Stroke and Embolic Events in Hypertrophic Cardiomyopathy
Risk Stratification in Patients Without Atrial Fibrillation

Shintaro Haruki, MD, PhD; Yuichiro Minami, MD, PhD; Nobuhisa Hagiwara, MD, PhD

Background and Purpose—Stroke and systemic embolic events are known to occur as complications of hypertrophic cardiomyopathy (HCM), and these complications are more common in patients with accompanying atrial fibrillation (AF). The diagnosis of AF is sometimes difficult, however, and it is possible that subclinical asymptomatic paroxysmal episodes or a first episode of AF in patients without previously documented AF may lead to embolic events. We investigated the prevalence of embolic events in patients with HCM and evaluated risk factors for these events in patients without documented AF.

Methods—This study enrolled 593 patients with clinically diagnosed HCM (age at diagnosis, 51.0±15.6 years) from 1980 to 2010.

Results—During a mean follow-up of 10.7±7.5 years, 68 (11.5%) experienced stroke and embolic events. AF had been documented before the event in 29 (42.6%) of them. AF was documented for the first time at the time of the event in 5 (7.4%) and after the event in 10 (14.7%). Among the 431 patients without previously documented AF (39 with events and 392 without events), older age at diagnosis and left atrial dimension ≥48 mm were identified as the independent determinants of the embolic event after adjusting for sex and classic prognostic markers related to HCM.

Conclusions—The incidence of stroke and embolic events was about 1.0% per year in the HCM cohort. AF had not been previously documented before the event in more than half of patients with events. Older age and enlarged left atrial dimension are possible risk factors for embolic events in patients with HCM without documented AF.

Key Words: atrial fibrillation ■ cardiomyopathies ■ heart atria ■ risk factors ■ stroke

Hypertrophic cardiomyopathy (HCM) is one of the most common genetic cardiac disorders, with markedly heterogeneous clinical manifestations and natural history. Although stroke and systemic embolic events are known to occur as complications of HCM, few data are available on the occurrence and profile of these events in this patient population. In a previous study, stroke and systemic embolic events showed an incidence of 0.8% per year, and these ominous and profound complications were more common in patients with atrial fibrillation (AF). Anticoagulation has proved effective in reducing the incidence of these events in patients with HCM and AF. Also, current guidelines state that anticoagulation is indicated in patients with HCM with paroxysmal, persistent, or chronic AF, regardless of known embolic risk factors such as those covered by the congestive heart failure, hypertension, age=75 years, diabetes mellitus, stroke score. Given the often paroxysmal and asymptomatic nature of AF, however, its diagnosis is sometimes difficult in real-world clinical practice. It is therefore possible that a subclinical, asymptomatic (silent) paroxysmal episode or a first paroxysmal episode of AF in patients without previously documented AF may lead to stroke and peripheral embolization. The epidemiology of these events in patients without documented AF is an important clinical issue. This is especially true for patients at high risk of embolization, such as those with HCM, although the connection remains unclear. The aim of this study was to investigate the frequency and clinical features of patients with HCM with stroke and systemic embolic events in a tertiary referral cohort in Japan and to clarify the epidemiology and risk factors of these events in patients with HCM without previously documented AF.

Methods

Patients

This observational study consecutively enrolled 593 patients with clinically diagnosed HCM from 1980 to 2010 at Tokyo Women’s Medical University Hospital, Tokyo, Japan. The initial evaluation in this trial was regarded as the first clinical assessment during which an echocardiographic diagnosis of HCM was made at our institution.
The most recent evaluation was defined as the patient review at a routine outpatient clinic visit or by telephone interview. This study was performed according to the principles of the Helsinki Declaration. The review board of Tokyo Women’s Medical University Hospital approved the protocol.

**Hypertrophic Cardiomyopathy**

HCM was diagnosed based on a standard definition. The diagnostic process consisted of 2-dimensional (2D) echocardiographic identification of a hypertrophied, nondilated left ventricle in the absence of any other cardiac or systemic disease capable of producing similar hypertrophy.\(^1,2\)

**Apical Hypertrophy and Aneurysm**

The diagnostic criteria for apical hypertrophy included asymmetrical left ventricular hypertrophy that was confined predominantly to the left ventricular apical region with apical wall thickness ≥15 mm.\(^9\) Left ventricular apical aneurysm was defined as a thin-walled dyskinetic or akinetic segment at the most distal part of the left ventricular chamber showing relatively wide communication with the left ventricular cavity.\(^10\)

**Arrhythmias**

Ambulatory electrocardiograms covering at least 24 hours were reviewed to detect nonsustained ventricular tachycardia and AF in all study patients during the initial evaluation. Nonsustained ventricular tachycardia was defined as a minimum of 3 consecutive ventricular extra beats at a rate of ≥120 per minute and lasting for <30 seconds.\(^11\) The presence of AF was documented by 12-lead resting electrocardiography or ambulatory electrocardiography performed either after the acute onset of symptoms or during a routine medical evaluation in patients without symptoms.\(^1,2\)

**Stroke and Systemic Embolic Events**

Stroke was defined as permanent neurological disability and impairment caused by vascular causes, including ischemic stroke and intracerebral hemorrhage.\(^3,12\) Stroke events had been classified by 2 studies as LAD ≥30 mm, nonsustained ventricular tachycardia, and LAD ≥48 mm. \(P=0.171\) and LAD (39.1±7.4 versus 38.8±8.4 mm; \(P=0.762\)). A \(P<0.05\) was considered to indicate statistical significance in all analyses.

**Statistical Analysis**

All analyses were performed with SAS 9.1 software (SAS Institute, Cary, NC). Data are presented as the mean±SD or as frequencies. Student \(t\) test was used to compare groups with normally distributed continuous variables, and the \(\chi^2\) or Fisher exact test (when an expected value was <5) was used to compare nominally scaled variables. Mann–Whitney \(U\) test was used to compare ordinal variables. Embolic event-free curves were estimated using the Kaplan–Meier method, and differences between curves were assessed by log-rank tests. Univariate and multivariate Cox proportional hazards models were used to evaluate the impact of various risk markers on the stroke and systemic embolic events. Multivariate models included age at the initial HCM diagnosis, sex, and the presence or absence of known risk markers related to HCM (family history of sudden cardiac death, unexplained syncope, left ventricular intracavitary gradient, maximum left ventricular wall thickness ≥30 mm, nonsustained ventricular tachycardia, and LAD ≥48 mm). In this study, 14.2% of patients were lost to follow-up. These patients were similar to those not lost to follow-up in study HCM cohort. That is, no statistically significant differences were observed between the 2 groups in terms of age at the initial diagnoses of HCM (53.2±18.3 versus 50.6±15.1 years; \(P=0.171\)) and LAD (39.1±7.4 versus 38.8±8.4 mm; \(P=0.762\)). A \(P<0.05\) was considered to indicate statistical significance in all analyses.

**Results**

**Prevalence of Stroke and Systemic Embolic Events**

Of the 593 studied patients with HCM (age at diagnosis, 51.0±15.6 years), 68 (11.5%) experienced stroke and systemic embolic events during the mean follow-up period of 10.7±7.5 years. The mean age at the event was 60.4±11.5 years (range, 23–83 years; Figure 1). Among the 68 study patients with events, cerebral ischemic stroke occurred in 62 patients (91.2%), including 4 patients with intracerebral hemorrhage. Six patients (8.8%) had embolic events to organs other than the brain: kidney (n=4), upper limb (n=1), and lower limb (n=1).

**Characteristics of Patients With and Without Embolic Events**

Clinical characteristics of the 593 studied patients with HCM with or without stroke and systemic embolic events

**Echocardiography**

Comprehensive 2D, M-mode, and Doppler echocardiographic studies were performed using commercially available ultrasonography systems. With the patient in the left lateral decubitus or supine position, we obtained parasternal short- and long-axis views, apical 4- and 2-chamber views, long-axis views, and subcostal views. The peak left ventricular intracavitary pressure gradient was quantified by continuous-wave Doppler echocardiography at the initial evaluation. A left ventricular outflow tract obstruction, caused by systolic anterior motion of the anterior mitral valve leaflet, was considered present when the estimated peak instantaneous gradient was ≥30 mm Hg at resting conditions.\(^13\) A left midventricular obstruction was diagnosed when we detected systolic apposition of the midleft ventricular walls (and often the papillary muscles), with abnormally high velocities (≥30 mm Hg at resting conditions), persisting through late systole and often with early diastolic paradoxical jet flow.\(^14\) The left atrial dimension (LAD) was measured from the parasternal long-axis view as the anteroposterior linear diameter at end-systole, as previously recommended.\(^15\) On the basis of previously published data, left atrial enlargement was defined in this study as LAD ≥48 mm.\(^15\)

![Figure 1. Age distribution of the patients at the time of the initial stroke and systemic embolic events in 68 patients with hypertrophic cardiomyopathy](http://stroke.ahajournals.org/)

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are shown in Table 1. The patients with events were slightly older at the initial HCM diagnosis than those without events, but the difference was not statistically significant. AF occurred more frequently throughout the follow-up period, anticoagulation (warfarin) was prescribed more often, and the LAD was larger in the event group than in the group without events. There were no significant differences with respect to sex, family history of sudden death, left ventricular phenotype (eg, presence or absence of intracavitary obstruction and apical aneurysm), maximum left ventricular wall thickness, history of syncope, or nonsustained ventricular tachycardia between the patients with and without events. Among 68 patients with embolic events, 15 (22.1%) had a congestive heart failure, hypertension, age=75 years, diabetes mellitus, stroke score of 0, 27 (39.7%) had a score of 1, 19 (27.9%) had a score of 2, and 7 (10.3%) had a score of 3. No patients had a score of 4 to 6 before embolic events. There was no significant difference with respect to congestive heart failure, hypertension, age=75 years, diabetes mellitus, stroke scores between the patients with and without embolic events (mean score of 1.3±0.9 versus 1.2±0.9; Mann–Whitney U test, P=0.681). Nineteen of the 68 patients with embolic events (27.9%) and 56 of the 525 patients without embolic events (10.7%) experienced episodes of progressive heart failure with an increase to ≥3 New York Heart Association functional class (P<0.001). As for HCM-related cardiac death (heart failure death and sudden death), 6 of the 68 patients with embolic events (8.8%) and 21 of the 525 patients without embolic events (4.0%) died with a cardiac cause during the follow-up period (P=0.111).

**Rhythm at the Embolic Events**

Rhythms at the time of the embolic events in the patients with HCM are shown in Figure 2. Of the 68 patients with events, AF was previously documented in 29 patients (42.6%; subset A in Figure 2). AF was first identified at the time of the embolic event in 5 patients (7.4%; subset B in Figure 2). AF was diagnosed only after the embolic event in 10 patients (14.7%; subset C in Figure 2). Overall, AF was diagnosed during the follow-up period in 44 of 68 patients with events (64.7%; subsets A, B, and C in Figure 2). AF was not found during the follow-up period, however, in the remaining 24 of the 68 patients with events (35.3%; subset D in Figure 2).

### Anticoagulation in Patients With Previously Documented AF

Among the 593 patients with HCM, AF had been documented before the event in 162 patients (27.3%; subsets A and F in Figure 2). Among them, 29 (17.9%; subset A in Figure 2) experienced stroke and systemic embolic events during a mean follow-up of 12.0±7.8 years. In patients with previously documented AF, 84 (51.9%) had been given anticoagulation with warfarin before their event. The incidence of embolic events was slightly higher among patients without anticoagulation (16/78 patients; 20.5%) than in those treated with warfarin (13/84 patients; 15.5%), but the difference was not statistically significant (P=0.528).

### Risk Stratification in Patients WithoutPreviously Documented AF

Among the 593 study patients, AF was not previously documented in 431 patients (72.7%; subsets B, C, D, and E in Figure 2). Of these 431 patients, 39 (9.0%; subsets B, C, and D in Figure 2) experienced stroke and systemic embolic events at a mean age of 59.2±9.9 years during the mean follow-up period of 10.2±7.4 years. The incidence of embolic events was slightly higher among patients without anticoagulation (16/78 patients; 20.5%) than in those treated with warfarin (13/84 patients; 15.5%), but the difference was not statistically significant (P=0.111).

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**Table 1. Patient Characteristics of Patients With Hypertrophic Cardiomyopathy With and Without Embolic Events**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients With Embolic Events (n=68)</th>
<th>Patients Without Embolic Events (n=525)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>29 (42.6)</td>
<td>191 (36.4)</td>
<td>0.383</td>
</tr>
<tr>
<td>Age at diagnosis, y</td>
<td>54.4±11.6</td>
<td>50.5±16.0</td>
<td>0.053</td>
</tr>
<tr>
<td>Family history of sudden death</td>
<td>8 (11.8)</td>
<td>61 (11.6)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Left ventricular outflow tract obstruction</td>
<td>15 (22.1)</td>
<td>117 (22.3)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Left ventricular midcavitary obstruction</td>
<td>6 (8.8)</td>
<td>50 (9.5)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Apical hypertrophy</td>
<td>14 (20.6)</td>
<td>167 (31.8)</td>
<td>0.080</td>
</tr>
<tr>
<td>Apical aneurysm</td>
<td>2 (2.9)</td>
<td>25 (4.8)</td>
<td>0.758</td>
</tr>
<tr>
<td>Left atrial dimension, mm</td>
<td>43.6±8.7</td>
<td>38.2±8.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum left ventricular wall thickness, mm</td>
<td>19.6±3.7</td>
<td>19.7±4.7</td>
<td>0.818</td>
</tr>
<tr>
<td>Unexplained syncope</td>
<td>14 (20.6)</td>
<td>92 (17.5)</td>
<td>0.650</td>
</tr>
<tr>
<td>Nonsustained ventricular tachycardia</td>
<td>32 (47.1)</td>
<td>195 (37.1)</td>
<td>0.147</td>
</tr>
<tr>
<td>Atrial fibrillation during follow-up period</td>
<td>44 (64.7)</td>
<td>133 (25.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anticoagulation during follow-up period</td>
<td>39 (57.4)</td>
<td>111 (21.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow-up duration, y</td>
<td>12.5±8.8</td>
<td>10.5±7.3</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Results are given as the mean±SD or the number (%).
anticoagulation (3/43 patients; 7.0%) in patients without previously documented AF, but the difference was not statistically significant (P=0.784). The clinical characteristics of 431 patients without prior documented AF are shown in Table 2 according to the presence or absence of embolic events. There was a higher proportion of female patients with events than without events, and the patients with events were older at the time of the initial HCM diagnosis than those without events. In addition, apical hypertrophy was less frequent and the LAD was larger in patients with events. The distribution of the LAD in patients without documented AF according to the presence or absence of events is shown in Figure 3A. Kaplan–Meier estimate revealed that patients with enlarged LAD (≥48 mm) had a significantly greater likelihood of embolic events than those without enlarged LAD among patients without documented AF (log-rank P<0.001; Figure 3B). The hazard ratios for stroke and systemic embolic events in patients with HCM without documented AF are shown in Table 3 according to their age at the time of the initial HCM diagnosis, their sex, and the presence or absence of classic risk markers related to HCM (family history of sudden cardiac death, unexplained syncope, left ventricular intracavitary gradient, maximum left ventricular wall thickness ≥30 mm, nonsustained ventricular tachycardia, and LAD ≥48 mm). The multivariate analysis, adjusted for the above markers of disease severity, revealed that older age at diagnosis and LAD ≥48 mm were independent determinants of the embolic events, although several findings (female sex and left ventricular intracavitary obstruction) were determinants on the univariate analysis.

**Discussion**

In this tertiary referral HCM cohort, the incidence of stroke and systemic embolic events was about 1.0% per year. In addition, patients with these events had a higher prevalence of AF throughout the follow-up period than those without an event. However, AF had not been previously documented in

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**Table 2. Patient Characteristics of Studied Patients With Hypertrophic Cardiomyopathy Without Documented Atrial Fibrillation According to the Presence or Absence of Embolic Events**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients With Embolic Events (n=39)</th>
<th>Patients Without Embolic Events (n=392)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>23 (59.0)</td>
<td>145 (37.0)</td>
<td>0.012</td>
</tr>
<tr>
<td>Age at diagnosis, y</td>
<td>55.8±11.2</td>
<td>49.5±16.6</td>
<td>0.022</td>
</tr>
<tr>
<td>Family history of sudden death</td>
<td>5 (12.8)</td>
<td>44 (11.2)</td>
<td>0.791</td>
</tr>
<tr>
<td>Left ventricular outflow tract obstruction</td>
<td>12 (30.8)</td>
<td>84 (21.4)</td>
<td>0.256</td>
</tr>
<tr>
<td>Left ventricular midcavitary obstruction</td>
<td>6 (15.4)</td>
<td>39 (9.9)</td>
<td>0.276</td>
</tr>
<tr>
<td>Apical hypertrophy</td>
<td>4 (10.3)</td>
<td>133 (33.9)</td>
<td>0.004</td>
</tr>
<tr>
<td>Apical aneurysm</td>
<td>1 (2.6)</td>
<td>20 (5.1)</td>
<td>0.709</td>
</tr>
<tr>
<td>Left atrial dimension</td>
<td>41.6±7.5</td>
<td>36.5±6.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum left ventricular wall thickness</td>
<td>18.9±3.6</td>
<td>19.9±4.7</td>
<td>0.215</td>
</tr>
<tr>
<td>Unexplained syncope</td>
<td>9 (23.1)</td>
<td>48 (12.2)</td>
<td>0.098</td>
</tr>
<tr>
<td>Nonsustained ventricular tachycardia</td>
<td>14 (35.9)</td>
<td>129 (32.9)</td>
<td>0.841</td>
</tr>
<tr>
<td>Follow-up duration, y</td>
<td>10.4±8.7</td>
<td>10.2±7.3</td>
<td>0.859</td>
</tr>
</tbody>
</table>

Results are given as the mean±SD or number (%).
more than half of the patients with events. Among the patients with HCM without previously documented AF, older age at diagnosis and enlarged LAD were identified as independent determinants of the embolic events.

This study confirms the results of a previous study that reported a 1% per year prevalence of stroke (including peripheral arterial embolization) in patients with HCM.3 Also, the characteristics of patients with embolic events in this study were almost identical to those in an earlier study.1

Anticoagulation has proved effective in reducing the incidence of embolic events in patients with HCM with AF. Current guidelines strongly recommend that anticoagulation with vitamin K antagonists be given to patients with paroxysmal (even for those with single or short episodes), persistent, or chronic AF and HCM, regardless of any known embolic risk factors such as the congestive heart failure, hypertension, age=75 years, diabetes mellitus, stroke score.1–3 Although not statistically significant, the incidence of embolic events in the present study was also lower among patients with AF given an anticoagulant (dose adjusted to a target prothrombin time expressed as an international normalized ratio of 2.0–3.0 and 1.6–2.6, for patients aged <70 and ≥70 years, respectively, in accordance with Japanese treatment guidelines16) than those who were not. Despite being based on a highly selected population of patients with HCM from a single tertiary referral center in Japan, the results of this study have revealed additional epidemiological information about the relationship between embolic events, AF, and anticoagulation in a relatively large HCM patient cohort.

Numerous previous studies have demonstrated that AF is common and is associated with high thromboembolic risk in patients with HCM.3,17–19 The reported prevalence of AF, however, varies considerably among studies in patients with HCM with stroke and systemic embolic events.3,18,19 In another study from Japan, AF was found in 67% of patients with HCM who had an ischemic stroke.18 From a large cohort in the United States and Italy, Maron et al3 reported that AF was found in 88% of patients with HCM with an embolic event. Finally, in another relatively small cohort study, such events occurred almost exclusively in patients with AF.19 These variations in reported prevalence could be the result of racial/ethnic differences, selection bias, or under-recognition of AF, especially subclinical, asymptomatic paroxysmal episodes of AF. In addition, the onset and time course of AF (before or after embolic events) was unclear in the above reports, and patients who had developed AF after their first event may also have been included in the group with AF. Therefore, in this study, we tried to clarify the heart rhythm at the time of

Table 3. Predictors of Embolic Events in Patients With HCM Without Documented Atrial Fibrillation

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude Hazard Ratio (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Age at initial HCM diagnosis (per 1 increase)</td>
<td>1.04 (1.02–1.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>2.59 (1.37–4.90)</td>
<td>0.003</td>
</tr>
<tr>
<td>Family history of sudden death</td>
<td>0.93 (0.35–2.46)</td>
<td>0.882</td>
</tr>
<tr>
<td>Maximum left ventricular wall thickness ≥30 mm</td>
<td>0.57 (0.08–4.19)</td>
<td>0.584</td>
</tr>
<tr>
<td>Nonsustained ventricular tachycardia</td>
<td>1.01 (0.52–1.95)</td>
<td>0.977</td>
</tr>
<tr>
<td>Unexplained syncope</td>
<td>2.02 (0.95–4.28)</td>
<td>0.066</td>
</tr>
<tr>
<td>Left ventricular intracavitary obstruction</td>
<td>2.20 (1.16–4.17)</td>
<td>0.016</td>
</tr>
<tr>
<td>Enlarged left atrial dimension ≥48 mm</td>
<td>3.77 (1.78–8.00)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; and HCM, hypertrophic cardiomyopathy.
the event in the HCM cohort (Figure 2). Our results showed that AF was previously documented in only about 40% of the patients with HCM with events. Additionally, AF was first documented at the time of the event or afterward in about 20% of patients with events. Altogether, >60% of patients with events had AF sometime during the follow-up period, a result that is almost identical to that of a previous report from a Japanese HCM cohort.18

The diagnosis of paroxysmal AF is sometimes difficult in real-world clinical practice, so patients without documented AF may nonetheless have subclinical, asymptomatic (silent) paroxysmal AF.4–8 It is also possible that an asymptomatic paroxysmal episode or a first paroxysmal episode of AF in patients without previously documented AF may lead to stroke and systemic embolic events.4–8 Asymptomatic AF is associated with at least the same risk for stroke as is symptomatic AF.5 In this respect, risk stratification of embolic events in patients without documented AF is extremely important and a critical issue, especially in patients at high risk of embolization, such as those with HCM. In our study cohort of patients with HCM without documented AF, an enlarged LAD was identified as an independent determinant of embolic events. An enlarged left atrium is an important prognostic factor in various heart diseases, and numerous previous studies have demonstrated that left atrial dilatation is related to adverse outcomes in cardiovascular patients.20,21 As for HCM, previous studies have reported that an enlarged left atrium is a marker of disease severity and predicts adverse cardiovascular events.15,22,23 In addition, left atrial dilatation is a sensitive, specific marker for the occurrence of AF.24,25 Therefore, patients with HCM with an enlarged LAD are thought to be predisposed to the development of AF—whether an asymptomatic paroxysmal episode or a first paroxysmal episode of AF—which in turn may cause stroke and systemic embolic events in patients without previously documented AF. However, such a hypothesis cannot account for all patients with HCM with an enlarged LAD and embolic events. Further studies are needed to clarify the relationship between the LAD and embolic risk in patients with HCM without documented AF. Hence, the prevention of stroke and ischemic embolic events (eg, by prophylactic anticoagulant therapy) in patients with HCM with an enlarged LAD without documented AF remains a clinical challenge.

Limitations
The study was performed at a single tertiary referral center in Japan, which may have resulted in certain inherent selection biases. Further multicenter, multinational, or population-based studies are therefore needed to confirm and extend our findings. The diagnosis of AF in this study was based on electrocardiograms and 24-hour ambulatory electrocardiograms, which are not fully reliable for detecting paroxysmal atrial arrhythmias. Therefore, it is likely that we underestimated the true prevalence of AF among studied patients with HCM. It remains unclear whether the use of additional electrocardiographic monitoring beyond 24 hours (eg, with an implantable loop recorder) is effective for the detection of subclinical AF in patients with HCM, and the most effective duration of monitoring has not been determined.4,6,8 In addition, it is unclear whether newly detected AF was causally related to the index embolic events because not all embolic events, even in patients with documented AF, are caused by the arrhythmia. Further studies are required to determine the most appropriate strategies for the detection of subclinical AF in patients with HCM, especially in patients with an enlarged LAD. We presented our data without making a precise distinction between cardioembolic and other stroke subtypes in our HCM cohort because of an acknowledged difficulty in definitively distinguishing cardioembolic stroke from other subtypes in individual patients. Although current guidelines recommend anticoagulation in patients with HCM with AF, only ≈50% of patients with AF in this study were given long-term anticoagulation, mainly because their AF occurred before the efficacy of warfarin had been established. Similarly, ≈40% of patients with AF had been under anticoagulation in a previous HCM patient cohort since the 1970s.2,15 We also did not measure the left atrial volume in this HCM cohort because of the large patient population that had accumulated since 1980 and the extended follow-up period. The LAD is a less precise surrogate of left atrial size than left atrial volume, which provides a more accurate and reproducible estimate of left atrial size and has a stronger association with disease severity and outcome.26 The LAD is more easily obtainable, however, and LAD measurements are already being used in conventional and standard echocardiographic studies.

Conclusions
In the studied HCM cohort, the incidence of stroke and systemic embolic events was about 1.0% per year, a result that is almost identical to that in a previous report on HCM. In addition, AF had not been documented before the embolic event in more than half of our patients with events. The multivariate analysis, adjusted for markers of disease severity, indicated that older age at the initial HCM diagnosis and enlarged LAD were independent determinants of embolic events in patients without previously documented AF. Prevention of stroke and systemic embolic events in elderly patients with HCM with an enlarged LAD without documented AF remains a clinical challenge.

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Disclosures
None.

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Stroke and Embolic Events in Hypertrophic Cardiomyopathy: Risk Stratification in Patients Without Atrial Fibrillation
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