ARTICLE

Clinical Characteristics and Risk Factors of Atrial Fibrillation in the Elderly

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ARTICLE INFO	ABSTRACT
	Objective: To investigate the epidemiobgical characteristics of the elderly with atrial fibrillation (AF) in age, gender, the types of AF and relative causes. And To analyze the risk factors of persistent AF (PeAF), then use them to guide to prevent and treat for AF in the elderly. **Methods:** Collect the data of elderly patients with AF who were admitted to Liaoning People's Hospital from September 1, 2016 to September 30, 2017, and summarize the epidemiological characteristics of AF in the elderly. The risk factors for PeAF were analyzed by Spearman correlation analysis and mltivariate logistic regression analysis. **Result:** 1. In the elderly, the number of AF cases increase with age. The group of 75-84 years old was the largest part. The number of older females was larger than male in all ages. It was important to pay more attention to old woman with AF. 2.In the elderly, nonvalvular atrial fibrillation is popular. The top three causes of AF in the elderly were CHD, hypertension and heart failure. In the elderly, comorbidities were frequent, and the management was a major therapeutic objective. 3.CRP, 1eft atria diameter were the independent risk factors for PeAF in the elderly.

1. Introduction

Atrial fibrillation (AF), as one of the most common tachyarrhythmias, is currently affecting 33 million people worldwide and growing at an annual rate of 5 million[1]. It is known as the "Cardiovascular Epidemiology in the 21st Century". Some reports showed that there are about 2.7 million to 6.7 million people with AF in the United States; and it is estimated that it will increase to 5.6 million to 15.9 million people by 2050[2,3]. In 2010, studies showed that about 8.8 million elderly people over 55 years of age in Europe suffered from AF. If the age and sex ratio remained stable, the number of people with AF is expected to double by 2060[4]. By 2050, there will be 7.2 million patients with AF and 2.9 million patients with atrial fibrillation-related stroke in Asia[5]. Most of the patients with AF are the elderly, and the incidence of AF increases with age. The Framingham study showed that the incidence of AF increased significantly after the age of 60, doubling on average every 10 years[6]; In 2004, Zhou et al. carried out a large-scale epidemiological study on 29079 cases of 14 natural populations. Among them, 224 patients with AF had a standardized prevalence rate of 0.61%, 0.5% in people aged 50-59, and 7.5% in those aged over 80[7]. Many studies have shown that the incidence of AF increases with age. Most of the patients are over 60 years old. Researchers suggest that AF research should be carried out for people over 60 years old.

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In the special group of the elderly, AF often coexists with a variety of diseases, showing a comorbid state, and mutual influence, mutual cause and effect. The occurrence of AF is often associated with many organic cardiovascular diseases, such as coronary heart disease, hypertension, heart failure, valvular disease, cardiomyopathy, sick sinus syndrome, etc., and is also closely related to other systemic diseases, such as hyperthyroidism, diabetes, sleep apnea syndrome, ischemic stroke, chronic kidney disease, etc. AF not only affects the quality of life of patients, but also significantly increases the risk of heart failure and stroke[8].

With the continuous progress of the aging of the social population, the number of patients with AF is also increasing. AF and aging are unavoidable medical and social problems all over the world, which is of great significance to conduct the in-depth study on AF in the elderly. At present, the treatment of AF is the research focus of most scholars, radiofrequency ablation of AF, left atrial appendage occlusion, pacemaker therapy and other diverse treatments. The cost of clinical treatment is high; the risk factors of intervention in AF can reduce the burden of AF to a certain extent. The occurrence of AF varies in different races and regions. According to the AHA/ACC/HRS guidelines for AF management in 2014, approximately 35% of patients with AF are older than 80 years old. In most atrial fibrillation-related studies, the selection conditions of the subjects are relatively broad and there is no specific age limit. As a result, the average age of the study cohort is about 5 years younger than that of the population with AF. Whether these findings are applicable to the elderly is still controversial[9]. Therefore, it is necessary to carry out relevant researches on the elderly with AF. This study was conducted in a single-center retrospective analysis of 700 elderly patients with AF who were over 65 years old and hospitalized in Liaoning People's Hospital. The clinical characteristics of elderly patients with AF were summarized, including age, sex, type of AF and related etiology. The related risk factors of elderly patients with persistent AF were analyzed to provide direction and reference for the prevention and treatment of elderly patients with AF.

2. Materials and Methods

2.1 Research Subjects

The medical records of elderly patients with atrial fibrillation who were admitted to the Heart Center of Liaoning People's Hospital from September 1, 2016 to September 30, 2017 were counted. Included subjects: Patients aged 65 years or older with evidences of AF such as electrocar-diogram or dynamic electrocardiogram or a clear history of AF. Excluded subjects: Patients with transient/reversible etiology. These include acute myocardial infarction, acute myocarditis, untreated hyperthyroidism and AF caused by recent electrophysiological examinations, angiography, pacemaker surgery, and cardiothoracic surgery, etc. The data of multiple hospitalized patients were based on the first hospitalization data and were counted only once.

2.2 Methods

2.2.1 Clinical Data Collection

It should be include patient age, gender, etiology and type of AF, past medical history, and related laboratory indicators, i.e., C-reactive protein (CRD), triglyceride (TG), cholesterol (TC), low-density lipoprotein (LDL), blood uric acid (BUA), serum creatinine (CREA) and so on, echocardiography recorded left atrial meridian (LAD), left ventricular ejection fractions(LVEF%).

2.2.2 Diagnostic Criteria for Major Diseases

(1) Elderly: age over 65

(2) Diagnostic criteria for atrial fibrillation: A. At least one ECG or 24 hour dynamic electrocardiogram (DCG) proved the diagnosis of AF.   B. A clear history of atrial fibrillation in the past. At least one of them should be met.

(3) Type of AF:

A. Paroxysmal atrial fibrillation: a kind of AF with a duration of <7 days, which can be converted within 48 hours, with self-limiting.

B. Persistent atrial fibrillation: a kind of AF with a duration of >7 days, which cannot be converted by itself.

C. Valvular atrial fibrillation: heart valve disease diagnosed by echocardiography, combined with AF. Heart valve diseases include rheumatic heart disease, senile degenerative valvular disease.

D. Non-valvular atrial fibrillation: exclusion of valvular heart disease by echocardiography, with other diseases such as coronary heart disease, cardiomyopathy, pulmonary heart disease, congenital heart disease, hypertension, hyperthyroidism, electrolyte imbalance, anemia, combined with AF.

E. Isolated atrial fibrillation: Clinical examination confirmed no combined heart disease such as coronary heart disease, cardiomyopathy, pulmonary heart disease, congenital heart disease, and other systemic diseases such as hypertension, hyperthyroidism, electrolyte imbalance, anemia, combined with AF.

(4) Cardiomyopathy: mainly including dilated cardiomyopathy, hypertrophic cardiomyopathy, etc.

(5) Hypertension: according to the 2010 Guidelines for the Prevention and Treatment of Hypertension in China, patients with systolic blood pressure($\geq$ 140 mm Hg) and/or diastolic blood pressure ($\geq$ 90 mm Hg), or who have previously diagnosed hypertension, who are receiving antihypertensive therapy and whose blood pressure level is within the normal range .

(6) Diagnostic criteria for heart failure: class II and above of cardiac function were diagnosed as heart failure according to the cardiac function classification of the New York Heart Association (NYHA).

(7) Diagnostic criteria for diabetes: using the diagnostic criteria proposed by the American Diabetes Association in 2012, i.e., fasting blood glucose $\geq$ 7.0 mmol/L and/or OGTT test was $\geq$11.1 mmol/L. Or a definite diagnosis of diabetes in the past.

(8) Diagnostic criteria for coronary heart disease: A. previous history of angina pectoris or significant ST-T changes showed by electrocardiogram, 24-hour DCG, exercise plate test, etc., during hospitalization; B. coronary artery stenosis ($\geq$ 50%) confirmed by coronary angiography; C. history of acute myocardial infarction or previous definite history of myocardial infarction. One of the above conditions should be met.

2.2.3 Cases Grouping

(1) 2 groups by gender: male and female.

(2) 3 groups by age: 65 to 74 years old, 75 to 84 years old, 85 years old and above.

(3) 2 groups according to the type of AF: A. Paroxysmal atrial fibrillation and persistent atrial fibrillation; B. valvular atrial fibrillation and non-valvular atrial fibrillation.

2.2.4 Statistical Methods

SPSS 18.0 program was used for statistical data processing; Chi-square test selected for counting data; t test selected for measurement data; $P < 0.05$ was statistically significant. Spearman correlation analysis was used for statistical significance indicators, and logistic regression analysis was conducted for correlative indicators.

3. Results

3.1 Clinical Features of Elderly Atrial Fibrillation

A total of 1144 patients with AF in the Hear Center of our hospital, from September 1st, 2016 to September 30th, 2017, were diagnosed as AF. According to the inclusion and exclusion criteria, 700 elderly patients with AF were enrolled, ranging in age from 65 to 99-year-old, with an average age of 77.1±6.9 years, accounting for 61.2% of all patients with AF. There were 316 male patients (45.1%) and 384 female patients (54.9%). The ratio of male to female was approximately 1:1.2.

3.1.1 Age and Gender Distribution

In the elderly population, the proportion of AF increased with age. The highest proportion of AF occurs in the 75-84 age group (49.9%) (Table 1). According to age, there were more female patients than male patients among different age groups. According to gender, the proportion of 75-84 years old group was the highest in both male and female patients. The chi-square test was performed according to the X-list. There was no significant difference between the groups ($P < 0.05$).

Table 1. Statistics of age and gender

Age	Male	Female	Total
65-74	110	132	242
75-84	156	193	349
85 and above	50	59	109
Total	316	384	700

3.1.2 Relevant etiological statistics

The causes and related factors of 700 elderly patients with AF were analyzed. As shown in figure 1, 481 cases (68.7%) of coronary heart disease, 406 cases (58.0%) of hypertension, 341 cases (48.7%) of heart failure, 191 cases (27.3%) of diabetes, 105 cases (15.0%) of valvular disease, 25 cases (3.6%) of cardiomyopathy, 21 cases (3.0%) of sick sinus syndrome and 20 cases (2.9%) of pulmonary heart disease, 15 cases (2.1%) of isolated atrial fibrillation and 2 cases (0.3%) of congenital heart disease were included. Among them, 41 cases were rheumatic valvular disease, accounting for 39.0% of valvular disease, accounting for 5.9% of the total number; 19 cases were senile valvular disease, accounting for 18.1% of valvular disease, accounting for 2.7% of the total number.
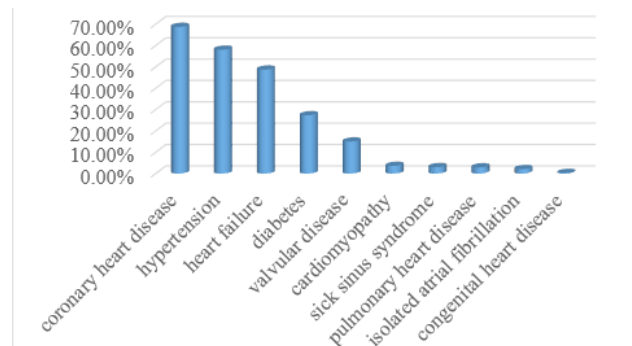
Figure 1. Analysis of the causes and related factors of 700 elderly patients with AF

3.1.3 Type distribution of atrial fibrillation

Among 700 patients with atrial fibrillation, according to the causes, there were 595 patients with non-valvular atrial fibrillation, accounting for 85.0% of the total number, including 271 male patients and 324 female patients. There were 105 patients with atrial fibrillation, including 45 male patients and 60 female patients. Both types of AF were more common in women; and non-valvular atrial fibrillation was common in both male and female patients. There was no significant difference between them (P > 0.05).

According to the duration of onset, 314 cases of paroxysmal atrial fibrillation, accounting for 44.9% of the total number, including 134 males and 180 females; 386 cases of persistent atrial fibrillation, accounting for 55.1% of the total number, including 182 males and 204 females. There was no significant difference between the type of atrial fibrillation and gender composition (P>0.05).

3.2 Risk Factors Associated with Persistent Atrial Fibrillation in the Elderly

3.2.1 Comparison of Observation Indexes between Paroxysmal Atrial Fibrillation and Persistent Atrial Fibrillation

The general clinical data between the two groups were compared. As shown in Table 2, Patients in the persistent atrial fibrillation group was older than those in the paroxysmal atrial fibrillation group; and the proportion of patients aged ≥75 years was higher. The proportion of patients' persistent atrial fibrillation combined with hypertension, diabetes, coronary heart disease, heart failure, valvular disease and ischemic stroke were higher. Among them, there were significant differences in age, hypertension, heart failure and valvular disease (P < 0.05), and no significant differences in other items (P > 0.05). The two groups of laboratory tests and cardiac color Doppler ultrasound indicators were compared, as shown in Table 3. In the persistent atrial fibrillation group, the levels of CRP, BUA, left atrial inner diameter were higher, and LVEF was lower. There were significant differences in CRP, uric acid, left atrial diameter and LVEF between the two groups (P < 0.05). There was no significant difference in the other indexes between the two groups (P > 0.05).

Table 2: Comparison of general medical records

	Paroxysmal atrial fibrillation (n = 314)	Persistent atrial fibrillation (n = 386)	Statistic value	P value
Age	75.81±6.58	78.25±6.96	t =4.728	0.000
≥75 years old	185	274	x^2=11169	0.001

Hypertension (cases)	196	210	x^2=4.568	0.033
Diabetes (cases)	86	105	x^2=0.003	0.956
Coronary heart disease (cases)	226	255	x^2=2.815	0.093
Heart failure (cases)	108	233	x^2=46.734	0.000
Valvular disease (cases)	14	91	x^2=49.628	0.000
Ischemic stroke (cases)	85	99	x^2=0.181	0.671

Table 3. Comparison of laboratory and cardiac ultrasound indicators

	Paroxysmal atrial fibrillation (n = 314)	Persistent atrial fibrillation (n = 386)	Statistic value	P value
CRP (mg/L)	815±2.65	18.15±5.95	t = -27.642	0.000
UA (μmol/L)	355.06±94.94	379.26±108.21	t = -3.108	0.002
Creatinine (μmol/L)	98.35±25.52	99.45±23.14	t = -0.596	0.551
TC (mmol/L)	3.93±0.92	3.91±0.89	t = 0.386	0.699
TG (mmol/L)	1.19±0.34	1.24±0.39	t = -1.572	0.116
LDL (mmol/L)	2.38±0.59	2.41±0.85	t = -0.486	0.627
Left atrial inner diameter (mm)	37.54±5.40	51.01±7.71	t = -5.053	0.000
LVEF(%)	53.68±7.04	47.53±4.75	t = -13.734	0.000

3.2.2 Spearman Correlation Analysis

Spearman correlation analysis was performed on the above eight statistically significant items, as shown in Table 4. The results showed that persistent atrial fibrillation was positively correlated with age, heart failure, valvular disease, CRP, uric acid, and left atrial diameter; and negatively correlated with LVEF, but not with hypertension.

Table 4. Spearman correlation analysis

	r value	P value
Age	0.181	0.000
Hypertension	-0.055	0.146
Heart failure	0.262	0.000
Valvular disease	0.266	0.000
CRP	0.820	0.000
Uric acid	0.166	0.000
Left atrial diameter	0.167	0.000
LVEF	-0.477	0.000

3.2.3 Multivariate Logistic Regression Analysis

Multivariate logistic regression analysis was performed on relevant 7 items including age, CRP, uric acid, left

atrial diameter, LVEF, heart failure, and valvular disease. The results showed that CRP level and left atrial inner diameter were independent risk factors for persistent atrial fibrillation in the elderly.

4. Discussion

4.1 Clinical Characteristics of Atrial Fibrillation in the Elderly

4.1.1 Age

Many studies have confirmed that age is an independent risk factor for atrial fibrillation, and is now widely recognized. Patients with atrial fibrillation aged 65 and over are specifically referred to as atrial fibrillation in the elderly[10]. The incidence of AF increases with age. The Framingham study showed that the incidence of AF was 0.5% in the 50-59 age group, 1.8% in the 60-69 age group, 4.8% in the 70-79 age group, and 8.8% in the 80-89 age group. The incidence of AF increased significantly after 60 years old, with an average annual increase of 1 fold[6]. According to a study published by the EHRA (European Heart Rhythm Association), the prevalence of AF in people younger than 60 years is about 1%; the prevalence of people aged 75-84 years is increased to 12%, and more than 1/3 after 80 years old[11]. The expert consensus of FSGG/FSC (French Society of Gerontology and Geriatrics/French Society of Cardiology) in 2013 pointed out that 70% of patients with AF are older than or equal to 75 years old [12]. At present, there is a lack of large-scale atrial fibrillation data statistics in China. In 2004, Zhou et al. carried out a large-scale epidemiological study on 29079 cases of 14 natural populations. Among them, the prevalence rate was 0.5% in the 50-59 age group, and 7.5% in the 80-year-old group[7].

The results of this study showed that in elderly patients with AF, patients over 75 years of age were the main patient group. This is consistent with the above findings. Patients aged 75-84 accounted for the majority of patients. Compared with that, the proportion of patients over 85 years of age did not increase significantly, which may be related to the small number of elderly hospitalized, population, regional differences and other factors.

The prevalence rate of AF increases with age; and it occurs more frequently in the elderly, which is associated with a series of body changes caused by aging. It has been suggested in the literature that when the human body enters the aging stage and develops further with the aging degree, the expression of L-type calcium channels and contractile proteins decreases at the gene and protein levels, and the left atrium (LA) may become more prominent

in the occurrence and development of AF. The specific reasons and possible mechanisms are not fully known and determined yet, which needs to be further studied[13].

4.1.2 Gender

The 38-year follow-up study of Framingham[6] in the United States showed that the prevalence of AF in men was 1-5 times higher than that in women. Studies in China have shown that the incidence of male AF is slightly higher than that of females[7,14]. But other studies have suggested further points. Feinberg et al. showed that male patients are more common than female patients before the age of 75; and after 75 years old, the proportion of female patients with atrial fibrillation increased, which was about 60%[15]. Other studies have shown that the prevalence of women in the age group >75 years old is twice that of men [16]. According to statistics from Switzerland, the prevalence of atrial fibrillation among women under 80 is lower than that of men, and women over 80 are higher than men [17]. In 2015, a study showed that the incidence of atrial fibrillation in China was 0. 05/100 patients · year. After age adjustment, the incidence and prevalence of atrial fibrillation in women were lower than in men, but the prevalence of atrial fibrillation in elderly women increased significantly [18]. This suggests that gender differences in atrial fibrillation may vary with age. The results of this study indicate that the prevalence of atrial fibrillation in older women is higher than that in men. The male to female ratio is about 1:1.2, and the prevalence of women in all age groups is high, which is roughly consistent with the above findings. The higher prevalence of atrial fibrillation in older women may be associated with changes in estrogen levels, autonomic dysfunction, increased risk factors for comorbidity in older women, and longer life expectancy in women. The specific reasons still need further discussion. Patients with atrial fibrillation have a faster ventricular rate and more pronounced symptoms. Compared with men, the quality of life is lower, and the mortality rate of female atrial fibrillation is not lower than that of men [19-21].

4.2 Risk Factors Associated with Persistent Atrial Fibrillation

4.2.1 Atrial Fibrillation and Heart Failure

In the American Flemingham study, the annual incidence of atrial fibrillation in heart failure patients was 54%, and the annual incidence of central dysfunction in patients with atrial fibrillation was 33% [22]. Atrial fibrillation interacts with heart failure. They have common risk factors such as age, smoking, obesity, hypertension, diabetes,

renal impairment, valvular heart disease, coronary artery disease, and obstructive sleep apnea. Pathophysiological mechanisms, neuroendocrine, electrophysiological and hemodynamic changes promote each other and form a vicious cycle [23]. Diastolic heart failure is common in the elderly population, and the incidence of arrhythmia is significantly higher than that of systolic heart failure. The results of this study suggest that heart failure is closely associated with persistent atrial fibrillation in the elderly. Increased volume load in patients with heart failure can lead to atrial dilatation, atrial stretch can activate ion channels, abnormal cardiac conduction, shortened refractory period and other changes, and increased blood volume can activate RASS system, which is conducive to the maintenance of atrial fibrillation. Meanwhile, the application of digoxin and other drugs has a certain impact on the progress of atrial fibrillation. In the later stage, the effects of heart function grading and anti-heart failure medication on persistent atrial fibrillation can be further studied.

4.2.2 Atrial Fibrillation and Hypertension

Hypertension is an independent predictor of newly onset atrial fibrillation and is almost linearly correlated with the occurrence of atrial fibrillation. Meanwhile, multiple studies have confirmed that prehypertension is also a high-risk factor related to atrial fibrillation [24-26]. Most old people have arteriosclerosis, and the difference in pulse pressure is large. Foreign studies suggest that an increase of 20mmHg in pulse pressure can increase the risk of atrial fibrillation [27]. Studies on elderly patients with hypertension have found a certain correlation between non-arytenoid blood pressure and the occurrence of atrial fibrillation [28]. It is suggested that reducing blood pressure variability in hypertensive patients can reduce the recurrence of atrial fibrillation and related target organ damage. Meanwhile, other scholars have put forward different conclusions. A meta-analysis conducted by Webb et al. pointed out that the blood pressure variability in patients with hypertension did not reduce the risk of new atrial fibrillation [29]. Blood pressure variability can be used as a predictor of risk, but may not be suitable as a therapeutic target. Whether it is an independent risk factor for atrial fibrillation needs further study. In this study, hypertension was associated with persistent atrial fibrillation. The left atrial structure changes induced by chronic hypertension provide conditions for the maintenance of atrial fibrillation. The vascular endothelium is damaged by hypertension, which further leads to atherosclerosis. Increased arterial stiffness is characterized by increased pulse differential pressure, which increases the risk of atrial fibrillation. In this study, the relationship between hypertension and atrial fibrillation was not further studied in terms of grading of hypertension and pulse pressure, which is the deficiency of this study.

5. Conclusion

(1) In elderly patients with atrial fibrillation, the proportion of atrial fibrillation increases with age. The age group between 75 and 84 years old accounted for the largest proportion, and the proportion of elderly women patients was higher, and slightly higher than that of men in all age groups. Elderly women with atrial fibrillation need to be taken seriously.

(2) Non-valvular atrial fibrillation is most common in elderly patients with atrial fibrillation. The most common first three related causes or risk factors are coronary heart disease, hypertension, and heart failure. The comorbidity of elderly patients with atrial fibrillation is common, and comorbid management is the prevention and treatment target of atrial fibrillation in the elderly.

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