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Association between cardiometabolic comorbidity and mortality in patients with atrial fibrillation

Zhaojie Dong^{1,2}, Chao Jiang³, Liu He³, Mingyang Gao³, Ribo Tang³, Nian Liu³, Ning Zhou³, Caihua Sang^{3*}, Deyong Long³, Xin Du^{3,4,5}, Jianzeng Dong³ and Changsheng Ma^{3*}

Abstract

Background Patients with atrial fibrillation (AF) often suffer from cardiometabolic comorbidities, but the impact of the type and number of cardiometabolic comorbidities on the prognosis of AF patients remain unclear.

Methods From August 2011 to December 2018, 23,838 AF patients from the Chinese Atrial Fibrillation Registry (China-AF) Study were enrolled in this study. The all-cause and cardiovascular-cause mortality was described. The Cox proportional hazard model was employed to explore the associations of the type and number of cardiometabolic comorbidities with all-cause and cardiovascular-cause mortality.

Results During an average follow-up of 4.07 ± 1.96 years, 2,140 (8.98%) deaths were identified. The mortality in AF patients with cardiometabolic conditions was significantly higher than that in AF patients without cardiometabolic conditions. Cardiovascular events contributed the most to the death of AF patients, particularly heart failure. AF complicated with heart failure was associated with the highest risk of all-cause mortality [hazard ratio (HR) 1.92, 95% confidence interval (CI) 1.74–2.13], followed by thromboembolism, diabetes mellitus, and vascular diseases. Whereas, the presence of co-morbid hypertension did not have a significant association with all-cause mortality (HR 0.97, 95%CI 0.86–1.09). The adjusted HRs for all-cause mortality in AF patients were 1.21 (95%CI 0.99–1.47), 1.71 (95%CI 1.40-2.08), 2.55 (95%CI 2.07-3.13), and 3.39 (95%CI 2.71-4.24) for 1, 2, 3, and ≥4 cardiometabolic comorbidities, respectively.

Conclusion The increase in the number of cardiometabolic comorbidities is associated with mortality in AF patients. Hence, strengthening the management of cardiometabolic comorbidities is critical to reducing the mortality of patients with AF.

Trial Registration URL: http://www.chictr.org.cn/showproj.aspx?proj=5831. Registration number: ChiCTR-OCH-13003729. Date of the registration is October 22, 2013.

Keywords Cardiometabolic, Multimorbidity, Atrial fibrillation, Mortality

*Correspondence: Caihua Sang sch9613070@sina.com Changsheng Ma chshma@vip.sina.com Full list of author information is available at the end of the article



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Background

Atrial fibrillation (AF), the most commonly described cardiac arrhythmia, has progressed to a global pandemic health problem accompanying the aging of populations, extended lifespan of the cardiovascular disease population, and intensifying AF detection [1-3]. Recent data from the Global Burden of Disease Study 2021 highlight that AF and atrial flutter (AFL) contributed to 8.36 million disability-adjusted life years (DALYs) and 0.34 million deaths globally in 2021, with marked regional disparities influenced by socio-demographic factors [4]. AF leads to significant disabilities and mortality in this population. Previous studies have shown that AF patients have a 1.5- to twofold greater risk of mortality compared with the general population [5, 6]. Cardiovascular death accounts for approximately 50% of all deaths, whereas fatal stroke or fatal bleeding just represents 6% to 7% of all-cause mortality [7, 8]. At present, the prevention of thromboembolism remains the cornerstone for the management of AF, which can effectively reduce the risk of stroke and severe bleeding. However, AF still exhibits high mortality and causes severe adverse events. Moreover, catheter ablation has emerged as an important therapeutic modality for AF, but its role in improving the survival of AF remains controversial [9, 10]. Therefore, it is imperative to identify modifiable risk factors/comorbidities to improve the survival of AF patients.

Cardiometabolic comorbidity is considerably prevalent in AF patients. It is estimated that 80%-90% of AF patients have at least one cardiometabolic comorbidity such as hypertension, coronary artery disease (CAD), and heart failure, etc [11-13], which may be causative, synergistic, or coincidental. These cardiometabolic comorbidities may complicate the diagnosis and treatment of AF and even negatively impact the prognosis of patients. Accumulating evidence has demonstrated that a concomitant single cardiometabolic comorbidity can increase the risk of mortality in AF patients. However, due to incomplete cardiometabolic disease records and the fact that clinical studies usually exclude patients with multimorbidity, few studies have evaluated the effect of multiple cardiometabolic comorbidities on the prognosis of patients with AF.

Emerging evidence from large-scale registries such as the GLORIA-AF Registry underscores the critical role of comorbidity patterns in shaping treatment decisions and prognosis. Latent class analysis of 32,560 AF patients identified six distinct phenotypes, ranging from low complexity to high complexity, with the latter groups exhibiting higher oral anticoagulant (OAC) use but also significantly elevated risks of all-cause death and major adverse cardiovascular events (MACE) (adjusted HR up to 1.47) [14]. These findings align with studies on specific comorbidities like peripheral artery disease (PAD) and chronic obstructive pulmonary disease (COPD), which are associated with reduced OAC adherence and worse outcomes, particularly in younger patients and those with concurrent cardiovascular risks [15, 16]. For example, COPD in AF patients correlates with a 78% higher risk of the composite outcome (all-cause death/MACE) and doubled mortality risk, despite higher OAC prescription rates [16].The Atrial fibrillation Better Care (ABC) pathway, validated in the mAFA-II trial, demonstrates improved outcomes across comorbidity phenotypes, with the greatest benefit in low-morbidity patients (HR 0.08 for primary outcomes), yet challenges persist in highcomplexity groups [17].

However, these studies lack insights into the impact of cardiometabolic comorbidities on AF prognosis in a Chinese population. Thus, we designed a study to analyze data from the China Atrial Fibrillation (China-AF) Registry to investigate the association between the type and number of cardiometabolic comorbidities and mortality in patients with AF.

Methods

Study Participants

The data of studies conducted in thirty-one tertiary and non-tertiary hospitals in Beijing from August 2011 to December 2018 were collected from the China-AF. As described previously [18], China-AF is a prospective, multicenter, and hospital-based ongoing registry study. All participating hospitals provided clinical management services for AF patients. Patients who met all the following criteria were included in this analysis: (1) \geq 18 years old, (2) with recorded information on concurrent cardiometabolic diseases at the baseline, (3) recorded cause-specific deaths, and (4) more than 6 months of follow-up. Written informed consent from all patients was obtained prior to data collection, and this study was approved by the Ethics Committee on Human Research of Beijing Anzhen Hospital, the Capital Medical University.

Data collection

The demographic data, cardiovascular risk factors, medical history, clinical presentation, vital signs, laboratory examination indicators, imaging examination findings, and medications of each patient were collected by trained staff. At the time of study recruitment, the comorbidity status was recorded according to standardized definitions and then subjected to retrospective analysis through complete paper or electronic records. The cardiometabolic conditions defined herein were hypertension, heart failure (HF), vascular diseases [including myocardial infarction (MI) and other CADs such as coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), coronary angiography findings of coronary stenosis \geq 50%, positive reaction in the load test, and specific manifestations in imaging examination], thromboembolism [including ischemic stroke (IS), transient ischemic attack (TIA), and peripheral arterial thromboembolism], and diabetes mellitus. Multiple cardiometabolic comorbidities, namely, the presence of 2 or more cardiometabolic diseases, were classified based on the count of comorbidities into 2 comorbidities, 3 comorbidities, and more than 4 comorbidities.

Outcomes

During the follow-up of the patient cohort in this study, the primary outcome was all-cause mortality and the secondary outcome was cardiovascular-cause mortality. The enrolled patients were followed up every 6 months by outpatient clinic visits or telephone interviews. The cause of patient death was adjudicated by an independent committee. All-cause mortality was defined as the mortality from all causes of death. Cardiovascular-cause death referred to death caused by cardiovascular events, mainly including death from MI, HF, sudden cardiac death (SCD), bleeding, IS, or other cardiovascular diseases.

Statistical analysis

Continuous data were presented as mean and standard deviation (SD), and categorical data as frequencies and percentages. Univariate differences in baseline variables between AF patients with and without cardiometabolic comorbidity were evaluated using 2-sample t tests for continuous variables and chi-square tests for categorical variables. The mortality rate of all-cause and cardiovascular-cause was calculated as the ratio of annual death events per 100 patients to follow-up time. Cox proportional hazard regression model was used to adjust age, gender, body mass index (BMI), smoking, AF type, noncardiovascular diseases, and treatment to evaluate the association of the type and number of cardiometabolic comorbidities with all-cause and cardiovascular-cause mortality among AF patients. Hazard ratio (HR) and 95% confidence interval (CI) were reported. Moreover, subgroup analysis based on gender stratification was performed. All analyses were performed using SAS statistical software version 9.4 (SAS Institute Inc., Cary, NC).

Results

Patient baseline characteristics

At baseline, the average age of patients was 63.9 ± 12.0 years old, and 37.9% were female. There were 17847 (74.9%) AF patients with coexisting cardiometabolic comorbidity, including 14517 (60.9%) cases with hypertension, 4998 (21.0%) cases with HF, 3589 (15.1%) cases with vascular diseases, 3393 (14.2%) cases with thromboembolism, and 5477 (23.0%) cases with diabetes mellitus. The baseline characteristics of patients are shown in Table 1. AF patients with cardiometabolic comorbidity were older than those without cardiometabolic comorbidity (with a median age of 66 years vs. 57 years, *P*<0.001). Female AF patients (40.1% vs. 31.2%, P < 0.001) and persistent AF (38.3% vs. 27.0%, P < 0.001) were more frequently associated with cardiometabolic comorbidity. Overweight, and current or preexisting non-cardiovascular conditions [including chronic obstructive pulmonary disease (COPD) and renal dysfunction] were associated with a higher prevalence of cardiometabolic comorbidity in AF patients. Among AF patients with cardiometabolic comorbidity, the proportion of patients receiving ventricular rate control drugs, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin II type 1 receptor blockers (ARBs), or statins was relatively large (all P < 0.01), while AF patients without cardiometabolic comorbidity tended to radiofrequency catheter ablation (RFCA). A summary of the distribution of AF patients with different numbers of cardiometabolic comorbidities is shown in Table 2.

Mortality and causes of death

A total of 2140 (9.0%) deaths were recorded during an average of 4.1 ± 2.0 years of follow-up. The all-cause mortality of AF patients without a history of cardiometabolic comorbidity was 0.69 per 100 patient-years, and the cardiovascular-cause mortality was 0.24 per 100 patient-years. The all-cause and cardiovascular-cause mortality of AF patients with a history of ≥ 1 cardiometabolic comorbidity was 2.65 per 100 patient-years and 1.44 per 100 patient-years respectively. The leading cause of AF deaths was cardiovascular events, among which HF accounted for the highest proportion, followed by sudden cardiac death and IS. Figure 1 shows the specific causes of death in AF patients.

Association of the types of cardiometabolic comorbidity with all-cause mortality and cardiovascular-cause mortality

After adjustment for age, gender, BMI, smoking, AF types, non-cardiovascular diseases, and treatment, AF patients complicated with HF (HR 1.92, 95% CI 1.74–2.13, P<0.01) showed the highest risk of all-cause mortality, followed by thromboembolism (HR 1.45, 95%CI 1.31–1.60, P<0.01), diabetes mellitus (HR 1.31, 95%CI 1.18–1.44, P<0.01), and vascular diseases (HR 1.25, 95%CI 1.12–1.39, P<0.01). Whereas, the presence of comorbid hypertension did not have a significant association with all-cause mortality (HR 0.97, 95%CI 0.86–1.09, P=0.62) (Fig. 2, Table S1). The adjusted HRs for cardiovascular-cause mortality were similar to the adjusted

Characteristics	All patients (N=23,838)	AF + None Cardiometabolic Comorbidities (N = 5991)	$AF + \ge 1$ Cardiometabolic Comorbidities ($N = 17,847$)	Р
Age, year (SD)	63.9±12.0	57.4±12.6	66.1±11.0	< 0.01
Female, n (%)	9031 (37.9%)	1870 (31.2%)	7161 (40.1%)	< 0.01
BMI, n (%)				< 0.01
Normal (< 24 kg/m²)	7071 (33.1%)	2043 (40.2%)	5028 (30.8%)	
Overweight (24–28 kg/m ²)	9734 (45.5%)	2252 (44.3%)	7482 (45.9%)	
Obese (BMI≥28 kg/m²)	4587(21.4%)	784 (15.4%)	3803 (23.3%)	
Smoking, <i>n</i> (%)	3659 (15.3%)	991 (16.5%)	2668 (15.0%)	< 0.01
Persistent AF	8454 (35.5%)	1616 (27.0%)	6838 (38.3%)	< 0.01
Cardiometabolic Comorbidities, n (%)				
Hypertension	14,517 (60.9%)	-	14,517 (81.3%)	
Heart failure	4998 (21.0%)	-	4998 (28.0%)	
Vascular disease	3589 (15.1%)	-	3589 (20.1%)	
Thromboembolism	3393 (14.2%)	-	3393 (18.0%)	
Diabetes mellitus	5477(23.0%)	-	5477 (30.7%)	
Non-CVD, <i>n</i> (%)				
COPD	203 (0.9%)	16 (0.3%)	187 (1.1%)	< 0.01
Renal dysfunction	684 (2.9%)	35 (0.6%)	649 (3.6%)	< 0.01
Treatment, n (%)				
Antiarrhythmic drugs	8124 (34.1%)	2417 (40.3%)	5707 (32.0%)	< 0.01
Ventricular rate control	10,090 (42.3%)	1327 (22.2%)	8763 (49.1%)	< 0.01
Anticoagulants	14,648 (61.4%)	3711 (61.9%)	10,937 (61.3%)	0.37
ACEIs/ARBs	7628 (32.0%)	362 (6.0%)	7266 (40.7%)	< 0.01
Statin	8392 (35.2%)	1000 (16.7%)	7392 (41.4%)	< 0.01
History of RFCA, n (%)	11,798 (49.5%)	3955 (66.0%)	7843 (44.0%)	< 0.01

Table 1 Baseline characteristics of AF patients with cardiometabolic comorbidities and those without cardiometabolic comorbidities

AF Atrial fibrillation, *BMI* Body mass index, *CVD* Cardiovascular disease, *COPD* Chronic obstructive pulmonary disease, *ACEIs* Angiotensin-converting enzyme inhibitors, *ARBs* Angiotensin II receptor blockers, *RFCA* Radiofrequency catheter ablation, eGFR (ml/min·1.73m²) = $186 \times \text{Scr-1.154} \times \text{age-0.203} \times 0.742$ (if female) $\times 1.233$ (if Chinese). Renal dysfunction was defined as eGFR < $60 \text{ ml/min·1.73m}^2$

Table 2 The distribution of AF patients with different numbers of cardiometabolic comorbidities

No. of Cardiometabolic Comorbidities	Patients (N = 23,838)		
0	5991 (25.1%)		
1	8530 (35.8%)		
2	5708 (23.9%)		
3	2566 (10.8%)		
4	885 (3.7%)		
5	158 (0.7%)		

HRs for all-cause mortality, with the highest HR in AF patients complicated with HF (HR 2.36, 95% CI 2.05–2.73, P<0.01) and no significant relevance between hypertension and cardiovascular-cause mortality (HR 1.04, 95% CI 0.88–1.23, P=0.68) (Fig. 2, Table S2). Additionally, as shown in Supplementary Tables S1 and S2, we compared the risks of cardiovascular and all-cause mortality between persistent or permanent atrial fibrillation

(AF) and paroxysmal AF. These results indicate that persistent AF is associated with a significantly increased risk of both all-cause mortality (HR 1.20, 95% CI 1.09–1.32, P<0.01) and cardiovascular mortality (HR 1.25, 95% CI 1.09–1.43, P<0.01) compared to paroxysmal AF.

Association of the number of cardiometabolic comorbidity with all-cause mortality and cardiovascular-cause mortality

The association between the number of comorbidity and all-cause and cardiovascular-cause mortality was analyzed. The adjusted HRs for all-cause mortality were 1.21 (95% CI: 0.99-1.47) for one comorbidity, 1.71 (95% CI: 1.40-2.08) for two comorbidities, 2.55 (95% CI: 2.07-3.13) for three comorbidities, and 3.39 (95% CI:2.71-4.24) for \geq four comorbidities, compared with AF patients without any cardiometabolic comorbidity (Fig. 3). The effect of the number of cardiometabolic comorbidity on cardiovascular-cause mortality was similar to that on all-cause mortality, but to a greater extent. The adjusted HRs for cardiovascular-cause mortality in

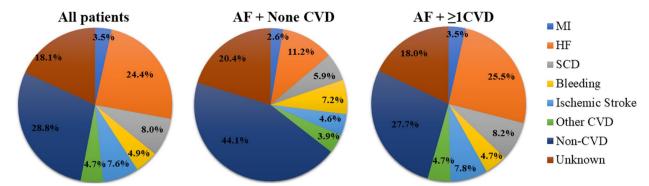


Fig. 1 The specific causes of death in AF patients with and those without cardiometabolic comorbidities. AF, atrial fibrillation; MI, myocardial infarction; HF, heart failure; SCD, sudden cardiac death; CVD, cardiovascular disease

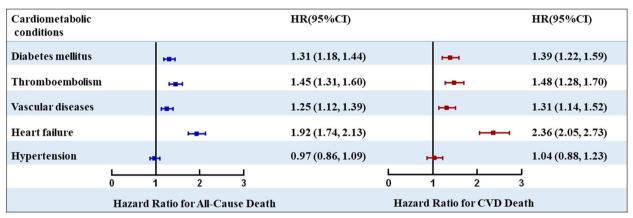


Fig. 2 Association of the types of cardiometabolic comorbidity with all-cause mortality and cardiovascular-cause mortality. CVD, cardiovascular disease

AF patients with only one cardiometabolic comorbidity was 1.52 (95% CI: 1.10–2.09), whereas that for those with a history of more than four cardiometabolic comorbidities increased to 5.37 (95% CI: 3.80–7.58) (Fig. 3). In addition, male AF patients had a larger relative effect size between a higher number of cardiometabolic comorbidities and a higher mortality risk than female AF patients (Figure S1. in the Supplemental material).

Discussion

This analysis demonstrated that approximately threequarters of the AF participants had at least one cardiometabolic comorbidity. Independent of cardiometabolic comorbidity, cardiovascular events showed the dominant cause of death, especially HF. The presence of HF was associated with the highest risk of all-cause and cardiovascular-cause mortality among AF patients. Thromboembolism, diabetes mellitus, and vascular diseases were also associated with significantly increased mortality among AF participants, with the exception of hypertension. The mortality of AF patients showed an additive increase trend with the increase in the number of cardiometabolic comorbidities.

Multiple cardiometabolic comorbidities commonly occur in AF patients. The prevalence of cardiometabolic comorbidity in AF patients in our study was consistent with the previously reported data [12, 13]. The mortality of AF patients with cardiometabolic comorbidity was significantly higher than that of AF patients without cardiometabolic comorbidity. A UK Biobank study of 3651 AF patients aged 40-70 years found that the mortality of AF patients with comorbidity was four times higher than that of AF patients without any comorbidity, and the presence of a single cardiometabolic condition was associated with an 83% higher risk of mortality [19]. Similar results were obtained in our study, as the mortality of AF patients with cardiometabolic comorbidity was 2.65 per 100 patientyears, which was about 4 times higher than that of AF patients without cardiometabolic comorbidity (0.69

No. of Cardiometabolic Comorbidity	No. of Patients	No. of All- Cause Death	All-Cause Mortality Rate (per 100 patient-years)		HR (95%CI)
0	5991	152	0.69		Ref
1	8530	449	1.27	-	1.21 (0.99, 1.47)
2	5708	629	2.59		1.71 (1.40, 2.08)
3	2566	562	5.11		2.55 (2.07, 3.13)
≥4	1043	348	8.12		3.39 (2.71, 4.24)
				0 1 2 3 4	5

No. of Cardiometabolic Comorbidity	No. of Patients	No. of All- Cause Death	CVD-Cause Mortality Rate (per 100 patient-years)		HR (95%CI)
0	5991	54	0.24	ł	Ref
1	8530	205	0.58		1.52 (1.10, 2.09)
2	5708	334	1.37		2.50 (1.82, 3.43)
3	2566	334	3.03		4.05 (2.92, 5.61)
≥4	1043	208	4.85		5.37 (3.80, 7.58)
			0	1 2 3 4 5 6 7 8	

Fig. 3 Association of the number of cardiometabolic comorbidity with all-cause mortality and cardiovascular-cause mortality. CVD, cardiovascular disease

per 100 patient-years). In addition, several studies [8, 20, 21] have demonstrated that cardiovascular death accounts for the highest proportion of all-cause deaths in AF patients, independent of cardiometabolic comorbidity, suggesting that cardiometabolic comorbidity burden may represent an important factor in AF mortality patterns.

There exists a strong association between HF and mortality in AF patients. According to the data from ETNA-AF-Europe registry study [22], HF is associated with a 65% increased risk of major bleeding and a 140% increased risk of all-cause mortality in AF patients. Furthermore, data from the Western Australian Hospitalization Morbidity Data Collection showed that the AF patients hospitalized for new HF is common and independently associated with a threefold hazard for allcause death [23]. Besides, a UK Biobank study [19] has also revealed the association between the presence of comorbid HF and the highest mortality risk of cardiometabolic conditions. Similarly, our data suggested that HF roughly doubled the risk of death in AF patients, and HF constituted the highest attributed risk for all-cause and cardiovascular-cause death compared with other cardiometabolic comorbidities. Hence, AF patients complicated with HF should be given more intense management of risk factors.

Moreover, our findings indicated that thromboembolism, diabetes mellitus, and vascular diseases also showed significant mortality correlations in AF patients, their effect sizes (30-40% increases) were smaller than HF's. However, whether thromboembolism, diabetes, and vascular disease significantly can increase the risk of allcause mortality in AF patients remains controversial. A study in the United States did not support the association between CAD and diabetes and the increased risk of AF mortality [24]. On the contrary, the UK Biobank study [19] pointed out that CAD and diabetes doubled the risk of death in AF patients, while IS/TIA was not responsible for the increased risk of death in AF patients. MI was identified as the strongest predictor of death in the Geisinger Health System. Such a difference in these findings might be attributed to the different severity of the disease, ethnic disparity, and health care services at different economic levels [25]. Although hypertension is the most common comorbidity in patients with AF, it does not increase the risk of all-cause and cardiovascular-cause mortality. However, the association between hypertension and all-cause and cardiovascular-cause death cannot be completely denied. Since there is a continuous loglinear relationship between blood pressure and the risk of cardiovascular events, the effect of hypertension on prognosis may be underestimated by categorizing only

elevated blood pressure as a binary variable in previous studies and our study [26].

In addition to evaluating the impact of each type of cardiometabolic comorbidity on all-cause and cardiovascular-cause mortality in AF patients, our study also quantified the association of cardiometabolic comorbidity with all-cause and cardiovascular-cause mortality. An additive-response association between the number of cardiovascular comorbidities and all-cause mortality was observed, with the increased number of cardiometabolic comorbidity leading to high mortality. Further, cardiometabolic comorbidity exerted a significant contribution to cardiovascular-cause mortality in AF patients, obviously exceeding its effect on all-cause mortality. The HR for all-cause mortality was about 1.5 in AF patients with only 1 comorbidity; for AF patients with 2 comorbidities, the HR was about 2; for 3 comorbidities, the HR was about 3, and for \geq 4 comorbidities, the HR was about 4. The effect of cardiometabolic comorbidity on mortality in patients with AF was essentially non-overlapping. Similarly, a study published in JAMA [27] investigated the effect of cardiometabolic disease on mortality among the general population (HR 2 for 1 cardiometabolic condition, HR 4 for 2 conditions, and HR 8 for 3 conditions). The effect of cardiometabolic disease on mortality in the general population reported in the study of JAMA was more significant than that of cardiometabolic disease on mortality in the AF population observed in our study, which might be due to the severer definition of cardiometabolic diseases (including diabetes, stroke, and MI) in the study of JAMA. A Chinese study found that the effect size of evaluating cardiometabolic diseases on mortality in the general population was slightly weaker when cardiometabolic diseases were defined as hypertension, diabetes, and cardiovascular diseases (including CAD and cerebrovascular diseases) [28]. Collectively, evidence from our study and prior experimental data strongly implicate the pivotal and independent role of multiple cardiometabolic comorbidities in all-cause and cardiovascular-cause death and highlight the importance of intensive management of these cardiometabolic comorbidities in reducing mortality.

Recent studies have further emphasized the importance of personalized management strategies for AF patients with complex comorbidities. For instance, a biomarker-based approach has been proposed to predict sinus rhythm persistence in AF patients, which could help tailor treatment strategies to individual patient profiles [29]. Additionally, the GLORIA-AF Registry highlighted that features of clinical complexity, such as frailty, chronic kidney disease (CKD), and a history of bleeding, are associated with lower use of OAC and higher risks of adverse outcomes [30]. These findings align with our results, underscoring the need for comprehensive and individualized care in managing AF patients with multiple comorbidities.

Limitations

There are some limitations in our study. Firstly, AF patients complicated with non-cardiovascular diseases were not completely excluded. For non-cardiovascular diseases, this study only corrected renal insufficiency and COPD, but failed to correct other non-cardiovascular diseases. Additionally, potential confounders such as medication adherence and the severity of individual comorbidities were not considered, which may have influenced mortality outcomes. Secondly, we did not combine specific cardiometabolic diseases, because it would produce 32 possible disease combinations, which was too much for stability analysis. Furthermore, while we included hypertension, heart failure, vascular diseases, thromboembolism, and diabetes mellitus as cardiometabolic comorbidities, other relevant conditions such as CKD were not explicitly included. The exclusion of these conditions may have influenced the results, particularly in relation to mortality. Thirdly, we merely used the state of cardiometabolic diseases at baseline to assess their effects on mortality in AF patients, but did not update the changes in the state of cardiometabolic diseases during follow-up. This lack of time-updated comorbidity data might have led to an underestimation of the true impact of comorbidities on mortality, as newly developed conditions or changes in disease severity during follow-up were not accounted for. Finally, the AF patients enrolled in this study mainly came from cities and suburbs, with relatively high medical levels and relatively good management of cardiometabolic diseases, which may underestimate the impact of cardiometabolic diseases on mortality in AF patients in real life.

Conclusions

The high burden of cardiometabolic comorbidities may be the primary contributor to the high mortality in AF patients. HF is associated with the highest risk of death, followed by diabetes mellitus, thromboembolism, and vascular diseases. The mortality risk of AF patients presents an additive increase trend with the increase of the number of cardiometabolic comorbidities, especially cardiovascular-related mortality risk, as the impact of cardiometabolic comorbidity on mortality is almost non-overlapping. Our study provides a clearer understanding of the effects of cardiometabolic comorbidity and multiple cardiometabolic comorbidities on AF mortality, which can facilitate healthcare providers to assess the prognosis of patients. AF patients with multiple cardiometabolic comorbidities demand more healthcare services, but currently, the healthcare model for multimorbidity has not been widely implemented yet. Therefore, there is a compelling need to develop and implement multidisciplinary-integrated management to deliver high-quality care to AF individuals with multiple cardiometabolic conditions.

Abbreviations

AF	Atrial Fibrillation
ACEIs	Angiotensin-Converting Enzyme Inhibitors
ARBs	Angiotensin II Receptor Blockers
BMI	Body Mass Index
CAD	Coronary Artery Disease
CABG	Coronary Artery Bypass Grafting
China-AF	Chinese Atrial Fibrillation Registry
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CVD	Cardiovascular Diseases
DM	Diabetes Mellitus
HF	Heart Failure
HR	Hazard Ratio
HTN	Hypertension
IS	Ischemic Stroke
MI	Myocardial Infarction
RFCA	Radiofrequency Catheter Ablation
SCD	Sudden Cardiac Death
SD	Standard Deviation
TIA	Transient Ischemic Attack

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12872-025-04784-8.

Supplementary Material 1: Figure S1. Association of the Number of Cardiometabolic Comorbidity with All-cause Mortality and Cardiovascular-cause Mortality in AF Patients of Different Genders. CVD, cardiovascular disease.

Supplementary Material 2.

Acknowledgements

Not applicable.

Authors' contributions

CS-M, CH-S and ZJ-D have designed the study. ZJ-D analyzed and interpreted the results of patients' statistic data and was a major contributor in writing the manuscript. L–H performed data statistic analysis. C-J, MY-G, DY-L, RB-T, N-L, N-Z, X-D, JZ-D contributed to refining the ideas and edited the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee on Human Research of Beijing Anzhen Hospital, the Capital Medical University and conformed to the ethical standards of the Declaration of Helsinki. All participants provided written informed consent prior to data collection.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Cardiology, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China. ²Heart Center and Beijing Key Laboratory of Hypertension, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China. ³Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, National Clinical Research Centre for Cardiovascular Diseases, No.2 Beijing Anzhen Road, Chaoyang District, Beijing 100029, People's Republic of China. ⁴Heart Health Research Center, Beijing, China. ⁵The George Institute for Global Health, Faculty of Medicine, University of New South Wales, Sydney, Australia.

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