Original Article

Prevalence and Risk Factors of Atrial Fibrillation in Chinese Elderly: Results from the Chinese Longitudinal Healthy Longevity Survey

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Abstract

Background: Prevalence of atrial fibrillation (AF) is increasing as the world ages. AF is associated with higher risk of mortality and disease, including stroke, hypertension, heart failure, and dementia. Prevalence of AF differs with each population studied, and research on non-Western populations and the oldest old is scarce.

Methods: We used data from the 2012 wave of the Chinese Longitudinal Healthy Longevity Survey, a community-based study in eight longevity areas in China, to estimate AF prevalence in an elderly Chinese population ($n = 1418$, mean age = 85.6 years) and to identify risk factors. We determined the presence of AF in our participants using single-lead electrocardiograms. The weighted prevalence of AF was estimated in subjects stratified according to age groups (65–74, 75–84, 85–94, 95 years and above) and gender. We used logistic regressions to determine the potential risk factors of AF.

Results: The overall prevalence of AF was 3.5%; 2.4% of men and 4.5% of women had AF ($P < 0.05$). AF was associated with weight extremes of being underweight or overweight/obese. Finally, advanced age (85–94 years), history of stroke or heart disease, low high-density lipoprotein levels, low triglyceride levels, and lack of regular physical activity were associated with AF.

Conclusions: In urban elderly, AF prevalence increased with age ($P < 0.05$), and in rural elderly, women had higher AF prevalence ($P < 0.05$). Further exploration of population-specific risk factors is needed to address the AF epidemic.

Key words: Atrial Fibrillation; China; Elderly; Oldest Old; Prevalence; Risk Factors

Introduction

Atrial fibrillation (AF), the most common type of arrhythmia, is associated with an increased risk of mortality and diseases, including hypertension, heart failure, stroke, and dementia.[1-3] AF accounts for 39% of strokes in individuals over 80 years and is also independently associated with prestroke cognitive impairment.[2,4]

Reported AF prevalence differs across populations. For instance, in Western populations, AF affects approximately 5–8% of those older than 65 years,[5-8] while in Asian populations, 1.6–2.6% of older adults have been reported to have AF,[9-12] suggesting that Asians may have a lower risk of AF compared to Caucasians.[13] However, there is limited

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data on AF in Asian populations, especially in those aged 80 years and above.

AF prevalence may also vary according to gender and urban/rural regions. Most studies on AF have found that men have a higher prevalence than women.[9,14] Findings on urban/rural location, however, are mixed and scarce. One study from the United Kingdom reported no difference in active prevalence of AF between urban and rural dwellers,[15] but a recent study from China indicated that AF prevalence in urban areas is higher than in rural areas.[16]

Previous studies have also demonstrated that advanced age, gender, obesity, diabetes, hypertension, and alcohol consumption increase the risk of developing AF.[17,18] Conversely, low-density lipoprotein (LDL) cholesterol and total cholesterol are associated with a lower risk of developing AF.[19] Further, nontraditional risk factors such as high sensitivity C-reactive protein (hsCRP) are associated with increased risk of AF.[20] However, most of these risk factors were identified in studies on Western populations. In China, only few studies have examined AF risk factors.[16,21,22] Since AF prevalence is population-specific, the risk factors for AF may also vary with clinical and socio-demographic characteristics.[16]

The rising prevalence of AF will likely lead to higher human and healthcare-related costs.[23,24] Hence, the identification of other potentially modifiable risk factors in addition to traditional risk factors for AF is important for effective healthcare planning and prevention. Our study examined the prevalence of AF and identified risk factors of AF in an elderly population from China to add to the scarce research on AF in Asian populations and in the oldest old (≥85 years). We used data from the 2012 wave in the Chinese Longitudinal Healthy Longevity Survey (CLHLS), a community-based study in eight longevity areas in China.

Methods

Subjects

CLHLS was an ongoing longitudinal data collection and research project established in 1998. The baseline and follow-up surveys were conducted in half of the counties and cities in the selected 22 provinces in 1998, 2000, 2002, 2005, 2008–2009, and 2011–2012. All local residents aged 100, and above were invited to participate in the study. An equal number of their neighbors in each of the age groups (40–59, 60–79, 80–99, and 100+) matched by gender and closest residence were also invited to participate. Details of this survey have been described elsewhere.[25] In 2012, a biomarker substudy of CLHLS was conducted in eight longevity areas in Shandong, Henan, Hubei, Hunan, Guangxi, Guangdong, Hainan and Jiangsu Provinces during the sixth wave of CLHLS. A total of 2252 subjects aged 65 years and above were recruited in the biomarker substudy.

Written informed consent was obtained from all participants or their proxies. The Ethics Committees of Peking University and the National University of Singapore approved this study.

Determination of atrial fibrillation

A single-lead (lead I) electrocardiogram (ECG) was recorded for five minutes with a handheld ECG device (DailyCare BioMedical Inc., Chungli, Taiwan, China). The recordings were then transferred to a computer for interpretation. Each ECG rhythm strip was separately read by two trained members of the research team. All AF and uncertain AF cases were reviewed by a cardiologist. In addition, 10% of ECG recordings deemed to be normal sinus rhythm were randomly sampled for review by the cardiologist. The diagnostic criteria for AF were: Consistently absent *P* waves, irregularly irregular rhythm, and presence of rapid, irregular F waves.

Independent variables

Data on the following socio-demographic indicators and health variables were collected through home interviews: Age, gender, residence (urban/rural), current smoker, current drinker, self-reported: Hypertension, diabetes, stroke history, and heart diseases, and physical activity. Physical activity was determined by one question: Do you exercise regularly at present? Subjects were defined to have physical activity if they answered "yes" for the question.

Height, weight, and waist circumference were measured, and body mass index (BMI) was calculated as weight (kg)/height (m^2) and was categorized using international cut-offs:[26] underweight (<18.5 kg/m^2), normal (range: 18.5–24.9 kg/m^2), overweight (range: 25.0–29.9 kg/m^2), and obese (≥30 kg/m^2). The number of obese participants in our sample was small (2%) so we combined those who were overweight and those who were obese in the same overweight/obese category.

Blood pressure (BP) measurements and phlebotomy were performed by trained medical personnel. Fasting blood samples were collected from participants who consented to a blood test (n = 1376). The following biomarkers were measured by an Automatic Biochemistry Analyzer (Hitachi 7180, Japan) using commercially available diagnostic kits (Roche Diagnostic, Mannheim, Germany): plasma lipids/lipoprotein (total cholesterol, triglycerides, high-density lipoprotein (HDL), LDL, fasting plasma glucose, plasma creatinine, and plasma hsCRP.

Hypertension was defined as systolic BP ≥140 mmHg and/or diastolic BP (DBP) ≥90 mmHg or self-reported hypertension. Diabetes was defined as fasting plasma glucose ≥7.0 mmol/L or self-reported diabetes.

Estimated glomerular filtration rate (eGFR) was calculated using the modification of diet in renal disease equation: eGFR ($ml \cdot min^{-1} \cdot 1.73\ m^{-2}$) = 186 × (creatinine/88.4) − 1.154 × (age) − 0.203× (0.742 if female).[27]

Statistical analysis

Of the 2252 participants who were recruited in the biomarker substudy, we excluded those without interpretable ECG rhythm strips (n = 834). The final sample for analysis included 1418 (645 men and 773 women).

Weighted means were calculated for continuous variables and weighted proportions were calculated for categorical variables. The differences in continuous variables and categorical variables across levels of categorical variables were evaluated using the unpaired Student's *t*-test, ANOVA, or Chi-square test. The weighted prevalence and 95% confidence intervals (*CIs*) of AF were estimated in subjects stratified according to age groups (65–74, 75–84, 85–94, 95 years and above) and gender. The Cochran-Armitage test was used to test for linearity in the prevalence of AF across age groups. A $P < 0.05$ was considered to be statistically significant. To compare AF prevalence across published studies, we calculated age-standardized prevalence using data from WHO World Standard Population.[28] The WHO World Standard Population is an average of the world population age structure estimated from the year 2000 to 2025. Further, its terminal age group has been extended out to 100 years and over rather than 85 and over.[28]

We used stepwise logistic regressions to determine the potential risk factors of AF in multivariable analysis, using socio-demographic indicators and clinical measurements mentioned in the section above as independent variables. We set a significant level of 0.25 for a variable to enter the model and a significant level of 0.15 for a variable to stay in the model. We determined the odds ratio and 95% *CIs* for each statistically significant independent variable.

The analysis was weighted using survey sampling weights to adjust for survey sample distribution into the total population distribution in eight longevity areas. For all analyses, we used SAS for Windows Version 9.3 (SAS, Cary, NC, USA).

Results

Of 2252 individuals in the biomarker study, 1418 (645 men and 773 women) had interpretable ECG rhythm strips. The mean age of the study population was 85.6 ± 12.2 years (80.4 ± 10.8 years for men, 89.9 ± 11.6 years for women). In the eight longevity areas, 83–99% of ECG rhythm strips were mostly interpretable in Henan, Hubei, Hunan, and Guangxi, 42–52% were interpretable in Jiangsu, Guangdong, and Hainan, and 15% were interpretable in Shandong. Those without ECG rhythm strips were more likely to reside in rural area (86% vs. 81%), more likely to be a current drinker (18% vs. 13%), have more physical activity (23% vs. 11%), and lower stroke prevalence (6% vs. 9%) compared to those without missing data ($P < 0.01$ for all).

Table 1 shows the characteristics of participants stratified by gender. There were statistically significant gender differences in age distribution, waist circumference, DBP, total cholesterol levels, HDL cholesterol level, smoking status, and drinking status ($P < 0.05$ for all).

Table 1: Characteristics of participants

Items	Weighted % (*n*) or mean ± SD[§,‖]		
	Total (*n* = 1418)	Men (*n* = 645)	Women (*n* = 773)
AF			
65≤ Age <80 (years)	3.5 (93)	2.4 (40)	4.6 (53)
Age ≥80 (years)	8.8 (80)	9.1 (34)	8.6 (46)
Age group (in years)			
65–74	60.3 (339)	64.1 (232)	56.4 (107)*
75–84	31.6 (344)	30.5 (198)	32.6 (146)
85–94	7.8 (318)	5.2 (130)	10.4 (188)
≥95	0.3 (417)	0.1 (85)	0.6 (332)
Residence			
Urban	47.9 (265)	46.5 (109)	49.3 (156)
Rural	52.1 (1153)	53.5 (536)	50.7 (617)
Body mass category (kg/m^2)			
Underweight	12.6 (348)	11.5 (115)	13.7 (233)
Normal	69.5 (840)	70.6 (418)	68.4 (422)
Overweight	15.8 (138)	15.6 (79)	16.0 (59)
Obese	2.1 (29)	2.2 (14)	1.9 (15)
Waist circumference (cm)	81.4 ± 0.7	82.7 ± 0.9	80.0 ± 1.0*
Systolic blood pressure (mmHg)	137.4 ± 1.1	136.3 ± 1.4	138.5 ± 1.6
Diastolic blood pressure (mmHg)	82.8 ± 0.6	83.9 ± 0.9	81.6 ± 0.8*
Fasting glucose (nmol/L)	4.32 ± 0.14	4.27 ± 0.21	4.27 ± 0.20
Total cholesterol (mmol/L)	4.30 ± 0.05	4.15 ± 0.07	447 ± 0.07†
HDL (mmol/L)	1.30 ± 0.02	1.26 ± 0.03	1.35 ± 0.03*
LDL (mmol/L)	2.43 ± 0.05	2.34 ± 0.07	2.50 ± 0.06
Triglyceride (mmol/L)	1.25 ± 0.07	1.15 ± 0.10	1.35 ± 0.09
Creatinine (μmol/L)	79.6 ± 1.4	88.8 ± 2.0	70.1 ± 1.1
hs-CRP (mg/dl)	2.73 ± 0.25	2.85 ± 0.37	2.60 ± 0.34
eGFR (ml·min^{-1}·1.73 m^{-2})	82.6 ± 1.1	84.2 ± 1.6	80.9 ± 1.4
Hypertension	58.7 (848)	59.2 (362)	58.2 (486)
Diabetes	7.8 (109)	7.0 (54)	8.4 (55)
Stroke	6.9 (127)	6.0 (49)	7.8 (78)
Heart disease	8.2 (98)	5.6 (38)	10.8 (60)
Physical activity	16.5 (157)	14.1 (85)	19.0 (72)
Current smoker	18.8 (232)	31.6 (199)	5.6 (33)‡
Current drinker	14.8 (187)	26.3 (154)	3.0 (33)‡

*P<0.05; †P<0.01; ‡P<0.001. §Weight variables percentage or means: Adjusted for survey sample distribution into the total population distribution of eight longevity areas via survey-sampling weight. Differences between genders were assessed by *t*-test and Chi-square test; ‖Percentages and means calculation may not base on the total number of subjects due to missing values: BMI (*n* = 63), waist (*n* = 36), blood sample (*n* = 42), hypertension (*n* = 16), diabetes (*n* = 58), stroke (*n* = 16), heart disease (*n* = 29), physical activity (*n* = 43). SD: Standard deviation; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; hs-CRP: High sensitivity C-reactive protein; eGFR: Estimated glomerular filtration rate; BMI: Body mass index; AF: Atrial fibrillation.

Prevalence of atrial fibrillation

The overall prevalence of AF was 3.5% in our study population; 2.4% of men and 4.6% of women had AF. For those aged 80 years and above, the prevalence of AF was 8.8%; 9.14% of men and 8.6% of women had AF [Table 1]. There was no significant difference in prevalence between men and women ($P = 0.07$). AF prevalence in our sample increased with age: 2.1% for those 65–74 years old, 4.0% for those 75–84 years old, 11.8% for those 85–94 years old, and 17.7% for those 95 years and above [Figure 1].

Prevalence of AF was higher in rural residents compared to urban residents (4.6% vs. 2.3%) but this was not a statistically significant difference ($P = 0.06$). For urban

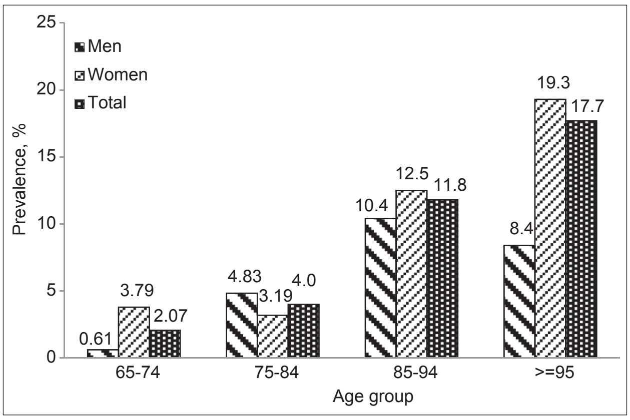

Figure 1: Age- and gender-specific weighted prevalence of atrial fibrillation.

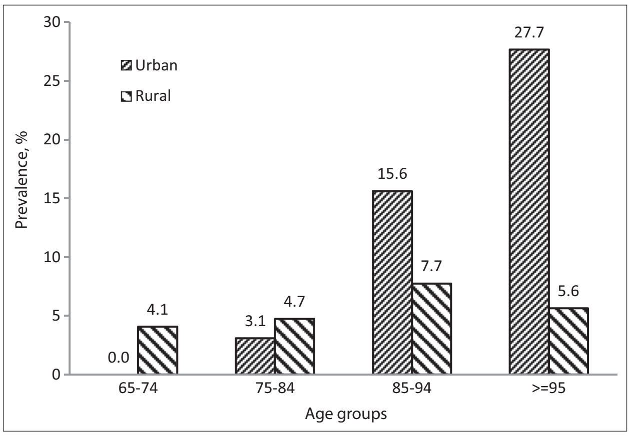

Figure 2: Age- and residence-specific weighted prevalence of atrial fibrillation.

residents, the prevalence of AF increased with age (P for trend <0.0001), however, for rural residents, there was no evidence of prevalence increasing with age (P for trend = 0.276) [Figure 2]. There was no gender difference in the prevalence of AF in urban residents (2.6% women vs. 2.0% men; $P = 0.6$); however, rural women had higher AF prevalence compared to men (6.5% women vs. 2.8%; $P = 0.04$) (data not shown).

Determinants of atrial fibrillation

In the multivariable analysis, serum cholesterol/LDL was excluded to avoid collinearity; there was a strong linear correlation between serum cholesterol and serum LDL-cholesterol ($r = 0.91$, $P < 0.0001$ by Pearson's method). The multivariable stepwise regression yielded the following statistically significant risk factors for AF: 85–94 years old, underweight, overweight, and obese, self-reported stroke history, self-reported heart disease history, decreased HDL and serum triglyceride, and no regular physical activity [Table 2].

Discussion

In our elderly Chinese population, we found that the overall prevalence of AF was 3.5% and no significant gender difference was observed. Prevalence of AF was higher in rural areas compared to urban areas. AF prevalence in women was significantly higher than men in rural but not in urban areas. AF prevalence increased with age in urban but not in rural areas. Our multivariable logistic regressions showed that the primary risk factors for AF were: Advanced age (85–94 years), extreme weight categories (underweight or overweight/obese), history of stroke or heart disease, low HDL, low triglycerides, and lack of regular physical activity.

Overall, age-standardized AF prevalence (3.4%) in our population for those 65 years and older was similar to another study in China (3.3%, age-standardized).[12] It was slightly higher than reported for other Asian countries - Singapore (2.0%, age-standardized) and Korea (2.4%, age-standardized).[9,10] However, it was still lower than the prevalence reported in the United States (age-standardized range: 4.69–5.43%)[5,14] and European populations (age-standardized range: 4.4–8.4%).[6-8,29] On the other hand, the prevalence for those 80 years and older in our study (7.6%, age-standardized) was comparable with the age-standardized prevalence reported in United States (age-standardized range: 7.3–9.2%)[5,14] and in European populations (7.2–15.4%)[6-8,29,30] (data not shown). The Rotterdam study, which used ECG data and survey of general practitioner files, reported higher prevalence compared to previous studies (age-standardized, 15.4% for those 80 years and older).[6] Because the Rotterdam study screened general practitioner files of all participants for the presence of AF at or before baseline and used 12-lead ECGs to determine AF, prevalence estimates from the study were higher compared to studies using only one method (ECGs or insurance/doctor reports).

Most studies on AF reported a higher prevalence in men than in women.[9,14] In our population, however, the inverse was observed (4.6% in women compared to 2.4% in men), although this difference was not statistically significant ($P = 0.06$). The risk of AF increases with age,[17] and in China, there are more women than men in older age groups.[31] In our sample, 61% of AF patients aged 75–84 years and 55% of AF patient aged 85–94 years were men. Conversely, 76% of the AF patients over 95 years old were women. While women outlive men, they live longer with disabilities.[31] In China, one study has shown that women have lower health status than men.[32] Because of gender differences in life expectancy and the accumulation of chronic health conditions, it is plausible that AF prevalence is higher in women.

Research on urban-rural divides in AF is scarce. In our study, we found that those who lived in rural areas had higher AF prevalence compared to their urban counterparts. This is unsurprising because urban dwellers generally have a higher socioeconomic standing and better healthcare access compared to their rural peers.[32] In China, particularly, urban and rural areas have many health and socio-economic disparities. For example, life expectancy in urban and rural China is 75.2 and 69.6 years, respectively.[32] Health and

Table 2: Univariable and multivariable logistic regression analysis of AF and related variables

Items	Univariate *OR* (95% *CI*)	Multivariable *OR*§,‖ (95% *CI*)
Age group (in years)		
65–74	Reference	Reference
75–84	1.97 (0.74–5.24)	1.49 (0.70–3.17)
85–94	6.30 (2.33–17.0)‡	4.12 (1.63–10.4)†
≥95	10.1 (3.05–33.6)‡	3.85 (0.19–77.6)
Gender		
Women	1.94 (1.09–3.46)*	
Men	Reference	
Residence		
Urban	0.49 (0.23–1.07)	
Rural	Reference	
Body mass category (kg/m^2)		
Underweight	3.60 (1.77–7.33)†	2.74 (1.12–6.73)*
Normal	Reference	Reference
Overweight and obese¶	2.31 (1.12–4.74)*	4.51 (1.72–11.8)†
Waist circumference (cm)	0.97 (0.95–1.00)*	0.97 (0.93–1.01)
Systolic blood pressure (mmHg)	0.99 (0.98–1.01)	
Diastolic blood pressure (mmHg)	0.99 (0.96–1.01)	
Hypertension	1.04 (0.59–1.85)	
Fasting glucose (nmol/L)	1.06 (0.97–1.15)	
Diabetes	1.21 (0.44–3.32)	
Total cholesterol (mmol/L)	0.57 (0.41–0.81)†	
HDL (mmol/L)	0.55 (0.25–1.21)	0.30 (0.11–0.83)*
LDL (mmol/L)	0.78 (0.53–1.14)	
Triglyceride (mmol/L)	0.30 (0.14–0.63)†	0.29 (0.13–0.64)†
Creatinine, (μmol/L)	1.00 (0.99–1.01)	
hs-CRP (mg/dl)	1.03 (1.00–1.06)*	
eGFR (ml·min^{-1}·1.73 m^{-2})	1.00 (0.98–1.01)	
Stroke	3.61 (1.75–7.43)‡	2.89 (1.22–6.86)*
Heart disease	9.59 (5.28–17.4)‡	12.9 (6.1–27.2)‡
Physical activity	0.31 (0.10–0.97)*	0.16 (0.03–0.97)*
Current smoker	0.56 (0.24–1.33)	
Current drinker	0.31 (0.09–1.06)	0.89 (0.22–3.64)

*P<0.05; †P<0.01; ‡P<0.001. §Only variables which meet the entry (P=0.25) and stay (P=0.15) criteria in the stepwise multivariable analysis were included; ‖Stepwise multivariable analysis was performed after excluding total cholesterol because there was a highly significant linear correlation between total cholesterol and LDL-cholesterol (r=0.91, P<0.0001); ¶Overweight and obese were combined due the small number of obese individuals in the sample (2%). HDL: High-density lipoprotein; LDL: Low-density lipoprotein; *OR*: Odds ratio; hs-CRP: High sensitivity C-reactive protein; eGFR: Estimated glomerular filtration rate; AF: Atrial fibrillation.

healthcare access inequalities explain why Chinese urban elderly have lower AF prevalence compared to rural elderly. Further, we found that in urban residents, AF prevalence increased with age, a trend consistent with studies done on other aging populations.[17] This was not observed among rural residents although rural women had higher AF prevalence compared to rural men. Gender may be a more powerful determinant of AF compared to age as a result of gender inequalities in health status in rural China.[32] Rural women reported lower health status compared to rural men,[32] and this may have contributed to higher AF prevalence in rural women in our study. An in-depth investigation of urban-rural disparities in AF prevalence is needed to design effective public health campaigns.

This study highlighted that being either underweight or overweight/obese was significantly associated with AF in an elderly Chinese population. Previous prospective studies[18,21] have highlighted the latter but did not report any association between AF and being underweight. A recent meta-analysis study showed that in adults aged 65 and older, the association between BMI and mortality was U-shaped.[33] BMI <18 kg/m^2 was associated with higher mortality from circulatory diseases, ischemic heart disease, and cerebrovascular disease,[34] suggesting that older adults with low BMI may have comparably high risk of AF compared to those with high BMI. However, previous studies[18,21] have only focused on the overweight/obese category, neglecting the underweight category. Additionally, since older adults are more susceptible to chronic diseases, which can lead to a lower BMI, they are often predisposed to AF. The mean age in our study was higher than other similar studies[18,21] (86 years compared to 56–65 years), suggesting that both advanced age and a low BMI (P for interaction = 0.002) could be underlying risk factors for AF.

Most of the risk factors we identified were consistent with the extensive evidence from other studies on AF. The risk of AF increasing with age,[14] and advanced age (85–94 years) was one of the primary risk factors in our study. The inverse association observed between HDL cholesterol levels, and AF was in line with the Niigata Preventive Medicine Study.[35] Heart disease and stroke were also associated with AF, which was consistent with the Framingham Heart Study and the REGARDS study;[17,36,37] the Framingham Heart Study reported that the relative risk of stroke for the oldest old (80–89 years) with AF was 4.5 compared to those without AF.[37] Further, our study suggested that those with less physical activity were more likely to have AF, a finding corroborated by the Cardiovascular Health Study.[38] We found that triglyceride levels were inversely associated with AF, which was inconsistent with earlier studies that reported no association.[19,35] On the other hand, our result was consistent with a recent study[22] in men in China (mean age: 53.2; range: 18–98 years). One potential explanation for our finding is that low triglycerides may be a marker of poor nutrition and AF-related chronic disease in an elderly population.[39]

Our study had a few limitations. First, Jiangsu, Guangdong, Hainan, and Shandong had relatively low percentages of interpretable ECG rhythm strips compared to Henan, Hubei, Hunan, and Guangxi. This was related to the lack of experience and training in handling the ECG device in study sites with low percentages. Second, AF was determined using only a 5-min single lead ECGs in the present study, which may not have been suitably sensitive, leading to an underestimation of AF in our sample. Third, we only had access to self-reported information on heart disease and stroke, which could have led to the under-reporting of chronic conditions. However, the prevalence of chronic conditions in our study is higher than or comparable to prevalence data in other Chinese national studies,[40] suggesting that under-reporting may not be a significant issue in our dataset. Other limitations of the present study include its sample size and study design. The cross-sectional study design limited our ability to establish a causal relationship between risk factors and AF. Thus, prospective studies with larger numbers of elderly are needed to clarify the association. As our sample was recruited from eight longevity areas in China, our findings may have limited generalizability to all elderly population in China.

Despite its limitations, our study contributes to our understanding of AF in a non-Western population and raises several important questions about AF risk factors. In our elderly Chinese population, we found that overall AF prevalence increases with age, specifically in urban (and not rural) residents. No significant gender difference was found although women had a higher overall prevalence compared to men. Finally, AF is associated with weight category extremes (underweight or overweight/obese), low HDL levels, low triglyceride levels, self-reported stroke, self-reported heart disease, and lack of regular physical activity.

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Conflicts of interest

There are no conflicts of interest.

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