Effects of Atrial Fibrillation on Long-Term Outcomes in Patients Hospitalized for Heart Failure in Japan

— A Report From the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) —

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Background: Atrial fibrillation (AF) is a common arrhythmia in patients with heart failure (HF), but its prognostic importance is controversial. The effect of AF on long-term outcomes, including mortality and rehospitalization, among unselected HF patients hospitalized with HF in routine clinical practice in Japan was assessed in the present study.

Methods and Results: The Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) prospectively studied the characteristics and treatment strategies of a broad sample of patients hospitalized with worsening HF and the outcomes were followed with an average of 2.4 years of follow-up. The study cohort (n=2,659) was grouped according to the presence (n=937; 35.2%) or absence (n=1,722; 64.8%) of AF at baseline. After multi-variable adjustment, patients with and without AF had a comparable risk for all-cause death (adjusted hazard ratio (HR) 0.931, 95% confidence interval (CI) 0.690–1.258, P=0.643), cardiac death (adjusted HR 0.949, 95%CI 0.655–1.377, P=0.784), rehospitalization because of the worsening HF (adjusted HR 1.028, 95%CI 0.816–1.295, P=0.816), and all-cause death or rehospitalization (adjusted HR 1.039, 95%CI 0.842–1.281, P=0.722).

Conclusions: Among patients hospitalized for HF in Japan, AF was common, but was not an independent risk for long-term adverse outcomes, including death or rehospitalization, in routine clinical practice. (Circ J 2009; 73: 2084–2090)

Key Words: Atrial fibrillation; Heart failure; Mortality; Outcomes; Rehospitalization

Atrial fibrillation (AF) is common in patients with chronic heart failure (HF). In the previous studies, the prevalence of AF in patients with HF has been reported to be 10–50%.^{1–6} It may cause hemodynamic deterioration and worsen HF by several mechanisms, including loss of atrial contraction, rapid ventricular rate, and irregular ventricular filling time. However, previous studies that investigated the prognostic impact of AF in HF have reported controversial results.^{2,3,5–16} Some studies reported that AF was associated with worse outcomes,^{2,7–13} whereas in others, AF was not an independent predictor of mortality.^{3,5,6,14–16} These discrepancies among the reports are partly attributable to differences in both the patients studied and the definition of AF. Therefore, better understanding of the prevalence, demographics, and clinical characteristics of HF patients with AF, and the relationship of AF to long-term outcomes including mortality and hospitalization, is needed. Moreover, most previous studies of this important issue have been reported from the United States and Europe,^{2,3,5–16} so the effect of AF on HF patient outcomes needs to be

assessed in a representative cohort in Japan.

The Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) prospectively studied the characteristics and treatments used in a broad sample of patients hospitalized with HF in Japan from January 2004 to June 2005 and the outcomes, including death and rehospitalization, were followed through 2007.¹⁷ The JCARE-CARD program enrolled in a web-based registry 2,675 patients admitted with HF at 164 participating hospitals and with an average follow-up of 2.4 years.

The aim of the present study was to use the JCARE-CARD database to analyze the prognostic value of AF on long-term mortality and rehospitalization in a broad sample of Japanese patients hospitalized with HF.

Methods

Study Patients

The details of the JCARE-CARD have been described previously.¹⁷ Briefly, eligible patients were those hospitalized

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Table 1. Baseline Patient Characteristics

	Total (n=2,659)	AF (n=937)	No AF (n=1,722)	P value
Demographic data				
Age, years (mean±SD)	71.0±13.4	72.6±11.6	70.1±14.2	0.001
Male, %	59.8	61.9	58.7	0.103
BMI, kg/m ²	22.3±4.1	22.1±3.9	22.4±4.2	0.178
Cause of heart failure, %				
Ischemic heart disease	32.0	19.2	39.0	<0.001
Valvular heart disease	27.8	41.2	20.5	<0.001
Hypertensive heart disease	24.4	19.9	26.9	<0.001
Dilated cardiomyopathy	18.2	16.6	19.0	0.126
Hypertrophic cardiomyopathy	2.2	2.2	2.2	0.954
Medical history, %				
Hypertension	52.8	47.0	56.0	<0.001
Diabetes mellitus	29.9	22.1	34.1	<0.001
Hyperlipidemia	24.8	17.8	28.7	<0.001
Hyperuricemia	46.9	50.1	45.2	0.017
Prior stroke	15.0	17.7	13.5	0.004
COPD	6.7	6.2	7.0	0.462
Smoking	37.7	35.3	39.0	0.067
Prior MI	26.9	15.3	33.2	<0.001
Sustained VT/VF	6.2	5.6	6.5	0.364
Procedures, %				
PCI	17.7	9.8	22.0	<0.001
CABG	9.3	6.2	10.9	<0.001
Valvular surgery	6.7	11.6	4.0	<0.001
PPM	1.1	1.1	1.0	0.958
ICD	2.1	1.9	2.1	0.705
CRT	1.6	2.0	1.4	0.238
Vital signs at discharge				
NYHA functional class	1.8±0.7	1.8±0.7	1.8±0.7	0.215
Heart rate, beats/min	70.5±12.0	70.6±12.5	70.4±11.8	0.950
SBP, mmHg	117.0±18.6	114.8±16.9	118.2±19.4	<0.001
DBP, mmHg	66.1±11.6	65.8±11.2	66.2±11.8	0.372
Laboratory data				
Serum creatinine, mg/dl	1.4±1.2	1.2±0.7	1.5±1.4	0.078
Hemoglobin, g/dl	12.0±3.3	12.3±2.8	11.9±3.5	0.025
Plasma BNP, pg/ml	389±507	339±328	413±575	0.884
Echocardiographic data at discharge				
LV EDD, mm	55.5±10.3	54.3±9.8	56.1±10.5	0.006
LV ESD, mm	43.0±12.3	40.8±11.7	44.0±12.4	<0.001
LVEF, %	44.2±16.5	47.9±16.5	42.3±16.1	<0.001

Values are percent or mean±SD.

AF, atrial fibrillation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; VT/VF, ventricular tachycardia/fibrillation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; PPM, permanent pacemaker; ICD, implantable cardioverter defibrillator; CRT, cardiac resynchronization therapy; NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; BNP, B-type natriuretic peptide; LV, left ventricular; EDD, end-diastolic diameter; ESD, end-systolic diameter; EF, ejection fraction.

because of worsening HF as the primary cause of admission. The study hospitals were encouraged to register the patients as consecutively as possible. For each patient, baseline data included (1) demography; (2) cause of HF; (3) precipitating cause; (4) comorbidities; (5) complications; (6) clinical status; (7) electrocardiographic and echocardiographic findings; (8) plasma brain-type natriuretic peptide level; and (9) treatments, including discharge medications. Ischemic heart disease was defined as present if the patient had 1 of the following: (1) documented history of myocardial infarction, angina or prior coronary revascularization, (2) pathologic Q waves on ECG, (3) reversible defects on a thallium stress test, or (4) >75% stenosis in 1 or more coronary arteries on coronary angiograms. The data were entered using a web-based electronic data capture (EDC) system licensed by the JCARE-CARD (www.jcare-card.jp).

The JCARE-CARD enrolled a total of 2,675 patients hospitalized for HF at 164 participating hospitals from January 2004 to June 2005. Only patients who survived the initial

hospitalization were included in the follow-up analysis. The diagnosis of AF was based on a 12-lead standard ECG performed at the time of inclusion in the study. Sixteen patients were excluded because of missing ECG data, resulting in 2,659 patients included in this analysis. They were divided into 2 groups according to the presence (n=937; 35.2%) or absence (n=1,722; 64.8%) of AF.

Outcomes

The status of all patients was surveyed on June 2006 at least 1 year after discharge and the following information was obtained from the participating cardiologists using the web-based EDC system: (1) survival, (2) cause of death, and (3) rehospitalization because of exacerbation of HF that required more than continuation of their usual therapy on prior admission. Follow-up data were obtained for 2,105 of the 2,659 patients (79.2%) and for 742 of the 937 AF patients (79.2%). Mean post-discharge follow up was 884±255 days (2.4±0.6 years).

Table 2. Medication Use at Hospital Discharge

	Total (n=2,659)	AF (n=937)	No AF (n=1,722)	P value
ACE inhibitor, %	37.4	35.9	38.3	0.236
ARB, %	44.3	42.7	45.2	0.230
β -blocker, %	48.7	44.5	50.9	0.002
Carvedilol, %	40.1	35.1	42.8	<0.001
Bisoprolol, %	3.6	3.8	3.5	0.715
Metoprolol, %	3.1	3.1	3.0	0.892
Other β -blockers, %	2.0	2.6	1.6	0.105
Diuretics, %	88.2	91.5	86.4	<0.001
Digitalis, %	30.9	51.9	19.5	<0.001
Calcium-channel blocker, %	25.2	25.6	24.9	0.731
Nitrates, %	23.3	17.8	26.3	<0.001
Antiarrhythmics, %	16.6	14.5	17.8	0.033
Amiodarone, %	7.1	6.8	7.2	0.750
Other antiarrhythmics, %	9.5	7.6	10.6	0.015
Aspirin, %	47.2	38.9	51.7	<0.001
Other antiplatelet drugs, %	11.9	8.5	13.8	<0.001
Warfarin, %	40.8	70.1	24.9	<0.001
Statin, %	19.9	14.8	22.7	<0.001

ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker. See Table 1 for other abbreviation.

Figure. Kaplan-Meier event-free curves free from all-cause death (A), cardiac death (B), rehospitalization for worsening heart failure (C), and all-cause death or rehospitalization (D) comparing patients with atrial fibrillation (AF) (red lines) and without AF (black lines).

Table 3. Subgroup Analysis of All-Cause Death by the Presence of AF

Subgroup	n	Hazard ratio for mortality AF vs No AF	95%CI	P value
Males	1,255	0.894	0.596–1.342	0.589
Females	850	0.964	0.602–1.542	0.878
Age ≥65 years	1,506	0.983	0.712–1.359	0.919
Age <65 years	599	1.069	0.472–2.421	0.873
Ischemic	658	0.772	0.446–1.337	0.355
Non-ischemic	1,447	1.058	0.720–1.552	0.775
Hypertensive heart disease	501	0.866	0.428–1.750	0.688
No hypertensive heart disease	1,604	1.003	0.714–1.409	0.985
Valvular	594	0.908	0.548–1.507	0.709
Non-valvular	1,511	0.959	0.661–1.390	0.824
Diabetes mellitus	618	1.246	0.665–2.336	0.493
No diabetes mellitus	1,483	0.798	0.561–1.135	0.209
Prior stroke	307	0.795	0.360–1.757	0.571
No prior stroke	1,769	1.007	0.723–1.402	0.969
β-blocker use	1,024	1.102	0.657–1.850	0.713
No β-blocker use	1,081	0.824	0.566–1.199	0.311
LVEF <40%	414	0.947	0.412–2.177	0.897
LVEF ≥40%	532	1.271	0.658–2.453	0.476

CI, confidence interval. See Table 1 for other abbreviations.

Statistical Analysis

Patient characteristics and treatments were compared using the Pearson chi-square test for categorical variables, Student's t-test for normally distributed continuous variables, and the Mann-Whitney U test for continuous variables not normally distributed. Cumulative event-free rates during follow-up were derived using the Kaplan-Meier method. The relationship between the presence of AF at baseline and the outcome among patients was evaluated with multivariable adjustment. Baseline clinical variables, treatment factors, and the severity of HF at discharge were used in developing the post-discharge Cox proportional hazard models. A P value of <0.05 was used as the criterion for variables to stay in the model. SPSS version 16.0 J for Windows (Chicago, IL, USA) was used for all statistical analyses.

Results

Patient Characteristics

The present study included 2,659 patients with a mean age of 71.0±13.4 years and 59.8% men (Table 1). The cause of HF was ischemic in 32.0%, valvular in 27.8%, hypertensive in 24.4%, and dilated cardiomyopathic in 18.2%. The mean left ventricular ejection fraction (LVEF) was 44.2±16.5% at discharge.

Patients with AF were significantly older and more often had valvular heart disease as the cause of HF, but less ischemic and hypertensive heart disease (Table 1). They were more likely to have had a prior stroke and hyperuricemia, but less often to have had hypertension, diabetes, hyperlipidemia, and a prior myocardial infarction. Their hemoglobin concentration was significantly higher and the LV end-diastolic diameters were smaller and LVEF greater than in the patients without AF.

Patients with AF were prescribed more often with diuretics, digitalis, and warfarin at discharge (Table 2). On the other hand, β-blockers, nitrates, antiarrhythmic, aspirin, antiplatelets, and statins were administered less in these patients.

Outcomes

During follow-up of 2.4 years after hospital discharge, the rates of adverse outcomes were as follows: all-cause death 21.2%, cardiac death 14.2%, rehospitalization because of worsening HF 35.5%, and all-cause death or rehospitalization 43.4%. These event rates were comparable between patients with and without AF (Figure).

After adjustment for covariates, patients with AF had a comparable risk for all-cause death (adjusted hazard ratio (HR) 0.931, 95% confidence interval (CI) 0.690–1.258, P=0.643), cardiac death (adjusted HR 0.949, 95%CI 0.655–1.377, P=0.784), rehospitalization because of worsening HF (adjusted HR 1.028, 95%CI 0.816–1.295, P=0.816), and all-cause death or rehospitalization (adjusted HR 1.039, 95%CI 0.842–1.281, P=0.722).

The results of subgroup analysis for all-cause death stratified by sex, age (≥65 vs <65 years), etiology (ischemic vs non-ischemic, hypertensive vs no hypertensive, and valvular vs non-valvular heart disease), comorbidity (diabetes vs no diabetes and prior stroke vs no prior stroke), medication use (β-blocker vs no β-blocker use), and LVEF (<40% vs ≥40%) are shown in Table 3. The finding on the primary analysis that the risk of adverse outcomes in patients with AF was not significantly different from those without AF was similarly found in each subgroup.

Of the patients with AF (n=937), 571 (60.9%) were treated with medications aimed at rate control, 129 (13.8%) were treated for rhythm control, and 192 (20.5%) had neither rate nor rhythm control therapy. Follow-up data were obtained in 497 of the 571 AF patients treated by rate control and in 111 of the 129 those treated by rhythm control. After adjustment for covariates, AF patients treated by rate or rhythm control had a comparable risk for all-cause death (adjusted HR 0.713, 95%CI 0.319–1.593, P=0.433), cardiac death (adjusted HR 0.591, 95%CI 0.206–1.697, P=0.329), rehospitalization because of worsening HF (adjusted HR 1.073, 95%CI 0.677–1.700, P=0.764), and all-cause death or rehospitalization (adjusted HR 0.933, 95%CI 0.598–1.455, P=0.759) (Table 4).

After adjustment for covariates, AF patients using warfarin had a significantly better outcome for all-cause death than those not using warfarin (adjusted HR 0.631, 95%CI

Table 4. Cox Analysis for HR of Outcomes Associated With the Treatment Strategy Among AF Patients

Outcome	n (%)		Adjusted HR	95%CI	P value
	Rate control (n=497)	Rhythm control (n=111)			
All-cause death	93 (18.7%)	21 (18.9%)	0.713	0.319–1.593	0.433
Cardiac death	63 (12.7%)	17 (15.3%)	0.591	0.206–1.697	0.329
Rehospitalization	191 (38.4%)	53 (47.7%)	1.073	0.677–1.700	0.764
All-cause death or rehospitalization	221 (44.5%)	55 (49.5%)	0.933	0.598–1.455	0.759

The Cox regression model used in the analysis adjusted for the following covariates: age, cause of heart failure (ischemic, hypertensive or valvular heart disease), medical history (diabetes, hyperlipidemia, hyperuricemia, prior stroke), serum creatinine, hemoglobin and BNP levels, LVEF, and medication use (diuretics, nitrates, aspirin, antiplatelet, warfarin, statin). AF patients treated for rate control were the reference group. BNP and LVEF at discharge were entered into the model as categorical variables; ie, BNP at discharge ≥ 240 pg/ml or < 240 pg/ml or unknown and LVEF at discharge $< 40\%$ or $\geq 40\%$ or unknown.

HR, hazard ratios. See Tables 1, 3 for other abbreviations.

Table 5. Cox Analysis for HR of Outcomes Associated With Warfarin Use Among AF Patients

Outcome	n (%)		Adjusted HR	95%CI	P value
	Warfarin (n=520)	No warfarin (n=222)			
All-cause death	88 (16.9%)	74 (33.3%)	0.631	0.403–0.990	0.045
Cardiac death	62 (11.9%)	48 (21.6%)	0.687	0.396–1.190	0.180
Rehospitalization	187 (36.0%)	85 (38.3%)	0.858	0.593–1.242	0.417
All-cause death or rehospitalization	219 (42.1%)	114 (51.4%)	0.826	0.596–1.145	0.251

The Cox regression model used in the analysis adjusted for the following covariates: age, cause of heart failure (ischemic, hypertensive or valvular heart disease), medical history (diabetes, hyperlipidemia, hyperuricemia, prior stroke), serum creatinine, hemoglobin, and BNP levels, LVEF, and medication use (β -blocker, diuretics, digitalis, nitrates, antiarrhythmic, aspirin, antiplatelets, statin). AF patients without warfarin use were the reference group. BNP and LVEF at discharge were entered into the model as categorical variables; ie, BNP at discharge ≥ 240 pg/ml or < 240 pg/ml or unknown and LVEF at discharge $< 40\%$ or $\geq 40\%$ or unknown.

See Tables 1, 3, 4 for abbreviations.

0.403–0.990, $P=0.045$). However, AF patients with and without warfarin use had a comparable risk for cardiac death (adjusted HR 0.687, 95%CI 0.396–1.190, $P=0.180$), rehospitalization because of worsening HF (adjusted HR 0.858, 95%CI 0.593–1.242, $P=0.417$), and all-cause death or rehospitalization (adjusted HR 0.826, 95%CI 0.596–1.145, $P=0.251$) (Table 5).

Discussion

The present study used the JCARE-CARD database and found that AF was seen in 35% of patients hospitalized with HF. These patients more often had a valvular etiology for HF and greater LVEF. They were prescribed more digitalis and warfarin. Importantly, the risk of unadjusted, as well as adjusted adverse outcomes, including all-cause death, cardiac death, and rehospitalization because of worsening HF, was comparable between the AF and no-AF groups during long-term follow-up of 2.4 years.

The present study results demonstrated that AF was not associated with adverse long-term outcomes in patients hospitalized with HF. However, the effect of AF on the mortality of HF patients is a controversial issue. Previous studies demonstrated that AF might be a prognostic factor in HF patients and this discrepancy might be associated with differences in the subjects and definitions of AF used among the studies. First, the present results consolidated previous studies conducted in selected patients as in the Veterans Affairs Vasodilator-Heart Failure Trial (V-HeFT) I and II,³ the PRIME-II,¹⁵ the Carvedilol or Metoprolol European Trial (COMET),⁵ the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity Echocardiographic Substudy (CHARMES),¹⁶ and reports

from Pennsylvania¹⁴ and France.⁶ In the V-HeFT I and II studies, AF did not increase major morbidity or mortality of patients with mild to moderate HF.³ Moreover, in the Prospective Randomized study of Ibopamine on Mortality and Efficacy (PRIME-II), the presence or development of AF in patients with severe HF was not independently related to adverse outcomes.¹⁵ The Framingham Heart Study demonstrated that preexisting AF was not associated with adverse survival in subjects with HF.¹¹ On the other hand, in a retrospective analysis of the Studies of Left Ventricular Dysfunction (SOLVD) trial, Dries et al reported that, after multivariate analysis, AF was significantly associated with all-cause mortality (adjusted HR 1.34, 95%CI 1.12–1.62, $P=0.002$), which could be largely related to progressive HF.⁷ In the VALsartan In Acute myocardial infarction (VALIANT) trial, both current and prior AF were associated with an increased risk of death and major cardiovascular events following acute myocardial infarction complicated by HF or LV dysfunction.¹² Similarly, the Candesartan in Heart failure-Assessment of Reduction in Mortality and morbidity (CHARM) study reported that AF predicted a high risk of cardiovascular morbidity and mortality in patients with HF and either reduced or preserved LVEF.¹³ Most of the previous data are from cohort studies and large-scale clinical trials. Although several studies have shown a comparable risk of AF in patients with HF, they are recognized as unrepresentative of the general HF population encountered in clinical practice. Therefore, uncertainty pertaining to the applicability of these findings to the population of patients with HF at large persists. It is of critical importance to analyze registry data of enrolled HF patients without any exclusion criteria. Moreover, results might be influenced by differences in the cause of HF or the medical

care, including length of hospital stay and medication use, of Japanese patients compared with Western patients. For instance, in comparison with community-based studies of HF from the USA and Europe, Japanese cohort studies have demonstrated that mean age, prevalence of preserved EF, and trends in seasonal variation are comparable, but that the incidence of HF is obviously lower.¹⁸ Therefore, it is of critical importance to analyze Japanese registry data enrolled HF patients. Previous Japanese cohort studies of HF patients have also reported that AF is not a significant risk factor for cardiac death.¹⁹ The present results from the JCARE-CARD supported previous reports that AF is not associated with long-term adverse outcomes in Japanese HF patients. Second, the present study divided the study patients into AF and non-AF groups according to the baseline ECG findings, so patients with a history of AF, but who were in sinus rhythm at baseline, were categorized as non-AF. Moreover, the present study had no data regarding the new onset of AF. The Framingham Heart Study and the COMET showed that preexisting AF was not associated with adverse outcomes, whereas new onset AF was associated with increased mortality and morbidity in HF patients.^{5,11} New onset AF might cause more drastic deterioration of hemodynamics than preexisting AF, which could be attributable to the worsening of HF. However, PRIME-II demonstrated the opposite result that neither preexisting nor new onset AF was independently related to adverse outcomes during long-term follow-up in patients with advanced chronic HF.¹⁵ Therefore, the effect of preexisting AF, as well as new onset AF, on the mortality of HF patients is still a controversial issue.

AF is the 1 of the most important precipitating factors related to diastolic dysfunction.^{16,20} However, data on the prognostic effect of AF in patients with HF and preserved EF are conflicting. In the subgroup analysis of the present study, HF patients with LVEF $\geq 40\%$ ($n=523$) also had a comparable risk between AF and no-AF for long-term adverse outcomes (**Table 3**). Our findings are consistent with those of CHARMES¹⁶ and the report from France,⁶ in which the risk of AF was comparable even in HF patients with preserved systolic function. However we are not in agreement with the findings of CHARM,¹³ in which that the presence of AF was associated with a greater increase in the risk of cardiovascular events and mortality in the group with preserved EF (EF $>40\%$) compared with reduced EF.

Current therapeutic options for HF patients with AF include rate or rhythm control to restore and maintain sinus rhythm.²¹ The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial could not demonstrate a significant difference in mortality between these 2 options in patients with AF after an average follow-up of 3.5 years.²² In the Rate Control vs Electrical cardioversion for persistent atrial fibrillation (RACE) study, the incidence of hospitalization with HF was 3.5% with rate control and 4.5% with rhythm control.²³ Similarly, there were no differences in the composite endpoint (overall mortality, cerebrovascular complications, cardiopulmonary resuscitation, and embolic events) in the Strategies of Treatment of Atrial Fibrillation (STAF) trial²⁴ or in the composite endpoint (death, thromboembolic complications, and major hemorrhage) in the How to Treat Chronic Atrial Fibrillation (HOT CAFE) study.²⁵ In the Atrial Fibrillation and Congestive Heart Failure (AF-CHF) trial, rhythm control did not reduce the rate of death from cardiovascular causes, as compared with rate control, in patients with LVEF $\leq 35\%$.²⁶ Moreover,

the present study demonstrated that AF patients treated for rate or rhythm control had a comparable risk for all-cause death, cardiac death, rehospitalization due to the worsening HF, and all-cause death or rehospitalization (**Table 4**).

In the present study, warfarin use reduced the rate of all-cause death of AF patients. However, the rates of cardiac death, rehospitalization because of worsening HF, and death or rehospitalization were comparable between patients with and without warfarin use. These results were consistent with the prospective cohort study by Suzuki et al in which the lack of anticoagulation was an independent predictor for mortality in AF patients.²⁷ They might be due to the efficacy of warfarin in the prevention of embolic stroke especially in patients with AF.

Study Limitations

Several limitations inherent in the design of the JCARE-CARD should be considered. First, documentation of AF at baseline might not accurately reflect the persistent presence of AF after hospital discharge. Moreover, the present study did not obtain data regarding new onset AF during follow-up, which has been reported to have a prognostic effect in HF patients.^{5,11,15} Thus in the present study we could not assess the effects of subsequent AF on the outcomes. Second, the JCARE-CARD is not a prospective randomized trial and, despite covariate adjustment, other measured and unmeasured factors might have influenced outcomes. We could not completely exclude other unmeasured factors that might also affect outcomes. Third, in the JCARE-CARD database, data of rhythm control therapy (eg, electrical cardioversion and catheter ablation) were not obtained, except for the use of antiarrhythmic drugs. Fourth, previous studies have demonstrated that the C-reactive protein (CRP) level is significantly higher in patients with AF than in those without AF and is associated with development of AF.^{28,29} However, in the JCARE-CARD database, data about systemic inflammatory markers such as CRP were not obtained. We thus could not assess the relation between inflammation and the outcomes of HF patients with and without AF in the present study. Finally, data were dependent on the accuracy of documentation and abstraction by the individual medical centers that participated in the program. A selection bias might exist in this study because the registration process was not strictly monitored. However, it was not the objective of this survey to restrict enrollment to the narrowly defined population of HF usually included in clinical trials, but rather to include a broad range of patients reflecting the current reality of clinical practice.

Conclusions

The present study demonstrated a higher prevalence of AF and no difference in the long-term outcomes of HF patients with and without AF in the “real world” of clinical practice in Japan.

Acknowledgments

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