Incident Atrial Fibrillation and the Risk of Congestive Heart Failure, Myocardial Infarction, End-Stage Kidney Disease, and Mortality Among Patients With a Decreased Estimated GFR

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Background: The association of atrial fibrillation (AF), estimated glomerular filtration rate (eGFR), and adverse events remains unknown.

Study Design: Population-based retrospective cohort study from Ontario, Canada.

Setting & Participants: 1,422,978 adult residents with eGFRs < 90 mL/min/1.73 m^2 from April 1, 2006, through March 31, 2015.

Factor: A diagnosis of AF at hospitalization.

Outcomes: Congestive heart failure (CHF), myocardial infarction (MI), end-stage kidney disease, all-cause mortality.

Results: All adverse events were more frequent in individuals with AF (93,414 propensity score matched) compared to no AF, and this difference was more pronounced within the first 6 months of the index date (CHF: 3.04% [AF] vs 0.28% [no AF], subdistribution HR [sHR] of 11.57 [95% CI, 10.26-13.05]; MI: 0.97% [AF] vs 0.21% [no AF], sHR of 4.76 [95% CI, 4.17-5.43]; end-stage kidney disease: 0.16% [AF] vs 0.03% [no AF], sHR of 5.84 [95% CI, 3.82-8.93]; and all-cause mortality: 6.11% [AF] vs 2.50% [no AF], HR of 2.62 [95% CI, 2.50-2.76]) than in the period more than 6 months after the index date (CHF: 6.87% [AF] vs 2.87% [no AF], sHR of 2.64 [95% CI, 2.55-2.74]; MI: 2.21% [AF] vs 1.81% [no AF], sHR of 1.24 [95% CI, 1.18-1.30]; end-stage kidney disease: 0.52% [AF] vs 0.32% [no AF], sHR of 1.75 [95% CI, 1.57-1.95]; and all-cause mortality: 15.55% [AF] vs 15.10% [no AF], HR of 1.07 [95% CI, 1.04-1.10]). The results accounted for the competing risk for mortality. eGFR level modified the effect of AF on CHF (*P* for interaction < 0.05).

Limitations: Observational study design does not permit determination of causality; only a single outpatient eGFR measure was used; medication data were not included.

Conclusions: Incident AF is associated with a high risk for adverse outcomes in patients with eGFRs < 90 mL/min/1.73 m^2. Because the risk is exceedingly high within the first 6 months after AF diagnosis, therapeutic interventions and monitoring may improve outcomes.

Complete author and article information provided before references.

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Chronic kidney disease (CKD) is a common medical problem[1-3] and carries a high burden of disease.[4] It is associated with increased risk for hospitalization, adverse cardiovascular outcomes, and death.[5-7] Among these adverse cardiovascular outcomes is increased risk for atrial fibrillation (AF).[8-14] AF is the most common arrhythmia,[15] affecting more than 33 million people worldwide,[16] with an incidence that continues to grow.[17] It negatively affects quality of life,[18] increases health care costs,[19] and also carries a high burden of disease. One of the most frequent complications is the development of cardioembolic stroke,[20-22] and multiple randomized controlled trials and evidence-based guidelines are available to guide therapeutic interventions in the non-CKD population. However, AF has a wide range of other cardiovascular effects, and studies have shown it to be associated with increased risk for congestive heart failure (CHF)[23-25] and myocardial infarction (MI),[26,27] as well as the development of CKD.[28] As such, AF and CKD are closely related diseases sharing common risk factors and showing similar adverse outcomes.[29]

Previous studies in patients with AF have focused on the end-stage kidney disease population. Patients with end-stage kidney disease have a much higher incidence of AF[31,32] and risk for adverse outcomes.[30,32-34] Recent studies suggest a high incidence of stroke, end-stage kidney disease, and all-cause mortality in patients with low estimated glomerular filtration rates (eGFRs) and AF.[35-38] There is limited information regarding the association of eGFR and other cardiovascular outcomes such as CHF and MI in patients with AF. Determination of the risk for other cardiovascular outcomes in patients with AF with low eGFRs would allow for improved risk stratification and identification of patients at high risk for adverse outcomes, allowing for possible preventative therapies.

We set out to examine the association between AF and cardiovascular outcomes (CHF and MI), end-stage kidney disease, and all-cause mortality in patients with a decrease in eGFR and whether different eGFR categories would influence these associations. We hypothesized that AF would be associated with higher risk for adverse events in patients with low eGFRs and the risk would differ by eGFR level.

Methods

Design and Setting

We conducted a population-based retrospective cohort study in the province of Ontario, Canada, using health care databases housed at the Institute for Clinical Evaluative Sciences (ICES). The study was conducted according to a prespecified protocol that was approved by the Research Ethics Board at Sunnybrook Health Sciences Centre (Toronto, Ontario, Canada). Informed consent was waived because deidentified information was used in the study.

Data Sources

We ascertained patient characteristics, laboratory data, and outcome data from linked databases. Gamma-Dynacare databases were used to obtain outpatient laboratory data. Gamma-Dynacare is a laboratory service provider that contains outpatient laboratory information for individuals who had bloodwork drawn at any of their 148 collection sites in Ontario. Demographics and vital status information were obtained from the Ontario Registered Persons Database, and physician specialization information was obtained from the ICES Physician Database. Diagnostic and procedural information from all hospitalizations was determined using the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD). Diagnostic information from emergency department visits was determined using the National Ambulatory Care Reporting System (NACRS). Information was also obtained from the Ontario Health Insurance Plan database, which contains all health claims for inpatient and outpatient physician services. We identified patients with a history of kidney transplantation or dialysis therapies (exclusion criteria) using the Canadian Organ Replacement Register (CORR). These data sets were linked using unique encoded identifiers and analyzed at ICES. When possible, we defined patient characteristics and outcomes using validated codes (Table S1).

Study Cohort

We included all patients with at least 1 outpatient eGFR obtained from April 1, 2006, to March 31, 2015, and looked forward 12 months for first evidence of AF.[39] Because our primary interest was the association of AF with clinical outcomes by eGFR, we included only patients with eGFRs < 90 mL/min/1.73 m^2. For each patient, the date of the first eligible incident AF diagnosis was taken as the index date. For patients who did not develop AF during the 12-month index period, a random index date was assigned based on the distribution of index dates in the AF group. We excluded patients younger than 18 years (due to the small sample size of younger individuals and their low risk for de novo AF), with any history of kidney transplantation, evidence of dialysis, or evidence of CHF or AF 5 years before their index date (Fig 1).

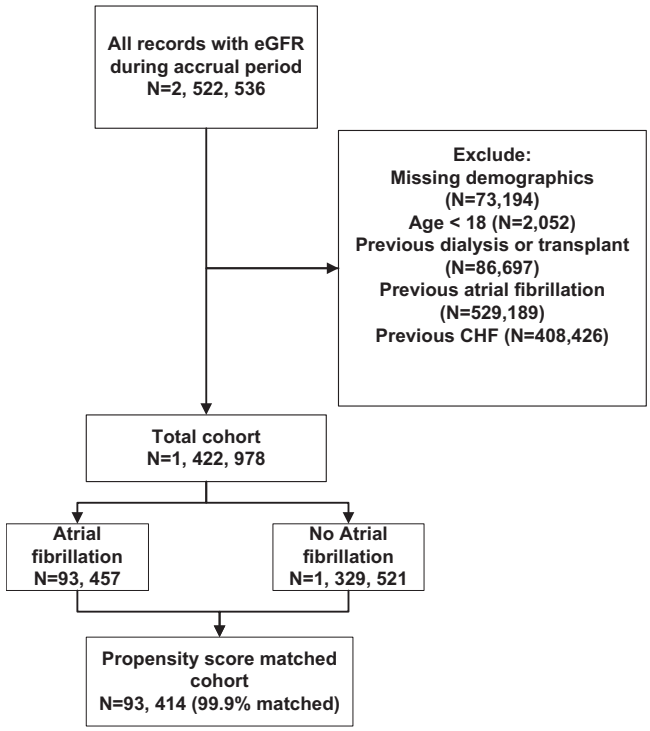

Figure 1. Cohort creation. Abbreviations: CHF, congestive heart failure; eGFR, estimated glomerular filtration rate.

Exposures, Comorbid Conditions, and Outcomes

We used the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation to calculate eGFR, which was categorized as 60 to <90, 30 to <60, and <30 mL/min/1.73 m^2.[21] Incident clinically identified AF was defined by a single *International Classification of Diseases* or billing code on first diagnosis during hospitalization, emergency department visit, or ambulatory care visit. The diagnosis of AF using *International Classification of Diseases*, Ontario Health Insurance Plan billing, and NACRS has been previously validated with specificities and sensitivities > 90%.[40] All eligible patients were followed up forward in time until receipt of dialysis, kidney transplantation, all-cause mortality, CHF, MI, or end-of-study follow-up period (March 31, 2015). Receipt of dialysis and/or kidney transplant for CHF, MI, end-stage kidney disease, and all-cause mortality had to occur more than 24 hours after the diagnosis of AF. CHF and MI were identified on first diagnosis during hospitalization, emergency department visit, or ambulatory care visit. End-stage kidney disease was defined as a long-term dialysis or kidney transplantation treatment code in CORR. Diagnoses for the study exposure and outcomes were identified using *International Classification of Diseases, Tenth Revision* codes in CIHI-DAD and NACRS, Ontario Health Insurance Plan diagnostic codes or treatment codes in CORR (Table S1). For all-cause mortality, patients were followed up until death (event of interest) or end of the study (a censoring event). For CHF, MI, or end-stage kidney disease, patients were followed up until