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Sex differences in clinical characteristics and inpatient outcomes among 2442 hospitalized Chinese patients with nonvalvular atrial fibrillation: The Nanchang Atrial Fibrillation Project

Qinmei Xiong [a,b], Alena Shantsila [b], Deirdre A. Lane [b], Qiongqiong Zhou [a], Ying Liu [a], Yang Shen [a], Xiaoshu Cheng [a], Kui Hong [a,1], Gregory Y.H. Lip [b,1,*]

[a] Cardiovascular Department, The Second Affiliated Hospital of Nanchang University, Nanchang, China
[b] University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom

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ABSTRACT

Background: Limited data exists on the impact of sex on clinical characteristics and outcomes among nonvalvular AF patients from China. We investigated the impact of gender on risk factors and inpatient mortality in a hospitalized nonvalvular AF cohort in Nanchang, China.
Methods: We studied consecutive patients hospitalized with nonvalvular AF between May 2011 and December 2013. Predictors of inpatient mortality were evaluated using multivariate regression analyses.
Results: We studied 2442 patients (43.7% female; mean age 71.8), with a median hospital stay of 10 days (IQR: 7–14). Inpatient mortality was 2.2%. Mean age, $CHADS_2$ and CHA_2DS_2-VASc scores were higher in females vs. males (all $p < 0.0001$). Oral anticoagulation use during hospitalization was 33.3% without sex differences, and length of stay and inpatient outcomes were comparable between sexes.
On multivariate analyses, the significant risk factors of inpatient death in females were previous ischemic stroke/transient ischemic attack (TIA)/thromboembolism (TE) (Odds Ratio (OR): 2.27; 95% Confidence Intervals (CI): 1.43–3.61), peripheral artery disease (OR: 5.75, 95% CI: 1.49–22.16) and chronic renal disease (OR: 5.68, 95% CI: 1.46–22.13). Among males, only age (OR: 1.06, 95% CI: 1.02–1.11) and previous ischemic stroke/TIA/TE (OR: 1.81, 95% CI: 1.25–2.63) were independent predictors of inpatient mortality.
Conclusion: Sex related differences in clinical characteristics and stroke risk profile were evident in Chinese nonvalvular AF patients, but no sex disparity was evident in the low antithrombotic therapy use or inpatient mortality. Previous ischemic stroke/TIA/TE was an important predictor of inpatient mortality in both female and male patients.

1. Introduction

Atrial fibrillation (AF) is the most common heart rhythm disorder and the global burden of AF and its high risk of stroke are well documented in both Western and Asia countries [1–4]. Findings from the prospective community-based Rotterdam study demonstrate that the number of AF patients aged >55 years old will be more than double to 17.9 million in European Union from 2010 to 2060 [5]. An investigation in the southwest of China has shown that the prevalence of AF had increased 20-fold over an 11-year period, while AF-related stroke increased 13-fold [4]. Due to the increasing epidemic of AF with an aging population, AF burden has become a growing public health concern worldwide.

In recent years, sex related differences in incidence, presentations, outcomes and clinical management among patients with nonvalvular AF have been demonstrated in previous epidemiologic studies from Western countries [6,7], with a greater prevalence of AF usually among males, while female patients are at higher risk of stroke and thromboembolism [8].

Indeed, females with AF tended to be older and sicker, with a worse cardiovascular risk profile and a lower quality of life [9]. In the original Framingham cohort, for example, AF was associated with a 1.9 fold higher risk of death among female patients compared to males [10]. The Anticoagulation and Risk factors In Atrial fibrillation (ATRIA) cohort prospectively studied 13 559 AF patients and have shown that females were at 1.6 fold higher risk for AF-related thromboembolism than males [11]. The increased risk of stroke among females with AF can be further demonstrated by a systemic review and meta-analysis [8]. Due to the higher risk of stroke among females AF patients, female sex has been incorporated in CHA_2DS_2-VASc score as a risk factor of stroke or systemic embolism among AF patients [12].

* Corresponding author.
E-mail address: g.y.h.lip@bham.ac.uk (G.Y.H. Lip).
[1] Joint senior authors.

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However, most sex-related investigations of AF are based on data from Western populations [8], while few studies have investigated the impact of sex on clinical characteristics and inpatient outcomes among nonvalvular AF patients from China.

Hence, the aim of this study was to investigate sex-related differences in clinical characteristics and inpatient outcomes among a hospitalized cohort of Chinese nonvalvular AF patients, in the Nanchang Atrial Fibrillation Project.

2. Methods

2.1. Study population

All consecutive patients with nonvalvular AF admitted to our tertiary care hospital, the second affiliated hospital of Nanchang university, from May 2011 till December 2013, were included. This is a teaching hospital which covers the health management of a population of over 5 million. Patients admitted with a concomitant diagnosis of AF were eligible for inclusion in this registry. Those with AF combined with the presence of valvular heart disease requiring management were excluded. The diagnosis of AF was made by the attending physician confirmed with an electrocardiogram or Holter monitor.

2.2. Data collection

The demographic and clinical characteristics of included patients were extracted from our hospital electronic data system, including date of birth, sex, length of stay, diagnoses and death prior to discharge. Medical records were reviewed by hospital personnel to determine the following data: current smoking; weight and height; systolic and diastolic blood pressure (BP) levels on admission; laboratory data during hospitalization; concomitant diseases; oral anticoagulant therapy before admission and during hospitalization. Both $CHADS_2$ (one point each for congestive heart failure, hypertension, age ≥ 75 years, diabetes; two points for previous stroke/transient ischemic attack (TIA)/Thromboembolism(TE)) and CHA_2DS_2-VASc (one point each for systolic heart failure, hypertension, age 65–74 years, diabetes, vascular disease and female sex; two points each for age ≥ 75 years and previous stroke/TIA/TE) scores were calculated to assess the risk of stroke and thromboembolism [12,13].

2.3. Definitions

Inpatient ischemic stroke was defined as a focal neurologic deficit of sudden onset newly diagnosed by a neurologist and confirmed by CT or MRI. Inpatient major bleeding was defined as intracranial or gastrointestinal hemorrhage which was newly diagnosed during the current admission. Inpatient death was defined as death from any cause occurring during hospitalization. Length of hospital stay was calculated as the number of nights spent in hospital.

Heart failure was defined as the presence of signs and symptoms of either right or left ventricular dysfunction, or both, confirmed by left ventricular ejection fraction (LVEF) <40%, documented by echocardiogram, or NYHA classification class ≥ II. All other concomitant diseases were collected on the basis of the medical notes, including hypertension, diabetes, coronary artery disease, peripheral artery disease, cardiomyopathy, chronic renal disease, hyperthyroidism and cancer. Any discrepancies were resolved by rechecking the medical records.

2.4. Statistical analysis

All analyses were performed using the IBM SPSS Version 21.0 (SPSS, Inc., Chicago, IL). The distribution of continuous variables was examined by the Kolmogorov–Smirnov test. Normally distributed variables are presented as mean (standard deviation, SD) and analyzed by *t*-test, while the non-normally distributed are presented as median with interquartile range (IQR) and analyzed by Mann–Whitney *U*-test. Categorical variables are presented as n (%) and analyzed using Chi-square test or a Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to evaluate the risk factors associated with inpatient death among both males and females. Variables for the multivariable logistic regression model included age, heart failure, hypertension, diabetes, previous ischemic stroke/TIA/TE, coronary artery disease, peripheral artery disease, and chronic kidney disease. The variables were selected after performing a univariate regression analysis first and then choosing those variables with a P value ≤ 0.2 as candidates for multivariate analysis. A two-sided $p < 0.05$ was considered statistically significant.

3. Results

In total, 3327 AF patients were admitted between May 2011 and December 2013. Of these, 875 (26.3%) were excluded due to the presence of valvular heart disease requiring management, and 10 were excluded for insufficient basic clinical data, leaving a final cohort population of 2442 non-valvular AF patients (Fig. 1). Of the whole cohort, there were 1453 patients hospitalized in the cardiovascular department, and 1030 patients admitted with a primary or secondary diagnosis of AF.

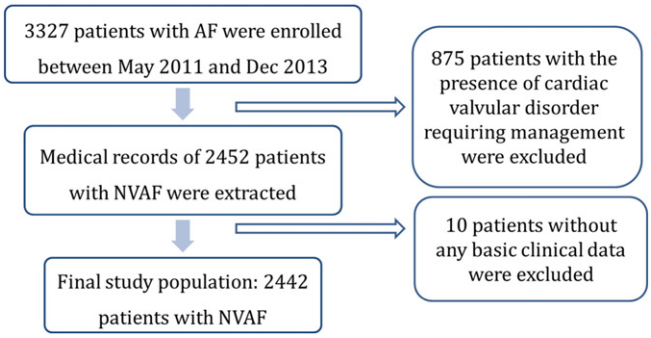

Fig. 1. Flow chart of the study cohort recruitment.

Males were more prevalent than females (56.3% vs 43.7%, P < 0.0001). Other demographic and clinical characteristics are summarized in Table 1. Overall mean ± SD age was 70.6 ± 11.3 years, with females being significantly older ($p < 0.0001$) and with more females aged ≥75 years (45.7% vs 39.8%; $p = 0.001$). Body mass index (BMI) was similar, but current smoking was more common in males Females had higher systolic BP on admission ($p < 0.0001$). Among the 1830 (74.9%) patients with LVEF assessed, almost three-quarters of the females had LVEF ≥ 55% and a significantly higher mean LVEF value ($p < 0.0001$).

Table 1
Baseline characteristics of the 2442 AF patients.

N (%)	Total	Males	Females	P value
No. of subjects	2442	1376 (56.3)	1066 (43.7)	<0.0001
Age				
Mean ± SD (years)	70.6 ± 11.3	69.6 ± 11.8	71.8 ± 10.4	<0.0001
<65	636 (26.0)	397 (28.9)	239 (22.4)	0.001
65–74	772 (31.6)	432 (31.4)	340 (31.9)	
≥75	1034 (42.3)	547 (39.8)	487 (45.7)	
Body mass index, n = 1150[a]				
mean ± SD (kg/m^2)	23.5 ± 3.9	23.6 ± 3.4	23.4 ± 4.4	0.53
Smoking status				
Never/former	2078 (85.1)	1035 (75.2)	1043 (97.8)	<0.0001
Current	364 (14.9)	341 (24.8)	23 (2.2)	
Blood pressure on admission, n = 2424[a]				
SBP, mean ± SD (mm Hg)	131.3 ± 21.4	129.9 ± 21.2	133.1 ± 21.5	<0.0001
DBP, mean ± SD (mm Hg)	78.4 ± 13.0	78.2 ± 12.9	78.7 ± 13.2	0.36
LVEF, n = 1830[a]				
mean ± SD	58.7 ± 11.7	57.6 ± 12.0	60.0 ± 11.2	<0.0001
<55%	537 (29.3)	332 (32.7)	205 (25.2)	<0.0001
≥55%	1293 (70.7)	683 (67.3)	610 (74.8)	
Type of AF				
Paroxysmal	357 (14.6)	188 (13.7)	169 (15.9)	0.13
Persistent/permanent	2085 (85.4)	1188 (86.3)	897 (84.1)	
Concomitant Conditions				
Previous Ischemic stroke/TIA/TE	624 (25.6)	347 (25.2)	277 (26.0)	0.67
Heart failure	872 (35.7)	474 (34.4)	398 (37.3)	0.15
Hypertension	1375 (56.3)	730 (53.1)	645 (60.5)	<0.0001
Diabetes	223 (9.1)	108 (7.8)	115 (10.8)	0.01
CAD	467 (19.1)	307 (22.3)	160 (15.0)	<0.0001
PAD	86 (3.5)	49 (3.6)	37 (3.5)	1.00
Cardiomyopathy	169 (6.9)	118 (8.6)	51 (4.8)	<0.0001
Chronic kidney disease	140 (5.7)	94 (6.8)	46 (4.3)	0.01
Hyperthyroidism	125 (5.1)	59 (4.3)	66 (6.2)	0.04
Cancer	142 (5.8)	97 (7.0)	45 (4.2)	0.003

AF, atrial fibrillation; CAD, coronary artery disease; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; PAD, peripheral artery disease; SBP, systolic blood pressure; TE, thromboembolism; TIA, transient ischemic attack.

[a] The number of patients with available data.