

## Postprint: Impact of Atrial Fibrillation on the Risk of Incident Myocardial Infarction in Hypertensive Populations

**Authors:** Yue Bocheng, Hou Qiqi, Han Quanle, Yang Bo, Wu Zheng, Wu Jianmei, Chen Shuohua, Wu Shouling

**Date:** 2022-10-28T00:00:00+00:00

### Abstract

**Background:** Global epidemiological studies have demonstrated that by 2019, the number of patients with hypertension worldwide had reached 1.28 billion, while patients with atrial fibrillation (AF) numbered approximately 59.7 million. Hypertension substantially increases the risk of AF, particularly among elderly hypertensive patients where the incidence of AF exceeds 60%. Concurrently, AF increases the risk of ischemic stroke, heart failure, myocardial infarction, chronic kidney disease, and dementia. For the vast hypertensive population, whether the development of AF increases the risk of new-onset myocardial infarction has been insufficiently studied, and whether this risk exhibits an interaction with age remains unclear.

**Objective:** To investigate and analyze whether AF in hypertensive populations increases the risk of new-onset myocardial infarction.

**Methods:** A prospective cohort study design was employed. From June 1, 2006 to October 31, 2007, 47101 hypertensive patients were selected from health examination populations of Kailuan Group employees. After excluding 2443 individuals with prior cardiovascular or cerebrovascular disease, 192 with malignant tumors, 860 with missing electrocardiographic data, and 773 who developed AF during follow-up, a total of 42833 individuals were included in the study. Annual follow-up was conducted, with new-onset myocardial infarction as the endpoint event. The final follow-up date was December 31, 2019, with a median follow-up duration of 13.01 years. Statistical analysis was performed to determine the effect of AF in hypertensive populations on the risk of new-onset myocardial infarction.

**Results:** (1) Ultimately, 42833 hypertensive patients were included and divided into AF and non-AF groups. The AF group comprised 270 individuals, aged

67.24±10.60 years, including 241 males (89.26±11.59 years, including 36132 males (84.89±10.05).

- (2) The number and proportion of new-onset myocardial infarction cases in the AF and non-AF groups were 15 cases (5.56%) and 1119 cases (2.63%), respectively. The follow-up person-years were 2737.20 and 547156.40, respectively. The cumulative incidence rates were 7.06% and 2.60%, respectively, with a statistically significant difference ( $\chi^2=15.48, P<0.01$ ). The incidence densities were 54.80‰ and 20.50‰. In the population aged  $\geq 60$  years, the number and proportion of new-onset myocardial infarction cases in the AF and non-AF groups were 6 cases (8.21%)<sup>{2}</sup> = 15.43,  $P < 0.01$ . The incidence densities were 48.74‰ and 33.05‰.  $P=0.28$ .
- (3) Proportional hazards regression model analysis revealed: After further adjustment for age, gender (male), BMI, TC, TG, diabetes history, alcohol consumption history, smoking history, and other factors, AF in hypertensive populations was identified as a risk factor for new-onset myocardial infarction, with an HR of 2.89 (95%CI: 1.74~4.82), and the associated risk remained significant ( $P<0.01$ ). Considering the interaction between age and AF, multivariate Cox proportional hazards regression analysis by age group demonstrated: For the population aged  $\geq 60$  years, after further adjustment for gender (male), BMI, TC, TG, diabetes history, alcohol consumption history, smoking history, and other factors, AF in hypertensive populations was identified as a risk factor for new-onset myocardial infarction, with an HR of 4.72 (95%CI: 2.11~10.56), and the associated risk was significantly present ( $P<0.01$ ). For the population aged  $>60$  years, after further adjustment for gender (male), BMI, TC, TG, diabetes history, alcohol consumption history, smoking history, and other factors, AF in hypertensive populations was identified as a risk factor for new-onset myocardial infarction, with an HR of 1.65 (95%CI: 0.85~3.20). The associated risk remained but was not statistically significant ( $P=0.14$ ).

Conclusion: AF in hypertensive populations in northern China constitutes a risk factor for new-onset myocardial infarction, particularly among hypertensive individuals aged  $\geq 60$  years, where AF represents an independent risk factor for new-onset myocardial infarction.

## Full Text

### Preamble

#### Effect of Atrial Fibrillation on the Risk of New-Onset Myocardial Infarction in Hypertensive Population

YUE Bocheng<sup>1</sup>, HOU Qiqi<sup>2</sup>, HAN Quanle<sup>1\*</sup>, YANG Bo<sup>1</sup>, WU Zheng<sup>3</sup>, WU Jianmei<sup>4</sup>, CHEN Shuohua<sup>5</sup>, WU Shouling<sup>5</sup>, LI Kangbo<sup>6</sup>

<sup>1</sup>Department of Cardiology, Tangshan Gongren Hospital, Tangshan 063000, China

<sup>2</sup>Department of Cardiology, Tangshan Gongren Hospital, Hebei Medical University, Tangshan 063000, China

<sup>3</sup>Department of Hepatobiliary Surgery, Tangshan Gongren Hospital, Tangshan 063000, China

<sup>4</sup>Department of Cardiac Surgery, Tangshan Gongren Hospital, Tangshan 063000, China

<sup>5</sup>Department of Cardiology, Kailuan General Hospital, Tangshan 063000, China

<sup>6</sup>School of Clinical Medicine, North China University of Science and Technology, Tangshan 063000, China

\*Corresponding author: HAN Quanle, Associate Professor, Master's Supervisor, Email: hanquanle@126.com

**Funding:** Key Medical Science and Technology Research Project of Hebei Province (20221777)

---

## Abstract

**Background:** Global epidemiological research indicates that by 2019, the number of hypertensive patients worldwide had reached 1.28 billion, while approximately 59.7 million people suffered from atrial fibrillation (AF). Hypertension substantially increases the risk of AF, with the incidence exceeding 60% among elderly hypertensive patients. Concurrently, AF elevates the risk of ischemic stroke, heart failure, myocardial infarction, chronic kidney disease, and dementia. However, few studies have examined whether AF increases the risk of new-onset myocardial infarction (MI) in the large hypertensive population, and whether this risk interacts with age remains unclear.

**Objective:** To investigate whether AF increases the risk of new-onset MI in hypertensive patients.

**Methods:** We conducted a prospective cohort study selecting 47,101 hypertensive patients from employees of Kailuan Group who underwent health examinations between June 1, 2006, and October 31, 2007. After excluding 2,443 patients with prior cardiovascular or cerebrovascular disease, 192 with malignant tumors, 860 with missing electrocardiogram data, and 773 who developed AF during follow-up, 42,833 patients were included in the final analysis. Participants were followed up annually, with new-onset MI as the endpoint event. The final follow-up date was December 31, 2019, with a median follow-up duration of 13.01 years. Statistical analysis was performed to assess the impact of AF on new-onset MI risk in the hypertensive population.

**Results:** (1) A total of 42,833 hypertensive patients were included and divided into AF and non-AF groups. The AF group comprised 270 patients (age  $67.24 \pm 10.60$  years, 241 males [ $89.26 \pm 11.59$  years], 36, 132 females [ $84.89 \pm 10.05$  years]).

- (2) New-onset MI occurred in 15 patients (5.56%) in the AF group and 1,119 patients (2.63%) in the non-AF group. The follow-up person-years were 2,737.20 and 547,156.40, respectively, with cumulative incidence rates of 7.06% and 2.60% ( $\chi^2=15.48, P<0.01$ ). The incidence density was 54.80‰ and 20.50‰, respectively. In participants aged  $\geq 60$  years, new-onset MI occurred in 6 AF patients (8.21‰) ( $\chi^2=15.43, P<0.01$ ), and incidence density of 67.35‰ and 15.54‰, respectively. In participants aged  $<60$  years, new-onset MI occurred in 9 AF patients (8.21‰) ( $\chi^2=0.01, P=0.28$ ), and incidence density of 48.74‰ and 33.05‰, respectively.
- (3) Multivariate Cox proportional hazards regression analysis, after adjusting for age, gender (male), BMI, TC, TG, diabetes history, alcohol consumption, and smoking, demonstrated that AF in hypertensive patients was a risk factor for new-onset MI (HR=2.89, 95%CI: 1.74-4.82,  $P<0.01$ ). Considering the interaction between age and AF, stratified analysis showed that in participants aged  $\geq 60$  years, AF remained a significant risk factor after multivariate adjustment (HR=4.72, 95%CI: 2.11-10.56,  $P<0.01$ ). In those aged  $>60$  years, AF was associated with increased risk but without statistical significance (HR=1.65, 95%CI: 0.85-3.20,  $P=0.14$ ).

**Conclusion:** AF is a risk factor for new-onset MI in hypertensive populations, particularly serving as an independent risk factor in hypertensive patients aged  $\geq 60$  years.

**Keywords:** Cardiology; Hypertension; Atrial fibrillation; New-onset myocardial infarction; Risk factors

---

## Introduction

The global prevalence of hypertension remains high. Data from 1,201 population-representative studies across 184 countries show that by 2019, the number of hypertensive patients worldwide had reached 1.28 billion [1], while global AF cases numbered approximately 59.7 million [2]. The Global Burden of Disease report identifies atrial fibrillation as one of the fastest-growing causes of mortality [3]. Epidemiological surveys of natural populations in 13 Chinese provinces and cities indicate that AF prevalence increases with age, affecting approximately 7.5% of individuals over 80 years [4]. The incidence of AF in elderly hypertensive patients exceeds 60% [5,6]. Studies demonstrate that AF increases the risk of ischemic stroke, heart failure, chronic kidney disease, cognitive dysfunction, and dementia [7-10]. While AF increases new-onset MI risk in the general population, research on its age-related correlation has yielded inconsistent conclusions [11,12]. Few studies have examined the relationship between AF and new-onset MI risk specifically in hypertensive populations. This study aims to investigate whether AF increases new-onset MI risk in hypertensive patients and whether age interacts with this relationship, providing data support for primary prevention of new-onset MI in hypertensive patients with AF.

### 1.1 Study Population

We selected 47,101 hypertensive patients from employees of Kailuan Group who underwent health examinations between June 2006 and October 2007. After excluding 2,443 patients with prior cardiovascular or cerebrovascular disease, 192 with malignant tumors, 860 with missing ECG data, and 773 who developed AF during follow-up, 42,833 patients were included in the final analysis. Patients were divided into AF and non-AF groups based on standard ECG diagnostic criteria for atrial fibrillation.

### 1.2 Inclusion Criteria

- (1) Age  $\geq$  18 years;
- (2) Hypertension diagnosis based on current antihypertensive medication use or, in the absence of medication, blood pressure measurements on different dates exceeding normal reference values (SBP  $\geq$  140 mmHg and/or DBP  $\geq$  90 mmHg) [13];
- (3) AF diagnosis: AF episodes recorded on standard ECG, Holter monitoring, or other cardiac recording devices (wearable or implanted) lasting  $>$ 30 seconds [14];
- (4) MI diagnosis: Presence of acute myocardial ischemia symptoms (typically  $>$ 10-20 minutes) with at least one serum cardiac troponin value above the upper limit of normal (99th percentile of reference values) [15];
- (5) Provided informed consent to participate in the study.

### 1.3 Exclusion Criteria

- (1) Patients who developed AF during follow-up;
- (2) Patients with cardiovascular or cerebrovascular disease, malignant tumors, severe hepatic or renal insufficiency, or immune system diseases;
- (3) Patients with incomplete research data.

#### 1.4.1 General Data Collection

Trained physicians conducted face-to-face interviews and completed questionnaires. Demographic data included age, gender, height, weight, personal history (smoking, alcohol consumption), past medical history (hypertension, diabetes, dyslipidemia), and ECG examinations (Holter or other cardiac monitoring data). Alcohol consumption was defined as  $>$ 1 standard drink per day (equivalent to 45 ml spirits/360 ml beer/120 ml wine) for  $>$ 1 year, including those who had quit

drinking within the past year. Smoking history was defined as  $\geq 1$  cigarette daily for  $>1$  year.

#### 1.4.2 Laboratory Data Collection

All participants provided 5 ml of fasting venous blood after 12 hours of fasting. Blood was collected in EDTA tubes, centrifuged at 3,000 rpm for 10 minutes within 30 minutes at room temperature, and serum was tested within 4 hours. Measurements included serum total cholesterol (TC), triglycerides (TG), fasting plasma glucose (FPG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). The estimated glomerular filtration rate (eGFR) was calculated using the formula shown in .

#### 1.5 Statistical Analysis

Data were analyzed using SAS 9.4 software. Categorical variables were expressed as n(%) and compared using  $\chi^2$  tests. Normally distributed continuous variables were expressed as mean $\pm$ SD and compared using t-tests. Non-normally distributed continuous variables were expressed as M(P25, P75) and compared using nonparametric tests. Cox proportional hazards regression models were used to analyze the effect of AF on new-onset MI risk.  $P \leq 0.05$  (two-sided) was considered statistically significant.

## Results

### 2.1 Baseline Characteristics

Patients were divided into AF and non-AF groups. The AF group included 270 patients (age  $67.24 \pm 10.60$  years, 241 males [89.26%], 36 females [13.33%]). Significant differences between groups were observed in age, DBP, TC, TG, LDL-C, and eGFR ( $P < 0.05$ ). No significant differences were found in male gender, FPG, SBP, BMI, HDL-C, smoking, alcohol consumption, or diabetes history ( $P > 0.05$ ) (see ).

New-onset MI occurred in 15 patients (5.56%) in the AF group and 1,119 patients (2.63%) in the non-AF group. Follow-up person-years were 2,737.20 and 547,156.40, respectively, with cumulative incidence rates of 7.06% and 2.60% ( $\chi^2 = 15.48$ ,  $P < 0.01$ ). The incidence density was 54.80‰ and 20.50‰, respectively. In participants aged  $\geq 60$  years, new-onset MI occurred in 6 AF patients ( $\chi^2 = 15.43$ ,  $P < 0.01$ ), and incidence density of 67.35‰ and 15.54‰, respectively. In particular,  $P = 0.28$ , and incidence density of 48.74‰ and 33.05‰, respectively (see ).

### 2.2 Multivariate Analysis

Using new-onset MI (yes=1, no=0) as the dependent variable and AF (yes=1, no=0) as the independent variable, multivariate Cox proportional hazards regression analysis adjusting for age, gender (male=1, female=0), BMI, TC, TG, diabetes (yes=1, no=0), alcohol consumption (yes=1, no=0), and smoking

(yes=1, no=0) showed that AF was a risk factor for new-onset MI in hypertensive patients (HR=2.89, 95%CI: 1.74-4.82,  $P<0.01$ ). Considering the interaction between age and AF, stratified analysis revealed that in participants aged  $\leq 60$  years, AF was a significant risk factor after multivariate adjustment (HR=4.72, 95%CI: 2.11-10.56,  $P<0.01$ ). In those aged  $>60$  years, AF was associated with increased risk but without statistical significance (HR=1.65, 95%CI: 0.85-3.20,  $P=0.14$ ) (see ).

## Discussion

This study demonstrates that AF is an independent risk factor for new-onset MI in hypertensive populations. After adjusting for gender (male), BMI, TC, TG, eGFR, diabetes history, alcohol consumption, and smoking, the association remained significant (HR=2.89, 95%CI: 1.74-4.82,  $P<0.01$ ). Notably, in hypertensive patients aged  $\leq 60$  years with AF, the risk of new-onset MI was markedly increased after multivariate adjustment (HR=4.72, 95%CI: 2.11-10.56,  $P<0.01$ ). These findings align with previous studies showing AF as an independent risk factor for new-onset MI in the general population [11,12].

The underlying mechanisms are primarily pathophysiological. During AF, the atrioventricular sequence of contraction and relaxation is lost, eliminating atrial kick and reducing ventricular filling. This decreases left ventricular ejection fraction and aortic pressure, impairing coronary perfusion during diastole and exacerbating myocardial ischemia [16,17]. Sustained rapid ventricular rates during AF increase myocardial energy consumption, remodeling, and ischemia [18,19]. Irregular atrioventricular contraction and relaxation cause adverse myocardial and coronary vascular remodeling while activating the renin-angiotensin-aldosterone system, leading to coronary fibrosis. Mechanical torsion increases atherosclerotic plaque instability and rupture risk, elevating the likelihood of acute thrombotic events [20-22]. Thromboembolism plays a crucial role in AF-related MI risk. Reduced left atrial flow velocity during AF creates stasis and vortex formation, with continuous impact forces damaging atrial endothelium. This exposes the extracellular matrix, facilitating coagulation factor activation and thrombus formation through both intrinsic and extrinsic pathways [23]. These mechanisms are consistent with Ilia R et al. [24], who found that AF patients with MI were predominantly elderly women with cardiovascular risk factors and valvular heart disease, often showing single-vessel coronary disease on angiography, suggesting thromboembolic etiology.

Beyond these pathophysiological mechanisms, other pathways require further investigation. Hypertension is a well-established risk factor for MI [25,26]. To exclude its confounding effect, this study specifically examined the hypertensive population. Acute MI represents the most severe manifestation of coronary atherosclerosis, typically resulting from plaque rupture and acute thrombosis. A study investigating AF's relationship with coronary atherosclerosis progression and major cardiovascular events [27] analyzed data from 4,966 coronary

artery disease patients undergoing PCI. Using intravascular ultrasound to assess atherosclerotic burden at 18-24 month intervals and propensity-weighted analysis, the study found that AF patients had lower baseline and progression rates of atherosclerotic volume but higher MI risk (HR=2.41, 95%CI: 1.74-3.35,  $P<0.001$ ) and major adverse cardiovascular event risk (HR=2.2, 95%CI: 1.66-2.92,  $P<0.001$ ). Kaplan-Meier analysis showed significantly higher two-year cumulative incidence of major adverse cardiovascular events (4.4% vs. 2.0%, log-rank  $P=0.02$ ) and MI (3.3% vs. 1.5%, log-rank  $P=0.05$ ) in AF patients. These findings suggest that AF increases MI risk independent of atherosclerotic burden, possibly through mechanical torsion causing plaque instability and rupture. Our results are consistent: new-onset MI incidence was 5.56% in the AF group versus 2.63% in the non-AF group, with cumulative incidence rates of 7.06% and 2.60% ( $\chi^2=15.48$ ,  $P<0.01$ ) and incidence density of 54.80‰ and 20.50‰, respectively. In participants aged  $\geq 60$  years, the incidence was  $8.21\% \pm 15.43$ ,  $P<0.01$ ) and incidence density of 67.35‰ and 15.54‰, respectively. These findings suggest that AF-related MI risk is not strongly correlated with coronary atherosclerosis, indicating other powerful influencing factors.

This study also identified male gender as a risk factor for new-onset MI in hypertensive patients with AF, contrasting with Soliman, E. Z. et al. [12], who found that AF increased MI risk, particularly in women and Black individuals. Their study of 23,928 participants aged  $>45$  years without prior coronary disease followed for 6.9 years showed that AF increased MI risk by 70% after adjusting for cardiovascular risk factors (HR=1.96, 95%CI: 1.52-2.52,  $P<0.001$ ). A meta-analysis of 30 studies with 4,371,714 participants [28] similarly concluded that women with AF have higher cardiovascular disease and mortality risk than men. These differences may reflect physiological and psychosocial variations between genders, such as women's higher risk of torsades de pointes and fatal events from antiarrhythmic medications [29], and evidence that smoking and diabetes confer greater coronary and stroke risk in women than men [30,31]. The Kailuan study population's male predominance (approximately 4:1 ratio) may have influenced these results; propensity-matched analyses in future studies may yield more consistent conclusions.

Our finding that AF significantly increased new-onset MI risk in hypertensive patients aged  $\geq 60$  years aligns with Hao Yujing et al. [11], who reported age-related AF risk (HR=2.11, 95%CI: 1.69-2.62,  $P<0.01$ ) in the general population, and with Han Quanle et al. [32], who identified age as a risk factor for acute MI in younger populations. However, our results differ from Soliman, E. Z. et al. [12], possibly because their study included only middle-aged participants ( $>45$  years), limiting the expression of age-related risk. In participants aged  $>60$  years, AF remained a risk factor (HR=1.65, 95%CI: 0.85-3.20,  $P=0.14$ ) but without statistical significance, likely because other MI risk factors such as hypertension, diabetes, and dyslipidemia accumulate with age, attenuating AF's independent effect.

This study identified age, BMI, smoking, TC, TG, eGFR, and diabetes history

as risk factors for new-onset MI across all hypertensive patients with AF, consistent with previous research [33-35]. Although AF-related MI risk appears independent of atherosclerotic burden [24], atherosclerosis remains the fundamental mechanism of MI. LDL-C is the primary atherogenic lipid component, while overweight and obesity promote metabolic syndrome, glucose intolerance, and diabetes, exacerbating endothelial injury and atherosclerosis. Atherosclerosis involving renal arteries reduces eGFR, which correlates with cardiovascular events in hypertensive patients [36]. In elderly individuals, reduced eGFR is independently associated with all-cause mortality, vascular mortality, and fatal and non-fatal coronary and heart failure events [37]. Smoking and secondhand smoke damage coronary endothelium and cause vasospasm, increasing MI risk [34,35].

Interestingly, alcohol consumption appeared protective against new-onset MI in this population (HR=0.75, 95%CI: 0.66-0.86,  $P<0.01$ ), consistent with Han Quanle et al. [32]. This may reflect moderate drinking patterns in the Kailuan population, as alcohol can dilate vessels, increase heart rate, improve circulation, and relieve stress when consumed in moderation. In contrast, studies identifying alcohol as a risk factor [38] typically included heavy drinkers, where high alcohol concentrations disrupt hemodynamics, reduce fibrinolytic components, impair endothelial function, and trigger coronary spasm, leading to hypercoagulability and thrombosis. In participants aged  $>60$  years, BMI (HR=1.02, 95%CI: 0.99-1.05,  $P=0.18$ ), smoking (HR=1.05, 95%CI: 0.77-1.37,  $P=0.64$ ), and alcohol consumption (HR=0.81, 95%CI: 0.61-1.07,  $P=0.14$ ) were no longer significant risk or protective factors, suggesting that risk factor profiles and weights change with age, requiring age-specific prevention strategies.

**Strengths:** This study utilized the large Kailuan cohort with long-term follow-up, yielding highly valuable scientific results. **Limitations:** First, the Kailuan Group's heavy industry workforce is predominantly male. Second, transient AF episodes may have been missed. Third, anticoagulant use in AF patients during that period was very low in China [39,40], potentially underestimating MI risk. These factors may introduce bias, which future studies will address through propensity matching.

In conclusion, hypertension, AF, and MI are common cardiovascular diseases that severely threaten human health. This study demonstrates that AF is an independent risk factor for new-onset MI in hypertensive patients, particularly those aged  $\geq 60$  years. Scientific management of these conditions, including blood pressure control and AF treatment, is essential for primary and secondary prevention of MI.

**Author Contributions:** YUE Bocheng and HAN Quanle conceived the study design and research proposal. HOU Qiqi, LI Kangbo, and WU Shouling conducted literature searches. YUE Bocheng, HOU Qiqi, YANG Bo, WU Zheng, and WU Jianmei collected data and conducted physical examinations. CHEN Shuhua and HOU Qiqi performed data analysis. YUE Bocheng drafted the manuscript. HAN Quanle revised the final version and takes overall responsibility.

ity.

**Conflict of Interest:** None declared.

---

## References

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants [J]. *Lancet* (London, England), 2021,398(10304):957-980. DOI:10.1016/S0140-6736(21)01330-1.
2. 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.
3. 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 Burden of Disease Study 2013 [J]. *Lancet* (London, England), 2015,385(9963):117-171. DOI:10.1016/S0140-6736(14)61682-2.
4. Zhou Z, Hu D. An epidemiological study on the prevalence of atrial fibrillation in the Chinese population of mainland China [J]. *J Epidemiol*, 2008,18(5):209-216. DOI:10.2188/jea.JE2008021.
5. Psaty BM, Manolio TA, Kuller LH, et al. Incidence of and risk factors for atrial fibrillation in older adults [J]. *Circulation*, 1997,96(7):2455-2461. DOI:10.1161/01.cir.96.7.2455.
6. 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*, 2001,285(18):2370-2375. DOI:10.1001/jama.285.18.2370.
7. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study [J]. *Stroke*, 1991,22(8):983-988. DOI:10.1161/01.str.22.8.983.
8. Thihalolipavan S, Morin DP. Atrial fibrillation and congestive heart failure [J]. *Heart failure clinics*, 2014,10(2):305-318. DOI:10.1016/j.hfc.2013.12.005.
9. Tapoi L, Ureche C, Sascau R, et al. Atrial fibrillation and chronic kidney disease conundrum: an update [J]. *Journal of nephrology*, 2019,32(6):909-917. DOI:10.1007/s40620-019-00630-1.

10. Bunch TJ, Weiss JP, Crandall BG, et al. Atrial fibrillation is independently associated with senile, vascular, and Alzheimer' s dementia [J]. *Heart rhythm*, 2010,7(4):433-437. DOI:10.1016/j.hrthm.2009.12.004.
11. Hao YJ, Yu J, Han QL, et al. Does atrial fibrillation increase the risk of new myocardial infarction? [J]. *Chinese General Practice*, 2022,25(17):2121-2126. DOI:10.12114/j.issn.1007-9572.2022.0056.
12. Soliman EZ, Safford MM, Muntner P, et al. Atrial fibrillation and the risk of myocardial infarction [J]. *JAMA internal medicine*, 2014,174(1):107-114. DOI:10.1001/jamainternmed.2013.11912.
13. Writing Group of 2018 Chinese Guidelines for the Management of Hypertension, Chinese Hypertension League, Chinese Society of Cardiology, et al. 2018 Chinese guidelines for the management of hypertension [J]. *Chinese Journal of Cardiovascular Medicine*, 2019,24(01):24-56. DOI:10.3969/j.issn.1007-5410.2019.01.002.
14. Chinese Society of Pacing and Electrophysiology, Chinese Society of Arrhythmias, Atrial Fibrillation Center Union of China. Current knowledge and management of atrial fibrillation: consensus of Chinese experts 2021 [J]. *Chin J Cardiac Arrhyth*, 2022,26(01):15-88. DOI:10.3760/cma.j.cn113859-20211224-00264.
15. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018) [J]. *Eur Heart J*, 2019,40(3):237-269. DOI:10.1093/eurheartj/ehy462.
16. Michniewicz E, Mlodawska E, Lopatowska P, et al. Patients with atrial fibrillation and coronary artery disease - Double trouble [J]. *Advances in medical sciences*, 2018,63(1):30-35. DOI:10.1016/j.advms.2017.06.005.
17. Bosch NA, Cimini J, Walkey AJ. Atrial Fibrillation in the ICU [J]. *Chest*, 2018,154(6):1424-1434. DOI:10.1016/j.chest.2018.03.040.
18. Packer DL, Bardy GH, Worley SJ, et al. Tachycardia-induced cardiomyopathy: a reversible form of left ventricular dysfunction [J]. *The American journal of cardiology*, 1986,57(8):563-570. DOI:10.1016/0002-9149(86)90836-2.
19. Shinbane JS, Wood MA, Jensen DN, et al. Tachycardia-induced cardiomyopathy: a review of animal models and clinical studies [J]. *Journal of the American College of Cardiology*, 1997,29(4):709-715. DOI:10.1016/s0735-1097(96)00592-x.
20. Yongjun Q, Huanzhang S, Wenxia Z, et al. From changes in local RAAS to structural remodeling of the left atrium: A beautiful cycle in atrial fibrillation [J]. *Herz*, 2015,40(3):514-520. DOI:10.1007/s00059-013-4032-7.

21. Sun Y. The renin-angiotensin-aldosterone system and vascular remodeling [J]. *Congestive heart failure* (Greenwich, Conn.), 2002,8(1):11-16. DOI:10.1111/j.1527-5299.2002.00723.x.
22. Goette A, Bukowska A, Dobrev D, et al. Acute atrial tachyarrhythmia induces angiotensin II type 1 receptor-mediated oxidative stress and microvascular flow abnormalities in the ventricles [J]. *European heart journal*, 2009,30(11):1411-1420. DOI:10.1093/eurheartj/ehp046.
23. Fatkin D, Kelly R, Feneley MP. Left atrial appendage blood velocity and thromboembolic risk in patients with atrial fibrillation [J]. *Journal of the American College of Cardiology*, 1994,24(5):1429-1430. DOI:10.1016/0735-1097(94)90133-3.
24. Ilija R, Weinstein JM, Wolak A, et al. Coronary thrombus in ST elevation myocardial infarction and atrial fibrillation [J]. *Journal of thrombosis and thrombolysis*, 2013,35(1):119-122. DOI:10.1007/s11239-012-0765-z.
25. Pedrinelli R, Ballo P, Fiorentini C, et al. Hypertension and acute myocardial infarction: an overview [J]. *Journal of cardiovascular medicine* (Hagerstown, Md.), 2012,13(3):194-202. DOI:10.2459/JCM.0b013e3283511ee2.
26. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study [J]. *Lancet* (London, England), 2004,364(9438):937-952. DOI:10.1016/S0140-6736(04)17018-9.
27. Bayturan O, Puri R, Tuzcu EM, et al. Atrial fibrillation, progression of coronary atherosclerosis and myocardial infarction [J]. *European journal of preventive cardiology*, 2017,24(4):373-381. DOI:10.1177/2047487316679265.
28. Emdin CA, Wong CX, Hsiao AJ, et al. Atrial fibrillation as risk factor for cardiovascular disease and death in women compared with men: systematic review and meta-analysis of cohort studies [J]. *BMJ* (Clinical research ed.), 2016,532:h7013. DOI:10.1136/bmj.h7013.
29. Roden DM, Kannankeril P, Darbar D. On the relationship among QT interval, atrial fibrillation, and torsade de pointes [J]. *Europace*, 2007,9(Suppl 4):iv1-3. DOI:10.1093/europace/eum165.
30. Huxley RR, Woodward M. Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies [J]. *Lancet*, 2011,378:1297-1305. DOI:10.1016/S0140-6736(11)60781-2.
31. Peters SAE, Huxley RR, Woodward M. Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events [J]. *Diabetologia*, 2014,57:1542-51. DOI:10.1007/s00125-014-3260-6.

32. Han QL, Mao RY, Yu J, et al. Analysis of risk factors of acute myocardial infarction in middle-aged and young people [J]. Chinese Journal of circulation, 2016,31(07):632-635. DOI:10.3969/j.issn.1000-3614.2016.07.003.
33. Kataoka Y, Shao M, Wolski K, et al. Multiple risk factor intervention and progression of coronary atherosclerosis in patients with type 2 diabetes mellitus [J]. Eur J Prev Cardiol. 2013 Apr,20(2):209-17. DOI:10.1177/2047487312437931.
34. Tolstrup JS, Hvidtfeldt UA, Flachs EM, et al. Smoking and risk of coronary heart disease in younger, middle-aged, and older adults [J]. Am J Public Health. 2014 Jan,104(1):96-102. DOI:10.2105/AJPH.2012.301091.
35. Neaton JD, Wentworth D. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. Multiple Risk Factor Intervention Trial Research Group [J]. Arch Intern Med. 1992 Jan,152(1):56-64.
36. Zhang R, Zheng L, Sun Z, et al. Decreased glomerular filtration rate is associated with mortality and cardiovascular events in patients with hypertension: a prospective study [J]. PLoS one, 2011,6(11):e27359. DOI:10.1371/journal.pone.0027359.
37. Ford I, Bezlyak V, Stott DJ, et al. Reduced glomerular filtration rate and its association with clinical outcome in older patients at risk of vascular events: secondary analysis [J]. PLoS medicine, 2009,6(1):e16. DOI:10.1371/journal.pmed.1000016.
38. Biyik I, Ergene O. Acute myocardial infarction associated with heavy alcohol intake in an adolescent with normal coronary arteries [J]. Cardiol Young. 2006 Apr,16(2):190-2. DOI:10.1017/S1047951106000187.
39. Liu J, Wang Y, Guo W, et al. Temporal trends of atrial fibrillation and/or rheumatic heart disease-related ischemic stroke, and anticoagulant use in Chinese population: An 8-year study [J]. Int J Cardiol, 2021 Jan 1,322:258-264. DOI:10.1016/j.ijcard.2020.08.046.
40. Guo J, Guan T, Fan S, et al. Underuse of Oral Anticoagulants in Patients With Ischemic Stroke and Atrial Fibrillation in China [J]. Am J Cardiol. 2018 Dec 15,122(12):2055-2061. DOI:10.1016/j.amjcard.2018.08.057.

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

*Source: ChinaXiv – Machine translation. Verify with original.*