Paroxysmal Atrial Fibrillation Coincident With Cardiac Decompensation is a Predictor of Poor Prognosis in Chronic Heart Failure

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Background The prognostic significance of atrial fibrillation (AF) in chronic heart failure (CHF) remains poorly understood.

Methods and Results Death and rehospitalization for CHF exacerbation for 427 consecutive patients hospitalized from 1996 to 2002 were retrospectively analyzed in relation to cardiac rhythm: sinus rhythm (SR; n=239) or AF (n=188). The AF group was classified according to an Intervention (n=57) or Non-Intervention (n=131) group for defibrillating AF. During the follow-up of 34±23 months, there was no significant difference of mortality or morbidity between the SR and AF groups, or between the Intervention and Non-Intervention groups, respectively. However, the Non-Intervention group consisted of 28 patients with paroxysmal AF (PAF), which spontaneously converted to SR during hospitalization, and 103 with chronic AF (CAF). The rehospitalization for CHF exacerbation was significantly higher in PAF than that in CAF and SR (p=0.00005 and 0.002, respectively). Multivariate Cox analysis demonstrated that, PAF, but not CAF, was a predictor of readmission (relative risk 2.30, p=0.004, 95% confidence interval 1.30 to 4.05).

Conclusions The present data implied that PAF coincident with cardiac decompensation could be a new predictor of prognosis for CHF. The management strategies of AF in CHF should be discussed according to the phenotype of AF. (Circ J 2005; 69: 823–830)

Key Words: Heart failure; Paroxysmal atrial fibrillation; Prognosis

Atrial fibrillation (AF) is the most common type of arrhythmia in clinical practice and it is responsible for substantial morbidity and mortality.^{1,2} Based on its pathophysiological and epidemiological background, it had long been believed that rhythm control for AF, including defibrillation and maintenance of sinus rhythm (SR), was the preferable type of management. However, the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study recently showed no significant difference in the overall prognosis of patients with AF between rate and rhythm control managements.³

Chronic heart failure (CHF) is an increasingly frequent cardiovascular disorder worldwide and it has been reported that AF is markedly more prevalent among patients with CHF than in the general population.^{4,5} The prognostic significance of AF in CHF, however, remains poorly understood. Although many clinical studies have supported the hypothesis that the presence or development of AF in patients suffering from CHF⁶ or left ventricular (LV) dysfunction,⁷ is associated with a higher mortality, there have been some reports with neutral conclusions^{8,9} or even finding a beneficial impact of AF on the prognosis of

CHF.¹⁰ Furthermore, the strategy for the treatment of AF in patients with CHF is still controversial.

The purpose of the present study was to investigate the clinical impact of AF on the prognostic value for CHF, especially according to the clinical forms of AF classified by its onset and persistence.

Methods

Patients

The study population consisted of consecutive patients with exacerbated heart failure diagnosed with congestive heart failure, according to the Framingham criteria, admitted to Kitasato University Hospital from January 1996 to September 2002. Patients with acute myocardial infarction or permanent pacemaker implantation and patients who dropped out from the outpatient management in this hospital were excluded. The patients were divided into 2 groups according to basic cardiac rhythm during hospitalization: 239 patients were in sinus rhythm with no documentation of AF during hospitalization (SR Group) and 188 patients were diagnosed with AF during hospitalization (AF Group). Patients in the AF Group were further classified into 2 groups according to the management for AF retrospectively: 57 patients who had electrical or pharmacological defibrillation, or had been administered antiarrhythmic agents for the prevention of AF recurrence were included in the Intervention Group, and 131 who did not have aggressive therapy for AF stated as above, with the exception of ventricular rate control, were included in the Non-Intervention

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Table 1 Baseline Characteristics of Patients in the SR and AF Groups

	SR group (n=239)	AF group (n=188)
Age, mean, years (SD)	65.2 (14.5)	66.9 (12.5)
Female, no. (%)	99 (41.4)	54 (28.7)**
On admission		
NYHA, II:III:IV	10:63:166	4:59:125
LAD, mm (SD)	41.5 (8.7)	46.9 (11.2)
LVDd, mm (SD)	58.8 (10.6)	55.8 (9.4)**
LVEF, % (SD)	34.7 (14.9)	39.3 (16.2)**
BNP, pg/ml (SD)	810 (635)	603 (520)**
On discharge		
LAD, mm (SD)	38.9 (6.7)	43.9 (10.2)
LVDd, mm (SD)	58.4 (10.1)	54.4 (9.9)**
LVEF, % (SD)	38.6 (15.1)	45.8 (14.6)**
BNP, pg/ml (SD)	219 (274)	204 (246)
Underlying cardiovascular disease no. (%)		
IHD	124 (51.9)	65 (34.6)**
DCM	65 (27.2)	37 (19.7)
HCM	4 (1.7)	4 (2.1)
VHD	37 (15.5)	75 (39.9)**
HHD	40 (16.7)	30 (20.0)
Other	11 (4.6)	7 (3.7)
Underlying complications no. (%)		
DM	88 (36.8)	47 (25.0)**
HT	151 (63.2)	98 (52.1)*
CVD	26 (10.9)	26 (13.8)
Medication use no. (%)		
-blockers	81 (33.9)	66 (35.1)
ACE inhibitors/ARB	199 (83.3)	152 (80.9)
Digoxin	77 (32.2)	120 (63.8)**
Diuretics	211 (88.3)	162 (86.2)
Aspirin	142 (59.4)	97 (51.6)
Warfarin	69 (28.9)	94 (50.0)**
Death no. (%)		
Total death	45 (18.8)	31 (16.5)
CHF	19	11
CPA	7	6
VF/VT	2	1
AMI	1	0
Stroke	2	11
Other	13	2
Readmission for		
CHF exacerbation	89 (37.2)	60 (31.9)
Other reasons		
CPA	7 (2.9)	4 (2.1)
VF/VT	7 (2.9)	8 (4.3)
AMI	3 (1.3)	0 (0.0)
Cerebral infarction	8 (3.3)	11 (5.9)
Cerebral hemorrhage	3 (1.3)	0 (0.0)
Bleeding	4 (1.7)	7 (3.7)
Embolic event	1 (0.4)	2 (1.1)

NYHA, New York Heart Association; LAD, left atrial dimension; LVDd, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; BNP, B-type natriuretic peptide; IHD, ischemic heart disease; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; VHD, valvular heart disease; HHD, hypertensive heart disease; DM, diabetes mellitus; HT, hypertension; CVD, cerebrovascular disease; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; CPA, cardiopulmonary arrest; VF, ventricular fibrillation; VT, ventricular tachycardia; AMI, acute myocardial infarction.

**p<0.05 and p<0.01 vs SR group, respectively.

Group. The in-hospital management strategy against AF for individual patients was decided based on the consensual opinion of 2 experienced cardiologists. Total death and rehospitalization for CHF exacerbation were retrospectively analyzed from hospital discharge until September 2002 (follow-up period of 1–72 months; 34.3±23.3 months).

Fig 1. Kaplan–Meier survival curves estimated for the SR and AF group. There was no significant difference in morbidity between patients with CHF in SR or in AF. HF-Event-Free Survival indicates the event-free rate for CHF exacerbation with readmission.

Clinical Measurement of CHF

Clinical parameters at discharge were analyzed as the patient baseline characteristics for CHF. Venous blood samples for neurohumoral factors were taken from an antecubital vein after 15 min of rest. Plasma B-type natriuretic peptide (BNP) was determined by sensitive noncompetitive immunoradiometric assays (Shionoria BNP®). Findings on ultrasonic cardiography were recorded by a SONOS 500 (Hewlett Packard, USA). The dimension of each chamber was measured in the left parasternal view using M mode, and the ejection fraction (EF) was calculated using a modified Simpson method.

Statistical Analysis

Continuous data are expressed as mean±SD. Patient characteristics were compared using the chi-squared test and Mann–Whitney U-test. The event-free rates among the groups were calculated using the Kaplan–Meier method, and the difference among the groups was detected using the log-rank test. Statistical significance was defined as a p-value of <0.05 (one-sided) for all analyses. The Cox proportional hazards model was applied to evaluate differences in the occurrence of death or rehospitalization for CHF exacerbation among the groups after taking into account the effect of several potential confounders using SPSS software (11.0.1J for Windows, SPSS Inc, Chicago, USA).

Results

Prognostic Value of AF in CHF

As shown in Table 1, the clinical background was similar between the SR Group and AF Group, although there were significant differences in left atrial dimension (LAD), LVEF, basal heart diseases and the administered frequency of digitalis and warfarin. Approximately one-third of each group was readmitted for CHF exacerbation during the 72-month-follow-up period. There was no significant difference in mortality (p=0.41, data not shown) or morbidity between these 2 groups (p=0.64, Fig 1).

Table 2 Baseline Characteristics of Patients in the I and NI Groups

	I group (n=57)	NI group (n=131)
Age, mean, years (SD)	61.8 (12.9)	69.3 (11.9)**
Female, no. (%)	10 (17.5)	44 (33.5)*
On admission		
NYHA, II:III:IV	3:10:44	1:49:81*
LAD, mm (SD)	44.2 (8.8)	48.0 (11.9)**
LVDd, mm (SD)	55.4 (7.9)	56.0 (10.0)
LVEF, % (SD)	39.0 (17.8)	39.4 (15.7)
BNP, pg/ml (SD)	533 (435)	642 (561)
On discharge		
LAD, mm (SD)	41.6 (9.0)	44.9 (10.6)*
LVDd, mm (SD)	52.9 (9.8)	55.0 (10.0)
LVEF, % (SD)	46.0 (14.4)	45.7 (14.8)
BNP, pg/ml (SD)	146 (175)	239 (275)**
Underlying cardiovascular disease no. (%)		
IHD	19 (33.3)	46 (35.1)
DCM	19 (33.3)	18 (13.7)*
HCM	3 (5.3)	1 (0.8)
VHD	15 (26.3)	60 (45.8)*
HHD	6 (10.5)	24 (18.3)
Other	1 (1.8)	6 (4.6)
Underlying complications no. (%)		
DM	10 (17.8)	37 (28.2)
HT	19 (33.3)	79 (60.3)**
CVD	5 (8.8)	21 (16.0)
Medication use no. (%)		
-blockers	27 (47.4)	39 (29.8)*
ACE inhibitors/ARB	47 (82.5)	105 (80.2)
Digoxin	32 (56.1)	88 (67.2)
Diuretics	46 (80.1)	116 (88.5)
Aspirin	29 (50.9)	68 (51.9)
Warfarin	28 (49.1)	66 (50.4)
Death no. (%)		
Total death	7 (12.3)	24 (18.0)
CHF	3	8
CPA	1	5
VF/VT	1	0
AMI	0	0
Stroke	0	11
Other	2	0
Readmission for		
CHF exacerbation	13 (22.8)	47 (35.3)
Other reasons		
CPA	2 (3.5)	2 (1.5)
VF/VT	3 (5.3)	5 (3.8)
AMI	0 (0.0)	0 (0.0)
Cerebral infarction	5 (8.8)	6 (4.5)
Cerebral hemorrhage	0 (0.0)	0 (0.0)
Bleeding	1 (1.8)	6 (4.5)
Embolic event	1 (1.8)	1 (0.8)

I group, Aggressive Intervention group; NI group, Non-Intervention group; other abbreviations as Table 1.

*,** $p<0.05$ and $p<0.01$ vs I group, respectively.

Prognostic Value of Treatment Strategy for AF in CHF

As shown in Table 2, clinical parameters were very similar between the Intervention Group and Non-Intervention Group except age, LAD, plasma BNP and basal heart diseases. There was no significant difference of mortality ($p=0.37$, data not shown) or morbidity ($p=0.20$, Fig 2) between these 2 groups.

Paroxysmal AF (PAF) as a Prognostic Indicator for CHF

The AF Group could further be classified according to the clinical forms of AF by its onset and persistence as shown in Fig 3. The Non-Intervention Group consisted of 28 patients with PAF, which spontaneously converted to SR during hospitalization and another 103 with chronic AF

Fig 2. Kaplan-Meier survival curves estimated for the Intervention and Non-Intervention groups of the AF group. There was no significant difference of morbidity between patients with or without attempting defibrillation of AF.

(CAF). When we compared the prognosis of these 2 groups, the rehospitalization rate due to CHF exacerbation was significantly higher in PAF than that in CAF ($p=0.00005$, Fig 4) at the statistical power of 80%, although there was no significant difference in total death. It was remarkable that 25.0% of the patients had died and a further 64.3% suffered CHF exacerbation leading to readmission during the follow-up period in the PAF group (Table 3). When comparing the prognosis with that of the SR Group, there was no significant difference between SR and CAF while the rehospitalization rate was significantly higher in PAF than that in SR ($p=0.002$; Fig 4). As shown in Table 3, there was no significant difference in the clinical parameters with the exception of LAD, complicated frequency of myocardial ischemia and diabetes mellitus between PAF and CAF, and with the exception age between PAF and SR. In multivariate Cox analysis, the existence of PAF, but not CAF, was a significant predictor of readmission for CHF exacerbation (relative risk 2.30, $p=0.004$, 95% confidence interval 1.30 to 4.05) (Table 4).

Further analysis of PAF during the follow-up period after discharge demonstrated that 25 out of 28 cases (89%) maintained SR while they had a stable CHF status as outpatients, while PAF was again documented at hospital readmission with CHF exacerbation in 12 out of 17 cases (70%).

Discussion

Pathophysiological and Prognostic Contribution of AF to CHF

It has been emphasized that AF may compromise LV systolic function and worsen CHF through poor rate control, irregularity of the ventricular response, and loss of atrial transport,¹ as well as tachycardia-induced cardiomyopathy.¹² Conversely, some reports insisted that CHF itself could

On admission

Exacerbated heart failure and AF

Fig3. The Non-Intervention group included patients with paroxysmal AF (PAF), which spontaneously converted to SR during hospitalization with the improvement of CHF and chronic AF (CAF).

Fig4. Kaplan–Meier survival curves estimated for patients with SR, CAF and PAF. There was no significant difference of morbidity between patients with SR or CAF. However, rehospitalization for exacerbated CHF was markedly higher in patients with PAF than those with SR or CAF.

contribute to the prevalence of complicated AF through atrial remodeling or activated neurohumoral factors, including sympathetic and renin-angiotensin-aldosterone systems^{13,14}

Although it is recognized that individuals with AF are at an increased risk of death in the general population,² the impact of AF on CHF mortality has remained controversial despite being examined extensively. V-HeFT trials found that baseline AF was not related to overall mortality or sudden death⁹ SOLVD trials, however, reported that AF was associated with increased mortality⁷ Studies based on CHF patients at transplant centers have reached conflicting

conclusions^{15,16} Some studies have even reported that AF has a beneficial impact on the prognosis in CHF¹⁰ Disparities between prior studies may be derived from several biases that reflect the focus on prevalence rather than the incidences of the disease^{7,9,16} varying duration of AF and CHF^{9,15} and the characteristics of different referral populations^{9,10,15} It has been suggested that AF is only independently associated with increased mortality rates in patients with relatively preserved LV function, while the relationship is more complicated and dependent on other variables in individuals with advanced disease^{8,15} Wang et al reported that antecedent AF was not a significant predictor of mor-

Table 3 Baseline Characteristics of Patients With SR, PAF and CAF

	SR (n=239)	PAF (n=28)	CAF (n=103)
Age, mean, years (SD)	65.2 (14.5)	70.6 (13.6)**	68.7 (11.1)**
Female, no. (%)	99 (41.4)	6 (21.4)	38 (27.3)
Time of previous admission (SD)	1.4 (0.9)	1.4 (0.7)	1.6 (1.1)
On admission			
NYHA, II:III:IV	10:63:166	0:08:20	1:41:61*
LAD, mm (SD)	41.5 (8.7)	41.6 (8.0)	49.9 (12.0)**§
LVDd, mm (SD)	58.8 (10.6)	55.4 (10.5)	56.2 (9.9)*
LVEF, % (SD)	34.7 (14.9)	37.1 (13.8)**	40.0 (16.1)**
BNP, pg/ml (SD)	810 (635)	903 (723)	570 (491)**†
On discharge			
LAD, mm (SD)	38.9 (6.7)	37.4 (6.3)	46.9 (10.6)**§
LVDd, mm (SD)	58.4 (10.1)	54.5 (11.1)	55.2 (9.7)*
LVEF, % (SD)	38.6 (15.1)	43.4 (13.1)*	46.3 (15.2)**
BNP, pg/ml (SD)	219 (274)	291 (301)	223 (268)
Underlying cardiovascular disease no. (%)			
IHD	124 (51.9)	18 (64.3)	28 (27.2)**§
DCM	65 (27.2)	3 (10.7)	15 (14.6)*
HCM	4 (1.7)	0 (0.0)	1 (1.0)
VHD	37 (15.5)	4 (14.3)	56 (54.4)**§
HHD	40 (16.7)	7 (25.0)	17 (16.5)
Other	11 (4.6)	0 (0.0)	6 (5.8)
Underlying complications no. (%)			
DM	88 (36.8)	15 (53.6)	22 (21.4)**§
HT	151 (63.2)	18 (64.3)	61 (59.2)
CVD	26 (10.9)	2 (7.1)	19 (18.4)
Medication use no. (%)			
-blockers	81 (33.9)	12 (42.9)	27 (26.2)
ACE inhibitors/ARB	199 (83.3)	22 (78.6)	83 (80.6)
Digoxin	77 (32.2)	11 (39.3)	77 (74.8)**§
Diuretics	211 (88.3)	22 (78.6)	94 (91.3)
Aspirin	142 (59.4)	19 (67.9)	49 (47.6)*
Warfarin	69 (28.9)	12 (42.9)	54 (52.4)**
Death no. (%)			
Total death	45 (18.8)	17 (62.2)	7 (25.0)
CHF	19	5	3
CPA	7	4	1
VF/VT	2	0	0
AMI	1	0	0
Stroke	2	8	3
Other	13	0	0
Readmission for			
CHF exacerbation	89 (37.2)	29 (27.6)	18 (64.3)
Other reasons			
CPA	7 (2.9)	1 (1.0)	1 (3.6)
VF/VT	7 (2.9)	4 (3.8)	1 (3.6)
AMI	3 (1.3)	0 (0.0)	0 (0.0)
Cerebral infarction	8 (3.3)	5 (4.8)	1 (3.6)
Cerebral hemorrhage	3 (1.3)	0 (0.0)	0 (0.0)
Bleeding	4 (1.7)	3 (2.9)	3 (10.7)
Embolic event	1 (0.4)	1 (1.0)	0 (0.0)

SR, sinus rhythm; PAF, paroxysmal atrial fibrillation; CAF, chronic atrial fibrillation; other abbreviations as Table 1.

*,**p<0.05 and p<0.01 vs SR patients, †and §p<0.05 and p<0.01 vs PAF patients, respectively.

tality in subjects with CHF because the high mortality associated with CHF in the community might overwhelm the modest influence of preexisting AF, particularly after adjustment for other cardiovascular conditions.¹⁷ We found in the present study population that the persistent or temporal existence of AF during the hospitalized course of CHF exacerbation was associated with morbidity. These fundamental data could lead us to focus on how to categorize and to deal with AF coincident with exacerbated CHF in further studies.

PAF as a New Predictor of Prognosis for CHF

In the present study, we found a unique impact of PAF on the prognosis of CHF as a new predictor. The PAF

group categorized in our study had the peculiarity that AF was documented with CHF exacerbation and restored to SR with stabilizing CHF status. Although one report showed conflicting data that patients with PAF have a better prognosis than those with CAF in the general population,¹⁸ its clinical value to patients with CHF has scarcely been investigated so far. To consider the causative mechanism of PAF on a worse prognostic value for CHF, we should focus on 2 paradigms: the patients' cardiac status predisposed them to the occurrence of AF; and acute hemodynamic alteration mainly derived from the cessation of regular sinus rhythm.

The predisposition of CHF to AF roughly consists of 2 pathomechanisms: irreversible and reversible processes.

Table 4 Variables in the Cox Proportional Hazards Model

Variables	Readmission for CHF exacerbation end-point			Death end-point		
	RR	95% CI	p value	RR	95% CI	p value
CAF	0.637	0.361–1.125	0.121	0.952	0.436–2.078	0.901
PAF	2.297	1.302–4.053	0.004	1.765	0.715–4.360	0.218
Male	1.527	1.021–2.283	0.039	1.346	0.767–2.362	0.300
Age	1.034	1.015–1.053	0.000	1.018	0.992–1.044	0.175
On admission						
NYHA	0.870	0.625–1.211	0.410	1.236	0.753–2.029	0.401
LAD	1.016	0.993–1.040	0.184	1.019	0.986–1.053	0.268
LVDd	0.994	0.969–1.019	0.625	1.000	0.964–1.039	0.980
EF	1.004	0.989–1.020	0.585	1.000	0.977–1.024	0.985
BNP	1.000	0.999–1.000	0.155	1.000	1.000–1.001	0.598
On discharge						
NYHA	1.630	1.111–2.392	0.012	1.603	0.905–2.840	0.106
LAD	1.009	0.975–1.044	0.611	1.037	0.991–1.086	0.116
LVDd	1.018	0.989–1.048	0.216	0.992	0.951–1.035	0.712
EF	1.005	0.986–1.024	0.631	0.980	0.952–1.009	0.170
BNP	1.002	1.001–1.003	0.000	1.001	1.000–1.002	0.127
Underlying cardiovascular disease						
IHD	1.234	0.720–2.115	0.444	0.660	0.301–1.448	0.300
DCM	1.191	0.589–2.407	0.627	0.670	0.248–1.811	0.430
VHD	0.866	0.509–1.475	0.597	0.407	0.177–0.939	0.035
HHD	0.889	0.499–1.583	0.689	1.380	0.635–2.999	0.416
Underlying complications						
DM	1.206	0.795–1.829	0.379	0.982	0.516–1.869	0.956
HT	1.018	0.680–1.525	0.930	1.370	0.745–2.520	0.311
CVD	1.296	0.764–2.198	0.336	1.664	0.787–3.518	0.182
Medication use						
-blockers	0.815	0.524–1.270	0.366	0.415	0.200–0.861	0.018
ACE inhibitors/ARB	0.789	0.509–1.222	0.288	1.119	0.587–2.130	0.733
Digoxin	1.048	0.696–1.577	0.823	1.063	0.577–1.957	0.845
Diuretics	1.833	0.910–3.692	0.090	0.531	0.245–1.150	0.108
Warfarin	0.494	0.308–0.794	0.004	0.505	0.255–1.001	0.050
Aspirin	0.889	0.591–1.338	0.573	0.294	0.165–0.525	0.000

RR, Risk ratio; 95% CI, 95% confidence interval; other abbreviations as Tables 1 and 3.

The former originates from organic changes, including atrial fibrosis, regional conduction abnormalities and electrophysiological changes such as a shortened atrial refractory period chronically caused by CHF^{19,20}. The latter occurs via acutely increased atrial filling pressure and atrial dilatation⁸. The significant impact of PAF should be derived from the reversible hemodynamic or cardiac background considering the pathomechanism stated above. Diastolic ventricular dysfunction causes a secondary increase in filling pressure and mediates atrial remodeling, and is associated with a 5.26-fold increase of the risk of AF development compared with normal diastolic function²¹. Complications of abnormal parameters for diastolic dysfunction, such as ischemic heart disease, hypertensive heart disease and diabetes mellitus, in the PAF group, although not significant, might contribute to the prevalence of PAF. Because it has been demonstrated that diastolic dysfunction could induce a poorer prognosis among CHF patients, similar to systolic function²², the diastolic property needs to be elucidated to better understand the causative mechanism. Left atrial dilatation is the only parameter that differentiates CAF from PAF. Because chronic atrial dilatation in the absence of overt CHF leads to increased vulnerability to AF through chronic regional inflammation and increased interstitial fibrosis²³, the existence of AF in CAF may not be affected by atrial stretch stimulation with exacerbated CHF.

In contrast, the clinical characteristic of PAF is represented as an 'alteration' compared to CAF. It was demon-

strated that the later development of AF, but not antecedent AF, was associated with increased mortality in CHF subjects¹⁷. Another report showed that the later onset of AF during the CHF course is associated with clinical and hemodynamic deterioration, and may predispose patients to systemic thromboembolism and a poorer prognosis²⁴. We observed the reproducibility of PAF in conjunction with cardiac decompensation in most of the eventful PAF cases during the follow-up period. It should be reasonable to consider, therefore, that the later onset of AF, presented as PAF in the present study, can cause deteriorated hemodynamics leading to a poorer prognosis, while CAF can not.

Clinical Implications and Future Prospects: Application to New Management of AF in CHF

The choice of long-term therapy of AF in CHF is the object of intense debate. Although it is unclear whether to control the rate vs rhythm despite the subgroups analysis of AFFIRM and RACE^{3,25}, which tended to support rhythm control, the results of studies specifically designed to examine populations of patients with CHF, such as AF-CHF²⁶, are needed to draw more definite conclusions. The consensus up until now, reflected in current ACC/AHA/ESC guidelines on management of AF, was that rhythm control should not be vigorously pursued in this clinical setting²⁷.

We did not demonstrate a beneficial outcome of the predominance of the rhythm control strategy in the present study, as indicated by the Intervention Group compared to rate control strategy in the Non-Intervention Group. It is

true that the present study reached a limited conclusion for the treatment strategy for AF coincident with CHF because of its non-randomized, retrospective fashion. We could emphasize, however, that the prognosis of the PAF group was only comparable to that of the CAF group among the Non-intervention group in which no aggressive therapy for AF except ventricular rate control was undertaken. In other words, it is a reliable interpretation, even in this retrospective study, that the existence of PAF has prognostic significance. Therefore, we need to discuss which therapy should be recommended for AF in CHF patients, distinguishing PAF from CAF.

Except for the emergent cases with deteriorated circulatory hemodynamics due to the additive occurrence of AF, conventional CHF management and rate control strategy without the defibrillation procedures should first of all be recommended in CHF patients with AF. When we encounter patients whose cardiac rhythms spontaneously convert from AF to SR with improving CHF status, we may propose specific management strategies. Therefore, the strategy for AF treatment can be optimized according to the pattern of AF onset and persistence because a phenotypic difference of AF could lead to a different clinical outcome in CHF. We might consider 2 ways of intervention for these PAF patients to improve the prognosis according to the presumable pathomechanisms stated above. The first possibility is the prevention of AF recurrence predominantly through the administration of preferable antiarrhythmic agents. For this purpose, amiodarone is an optimal candidate with significant potential to maintain SR, leading to lower mortality in CHF.²⁸ An AFFIRM study, however, demonstrated that only 35% of cases could maintain SR under the administration of amiodarone,³ while it was reported that PAF eventually developed into its chronic form in 77.2% of patients under conventional antiarrhythmic therapy during a 14-year-follow-up.²⁹ Komatsu et al reported that the long-term prognosis of patients with PAF varies with the response to antiarrhythmic drug therapy.³⁰ The limitations of the rhythm control therapy may be recognized, considering the altered management policy of rate control, if AF has repeatedly occurred under the antiarrhythmic drug therapy. The other option is strict CHF control unless CHF status worsens, leading to the occurrence of AF. Optimal pharmacotherapy under established guidelines or a BNP-guided management might approach this target.^{31,32} Further prospective studies are warranted to determine the optimal management strategy for CHF patients with AF.

Study Limitations

Some limitations of the study must be acknowledged: (1) the study was carried out inside a single center in both a retrospective and nonrandomized fashion. The acquired data might be biased because the clinical judgment depended on the clinical status of each patient. (2) It would be ideal if there was no significant difference in the clinical backgrounds between SR and AF patients. This, however, must be impossible because AF itself may lead to pathological and hemodynamic changes. (3) Although patients were carefully followed up, asymptomatic AF cannot be ruled out completely, and conversely, spontaneous termination and reinitiation of persistent AF cannot be distinguished from CAF. Despite these limitations, the present study focused for the first time on the clinical significance of PAF coincident with cardiac decompensation in CHF management. This finding raises the possibility that prophylactic

therapies reduce the repeated cardiac events of exacerbated CHF to these high-risk patients. Further studies addressing the pathogenesis, prevention, and the optimal management of the AF and CHF according to the phenotype of AF seem warranted.

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