Prevalence and Prognosis of Patients With Atrial Fibrillation in Japan

— A Prospective Cohort of Shinken Database 2004 —

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Background Prognosis of Japanese patients with atrial fibrillation (AF) should be determined in a prospective cohort study.

Methods and Results A prospective cohort of The Shinken Database 2004 comprised details on all the new patients who visited The Cardiovascular Institute Hospital in 2004 ($n=2,412$), which included 286 AF patients (11.8%, 205 males, 64.1 ± 12.3 years, 165 paroxysmal). In this Japanese cohort of AF patients, the prevalence of congestive heart failure (CHF) was low compared with that in Westerners. Total mortality and cardiovascular morbidity of these patients were also quite low, 1.7% and 11.2% at 1 year, respectively. However, patients with CHF exhibited higher mortality (7.3%), and hospitalization for CHF increased the rate to 22.6%. There was no significant difference in mortality between paroxysmal and persistent AF. Multiple Cox-hazard regression analysis identified hospitalization at initial visit and lack of anticoagulation as independent predictors for mortality, and existence of CHF as the only independent predictor for cardiovascular morbidity.

Conclusions The present study identified the mortality (1.7%) and morbidity (11.2%) of Japanese AF patients during 1 year after initial visit. Hospitalization for CHF and lack of anticoagulation were independent predictors for mortality, suggesting important roles of co-morbidities of Japanese AF patients. (*Circ J* 2008; 72: 914–920)

Key Words: Atrial fibrillation; Epidemiology; Morbidity; Mortality; Prognosis

Atrial fibrillation (AF) is the most common chronic arrhythmia associated with increased mortality and morbidity. This arrhythmia is well-known to be closely associated with older age¹ and therefore, becomes an important medical problem in regards to an aging society.

Recently, medical practice for AF has been strongly influenced by many large-scale randomized control trials (RCT) performed in Western countries. In particular, Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)² and RAte Control vs Electrical cardioversion for persistent atrial fibrillation (RACE) studies³ which found no difference in mortality between patients under rhythm and rate control strategy, had a great impact on treatment of AF in the world. However, it should be noted that these RCT were planned on the basis of prospective cohorts, including the Framingham study. The study has revealed that the incidence of AF is closely associated with increasing age, gender and other co-morbidities including congestive heart failure (CHF), valvular diseases, hypertension (HT),

diabetes mellitus (DM) and myocardial infarction (MI),⁴ and also has revealed that the existence of AF is associated with increased incidence of mortality,⁵ stroke⁶ and CHF⁷.

In Japan, however, there have been lacking in prospective cohort data of Japanese AF patients. Although physicians in Japan have depended on the clinical evidence in the USA and Europe,^{5,8–11} there could be many differences from Western countries: medical circumstances, clinical backgrounds of AF patients, and their consequent prognosis.^{12–14} Thus, emphasizing the needs of own evidence in Japan, the J-RHYTHM study has been started in 2003.¹⁵

Similarly, a prospective cohort data of Japanese AF patients should be required, because RCTs and prospective cohort data complement one another. The purpose of the present study was to identify clinical backgrounds, mortality and morbidity of Japanese AF patients in a prospective cohort study.

Methods

Study Patients

A prospective cohort study of the Shinken Database 2004 was conducted to investigate the mortality and morbidity of cardiovascular diseases in Japan. The database comprises details on all of the new patients who visited The Cardiovascular Institute Hospital between April 2004 and March 2005 ($n=2,412$). It included 286 patients with AF (11.8%; 205 males, 64.1 ± 12.3 years old, 165 paroxysmal

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Table 1 Characteristics of the Study Patients

	All (n=286)
Male (%)	205 (71.7)
Age (years)	64.1±12.3
BMI (kg/m ²)	22.7±4.7
Type of AF	
Paroxysmal AF (%)	165 (57.7)
Persistent AF (%)	121 (42.3)
Echocardiographic parameters at the initial visit to hospital ^{*1}	
LVDd (mm)	48.0±6.2
LVDs (mm)	31.5±7.4
EF (%)	63.1±12.8
LAD (mm)	42.1±8.8
Underlying cardiovascular diseases	
CHF (%)	65 (22.7)
Valvular disease (%)	41 (14.3)
MI (%)	10 (3.5)
AP (%)	11 (3.8)
DCM (%)	4 (1.4)
HCM (%)	10 (3.5)
No cardiac disease (%)	218 (76.2)
CI (%)	9 (3.1)
TIA (%)	5 (1.7)
Underlying complications	
HT	92 (32.2)
DM	34 (11.9)
Risk score and medication for stroke	
CHADS ₂ score (points) ^{*2}	0.94±1.01
No. of Warfarin administration (%)	140 (49.0)

BMI, body mass index; AF, atrial fibrillation; LVDd, left ventricular diameter of diastole; LVDs, left ventricular diameter of systole; EF, ejection fraction; LAD, left atrium diameter; CHF, congestive heart failure; MI, myocardial infarction; AP, angina pectoris; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; CI, cerebral infarction; TIA, transient ischemic attack; HT, hypertension; DM, diabetes mellitus.

^{*1}Echocardiographic parameters were derived from 257 patients in total patients.

^{*2}CHADS₂ score is calculated by adding 1 point for each of the following conditions: recent CHF, HT, age at least 75 years, or DM and adding 2 points for having had previous stroke.

AF), which were the study patients of the present study.

Data Collection

In each patient, after obtaining electrocardiogram and chest X-ray, evaluation of cardiovascular status was performed using echocardiography, exercise test, 24-h Holter recordings and blood laboratory data according to the attending physicians' decision within 3 months after the first visit. In the present study, the following information has been collected as the initial clinical parameters: gender, age, body mass index, type of AF (paroxysmal or persistent), type of antithrombotic therapy (warfarin, aspirin, or none), coexisting conditions including CHF, valvular diseases, MI, angina pectoris (AP), hypertrophic cardiomyopathy, dilated cardiomyopathy, HT and DM. In some patients, the following cardiographic parameters were also collected including left ventricular diameter of diastole, left ventricular diameter of systole, left atrium diameter and ejection fraction (EF).

Primary Objective

The primary objective of the present study was to determine the mortality and morbidity of Japanese AF patients. The endpoints included total mortality, cardiovascular mortality, incidences of cardiovascular events and AF-associated events.

In the present study, cardiovascular events were defined

Fig 1. (A) Patients distribution according to CHADS₂ score. Horizontal axis shows the CHADS₂ score (0 to 6); vertical axis, the number of patients in each score. (B) Prescription rates of oral anticoagulant according to CHADS₂ score. Horizontal axis shows the CHADS₂ score (0 to 6); vertical axis, the prescription rates of oral anticoagulant for patients in each score.

as emergent hospitalizations for CHF, MI, unstable AP, cerebral infarction and intracranial bleeding. AF-associated events were defined as hospitalizations with AF-related causes including those for cardioversion, catheter ablation and medical treatment to improve patients' quality of life.

Secondary Objectives

The secondary objective was to determine the role of clinical characteristics at the initial visit for the mortality and the morbidity of Japanese AF patients. Because CHF and AF types, both of which represent important characteristics of the AF patients, have long been believed to have a great impact on the prognosis, we first determined the effects of each factor on the mortality and morbidity of our AF patients. Second, to determine the role of other clinical characteristics of the patients, we sought independent risk factors for the mortality and morbidity of AF patients, using all the other clinical variables obtained at the initial visit.

Statistical Analysis

Observed survivals were estimated using the Kaplan–Meier method and log rank tests were used for group comparisons. The association between the parameters at the initial visit and the endpoints was assessed using Cox proportional hazards models. Variables were compared between 2 groups using unpaired t-test. Proportion of patients was compared using chi-square test. Data (except percentage) were presented as mean±SD. Statistical significance was set at p<0.05.

Fig2. Prognosis of study patients. (A) Mortality—Kaplan–Meier survival curves for total atrial fibrillation (AF) patients. Vertical axis shows the survival rate at follow-up (0.8 to 1.0); horizontal axis, follow-up period (0 to 784 days). The solid line represents the survival rate of total mortality; the dotted line, that of cardiovascular mortality. (B) Event-free survival—Kaplan–Meier event-free survival curves for total AF patients. Vertical axis shows the event-free survival rate at follow-up (0.6 to 1.0); horizontal axis, follow-up period. The solid line represents the event-free survival rate of mortality and cardiovascular events; the dotted line, that of total events including mortality, cardiovascular events and AF-associated events.

Ethical Issues

Ethical Committee in the Cardiovascular Institute granted ethical permission for this study.

Results

1. Primary Objective

Patients Characteristics The characteristics of the study patients are shown in Table 1. The mean follow-up period was 430.9 ± 226.5 days. Patients' distribution on CHADS₂ scores and the prescription rate of oral anticoagulant are shown in Figs 1A and B. The mean age of the study patients was 64.1 ± 12.3 years. Of the patients, 71.7% were male and 42.3% had persistent AF. Patients without structural cardiac diseases accounted for 76.2% of the study patients, whose proportion was much higher than that in previous studies in USA⁵ and Europe⁹. Only 3.1% had a history of cerebral infarction, whereas 42.7% were at low risks for stroke. Anticoagulation therapy was given in 49.0% of the total patients.

Mortality During the observation period, the number of total deaths was 6 (2.1%; heart failure 3, cancer 3). The survival curves are shown in Fig 2A, which shows that the cumulative rates of total and cardiovascular death at 1 year were 1.7% and 1.3%, respectively. These figures were remarkably low compared with those of AF patients in USA⁵ and Europe⁹.

Cardiovascular Events and AF-Associated Events There were 31 cardiovascular events in total, the components of which were 26 CHF, 4 MI, 3 unstable AP, 1 cerebral infarction (3 events of MI were accompanied by CHF). The event-free survival curve shown in Fig 2B (solid line) represents the incidence of deaths and cardiovascular events, which shows that the cumulative rate of these events was relatively high, 11.2% at 1 year.

There were 38 AF-associated events (to improve patients' quality of life), the components of which were 6 for cardioversion, 4 for catheter ablation and 28 for medical treatment. The dotted line in Fig 2B represents the incidence of deaths, cardiovascular events and hospitalizations with AF-related causes, which shows that the total events occurred very frequently (26.1%) at 1 year.

These event-free survival curves not only clarified the cardiovascular morbidity of Japanese AF patients, but also showed that these cardiovascular events occurred frequently within 6 months after the initial visit to the hospital and decreased thereafter.

2. Secondary Objectives

Role of CHF In the present study, there were 65 (22.7%) patients complicated with CHF at the initial visit to our hospital. The characteristics of these 65 patients were compared with those without CHF in Table 2, which shows that the patients with CHF were significantly higher in age, prevalence of persistent AF, underlying cardiac diseases and also prescription rate of oral anticoagulation than those without CHF. In addition, the former showed more significantly impaired cardiac systolic function and renal function than the latter.

The event-free survival curves of the patients with and without CHF are shown in Figs 3A–D. There were significant differences in mortality between patients with and without CHF. The cumulative rate at 1 year of total and cardiovascular mortality with CHF vs without CHF were 8.3% vs 0.0% (log rank test, $p < 0.001$), 6.4% vs 0.0% (log rank test, $p = 0.001$), respectively. In morbidity, there were also significant difference between the former and the latter. The cumulative rate at 1 year of mortality and cardiovascular events in patients with and without CHF were 43.5% and 2.0%, respectively (log rank test, $p < 0.001$), whereas that of mortality, cardiovascular events and AF-associated events in the former and the latter were 53.0% and 17.4%, respectively (log rank test, $p < 0.001$).

When we closely examined the event-free survival curves (Figs 3C and D), most of the adverse events occurred on the day of the initial visit to our hospital. In fact, among the total number of 31 cardiovascular events, 25 occurred at their initial visit, which included 24 acute heart failure or exacerbation of CHF (including 4 acute MI; other 1 event was unstable AP without CHF). This implied the existence of a particular group: severely-diseased patients that required hospitalization at the initial visit with heart failure (Table 2). This particular group of 24 patients accounted for 8.3% of the total study patients, which showed extremely high total mortality and cardiovascular mortality (22.6%

Table 2 Characteristics of AF Patients With and Without CHF

	AF with CHF (n=65)	Group A Patients requiring hospitalization at initial visit with CHF (n=24)	Group B Others (n=41)	p value (Group A vs Group B)	AF without CHF (n=221)	p value (with CHF vs without CHF)
Male (%)	47 (72.3)	14 (58.3)	33 (80.5)	0.084 ^{*3}	158 (71.5)	0.000 ^{*3}
Age (years)	67.3±10.6	69.0±9.6	66.2±11.1	0.291 ^{*4}	63.1±12.6	0.016 ^{*4}
BMI (kg/m ²)	22.5±4.7	21.8±6.2	22.8±3.7	0.405 ^{*4}	22.8±4.7	0.591 ^{*4}
Type of AF						
Paroxysmal AF (%)	22 (33.8)	7 (29.2)	15 (36.6)	0.597 ^{*3}	143 (64.7)	<0.001 ^{*3}
Persistent AF (%)	43 (66.2)	17 (70.8)	26 (63.4)		78 (35.3)	
Echocardiographic parameters at the initial visit to hospital ^{*1}						
LVDd (mm)	51.8±8.0	51.0±8.5	52.3±7.7	0.534 ^{*5}	46.8±5.0	<0.001 ^{*5}
LVDs (mm)	36.3±10.2	37.9±11.5	35.3±9.3	0.344 ^{*5}	29.9±5.4	<0.001 ^{*5}
EF (%)	55.7±18.5	49.5±21.3	59.6±15.7	0.037 ^{*5}	65.4±9.2	<0.001 ^{*5}
LAD (mm)	48.1±9.6	51.2±9.6	46.2±9.3	0.046 ^{*4}	40.4±7.7	<0.001 ^{*3}
Underlying cardiovascular diseases						
CHF (%)	—	—	—	—	—	—
Valvular disease (%)	28 (43.1)	9 (37.5)	19 (46.3)	0.606 ^{*3}	13 (5.9)	<0.001 ^{*3}
MI (%)	7 (10.8)	5 (20.8)	2 (4.9)	0.091 ^{*3}	3 (1.4)	0.002 ^{*3}
AP (%)	6 (9.2)	3 (12.5)	3 (7.3)	0.662 ^{*3}	5 (2.3)	0.020 ^{*3}
DCM (%)	4 (6.2)	3 (12.5)	1 (2.4)	0.138 ^{*3}	0 (0.0)	0.002 ^{*3}
HCM (%)	4 (6.2)	1 (4.2)	3 (7.3)	1.000 ^{*3}	6 (2.7)	0.242 ^{*3}
No cardiac disease (%)	21 (32.3)	6 (25.0)	15 (36.6)	0.416 ^{*3}	197 (89.1)	<0.001 ^{*3}
CI (%)	1 (1.5)	0 (0.0)	1 (2.4)	1.000 ^{*3}	8 (3.6)	0.689 ^{*3}
TIA (%)	0 (0.0)	0 (0.0)	0 (0.0)	—	5 (2.3)	0.592 ^{*3}
Underlying complications						
HT	20 (30.8)	8 (33.3)	12 (29.3)	0.785 ^{*3}	72 (32.6)	0.880 ^{*3}
DM	12 (18.5)	5 (20.8)	7 (17.1)	0.748 ^{*3}	22 (10.0)	0.080 ^{*3}
Risk score and medication for stroke						
CHADS ₂ score (points) ^{*2}	1.48±0.89	1.92±0.83	1.22±0.82	0.002 ^{*4}	0.78±0.99	<0.001 ^{*4}
No. of Warfarin administration (%)	45 (69.2)	17 (70.8)	28 (68.3)	1.000 ^{*3}	95 (43.0)	<0.001 ^{*3}

Group A, AF patients with CHF hospitalization at the initial visit; Group B, other AF patients with CHF. Other abbreviations are same as Table 1.

^{*1}Echocardiographic parameters were derived from 62, 195, 24 and 38 patients in those with CHF, without CHF, of Group A and of Group B, respectively.

^{*2}CHADS₂ score is explained in Table 1. ^{*3}Chi-square test. ^{*4}Student's *t*-test. ^{*5}Welch's *t*-test.

and 18.1%, respectively) at 1 year.

Role of Type in AF (Paroxysmal AF vs Persistent AF)

The characteristics of the patients showed that persistent AF was associated with older age (66.1 vs 62.6 years old, *p*=0.016), lower EF (59.3% vs 66.2%, *p*<0.001) and more coincidence of underlying cardiovascular diseases (33.9% vs 16.4%, *p*=0.001) than paroxysmal AF. Also, CHADS₂ score was higher in persistent AF than in paroxysmal AF (1.00 vs 0.73, *p*=0.023). The survival curves showed that cumulative rate at 1 year of total mortality, cardiovascular mortality, cardiovascular events and AF-associated events of paroxysmal vs persistent AF were 0.7% vs 3.1% (log rank test, *p*=0.178), 0.7% vs 2.2% (*p*=0.372), 6.5% vs 17.9% (*p*=0.004) and 25.2% vs 27.5% (*p*=0.607), respectively. There were no significant differences in mortality and incidence of AF-associated events between patients with paroxysmal and persistent AF, although the incidence of cardiovascular events was significantly higher in patients with the latter than in those with the former.

Risk Factors for Prognosis According to the results of analysis with Kaplan–Meier method and comparison with log rank test, CHF was related with higher mortality and morbidity in our study population, whereas the type of AF was related only with higher morbidity but not with mortality. However, the background characteristics of the patients were significantly different between the groups, and therefore the different outcome could result from many other co-existing factors. To determine the independent effects of CHF, AF types and also other clinical variables on the prog-

nosis of Japanese AF patients, multivariate analysis was performed.

The results of the multivariate analysis in total mortality are shown in Table 3 (A), which shows that hospitalization at the initial visit was closely associated with higher mortality (confidence interval (CI): 2.158–270.694, *p*=0.010) and that warfarin use was associated with lower mortality (CI: 0.003–0.446, *p*=0.010). For cardiovascular and AF-associated events, CHF was the only independent risk factor as shown in Table 3 (B and C), respectively. Otherwise, the type of AF was not an independent risk factor for mortality, cardiovascular events and AF-associated events.

Discussion

Major Findings

The major findings of the present study were as follows: (1) AF accounted for 11.8% of new patients visiting a cardiovascular hospital in 2004; (2) total mortality, cardiovascular mortality and morbidity of the total AF patients were 1.7%, 1.3% and 11.2%, respectively, at 1 year after the initial visit; (3) AF patients with CHF exhibited higher mortality (7.3%), and hospitalization for CHF at the initial visit increased the mortality up to 22.6%; (4) no significant differences in mortality was observed between paroxysmal and persistent AF, although persistent AF was more associated with cardiovascular events; and (5) multiple regression analysis revealed that hospitalization at the initial visit and lack of anticoagulation were independent predictors for

Fig 3. Prognosis of atrial fibrillation (AF) Patients with and without congestive heart failure (CHF). (A) Mortality—Kaplan–Meier survival curves for mortality. (B) Cardiovascular mortality—Kaplan–Meier event-free survival curves for cardiovascular mortality. (C) Mortality and cardiovascular events—Kaplan–Meier event-free survival curves for mortality and cardiovascular events. (D) AF-associated events and (C) Kaplan–Meier event-free survival curves for mortality, cardiovascular events and AF-associated events. The solid line represents the survival rate of patients with CHF (n=65); the dotted line, that of patients without CHF (n=221). Vertical axis shows the survival rate at follow-up (A, B; 0.6 to 1.0; C, D; 0 to 1.0); horizontal axis, follow-up period (0 to 784 days).

Table 3 Risk Factors for (A) Total Mortality, (B) (A)+Cardiovascular Events and (C) (B)+Hospitalizations With AF-Related Causes in Total AF Patients

	Hazard ratio	95% confidence interval	p value
<i>(A) Total mortality</i>			
Hospitalization at first visit with CHF	24.170	2.158–270.694	0.010
CHF	472,076.437	0.000–1.579×10 ⁹⁶	0.902
Persistent AF	1.511	0.210–10.891	0.682
Age	0.953	0.856–1.060	0.376
Female	3.448	0.326–36.452	0.304
BMI	1.040	0.855–1.265	0.692
Underlying cardiovascular disease	0.330	0.038–2.861	0.314
Warfarin use	0.035	0.003–0.446	0.010
<i>(B) (A)+Cardiovascular events</i>			
CHF	20.887	5.476–79.676	<0.001
Persistent AF	1.134	0.532–2.420	0.745
Age	1.011	0.972–1.051	0.585
Female	1.455	0.702–3.016	0.313
BMI	0.967	0.899–1.040	0.366
Underlying cardiovascular disease	1.886	0.769–4.629	0.166
Warfarin use	1.196	0.546–2.619	0.655
<i>(C) (B)+Hospitalizations with AF-related causes</i>			
CHF	4.015	2.184–7.384	<0.001
Persistent AF	0.710	0.430–1.171	0.180
Age	1.001	0.980–1.022	0.950
Female	1.314	0.797–2.165	0.284
BMI	0.969	0.922–1.018	0.208
Underlying cardiovascular disease	1.322	0.727–2.404	0.361
Warfarin use	1.261	0.767–2.073	0.362

Abbreviations are same as Table 1.

mortality and that CHF was the only independent predictor of cardiovascular events.

Prevalence of AF Patients

The prevalence of AF has been reported between 1% and 2% of the general population in the USA.^{6,8} In Japan, its prevalence seems somewhat lower, as a recent study reported (0.64% of the general population).¹² From hospital-based studies, the prevalence rose expectedly; 18% in a Danish study⁶ and slightly lower figure (14%) in a previous Japanese study.¹³ In the present study, 11.8% of new patients were with AF, as is consistent with these previous reports. At present, it should be noted that >10% of patients visiting cardiovascular clinics are complicated by AF in Japan, implying that the arrhythmia is one of medical problems of great concern.

Patients Backgrounds

In previous studies, differences and similarities in the characteristics of AF patients can be seen between foreign countries and Japan. (1) Mean age of AF patients were between 69 and 75 years in the USA,^{5,8-11} whereas the age was younger, at around 65 years in Japan.¹²⁻¹⁴ (2) The percentage of male was ~55% in the USA,^{10,11} whereas in Japan, it was lower (45%) in a general population-based study¹² and higher (around 65%) in hospital-based population studies.^{13,14} (3) Among hospital-based population, paroxysmal AF accounted 53% of AF patients in the USA,¹¹ whereas it was under 40% in Japan.^{13,14} (4) Prescription rate of warfarin has been recently increased from under 15–50% both in the USA^{17,18} and in Japan.^{13,14} (5) The prevalence of heart failure in AF patients was as high as up to 42% in the USA,¹⁹ whereas it was lower (22%) in Japan.¹⁶

In the present study, mean age (64.1 years), prescription rate of warfarin (49.0%) and the prevalence of heart failure (22.7%) were almost similar to those in the previous Japanese studies, whereas percentage of male (71.7%) and prevalence of paroxysmal AF (57.7%) was rather high.^{13,16}

Incidence Rate of Mortality

Total mortality of AF patients has been reported to be diverse. In a previous cohort study in the USA,⁵ total mortality of AF patients was over 10% at 1 year after diagnosis even in younger patients and increased dramatically with increasing ages. In another cohort study in Chile,⁹ total mortality was reported as 15% during 6 months. In contrast, that of Japanese AF patients seemed to be low: 2% per year in cardiovascular clinics¹³ and also a similar figure in a general population-based study.¹² The present results supported these Japanese studies by identifying similar total mortality (1.7% at 1 year). The mortality of Japanese AF patients was actually extremely low, which was almost comparable to that of AF patients without structural heart diseases in foreign studies.^{20,21} This difference deserves discussion, but could result from many clinical factors: age, prevalence of CHF, structural heart diseases, stroke, also medical environments including health insurance system and hospital access.

Role of CHF

CHF has a close relation to AF and plays a very important role in prognosis of AF patients.^{19,22} In foreign studies, the mortality rate of AF patients with CHF at 1 year after diagnosis was reported to be high between 13% and 20%.^{23,24} Also in the present study, mortality at 1 year of

Japanese AF patients with CHF should be estimated high (7.3%) as compared with those free from CHF, although there might be some differences in the figures between countries. Regarding the prevalence of CHF in AF patients, the present study showed much lower figure (22.7%) than that in the USA (42%).¹⁹ Because differences in the prevalence of CHF should affect the mortality of total AF patients, the lower mortality of Japanese AF patients could be attributed, in part, to the CHF prevalence.

Role of Type in AF (Paroxysmal vs Persistent)

Paroxysmal AF has been reported to develop to persistent AF at a rate of 7% per year in Western country²⁵ and 5.5–6.3% per year in Japan.^{26,27} Consequently, it has been believed that the prognosis of AF patients becomes worse according to the progression of AF. Actually, it has been reported that the mortality rates in patients with paroxysmal AF (0.9%)²⁸ was worse compared with those with persistent AF (2.6–3.7%).^{3,29} The present study also demonstrated similar figures: 0.7% in paroxysmal AF and 3.1% in persistent AF. However, in the present study, the patients' backgrounds were significantly different in many aspects between paroxysmal and persistent AF, and those with persistent AF were more associated with impaired patients' conditions, which could affect the difference in mortality between paroxysmal and persistent AF. Actually, the mortality rates were not significantly different between paroxysmal and persistent AF, possibly implying limited role of AF types on mortality, and rather important roles of co-morbidities of AF patients.

Independent Risk Factors for Mortality and Morbidity in Japanese AF Patients

There have been several factors that are considered to affect the mortality of AF patients, including older age, AF types and CHF.⁹ In the present study, all these clinical variables could not be determined as independent risk factors for mortality, although CHF was determined as the only independent risk factor for morbidity including cardiovascular events and AF-associated events. This might result from relatively short follow-up period and small number of events. However, we found a much more sensitive marker predicting mortality of Japanese AF patients, requirement of hospitalization for CHF at the initial visit. Actually, in the present study, those with this particular condition had extremely poor prognosis (22.7% of mortality) at 1 year after the initial visit, which was much greater than that of patients with CHF (7.3%) as well as total AF patients in the present study (1.7%). Furthermore, it should be expected because the marker represents the severity of CHF. Otherwise, in a relatively short-term perspective, it should be noted that AF types were not associated with mortality of Japanese AF patients.

Moreover in the present study, use of warfarin was significantly related with reduction of mortality, although there was no death associated with stroke in the total AF patients. This might appear strange, because AF patients without warfarin experienced no stroke-related death. However, half of the events in mortality could be attributed to malignancy. In patients with cancer, attending physicians avoided the use of warfarin, considering the risk of bleeding from the site of cancer. Therefore, use of warfarin could contribute to improved mortality as a surrogate marker for being free from malignancy, as is the case in the AFFIRM study.³⁰

Limitations

The present study has several limitations: (1) the present study was based on single center experience, and therefore it might be difficult to apply the results to the entire AF Japanese patients; (2) the number of study patients was rather small and the observation period was short in view of the long lives of AF patients; (3) treatment for AF itself and for co-morbidities in our patients had a wide range of drugs, and therefore could not be analyzed in view of other than anticoagulation therapy; and (4) the occurrence of AF-associated events that do not include emergent cardiovascular events could be biased by patients and physicians, because they were based on discussion between them.

Nevertheless, the present study identified the mortality and morbidity of Japanese AF patients in a prospective cohort fashion, thus providing important basis for decision-making in managing Japanese AF patients.

Conclusions

The present study described clinical characteristics of Japanese AF patients as a single center experience. The mortality and morbidity of Japanese AF patients during 1 year after an initial visit to a cardiovascular hospital were 1.2% and 11.2%, respectively. The role of co-morbidities might be substantiated more than expected, although the prevalence of CHF was very low in Japanese AF patients. However, Japanese AF patients without CHF showed remarkably good prognosis in a short-term perspective.

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