Postprint: Atrial Fibrillation and Risk of Incident Chronic Kidney Disease in a Northern Chinese Population

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Abstract

Background The Global Burden of Disease report shows that atrial fibrillation and chronic kidney disease (CKD) have become one of the fastest-growing causes of mortality in the past two decades. The concept of cardiorenal syndrome suggests that atrial fibrillation may increase the risk of incident chronic kidney disease; however, current research both domestically and internationally on the risk of atrial fibrillation increasing incident CKD remains limited, and the interaction with age is still unclear.

Objective To investigate whether atrial fibrillation (AF) increases the risk of incident chronic kidney disease (CKD) in a northern Chinese population.

Methods A prospective cohort study design was employed. Participants were selected from employees of the Kailuan Group in Hebei Province who underwent health examinations between June 1, 2006, and October 30, 2010 (n=135,168, aged 18-98 years). After excluding 19,883 individuals with missing data or a history of CKD, and 4,430 individuals with prior cardiovascular or cerebrovascular disease, malignant tumors, or those who developed AF during follow-up, a total of 110,855 participants were included in the study. Participants were divided into AF and non-AF groups based on the presence of AF, with 368 AF patients and 110,487 non-AF individuals. Follow-up was conducted annually, with the final follow-up date being December 31, 2020. The median follow-up duration was 13.46 (9.70, 14.05) years, and the endpoint event was incident CKD. Statistical analysis was performed to assess the effect of AF on the risk of incident CKD.

Results (1) The AF group comprised 368 individuals with a mean age of $(63.43\$\pm10.61)years, including338males(91.85\pm\$12.92)$ years, including 88,288 males (79.91%). Statistically significant differences were observed between the

AF and non-AF groups in age (years), sex (male), systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), high-sensitivity C-reactive protein (Hs-CRP), education level (high school diploma or above), alcohol consumption, physical exercise, hypertension, use of antihypertensive medication, diabetes, and use of hypoglycemic medication (P<0.01 or P<0.05). No statistically significant differences were found between the AF and non-AF groups in fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-C), smoking, or use of lipid-lowering medication (P>0.05).

(2) In the AF group, 95 individuals developed incident CKD, with a cumulative incidence of 30.40%. In the non-AF group, 22,725 individuals developed incident CKD, with a cumulative incidence of 21.77%. The difference in cumulative incidence between the two groups was statistically significant (^{2}=14.30, P<0.001). The incidence densities were 28.63 per 1,000 person-years and 18.48 per 1,000 person-years for the AF and non-AF groups, respectively.

(3) AF was associated with an increased risk of incident CKD compared with non-AF [HR=1.477, 95%CI (1.208, 1.806), P<0.001]. After stratification by age, AF increased the risk of incident CKD in individuals aged $ $65 years [HR=1.566, 95%CI (1.024, 2.035), P=0.001], but not in those aged >65 years [HR=0.970, 95%CI (0.707, 1.330), P=0.855]. After further adjustment for age and sex (male) using multivariate Cox proportional hazards regression analysis, AF was no longer associated with an increased risk of CKD in the overall population or in those aged >65 years [HR=1.167, 95%CI (0.954, 1.428), P=0.133; HR=1.007, 95%CI (0.734, 1.381), P=0.968, respectively]. However, in individuals aged $ $65 years, AF remained associated with an increased risk of CKD [HR=1.363, 95%CI (1.048, 1.769), P=0.021]. After further adjustment for alcohol consumption, smoking, physical exercise, education level, history of hypertension, use of antihypertensive medication, history of diabetes, use of hypoglycemic medication, use of lipid-lowering medication, BMI, TG, HDL-C, LDL-C, FPG, and Hs-CRP using multivariate Cox proportional hazards regression analysis, AF increased the risk of CKD only in individuals aged $ $65 years [HR=1.351, 95%CI (1.038, 1.755), P=0.025].

Conclusion AF is an independent risk factor for incident CKD in the northern Chinese population, particularly among middle-aged and young individuals aged $ $65 years.

Full Text

Preamble

Study on the Risk of Atrial Fibrillation for New-Onset Chronic Kidney Disease in Northern China

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Abstract

Background: The Global Burden of Disease report indicates that atrial fibrillation (AF) and chronic kidney disease (CKD) have become among the fastest-growing causes of mortality over the past two decades. The concept of cardiorenal syndrome suggests that AF may increase the risk of new-onset CKD, yet few studies have examined this relationship, and the interaction with age remains unclear.

Objective: To investigate whether AF increases the risk of new-onset CKD in a northern Chinese population.

Methods: We conducted a prospective cohort study using data from employees of the Kailuan Group in Hebei Province who participated in health examinations between June 1, 2006, and October 30, 2010 (n=135,168, aged 18-98 years). After excluding 19,883 individuals with missing data or a history of CKD, and 4,430 individuals with prior cerebrovascular/cardiovascular disease, malignancy, or incident AF during follow-up, 110,855 participants were included. Participants were divided into AF (n=368) and non-AF (n=110,487) groups based on AF status at baseline. Annual follow-up was conducted through December 31, 2020, with a median follow-up duration of 13.46 (9.70, 14.05) years. The endpoint was new-onset CKD.

Results: (1) The AF group (n=368) had a mean age of 63.43$\pm$10.61$years and 338 males (91.85\pm12.92 years and 8$

P<0.001). The incidence density was 28.63 per 1,000 person-years in the AF group and 18.48 per 1,000 person-years in the non-AF group. (3) AF was associated with increased risk of new-onset CKD [HR=1.477, 95%CI (1.208, 1.806), P<0.001]. After age stratification, AF increased CKD risk in participants $ $65 years [HR=1.566, 95%CI (1.024, 2.035), P=0.001] but not in those >65 years [HR=0.970, 95%CI (0.707, 1.330), P=0.855]. After multivariate Cox proportional hazards regression adjusting for age and sex, AF no longer increased CKD risk in the overall population [HR=1.167, 95%CI (0.954, 1.428), P=0.133] or in those >65 years [HR=1.007, 95%CI (0.734, 1.381), P=0.968], but remained significant in those $ $65 years [HR=1.363, 95%CI (1.048, 1.769), P=0.021]. After further adjustment for alcohol intake, smoking, physical exercise, education level, hypertension history, antihypertensive medication use, diabetes history, hypoglycemic medication use, lipid-lowering medication use, BMI, TG, HDL-C, LDL-C, FPG, and Hs-CRP, AF remained an independent risk factor only in participants $ $65 years [HR=1.351, 95%CI (1.038, 1.755), P=0.025].

Conclusion: AF is an independent risk factor for new-onset CKD in northern Chinese populations, particularly among individuals aged $ $65 years.

Keywords: Atrial fibrillation; Chronic kidney disease; Risk factors; Epidemiology; Prospective cohort study

Introduction

The Global Burden of Disease 2019 report shows that the prevalence of atrial fibrillation has gradually increased over the past three decades, with the global disease burden doubling over the last decade to approximately 59.7 million cases. The 2013 Global Burden of Disease Study identified AF and CKD as among the fastest-growing causes of death over the previous 20 years. Epidemiological surveys indicate that the age-adjusted prevalence of AF among Chinese adults is 1.6%, with incidence increasing markedly with age; over 60% of elderly hypertensive patients will develop AF. AF increases stroke risk nearly fivefold and elevates risks of cardiac pump failure, acute coronary ischemic events, and dementia. According to the cardiorenal syndrome concept, AF may increase the risk of new-onset CKD. Domestic research has demonstrated that AF reduces glomerular filtration rate, while international studies show that AF accelerates CKD progression, that AF and CKD frequently coexist and worsen each other, and that vitamin K antagonists may exacerbate eGFR decline in CKD patients. However, no studies have examined whether AF increases the risk of new-onset CKD in the general population. This study aims to investigate whether AF increases the risk of new-onset CKD in a Chinese general population, providing evidence-based support for comprehensive AF management and CKD prevention.

Methods

Study Population

We selected participants from employees of the Kailuan Group in Hebei Province who underwent health examinations between 2006 and 2010 (n=135,168, aged 18-98 years). After excluding 19,883 individuals with missing data or a history of CKD, and 4,430 individuals with prior cerebrovascular or cardiovascular disease, malignancy, or incident AF during follow-up, 110,855 participants were included in the final analysis. Participants were divided into AF (n=368) and non-AF (n=110,487) groups based on AF status at baseline.

Inclusion Criteria

(1) AF diagnosis: Documentation of AF episodes lasting >30 seconds on Holter monitoring, standard surface ECG, or implanted cardiac rhythm recording devices. (2) CKD diagnosis: Estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2 and/or proteinuria.

Exclusion Criteria

(1) Malignancy, cerebrovascular or cardiovascular disease, or incident AF during follow-up. (2) Incomplete relevant data.

Data Collection

General Information A detailed questionnaire recorded participants' information including sex, age, family history within three generations, personal history (smoking, alcohol consumption), medical history (coronary heart disease, diabetes, hypertension, hyperlipidemia), anthropometric measurements (height, weight, blood pressure), and ECG examinations (standard surface ECG, Holter monitoring, cardiac rhythm recording devices). Smoking was defined as a history of $ $1 year with $ $1 cigarette daily, or former smoking with cessation <1 year. Alcohol consumption was defined as drinking for $ $1 year with average intake >1 standard drink daily (equivalent to 45 ml spirits/360 ml beer/120 ml wine), or former drinking with cessation <1 year.

Laboratory Biochemical Data All participants fasted for $ $8 hours, with blood samples collected between 6:00-7:00 AM. Five milliliters of elbow venous blood was drawn into EDTA anticoagulant tubes, centrifuged at 3,000 rpm for 10 minutes at room temperature (24°C) within 30 minutes, and serum was separated. Biochemical tests including total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and fasting plasma glucose (FPG) were completed within 4 hours. eGFR was calculated using the formula shown in .

Endpoint Event Collection Follow-up was conducted annually through December 31, 2020, with a median follow-up duration of 13.46 (9.70, 14.05) years. The endpoint was new-onset CKD.

Statistical Analysis

Statistical analysis was performed using SAS 9.4. Categorical data were expressed as n (%) and compared using ^{2} tests. Non-normally distributed continuous data were expressed as median (P25-P75) and compared using nonparametric tests. Normally distributed continuous data were expressed as mean ± standard deviation and compared using one-way ANOVA. Kaplan-Meier survival curves were generated using SAS 9.4 to calculate cumulative incidence of CKD events in AF and non-AF groups, with differences tested using Log-Rank tests. Multivariate Cox proportional hazards regression models were used to analyze the effect of AF on new-onset CKD risk. Statistical significance was defined as P<0.05 (two-tailed).

Results

Baseline Characteristics

The AF group (n=368) had a mean age of $63.43\$\pm10.61 years, while the non-AF group (n = 110,487) had a mean age of 49.04±$12.92 years. The groups differed significantly in age, sex distribution, SBP, DBP, TC, LDL-C, BMI, TG, Hs-CRP, hypertension, diabetes, alcohol consumption, education level (high school or above), physical exercise, antihypertensive medication use, and hypoglycemic medication use (P<0.01 or P<0.05). No significant differences were observed in FPG, HDL-C, smoking status, or lipid-lowering medication use (P>0.05) (see).

Incidence of New-Onset CKD

New-onset CKD occurred in 95 individuals in the AF group (cumulative incidence 30.40%) and 22,725 individuals in the non-AF group (cumulative incidence 21.77%). The difference in cumulative incidence was statistically significant (^{2}=14.30, P<0.001). The incidence density was 28.63 per 1,000 person-years in the AF group and 18.48 per 1,000 person-years in the non-AF group (see).

Multivariate Cox Proportional Hazards Regression Analysis

Using new-onset CKD (yes=1, no=0) as the dependent variable and AF status (yes=1, no=0) as the independent variable, we performed multivariate Cox regression analysis. Model 1 included only AF as the independent variable. Model 2 adjusted for age (continuous) and sex (male=1, female=0). Model 3 further

adjusted for smoking (yes=1, no=0), alcohol consumption (yes=1, no=0), physical exercise (yes=1, no=0), education level (high school or above=1, junior high or below=0), hypertension history (yes=1, no=0), antihypertensive medication use (yes=1, no=0), diabetes history (yes=1, no=0), hypoglycemic medication use (yes=1, no=0), lipid-lowering medication use (yes=1, no=0), BMI (continuous), TG (continuous), HDL-C (continuous), LDL-C (continuous), FPG (continuous), and Hs-CRP (continuous).

The results showed that AF increased the risk of new-onset CKD [HR=1.477, 95%CI (1.208, 1.806), P<0.001]. After age stratification, AF increased CKD risk in participants $ $65 years [HR=1.566, 95%CI (1.024, 2.035), P=0.001] but not in those >65 years [HR=0.970, 95%CI (0.707, 1.330), P=0.855]. After adjusting for age and sex, AF no longer increased CKD risk in the overall population [HR=1.167, 95%CI (0.954, 1.428), P=0.133] or in those >65 years [HR=1.007, 95%CI (0.734, 1.381), P=0.968], but remained significant in those $ $65 years [HR=1.363, 95%CI (1.048, 1.769), P=0.021]. After full multivariate adjustment, AF remained an independent risk factor only in participants $ $65 years [HR=1.351, 95%CI (1.038, 1.755), P=0.025] (see).

Cumulative Incidence Over Time

With extended follow-up, the cumulative incidence of new-onset CKD increased annually in the AF group compared to the non-AF group in both the overall population and participants $ $65 years (see [Figure 1: see original paper] and [Figure 2: see original paper]). No difference in cumulative incidence was observed between groups among participants >65 years (see [Figure 3: see original paper]).

Discussion

This study, based on the Kailuan cohort, is the first to demonstrate that AF is an independent risk factor for increased new-onset CKD risk in northern Chinese populations, particularly among individuals aged $ $65 years. Our findings align with previous research on the correlation between AF and glomerular filtration rate. One cross-sectional study of 150 AF patients and non-AF controls found that increasing AF burden was associated with stepwise reductions in eGFR (P<0.05), with multivariate regression confirming that AF reduces glomerular filtration rate. The same research group subsequently confirmed this relationship prospectively, showing that radiofrequency ablation and restoration of sinus rhythm in 121 AF patients (105 paroxysmal, 16 persistent) led to increased eGFR at 6 and 12 months post-procedure (P<0.05), demonstrating that rhythm control improves renal function in AF patients. International studies have primarily confirmed that AF accelerates CKD progression and that vitamin K antagonists accelerate renal function decline in CKD patients, with warfarin having a greater impact than dabigatran, particularly in diabetic patients with

prior vitamin K antagonist use. While age, male sex, BMI, SBP, LDL-C, TG, hypertension, diabetes, cardiovascular disease history, hyperuricemia, residential area, and economic status are established CKD risk factors, our study demonstrates that AF remains an independent risk factor for new-onset CKD even after adjusting for all these variables.

The pathophysiological mechanisms linking AF to new-onset CKD likely involve hemodynamic effects as the most fundamental factor. Rapid ventricular rates, severe bradycardia, and prolonged R-R intervals during rapid AF lead to loss of atrioventricular synchrony, impairing atrial booster pump function. This reduces ventricular preload and stroke volume, ultimately causing prerenal hypoperfusion. Although not the first organ to receive oxygenated blood, the kidneys receive 25% of cardiac output. Their low-resistance circulation requires sufficient pressure differential between afferent arterioles and efferent venules to maintain renal blood flow and glomerular filtration. The low-resistance properties of renal vasculature and parenchyma, combined with the extremely low oxygen tension of the outer medulla, explain the kidney' s unique susceptibility to hypotension-induced injury, which exacerbates reductions in GFR. Additionally, inadequate renal afferent arterial flow activates the renin-angiotensin-aldosterone system (RAAS), increases sympathetic nervous system activity and arginine vasopressin secretion, enhances proximal tubular sodium and water reabsorption, and promotes fluid retention. This increases cardiac preload, further deteriorates cardiac pump function, and ultimately leads to oliguria and worsening congestive heart failure to maintain effective plasma volume. These renal hemodynamic regulatory mechanisms also explain elevated serum creatinine levels, supporting the cardiorenal syndrome framework and confirming that AF and CKD frequently coexist and worsen each other. Blood pressure fluctuations, which are more pronounced in AF patients, increase mechanical stress and tangential tension on arterial walls, promoting intimal and medial fibromuscular thickening and luminal narrowing that accelerate atherosclerotic progression, including renal artery involvement, ultimately reducing GFR.

The irregular cardiac contraction and relaxation during AF triggers dramatic arterial pressure fluctuations, promoting adverse systemic arterial remodeling and activating circulating RAAS. This can induce renal arteriolar fibrosis and, due to systemic fibrotic tendencies, lead to renal fibrosis and impaired renal function, increasing CKD risk through reduced GFR. Significant blood pressure variability in AF patients also activates vasoactive hormones and humoral factors, including increased angiotensin, catecholamine, and prostaglandin levels, which may contribute to atherosclerotic disease pathogenesis. Additionally, inflammatory cytokines and prothrombotic states exacerbate cardiovascular and cerebrovascular ischemic events. Chronic AF is associated with accelerated atherosclerosis, though it remains unclear whether this systemic inflammation results directly from AF or from the higher burden of cardiovascular risk factors in AF patients, as inflammation likely plays a pathogenic role in both conditions.

Thromboembolism may also importantly contribute to AF-related CKD risk.

Reduced left atrial flow velocity in AF patients causes blood stasis in the left atrial appendage, increasing local coagulation factor concentration and activation, raising blood viscosity, and promoting erythrocyte and platelet aggregation. Collagen in subendothelial connective tissue and tissue thromboplastin released from damaged atrial walls facilitate conversion of fibrinogen to fibrin, increasing thrombosis risk. As atrial enlargement progresses, damaged endothelium becomes exposed, extracellular matrix becomes edematous, and fibrocellular infiltration occurs, predisposing to left atrial platelet thrombus formation that can embolize to renal arteries.

Aging naturally leads to declining GFR in the general population, with proteinuria and CKD incidence increasing with age. Studies show that each additional year of age increases CKD risk by 5.5% (95% CI: 1.053-1.057), with CKD prevalence increasing across age groups (young, middle-aged, elderly) to 6.8%, 9.5%, and 24.4% in men and 7.6%, 14.5%, and 34.1% in women, respectively (all P<0.001). Therefore, we performed age-stratified analyses, which revealed that AF is an independent CKD risk factor in those $ $65 years (HR=1.351, 95% CI: 1.038-1.755, P=0.025) but not in those >65 years (HR=1.009, 95% CI: 0.735-1.384, P=0.957), suggesting that aging may attenuate the impact of AF on new-onset CKD risk.

Limitations and Strengths: First, the Kailuan Industrial Group comprises primarily mining and heavy manufacturing industries, resulting in a male-predominant study population; future analyses will include sex matching to minimize potential bias from this imbalance. Second, transient AF episodes may have gone undetected. However, the large sample size and long follow-up duration provide substantial scientific value.

In conclusion, AF and CKD are common cardiorenal diseases that severely threaten human health and produce various adverse outcomes. This study demonstrates that AF is an independent risk factor for new-onset CKD in the general population, particularly among those $ $65 years. Given the substantial family and societal impact of CKD in this age group, scientific AF management, rigorous control of related risk factors, and early AF intervention are essential to reduce CKD incidence, improve quality of life, and extend survival.

References

1. Roth GA, Mensah GA, Johnson CO, et al. Global burden of cardiovascular diseases and risk factors, 1990-2019: update from the GBD 2019 Study [J]. J Am Coll Cardiol, 2020, 76(25): 2982-3021. DOI: 10.1016/j.jacc.2020.11.010.

2. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Bur-

den of Disease Study 2013[J]. Lancet, 2015, 385(9963): 117-171. DOI: 10.1016/S0140-6736(14)61682-2.

3. Shi S, Tang Y, Zhao Q, et al. Prevalence and risk of atrial fibrillation in China: A national cross-sectional epidemiological study[J]. Lancet Reg Health West Pac, 2022, 23: 100439. DOI: 10.1016/j.lanwpc.2022.100439.

4. Psaty BM, Manolio TA, Kuller LH, et al. Incidence of and risk factors for atrial fibrillation in older adults[J]. Circulation, 1997 Oct 7, 96(7): 2455-61. DOI: 10.1161/01.cir.96.7.2455.

5. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study[J]. JAMA, 2001 May 9, 285(18): 2370-5. DOI: 10.1001/jama.285.18.2370.

6. Staerk L, Sherer JA, Ko D, et al. Atrial Fibrillation: Epidemiology, Pathophysiology, and Clinical Outcomes[J]. Circ Res, 2017 Apr 28, 120(9): 1501-1517. DOI: 10.1161/CIRCRESAHA.117.309732.

7. Lippi G, Sanchis-Gomar F, Cervellin G. Global epidemiology of atrial fibrillation: An increasing epidemic and public health challenge[J]. Int J Stroke, 2021 Feb, 16(2): 217-221. DOI: 10.1177/1747493019897870.

8. Thihalolipavan S, Morin DP. Atrial fibrillation and congestive heart failure[J]. Heart Fail Clin, 2014 Apr, 10(2): 305-18. DOI: 10.1016/j.hfc.2013.12.005.

9. Wu J, Hou Q, Han Q, et al. Atrial fibrillation is an independent risk factor for new-onset myocardial infarction: a prospective study[J]. Acta cardiologica, 2022: 1-8. DOI: 10.1080/00015385.2022.2129184.

10. Bunch TJ, Weiss JP, Crandall BG, et al. Atrial fibrillation is independently associated with senile, vascular, and Alzheimer's dementia[J]. Heart Rhythm, 2010 Apr, 7(4): 433-7. DOI: 10.1016/j.hrthm.2009.12.004.

11. Rangaswami J, Bhalla V, Blair JEA, et al. Cardiorenal Syndrome: Classification, Pathophysiology, Diagnosis, and Treatment Strategies: A Scientific Statement From the American Heart Association[J]. Circulation, 2019, 139(16): e840-e878. DOI: 10.1161/CIR.0000000000000664.

12. Han Q, Mao R, Cao L, et al. Study on the correlation between atrial fibrillation and glomerular filtration rate[J]. Modern Preventive Medicine, 2017, 44(05): 947-949+953.

13. Fauchier L, Bisson A, Clementy N, et al. Changes in glomerular filtration rate and outcomes in patients with atrial fibrillation[J]. American heart journal, 2018, 198: 39-45. DOI: 10.1016/j.ahj.2017.12.017.

14. Banerjee A, Fauchier L, Vourc' h P, et al. A prospective study of estimated glomerular filtration rate and outcomes in patients with atrial fibrillation:

the Loire Valley Atrial Fibrillation Project[J]. Chest, 2014, 145(6): 1370-1382. DOI: 10.1378/chest.13-2103.

15. Murphy A, Banerjee A, Breithardt G, et al. The World Heart Federation Roadmap for Nonvalvular Atrial Fibrillation[J]. Glob Heart, 2017 Dec, 12(4): 273-284. DOI: 10.1016/j.gheart.2017.01.015.

16. Chugh SS, Roth GA, Gillum RF, et al. Global Burden of Atrial Fibrillation in Developed and Developing Nations[J]. Glob Heart, 2014, 9(1): 113-119. DOI: 10.1016/j.gheart.2014.01.004.

17. Chinese Society of Pacing and Electrophysiology, Chinese Association of Arrhythmia, Chinese Atrial Fibrillation Center Alliance. Atrial fibrillation: current understanding and treatment recommendations (2021)[J]. Chinese Journal of Cardiac Arrhythmias, 2022, 26(01): 15-88. DOI: 10.3760/cma.j.cn113859-20211224-00264.

18. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate[J]. Ann Intern Med, 2009, 150(9): 604-612. DOI: 10.7326/0003-4819-150-9-200905050-00006.

19. Zhang C, Gao J, Guo Y, et al. Association of atrial fibrillation and clinical outcomes in adults with chronic kidney disease: A propensity score-matched analysis[J]. PloS one, 2020, 15(3): e0230189. DOI: 10.1371/journal.pone.0230189.

20. Han Q, Mao R, Cao L, et al. Effect of radiofrequency ablation on glomerular filtration rate in patients with non-valvular atrial fibrillation[J]. Chinese Journal of Arteriosclerosis, 2017, 25(12): 1242-1246.

21. Potpara TS, Ferro CJ, Lip GYH. Use of oral anticoagulants in patients with atrial fibrillation and renal dysfunction[J]. Nat Rev Nephrol, 2018, 14(5): 337-351. DOI: 10.1038/nrneph.2018.19.

22. Fauchier L, Bisson A, Clementy N, et al. Changes in glomerular filtration rate and outcomes in patients with atrial fibrillation[J]. Am Heart J, 2018, 198: 39-45. DOI: 10.1016/j.ahj.2017.12.017.

23. Böhm M, Ezekowitz MD, Connolly SJ, et al. Changes in Renal Function in Patients With Atrial Fibrillation: An Analysis From the RE-LY Trial[J]. J Am Coll Cardiol, 2015, 65(23): 2481-2493. DOI: 10.1016/j.jacc.2015.03.577.

24. Han Q, Zhang D, Mao R, et al. Research on the prevalence of chronic kidney disease and risk factors in northern populations of China[J]. Int J Clin Exp Med, 2018, 11(8): 8585-8592.

25. Zhang L, Wang F, Wang L, et al. Prevalence of chronic kidney disease in China: a cross-sectional survey[J]. Lancet (London, England), 2012, 379(9818): 815-822. DOI: 10.1016/S0140-6736(12)60033-6.

26. Khatib R, Joseph P, Briel M, et al. Blockade of the renin-angiotensin-aldosterone system (RAAS) for primary prevention of non-valvular atrial fibrillation: a systematic review and meta-analysis of randomized controlled trials[J]. Int J Cardiol, 2013, 165(1): 17-24. DOI: 10.1016/j.ijcard.2012.02.009.

27. Hollander W. Role of hypertension in atherosclerosis and cardiovascular disease[J]. Am J Cardiol, 1976 Nov 23, 38(6): 786-800. DOI: 10.1016/0002-9149(76)90357-x.

28. Burstein B, Qi XY, Yeh YH, et al. Atrial cardiomyocyte tachycardia alters cardiac fibroblast function: a novel consideration in atrial remodeling[J]. Cardiovasc Res, 2007, 76(3): 442-452. DOI: 10.1016/j.cardiores.2007.07.013.

29. Zuo H, Nygård O, Ueland PM, et al. Association of plasma neopterin with risk of an inpatient hospital diagnosis of atrial fibrillation: results from two prospective cohort studies[J]. J Intern Med, 2018, 283(6): 578-587. DOI: 10.1111/joim.12748.

30. Fatkin D, Kelly R, Feneley MP. Left atrial appendage blood velocity and thromboembolic risk in patients with atrial fibrillation[J]. J Am Coll Cardiol, 1994 Nov 1, 24(5): 1429-1430. DOI: 10.1016/0735-1097(94)90133-3.

31. D'Souza A, Butcher KS, Buck BH. The Multiple Causes of Stroke in Atrial Fibrillation: Thinking Broadly[J]. Can J Cardiol, 2018, 34(11): 1503-1511. DOI: 10.1016/j.cjca.2018.08.036.

32. Cohen E, Nardi Y, Krause I, et al. A longitudinal assessment of the natural rate of decline in renal function with age[J]. J Nephrol, 2014, 27(6): 635-641. DOI: 10.1007/s40620-014-0077-9.

33. Fox CS, Larson MG, Leip EP, et al. Predictors of new-onset kidney disease in a community-based population[J]. JAMA, 2004, 291(7): 844-850. DOI: 10.1001/jama.291.7.844.

34. Chen Y, Shen F, Chen S, Zheng Y. Analysis of renal function and related risk factors in hospitalized patients aged 80 years and older[J]. Chinese Journal of Geriatrics, 2015, 34(05): 530-533. DOI: 10.3760/cma.j.issn.0254-9026.2015.05.019

Note: Figure translations are in progress. See original paper for figures.