function.

Prevalence of ECG-Detected AF
There were 198 cases of ECG-detected AF among adults without CKD, and 83, 71, and 9 cases among adults with
stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively. The prevalence of ECG-detected AF increased across worsening CKD stages. Specifically, the prevalence of AF was 1.0% among adults without CKD, and 2.8%, 2.7%, and 4.2% among adults with stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively. After adjustment for age, race and sex, the ORs for AF were 2.67 (95% CI, 2.04 to 3.48), 1.68 (95% CI, 1.26 to 2.24), and 3.52 (95% CI, 1.73 to 7.15) for those with stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively, compared with participants without CKD (Table 2). These associations were attenuated but remained statistically significant, after further multivariable adjustment.

**Subgroup Analysis**

The Figure shows the multivariable-adjusted ORs for prevalent AF associated with stage 1 to 2 CKD and stage 3 to 5 CKD, separately, versus no CKD within subgroups of REGARDS participants. The associations were consistent (all probability values for interaction >0.10), with ORs >1 in all subgroups.

**Risk Factors for Prevalent AF**

The following variables were associated with prevalent AF in age-, race-, and sex-adjusted models among all participants: age, male sex, African-American race, elevated CRP, LVH, and symptoms of heart failure. Higher BMI and renin-angiotensin system inhibitors were significantly associated with prevalent AF among those without CKD, whereas CAD was significantly associated with AF among those with stage 3 to 5 CKD. Hypertension was not significantly associated with prevalent AF in age-, race-, and sex-adjusted models.

**Table 1. Characteristics of REGARDS Study Participants Stratified by CKD Stage**

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>No CKD (n=21 081)</th>
<th>Stage 1–2 (n=2938)</th>
<th>Stage 3 (n=2683)</th>
<th>Stage 4–5 (n=215)</th>
<th>P Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64.2 (9.0)</td>
<td>66.4 (9.5)</td>
<td>71.2 (9.1)</td>
<td>68.7 (9.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male, %</td>
<td>45.1</td>
<td>49.2</td>
<td>41.2</td>
<td>45.1</td>
<td>0.190</td>
</tr>
<tr>
<td>African-American, %</td>
<td>39.2</td>
<td>52.9</td>
<td>36.5</td>
<td>58.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke belt, %</td>
<td>34.8</td>
<td>34.6</td>
<td>32.3</td>
<td>29.8</td>
<td>0.005</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>16.3</td>
<td>39.6</td>
<td>31.1</td>
<td>55.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>53.6</td>
<td>74.7</td>
<td>79.9</td>
<td>86.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoking, %</td>
<td>14.2</td>
<td>20.6</td>
<td>11.0</td>
<td>13.1</td>
<td>0.565</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>29.1 (6.0)</td>
<td>30.4 (6.7)</td>
<td>29.6 (6.4)</td>
<td>31.0 (7.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAD,* %</td>
<td>11.1</td>
<td>17.3</td>
<td>23.5</td>
<td>33.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptoms of heart failure, †%</td>
<td>4.4</td>
<td>5.8</td>
<td>6.0</td>
<td>11.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Elevated serum cholesterol, %</td>
<td>38.9</td>
<td>44.3</td>
<td>52.5</td>
<td>56.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statins, %</td>
<td>28.7</td>
<td>34.3</td>
<td>44.4</td>
<td>48.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renin-angiotensin system inhibitors, %</td>
<td>29.2</td>
<td>43.6</td>
<td>52.4</td>
<td>57.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ECG, LVH, %</td>
<td>4.2</td>
<td>9.6</td>
<td>8.0</td>
<td>14.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP ≥3 mg/L, %</td>
<td>37.8</td>
<td>50.3</td>
<td>46.4</td>
<td>57.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Numbers in table are mean (standard deviation) or percentage.

*Prior self-reported myocardial infarction, coronary stenting, or coronary bypass.
†Based on self-reported symptoms of having to sleep on 2 or more pillows to help breathing or awakening caused by difficulty breathing.

**Table 2. ORs (95% CIs) for AF Defined by ECG**

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>No CKD (n=21 081)</th>
<th>Stage 1–2 (n=2938)</th>
<th>Stage 3 (n=2683)</th>
<th>Stage 4–5 (n=215)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases of AF, n</td>
<td>198</td>
<td>83</td>
<td>71</td>
<td>9</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1 (ref)</td>
<td>2.67 (2.04, 3.48)§</td>
<td>1.68 (1.26, 2.24)§</td>
<td>3.52 (1.73, 7.15)§</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)*</td>
<td>1 (ref)</td>
<td>2.20 (1.64, 2.94)§</td>
<td>1.51 (1.12, 2.05)‡</td>
<td>2.86 (1.38, 5.92)‡</td>
</tr>
</tbody>
</table>

*Adjusted for age, race, sex, geographic region (stroke belt versus non–stroke belt), current smoking, BMI, hypertension, diabetes, CAD, symptoms of heart failure, ECG-detected LVH, elevated cholesterol, statin and renin-angiotensin system inhibitor use, and CRP ≥3 mg/L.
‡P < 0.01; §P < 0.001.
The multivariable-adjusted associations between demographic and clinical variables and prevalent AF among those with no CKD, stage 1 to 2 CKD, and stage 3 to 5 CKD, separately, are shown in Table 3. Regardless of CKD stage, older age and male sex were associated with an increased OR for AF, whereas African-American race was associated with a lower OR for AF. There was no evidence of effect modification by CKD on the association between demographic and clinical variables and prevalent AF (all P interaction terms >0.10). Among those with stage 3 to 5 CKD, the multivariable-adjusted OR for prevalent AF associated with albuminuria was 2.13 (95% CI, 1.32 to 3.42).

**Self-Reported or ECG-Detected AF**

There were 1478 cases of AF defined by self-report or ECG among those without CKD and 308, 321, and 34 cases among adults with stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively. The prevalence of self-report of ECG-detected AF was 7.1% (95% CI, 6.7% to 7.5%) among adults without CKD and 10.7% (9.5% to 11.9%), 12.2% (11.0% to 13.4%), and 16.0% (11.1% to 20.9%) among those with stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively ($P$-trend <0.001). After adjustment for age, race, and sex, the ORs for self-report or ECG-detected AF were 1.52 (95% CI, 1.33 to 1.73), 1.52 (95% CI, 1.33 to 1.74), and 2.29 (95% CI, 1.58 to 3.33) for those with stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively, compared with participants without CKD. The multivariable-adjusted ORs for these groups were 1.29 (95% CI, 1.10 to 1.54) for those with stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively, compared with participants without CKD.

**Discussion**

In the present analysis of almost 27 000 US adults, CKD was associated with an increased prevalence of AF. The prevalence of AF was highest among those with stage 4 or 5 CKD, and the association between CKD stage and AF persisted after multivariable adjustment and was consistent across all of the subgroups examined. In addition, the association between CKD and AF was present whether AF was detected via ECG or self-report of a prior diagnosis of the arrhythmia.

In previous studies involving patients on hemodialysis, the prevalence of AF ranged from 5% to 27%, depending on the duration of dialysis therapy, associated risk factors, and patterns of AF (paroxysmal, persistent or permanent). After adjustment for age, race, and sex, the ORs for self-report or ECG-detected AF were 1.52 (95% CI, 1.33 to 1.73), 1.52 (95% CI, 1.33 to 1.74), and 2.29 (95% CI, 1.58 to 3.33) for those with stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively, compared with participants without CKD. The multivariable-adjusted ORs for these groups were 1.29 (95% CI, 1.10 to 1.54) for those with stage 1 to 2, stage 3, and stage 4 to 5 CKD, respectively, compared with participants without CKD.

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risk of mortality and stroke over 4 years compared with dialysis patients without AF, a magnitude of incremental risk similar to that observed in patients without end-stage renal disease.\textsuperscript{1,2} Our findings extend these observations, suggesting that the prevalence of AF is increased even in persons with less advanced CKD.

Community-based studies in The Netherlands and Japan have evaluated the associations between albuminuria and reduced eGFR, separately, and AF.\textsuperscript{20,21} In both studies, participants were recruited by mail and underwent examination in outpatient clinics or health screening programs. In The Netherlands study, microalbuminuria was associated with an OR for prevalent AF of 1.93 (95% CI, 1.10 to 3.37), similar in magnitude to the association we observed for stage 1 to 2 CKD. In the Japanese study, the OR for prevalent AF among participants with stage 3 to 5 CKD, suggesting that the high prevalence of hypertension may have limited our ability to detect an association between hypertension and AF. Longitudinal follow-up of the REGARDS cohort, including the ascertainment of incident AF, might clarify the relationship between hypertension and AF.

In addition, albuminuria was strongly associated with AF among participants with stage 3 to 5 CKD, suggesting that the burden of AF among individuals with both albuminuria and reduced eGFR may be substantially higher than in those with only 1 of these abnormalities. The current findings are also consistent with previous reports that other manifestations of CVD, such as peripheral arterial disease,\textsuperscript{23} are more frequent among individuals with both reduced eGFR and albuminuria compared with those with only 1 of these abnormalities.

Hypertension did not emerge as a significant correlate of AF, even among those without CKD. This is unexpected, given the established association of hypertension with AF in other studies.\textsuperscript{2,5} This discrepancy may be due to differences in the prevalence of hypertension and racial diversity in the REGARDS cohort compared with earlier studies. The prevalence of hypertension is 57% in the REGARDS study.\textsuperscript{24} The high prevalence of hypertension may have limited our ability to detect an association between hypertension and AF.

In addition to evaluating the prevalence of AF, we compared clinical correlates of AF among participants with and without CKD. Established risk factors for AF, such as advanced age, male sex, symptoms of heart failure, LVH, and CAD\textsuperscript{2,5,22} were associated with prevalent AF among those with CKD in the REGARDS cohort. The association between symptoms of heart failure, CAD, and AF was less precise and weaker in magnitude compared with earlier studies. This finding may be due to limited statistical power when conducting subgroup analyses. Participants may also have been misclassified as having either symptoms of heart failure or CAD because these conditions were based on subjective criteria or self-report. Elevated CRP, a biomarker associated with an increased risk for cardiovascular events in both the general and CKD populations, was associated with AF within each CKD strata.

<table>
<thead>
<tr>
<th>Multivariable-Adjusted ORs* (95% CI)</th>
<th>No CKD</th>
<th>Stage 1–2 CKD</th>
<th>Stage 3–5 CKD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per 10 y</td>
<td>2.84 (2.39, 3.38)¶</td>
<td>2.08 (1.57, 2.76)¶</td>
<td>2.05 (1.52, 2.76)¶</td>
</tr>
<tr>
<td>Male</td>
<td>3.16 (2.25, 4.44)¶</td>
<td>3.03 (1.71, 5.36)¶</td>
<td>2.94 (1.75, 4.91)¶</td>
</tr>
<tr>
<td>African-American</td>
<td>0.34 (0.23, 0.51)¶</td>
<td>0.43 (0.25, 0.72)¶</td>
<td>0.34 (0.18, 0.65)¶</td>
</tr>
<tr>
<td>BMI per 5 kg/m\textsuperscript{2}</td>
<td>1.26 (1.10, 1.46)[</td>
<td>1.04 (0.83, 1.29)</td>
<td>1.10 (0.88, 1.36)</td>
</tr>
<tr>
<td>CAD†</td>
<td>1.05 (0.73, 1.51)</td>
<td>1.07 (0.62, 1.84)</td>
<td>1.92 (1.20, 3.09)§</td>
</tr>
<tr>
<td>Symptoms of heart failure‡</td>
<td>1.40 (0.68, 2.90)</td>
<td>2.26 (0.93, 5.51)</td>
<td>1.45 (0.59, 3.55)</td>
</tr>
<tr>
<td>Renin-angiotensin system inhibitors</td>
<td>1.26 (0.92, 1.71)</td>
<td>1.41 (0.87, 2.29)</td>
<td>1.06 (0.66, 1.69)</td>
</tr>
<tr>
<td>CRP \textsuperscript{≥}3 mg/L</td>
<td>1.28 (0.94, 1.74)</td>
<td>1.42 (0.87, 2.32)</td>
<td>1.93 (1.20, 3.09) §</td>
</tr>
<tr>
<td>LVH</td>
<td>1.56 (0.80, 3.02)</td>
<td>2.46 (1.21, 5.01)§</td>
<td>1.64 (0.75, 3.57)</td>
</tr>
</tbody>
</table>

*Age, sex, race, BMI, CAD, symptoms of heart failure, renin-angiotensin system inhibitor use, CRP \textsuperscript{≥}3 mg/L, and ECG-detected LVH were included in 3 separate models; 1 each for no CKD, stage 1 to 2 CKD, and stage 3 to 5 CKD.
†Prior self-reported myocardial infarction, coronary stenting, or coronary bypass.
‡Based on self-reported symptoms of having to sleep on 2 or more pillows to help breathing or awakening caused by difficulty breathing.
§P\textless;0.05; ||P\textless;0.01; and ¶P\textless;0.001.
including interstitial collagen deposition, have been demonstrated early in the course of CKD and might also contribute to AF by enhancing intra-atrial reentry.

Quantifying the burden of AF among the population with CKD is clinically relevant and maintains public health importance because approximately 26 million US adults (13%) have CKD. The prevalence of CKD is projected to increase as the US population ages and the prevalence of risk factors for the development of renal disease increases. In contrast to other manifestations of CVD, such as aortic stiffness, vascular calcification, and LVH, the association between CKD and AF has not been extensively studied. AF may emerge as an important prognostic marker or even as a mediator of excess cardiovascular risk among patients with CKD. The relatively high prevalence of AF combined with its impact on morbidity and mortality due to CVD, highlight the importance of AF detection, but additional studies are needed to elucidate the mechanisms responsible for development of AF among people with CKD and to develop preventive strategies.

This study should be interpreted in the context of certain limitations. The most important may be its cross-sectional observational design. This precludes inferences about the temporal relation between CKD and AF. Furthermore, serum creatinine and albuminuria measurements were performed only once for each participant. The same was true of ECG recordings, raising the likelihood that many cases of paroxysmal AF were not detected. There were a limited number of cases of AF among participants with stage 4 to 5 CKD, rendering prevalence estimates for this group less reliable than those for other CKD stages. Insufficient power may have precluded our ability to detect important associations between various risk factors for AF among participants in different CKD stages. Multiple statistical tests performed in our subgroup analyses might have also resulted in Type I error inflation. In addition, both recall and misclassification bias might have confounded the association between various risk factors and AF as many medical conditions were based on self-reported history alone. Not only are we unable to establish causality between CKD and AF based on the present investigation, our cross-sectional design is also limited by inherent selection and survival biases. Despite these weaknesses, this may be the largest and most racially diverse population-based sample yet to assess the relationship between renal function and ECG-documented AF. Moreover, measurements of both serum creatinine and albuminuria allowed for estimation of the association of AF with renal impairment across the entire spectrum of CKD.

In conclusion, CKD was associated with an increased prevalence of AF in this large population-based sample of US adults. This association was present among individuals with stage 1 or 2 CKD, stage 3 CKD, and stage 4 or 5 CKD, remained consistent across several subgroups, and persisted after adjustment for multiple potential confounders. Given the large number of US adults with CKD and their high risk of CVD, these findings have important clinical implications. Additional prospective studies are needed to determine the mechanisms responsible for this association and incremental risk for stroke associated with AF among individuals with CKD.

Sources of Funding
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Dr Muntner had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Warnock and McClellan received research support and serve as consultants for AMGEN, Inc. Dr Halperin received honoraria from Portola Pharmaceuticals, Inc and has received consulting fees from Astellas Pharma, US, Bayer AG HealthCare, Boehringer Ingelheim, Daiichi Sankyo, Johnson & Johnson, Sanofi-Aventis, and Biotronik, Inc.

References
Atrial fibrillation (AF) is a common cardiac arrhythmia that substantially increases risk for cardiac death and ischemic stroke. Chronic kidney disease (CKD) is also highly prevalent and associated with excess cardiac morbidity and mortality. Although AF and CKD share many risk factors, most studies evaluating the association between CKD and AF have been limited to those with advanced dialysis-dependent CKD. We evaluated the association between ECG-documented AF and non–dialysis-dependent CKD among 26,917 community-dwelling US adults. In this study, the prevalence of AF was significantly higher in those with versus without CKD. Moreover, the prevalence of AF was higher at progressively more advanced renal disease. The association between CKD and AF remained statistically significant across numerous subgroups. We did not detect any important differences in the risk factors for AF among those with versus without CKD. These results may provide important insight on increased thrombotic risk in CKD populations. Screening for AF among those with predialysis CKD may be warranted.
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