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ORIGINAL ARTICLE

Clinical significance of new-onset atrial fibrillation in patients with hypertrophic cardiomyopathy

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Abstract

Aims There is limited information about the clinical significance of atrial fibrillation (AF), particularly new-onset AF, in patients with hypertrophic cardiomyopathy (HCM) in a community-based patient cohort. This study was carried out to clarify the prevalence and prognostic impact of AF in Japanese HCM patients.

Methods and results In 2004, we established a cardiomyopathy registration network in Kochi Prefecture as a prospective study, and finally, 293 patients with HCM were followed. In the patients' cohort, we recently reported the clinical outcomes including mortality and HCM-related morbid events. HCM-related adverse cardiovascular events were defined in the following: (i) sudden cardiac death (SCD)-relevant events including SCD, spontaneous sustained ventricular tachycardia, and appropriate implantable cardioverter defibrillator discharge; (ii) heart failure (HF) events with the composite of HF death and hospitalization for HF; and (iii) embolic events included embolic stroke-related death and admission for embolic events. In the present study, we focused on AF and conducted a detailed investigation. At registration, the mean age of the patients was 63 ± 14 years, and 86 patients (29%) had documented AF including paroxysmal AF. Patients with AF at registration were characterized by worse clinical profiles including more advanced age, more symptomatic, more advanced left ventricular, and left atrial remodelling at registration. During a mean follow-up period of 6.1 ± 3.2 years, a total of 77 HCM-related adverse events occurred, and the presence of AF at registration was associated with an increased risk of HCM-related adverse events, particularly heart failure events. During the follow-up period, an additional 31 patients (11%) had documentation of AF for the first time, defined as new-onset AF, with an annual incidence of approximately 1.8%, and finally, a total of 117 patients (40%) showed AF. The presence of palpitation and enlarged left atrial diameter, particularly left atrial diameter ≥50 mm, at registration were significant predictors of new-onset AF. Importantly, the incidence of overall HCM-related adverse events was further higher in patients with new-onset AF observed from AF onset than in patients with AF at registration.

Conclusions In our HCM registry in an aged Japanese community, a significant proportion developed AF. The presence of AF, particularly new-onset AF, was associated with increased incidence of HCM-related events. AF may not be just a marker of disease stage but an important trigger of adverse events.

Keywords Hypertrophic cardiomyopathy; Atrial fibrillation; Clinical outcome

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Introduction

Hypertrophic cardiomyopathy (HCM) is a primary myocardial disorder with heterogeneous morphologic, functional, and clinical features.[1–3] Atrial fibrillation (AF) is the most common arrhythmia in patients with HCM.[4–7] AF in HCM has been regarded as an important determinant responsible for a major impact on clinical outcomes including heart failure

(HF) and embolic stroke.[5–7] However, in contrast to previous reports, a recent study showed a more favourable clinical course of HCM patients with AF.[8] In 2004, we established Kochi Cardiomyopathy Network, named Kochi RYOMA (registry of myocardial diseases) study, to provide detailed information on the clinical features of HCM in a prospectively assembled regional Japanese patient cohort.[9] Regarding the prognostic factors in this cohort, multivariate analysis revealed that the presence of AF, severe symptoms judged by New York Heart Association (NYHA) class, lower left ventricular (LV) fractional shortening, and the presence of LV outflow tract obstruction at registration were independent risk factors for HCM-related adverse events.[10]

In this study, we investigated the prevalence and clinical significance of AF, particularly new-onset AF, in a prospectively assembled HCM patient cohort in an aged Japanese community.

Methods

Subjects

In 2004, we established Kochi Cardiomyopathy Network consisting of 9 hospitals serving as primary, secondary, and tertiary referral medical centres for cardiovascular patients in Kochi Prefecture, Japan, with about 800 000 inhabitants.[9] Between February 2004 and December 2013, 305 patients with a diagnosis of HCM were registered. The diagnosis of HCM was based on echocardiographic demonstration of left ventricular hypertrophy (LVH), that is, maximum LV wall thickness $\geq$15 mm, in the absence of another cardiac or systemic disease that could cause LVH. Patients with known metabolic disease or syndromic causes of LVH were excluded from the study. Shortly afterward, three of the patients were diagnosed as having specific cardiomyopathy: one patient with cardiac amyloidosis and two patients with cardiac involvement of Fabry disease. Finally, 302 patients were registered. In this longitudinal study, we excluded 9 patients with no follow-up data and the final study population consisted of 293 patients.

This investigation was performed according to the Declaration of Helsinki. The study was approved by the Ethics Committee on Medical Research of Kochi Medical School, and informed consent was obtained from all patients or their parents in accordance with the guidelines of the Ethics Committee.

Clinical evaluation

Evaluation of patients included medical history, clinical examination, 12-lead electrocardiography (ECG), M-mode, 2D and Doppler echocardiography, and ambulatory 24 h Holter ECG analysis. The severity and distribution of LVH were assessed in the parasternal short axis plane at mitral valve, papillary muscle, and apical levels. Left ventricular end-diastolic diameter (LVEDD) and end-systolic diameter (LVESD) were measured from M-mode and 2-D images obtained from parasternal long-axis views, and LV fractional shortening [LVFS = (LVEDD − LVESD)/LVEDD × 100] was calculated. LV outflow tract gradient was calculated from continuous-wave Doppler using the simplified Bernoulli equation. Assessment of mitral regurgitation included a comprehensive evaluation of 2D and Doppler colour flow echocardiographic images. We defined mitral regurgitation as significant mitral regurgitation if the degree was moderate or severe. Moderate mitral regurgitation was defined as a jet penetrating any depth and encompassing 30% to 50% of the left atrium. Severe mitral regurgitation was considered present when the a jet encompassed $>$50% of the left atrial area.[11]

Based on morphologic and hemodynamic assessments by echocardiography, we divided the patients into the following five groups: (i) hypertrophic obstructive cardiomyopathy (HOCM), defined as the presence of basal LV outflow tract obstruction (gradient $\geq$30 mmHg at rest); (ii) midventricular obstruction (MVO), defined as the presence of systolic LV cavity obliteration at the midventricle creating midventricular obstruction with a peak systolic gradient $\geq$30 mmHg at rest; (iii) end-stage HCM, defined as LV systolic dysfunction of global ejection fraction (EF) $<$ 50% (Global EF was determined from apical two- and four-chamber views by modified Simpson's method.); (4) apical HCM, defined as hypertrophy confined to the LV apex; and (5) hypertrophic non-obstructive cardiomyopathy (HNCM): HCM without obstruction other than end-stage HCM and apical HCM.[12]

Paroxysmal AF episodes are episodes that terminate spontaneously or with intervention that restores sinus rhythm $\leq$7 days after onset.[13] AF epidodes lasting $>$7 days and terminating spontaneously or with interventions (viz. persistent AF) are included within the paroxysmal AF category. Permanent AF episodes are episodes that persist until the patient and clinician make a shared decision together to cease further attempts to restore or maintain sinus rhythm.[13] Long-standing persistent AF (continuous AF lasting $>$12 months in duration) was considered as permanent AF. The definition of new-onset AF during the follow-up period was that AF was documented for the first time under the recommended annual ECG follow-up situation after the study registration in patients without documentation of AF before or at registration.[1,2]

For prognostic analysis, three modes of HCM-related adverse cardiovascular events were defined: (i) sudden cardiac death (SCD)-relevant events were the composite of SCD, spontaneous sustained ventricular tachycardia (VT) associated with hemodynamic instability, and appropriate implantable cardioverter defibrillator (ICD) discharge; (ii) HF events included HF death and hospitalization for HF; and (iii) embolic events were the composite of embolic stroke-related death and admission for arterial thromboembolic events. Data on

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survival and clinical status of patients were obtained during serial clinic visits or from records in their clinical charts including information from other institutes. The study closed on 31 December 2014.

Data analysis

All data are expressed as mean ± SD or frequency (percentage). Differences in continuous variables were assessed using Student's *t* test. Pearson's chi-square test was used for comparisons between non-continuous variables, and Fisher's exact test was used when the expected frequency was lower than 5. Event-free estimate curves were calculated by the Kaplan–Meier method, and the log rank test was used for comparison. Multivariate logistic regression analysis was performed to estimate the odds ratios for predictors of new-onset AF during the follow-up period in patients without AF at registration. The determinants included conventional factors and some variables with $P \leq 0.05$ in univariate analysis: gender, age at registration, LV end-diastolic diameter, left atrial diameter, and the presence of palpitation at registration. Regarding left atrial size, receiver-operator characteristic (ROC) analysis for predicting new-onset AF was performed and the area under the curve (AUC) for determining the cut-off value was used. Statistical significance was defined by $P \leq 0.05$. Statistical analysis was performed using SPSS version 21.0J (IPM Corp., Armonk, NY, USA).

Results

Baseline patient characteristics and factors with atrial fibrillation at registration

The clinical characteristics of the 293 patients with HCM at registration are summarized in *Table 1*.[10] The ages at registration and at diagnosis were 63 ± 14 (range: 7 to 88) and 56 ± 16 (range: 6 to 87) years, respectively, and 197 patients (67%) were men. Most of the 293 patients were completely asymptomatic or mildly symptomatic at registration: 163 patients (56%) were NYHA functional class I, 109 patients (37%) were NYHA class II, and only 21 patients (7%) were NYHA class III. At registration, 86 patients (29%) had documentation of AF (46 patients with paroxysmal AF and 40 patients with

Table 1 Clinical characteristics of the 293 HCM patients with and without AF at registration

	Overall cohort (n = 293)	AF (+) (n = 86)	AF (−) (n = 207)	P
Age at registration, years	63 ± 14	68 ± 9	61 ± 17	<0.001
Gender: male, *n* (%)	197 (67%)	58 (67%)	139 (67%)	0.961
Age at diagnosis of HCM, years	56 ± 16	58 ± 13	55 ± 17	0.209
Reason for diagnosis of HCM: symptoms, *n* (%)	136 (46%)	66 (77%)	70 (34%)	<0.001
Family history of HCM, *n* (%)	76 (26%)	22 (26%)	54 (26%)	0.928
Family history of sudden death, *n* (%)	52 (18%)	14 (16%)	38 (18%)	0.672
Symptoms at registration, *n* (%)				
NYHA functional class: III/IV	21 (7%)	18 (21%)	3 (1%)	<0.001
Chest pain	77 (26%)	19 (22%)	58 (28%)	0.294
Palpitation	67 (23%)	29 (34%)	38 (18%)	0.004
Syncope	12 (4%)	4 (5%)	8 (4%)	0.752
Echocardiographic data at registration				
Subtype, *n* (%)				0.011
HOCM	40 (14%)	10 (15%)	30 (14%)	
MVO	8 (3%)	2 (2%)	6 (3%)	
End-stage	13 (4%)	9 (10%)	4 (2%)	
Apical HCM	52 (18%)	10 (12%)	42 (20%)	
HNCM	180 (61%)	55 (64%)	125 (60%)	
Presence of LV outflow obstruction, *n* (%)	36 (12%)	9 (10%)	27 (13%)	0.544
Maximum LV wall thickness, mm	19.9 ± 3.9	18.9 ± 3.6	19.1 ± 4.1	0.824
LV end-diastolic diameter, mm	46.3 ± 6.0	48.1 ± 6.2	45.6 ± 5.8	0.001
LV fractional shortening, %	40.9 ± 8.5	37.5 ± 9.2	42.3 ± 7.7	<0.001
Left atrial diameter, mm	44.3 ± 7.5	50.1 ± 7.3	41.8 ± 6.1	<0.001
Significant mitral regurgitation, *n* (%)	16 (5%)	7 (8%)	9 (4%)	0.257
Medications at registration, *n* (%)				
Beta-blocker	119 (41%)	49 (57%)	70 (34%)	<0.001
Calcium antagonist	79 (27%)	35 (41%)	44 (21%)	0.001
ACEI or ARB	78 (27%)	35 (41%)	43 (21%)	<0.001
Diuretic	50 (17%)	38 (4%)	12 (6%)	<0.001
Amiodarone	11 (4%)	8 (9%)	3 (1%)	0.003
Anti-coagulation therapy	79 (27%)	73 (85%)	6 (3%)	<0.001

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; HNCM, hypertrophic non-obstructive cardiomyopathy (HCM without obstruction other than end-stage HCM and apical HCM); HOCM, hypertrophic obstructive cardiomyopathy; LV, left ventricular; MVO, midventricular obstruction; NYHA, New York Heart Association.

permanent AF). ICD implantation had been performed in four patients.

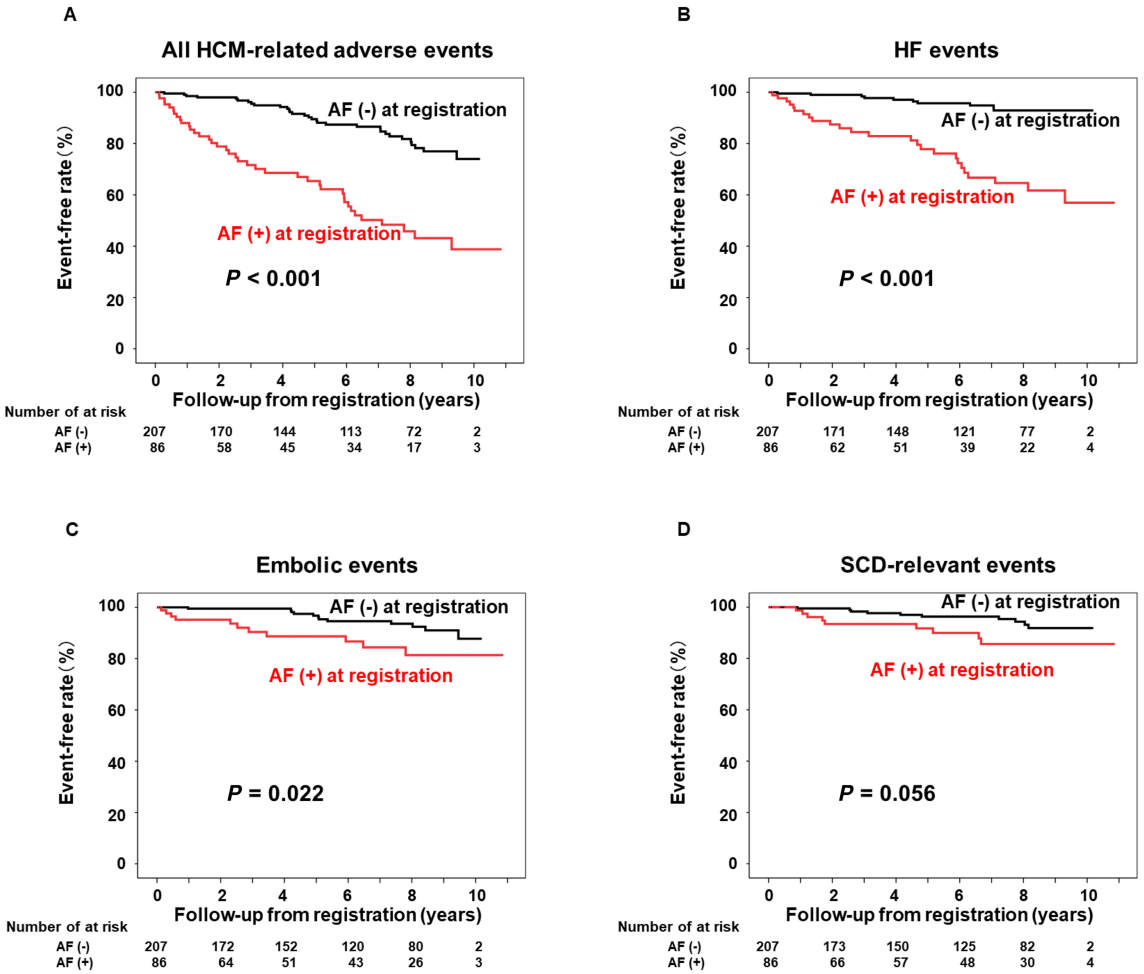
Clinical characteristics of patients with and those without AF at registration are shown in *Table 1*. Patients with AF were older, were more symptomatic, and had a more advanced disease stage (larger LV end-diastolic diameter, lower LVFS, and larger left atrial diameter) than patients without AF. Occurrence of significant mitral regurgitation was not different between the two groups. Regarding the treatments, more prescriptions including beta-blocker, diuretic, and amiodarone were used in patients with AF.

Atrial fibrillation at registration and clinical outcomes

As we previously reported,[10] in this patient cohort, there were 23 HCM-related deaths during the mean follow-up period of 6.1 ± 3.2 years. The HCM-related annual mortality rate was 1.3%, and the HCM-related 5-year survival rate was 94%. Regarding overall HCM-related cardiovascular events, a total of 77 adverse events in 70 patients occurred: SCD-relevant events in 19 patients including 9 SCDs, HF events in 35 patients including 11 HF deaths, and embolic events in 23 patients including 3 embolic stroke deaths. As we previously reported, the presence of AF, NYHA class III, lower LVFS, and the presence of LV outflow tract obstruction at registration were independent predictors of adverse events.[10]

Figure 1 shows HCM-related adverse events in HCM patients with and those without AF at registration: *Figure 1A* for all events, *Figure 1B* for HF events, *Figure 1C* for embolic events, and *Figure 1D* for SCD-relevant events. Patients with AF had more frequent HCM-related adverse events than did those without AF. This tendency was remarkable in HF events (*Figure 1B*).

Figure 1 HCM-related adverse events in HCM patients with and those without AF at registration: (A) For all events, (B) for HF events, (C) for embolic events, and (D) for SCD-relevant events. AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; HF, heart failure; SCD, sudden cardiac death.



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New-onset atrial fibrillation and clinical course

During the follow-up period, an additional 31 patients (11%) had documentation of AF for the first time, defined as new-onset AF, with an annual incidence of approximately 1.8%, and finally, a total of 117 patients (40%) in this regional cohort showed AF (*Figure 2*). The median period between the registration and documentation of new-onset AF was 4.2 years. We focused on the 31 patients who had new-onset AF.

Figure 2 Flow diagram showing the timing of detection of AF. AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy.

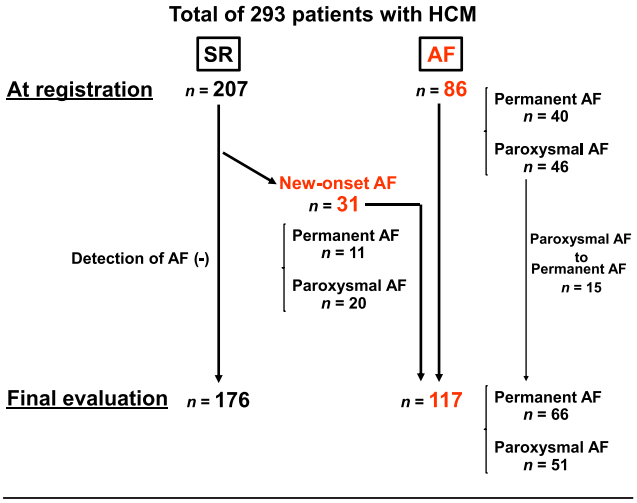


Table 2 shows the baseline characteristics of patients with and those without new-onset AF during the follow-up period among the 207 patients without AF at registration. The percentage of patients complaining of palpitation was higher in the new-onset AF group, although the presence of AF was not confirmed at registration in those patients. Patients with new-onset AF had more enlarged LV end-diastolic diameter and left atrial diameter. Multivariate logistic regression analysis was performed to clarify the determinants of new-onset AF. *Table 3* shows that the presence of palpitation and enlarged left atrial diameter were significant predictors among the five determinants. Regarding left atrial size for predicting new-onset AF, the AUC value determined by ROC analysis was 0.669 with the cut-off value of 43 mm. Left atrial diameter ≥50 mm at registration was significantly associated with new-onset AF in the univariate analysis (*Table 4*).

In the 31 patients with new-onset AF, 17 patients (55%) had the HCM-related adverse events during the follow-up period. Three patients suffered from the adverse events before

Table 2 Clinical characteristics of patients with and without new-onset AF during the follow-up period among the 207 HCM patients without AF at registration

	New-onset AF (+) (n = 31)	New-onset AF (–) (n = 176)	P
Age at registration, years	64 ± 12	60 ± 16	0.234
Gender: male, *n* (%)	24 (77%)	115 (65%)	0.187
Age at diagnosis of HCM, years	57 ± 14	55 ± 17	0.591
Reason for diagnosis of HCM: symptoms, *n* (%)	13 (42%)	57 (32%)	0.300
Family history of HCM, *n* (%)	8 (26%)	46 (26%)	0.969
Family history of sudden death, *n* (%)	6 (19%)	32 (18%)	0.876
Symptoms at registration, *n* (%)			
NYHA functional class: III/IV	0 (0%)	3 (2%)	1.000
Palpitation	12 (39%)	26 (15%)	0.002
Echocardiographic data at registration			
Subtype, *n* (%)			0.763
HOCM	5 (16%)	25 (14%)	
MVO	0 (0%)	6 (3%)	
End-stage	1 (3%)	3 (2%)	
Apical HCM	5 (16%)	37 (21%)	
HNCM	20 (65%)	105 (60%)	
Presence of LV outflow obstruction, *n* (%)	4 (13%)	23 (13%)	1.000
Maximum LV wall thickness, mm	18.2 ± 4.4	19.2 ± 4.0	0.187
LV end-diastolic diameter, mm	47.7 ± 6.5	45.2 ± 5.6	0.032
LV Fractional shortening, %	41.4 ± 8.7	42.5 ± 7.5	0.465
Left atrial diameter, mm	44.8 ± 5.5	41.3 ± 6.1	0.003
Significant mitral regurgitation, *n* (%)	2 (6%)	7 (4%)	0.626
Medications at registration, *n* (%)			
Beta-blocker	15 (48%)	55 (31%)	0.063
Calcium antagonist	6 (19%)	38 (22%)	0.779
ACEI or ARB	7 (23%)	36 (20%)	0.788
Diuretic	2 (6%)	10 (6%)	0.697
Amiodarone	1 (3%)	2 (1%)	0.387
Anti-coagulation therapy	4 (13%)	2 (1%)	0.005

ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; HCM, hypertrophic cardiomyopathy; HNCM, hypertrophic non-obstructive cardiomyopathy (HCM without obstruction other than end-stage HCM and apical HCM); HOCM, hypertrophic obstructive cardiomyopathy; MVO, midventricular obstruction; NYHA, New York Heart Association; LV, left ventricular.

Table 3 Predictors of new-onset AF during the follow-up period among the HCM patients without AF at registration (multivariate logistic regression analysis)

	Odds ratio (95% CI)	*P*
Gender, male	1.968 (0.701–5.523)	0.199
Age at registration, years	1.019 (0.986–1.053)	0.269
Presence of palpitation at registration	4.811 (1.912–12.102)	0.001
LV end-diastolic diameter, mm	1.040 (0.958–1.128)	0.351
Left atrial diameter, mm	1.089 (1.014–1.171)	0.020

AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; LV, left ventricular.

Table 4 Left atrial diameter at registration and new-onset AF during the follow-up period among the HCM patients without AF at registration

	Odds ratio (95% CI)	*P*
Left atrial diameter <43 mm	Reference	
Left atrial diameter ≥43 mm, <50 mm	2.273 (0.967–5.343)	0.060
Left atrial diameter ≥50 mm	3.409 (1.106–10.512)	0.033

AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy.

Figure 3 HCM-related adverse events in HCM patients with AF at registration, those with new-onset AF, and those without detection of AF during the follow-up period: (A) for all events, (B) for HF events, (C) for embolic events, and (D) for SCD-relevant events. AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; HF, heart failure; SCD, sudden cardiac death.

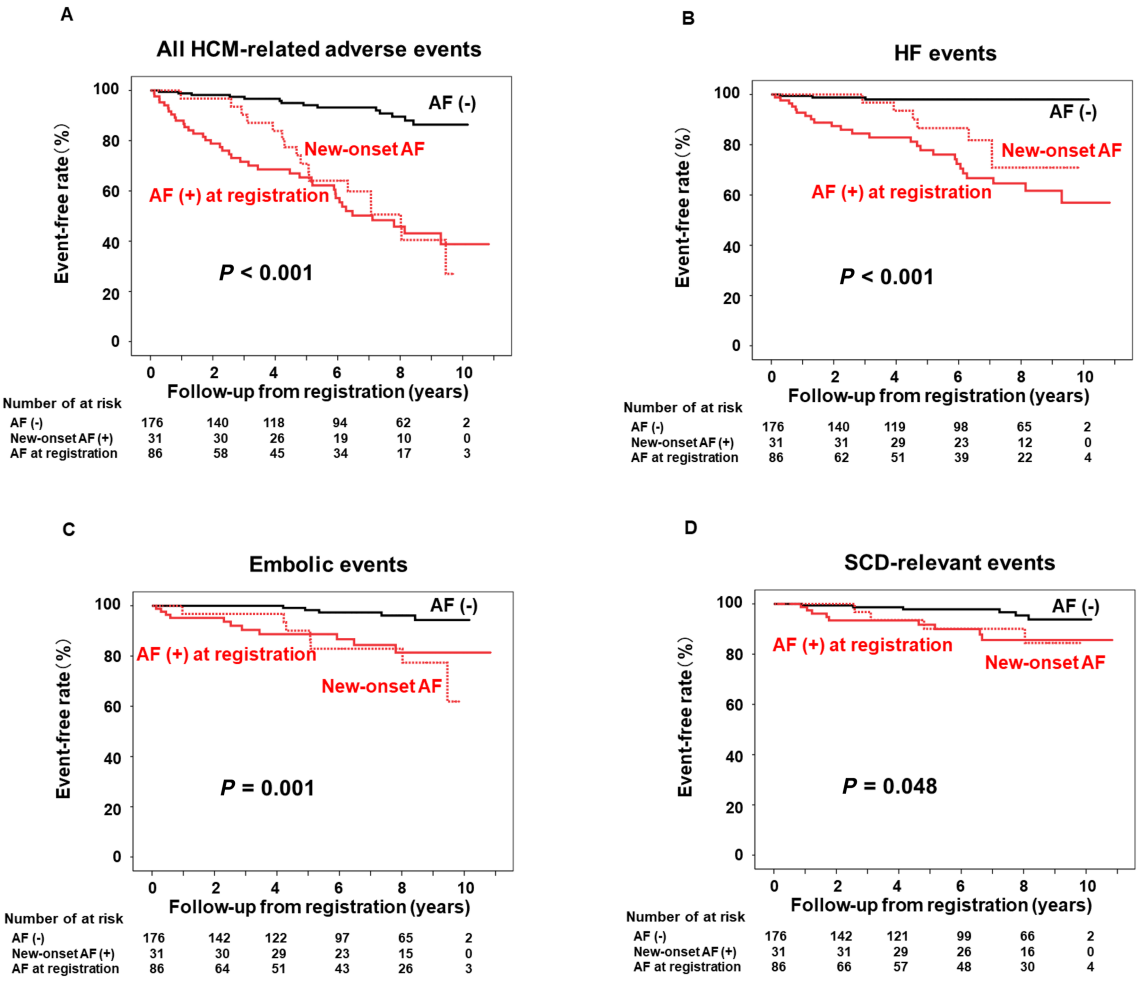
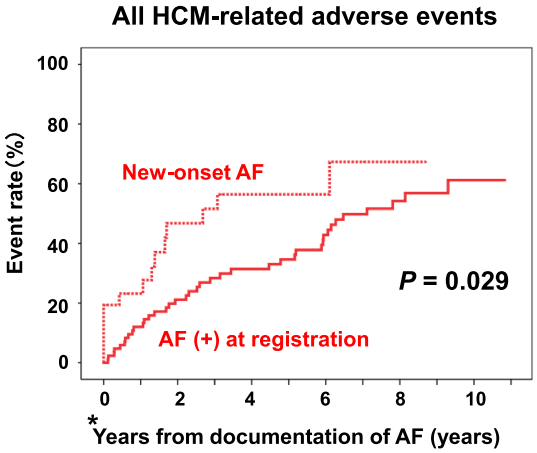


Figure 4 HCM-related adverse events in HCM patients with new-onset AF observed from AF onset and those with AF at registration. *In the patients with AF at registration who had documentation of AF (including paroxysmal AF) before or at registration, we have set a unified point at registration as the timing of AF detection in this prospective cohort study. AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy.



detection of AF (all had embolic stroke events) and one of the three patients had HF hospitalization after AF documentation. In the six of the 17 new-onset AF patients with the adverse events, AF was detected on the same day as occurring the HCM-related events: three patients with embolic events, two patients with HF admission, and one patient with sustained VT.

Figure 3 shows the HCM-related adverse events in HCM patients with AF at registration, those with new-onset AF, and those without detection of AF during the follow-up period: *Figure 3A* for all events, *Figure 3B* for HF events, *Figure 3C* for embolic events, and *Figure 3D* for SCD-relevant events. The rates of events in patients in the new-onset AF group rapidly approached those in patients with AF at registration. We focused on the period from the detection of AF to the occurrence of the HCM-related adverse events in *Figure 4*. Importantly, the incidence of all HCM-related adverse events was further higher in patients with new-onset AF observed from AF onset compared with those with AF at registration (*Figure 4*: the three embolic events before detection of AF were not included in the analysis in patients with new-onset AF). A certain number of the HCM-related adverse events seemed to be associated with new occurrence of AF.

Discussion

The major findings of our prospective study were that (i) about 30% of the HCM patients had a current or past history of AF at registration; (ii) patients with AF at registration were characterized by worse clinical profiles including more advanced age, more symptomatic, more advanced LV and left atrial remodelling at registration, and AF at registration was associated with an increased incidence of HCM-related adverse events, particularly HF events; (iii) approximately 1.8% of the patients without detection of AF at registration developed new AF annually, and the presence of palpitation and enlarged left atrial diameter, particularly left atrial diameter ≥50 mm, at registration were significant predictors of new-onset AF; and (iv) patients with new-onset AF had a further higher incidence of HCM-related adverse events observed from AF onset than did patients with AF at registration.

Atrial fibrillation represents the most common arrhythmia in patients with HCM. Although the reported prevalence of AF in several HCM populations was around 20%,[4–7] the prevalence of AF in our study was 29% at registration and finally reached 40% during the follow-up period. This relatively high prevalence of AF is probably due to our aged cohort. Age at our regional cohort in the Kochi RYOMA study was older than that of HCM cohorts in previous studies.[4–7] This age distribution of patients in the present study is probably because of the fact that Kochi Prefecture, where our study was performed, is located far from urban areas and is one of the most aged communities in Japan. We think that, at least in Japanese rural regions, many patients with this disease are middle-aged or elderly despite the fact that HCM is regarded as a genetic disorder. Maron *et al*. reported that the segment of an HCM cohort with advanced age (>50 years old) was most vulnerable to stroke and other peripheral vascular events and that this risk progressed with advance of age, probably due mainly to the more frequent occurrence of AF in older patients.[6]

Regarding HCM-related adverse events, it is well known that AF is a strong determinant of arterial embolic events.[14] Furthermore, there have been several retrospective studies showing that HCM patients with AF had increased risk for heart failure-related mortality and severe functional disability as well as stroke.[5–7] However, Rowin *et al*. recently showed in their retrospective study that AF is associated with a low rate of cardiovascular mortality and does not appear to be an independent determinant of HF morbidity.[8] On the other hand, in our prospective patient cohort, we recently reported that though mortality was favourable, clinically important morbid events frequently occurred and AF was an independent predictor of overall HCM-related adverse events.[10] In the present study, we focused on AF and conducted a detailed investigation. Patients with AF at registration were characterized by worse clinical profiles and AF at registration was strongly associated with increased incidence of HCM-related adverse events, particularly HF events. From these results, it is difficult to determine whether AF is just a marker of advanced stage of the disease or whether AF itself causes those events. Here, we further assessed the clinical significance of newly developed AF. If AF could be just a marker of the disease stage, we expected that they would be parallel graphs of HCM-related adverse events between in patients with new-onset AF and in

patients with AF at registration. However, as shown in *Figure 3A*, the rates of events in patients in the new-onset AF group rapidly approached those in patients with AF at registration. Then, we focused on the period from the detection of AF to the occurrence of the HCM-related adverse events and found that patients with new-onset AF had a higher incidence of HCM-related adverse events observed from AF onset compared with patients who had AF at the beginning of the registration (*Figure 4*). Based on these findings, we consider that AF may not be just a marker of disease stage but an important trigger of HCM-related adverse events although the direct cause-effect relationship was not provided in our observational registry study. In general, AF exerts negative hemodynamic effects by decreasing cardiac output via the loss of atrial contraction, impaired ventricular rate control and triggering ventricular arrhythmias. Yamauchi *et al*. found in their large-scale chronic HF registry (CHART-2) that onset of new AF, but not a history of AF, was associated with increased mortality in general chronic HF patients.[15] Therefore, more careful management of HCM patients with AF, particularly for those with new-onset AF, is needed. Furthermore, patients with HCM who develop AF even without any symptoms should be identified early in clinical practice. The results of our study showed that the presence of palpitation and enlarged left atrial diameter, particularly left atrial diameter ≥50 mm, are simple but useful findings predicting the development of new AF. The 2014 ESC Guidelines recommended that 48-hour ambulatory ECG monitoring every 6–12 months to detect AF should be considered in patients who are in sinus rhythm and have a left atrial diameter of ≥45 mm.[2]

Limitations

There are several limitations to be acknowledged in the present study. First, the number of study patients was relatively small and some of the statistical analyses might have been affected. In addition, our study cohort differs from tertiary center cohorts in which referral patterns are skewed toward patients perceived to be at high risk. The cohort in the present study was a community-based cohort and included less high-risk patients for sudden death than those in major referral centers. Second, only about 70% of the patients had Holter ECG monitoring during the follow-up period. Due to no systematic strategy of arrhythmic monitoring in this study, AF counted as new-onset could represent previously unrecognized arrhythmias and the prevalence of AF might have been underestimated both at the time of registration and at the time of last evaluation. Third, in this study, we did not find any clinical impact of therapeutic interventions for AF. This can be because even treatments aimed at rhythm control were not always successful. Given that AF might be a trigger for worsening disease condition in HCM, aggressive interventions such as AF catheter ablation or the Maze procedure at surgical myectomy can improve the outcomes.[8] Recently, the practice of AF catheter ablation has been increasing in our area, and it is necessary to investigate the therapeutic intervention in AF and the effects including maintenance rate of sinus rhythm and clinical course in our HCM population.

Conclusions

In our unselected registry in an aged Japanese community, 29% of the patients at registration had documentation of AF and the annual detection rate of new-onset AF was 1.8% during the follow-up period. Although HCM mortality was favourable, a considerable number of patients suffered from HCM-related adverse events. The presence of AF, particularly new-onset AF, was associated with unfavourable clinical outcomes. AF may not be just a marker of disease stage but an important trigger of HCM-related adverse events.

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Conflict of interest

None of the authors have conflict of interest to disclose in connection with our manuscript.

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