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Original Article

# Estimating the prevalence, clinical characteristics, and treatment patterns of hypertrophic cardiomyopathy in Japan: A nationwide medical claims database study

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ABSTRACT

*Background:* Limited data are available regarding therapies for hypertrophic cardiomyopathy (HCM). This study assessed the prevalence, clinical characteristics, and treatment patterns of HCM in Japan.
*Methods:* This retrospective database study analyzed data from 438 hospitals in the Japan Medical Data Vision database from 2016 to 2020. We identified 3913 patients (15 %) with obstructive HCM (oHCM) and 21,714 patients (85 %) with nonobstructive HCM (nHCM).
*Results:* The estimated total number of patients with oHCM and nHCM in 2020 among Japanese hospitals was 8500 and 43,500, respectively. The prevalence of oHCM and nHCM steadily increased by 27 % and 12 %, respectively, from 2016 to 2020, with a 1:5.2 ratio of oHCM to nHCM in 2020. The mean age of the oHCM and nHCM populations was 72 and 70 years, respectively, and comorbidities included atrial fibrillation (AF) (oHCM, 33.8 %; nHCM, 32.2 %), other arrythmia (30.1 %; 27.6 %), and stroke (16.6 %; 16.4 %). Furthermore, 45.0 % of oHCM and 37.7 % of nHCM patients had undergone at least one hospitalization. A substantial number of HCM patients aged between 20 and 59 years reported AF (oHCM, 17–37 %; nHCM, 4–24 %) and stroke (oHCM, 0–12 %; nHCM, 3–10 %). β-blockers (oHCM, 64.0 %; nHCM, 42.1 %) were the most frequently prescribed treatment, followed by Na channel blockers (29.5 %; 5.7 %), calcium channel blockers (18.1 %; 8.8 %), direct oral anticoagulants (14.5 %; 15.2 %), and warfarin (11.0 %; 11.4 %).
*Conclusions:* This study provides important information on the current epidemiological and clinical characteristics of HCM in Japan.


## Introduction

Hypertrophic cardiomyopathy (HCM) is a primary myocardial disorder with heterogeneous morphologic, functional, and clinical features [1–3]. HCM can be broadly categorized into obstructive HCM (oHCM) and nonobstructive HCM (nHCM) depending on the presence or absence of left ventricular outflow tract (LVOT) obstruction [1,2,4]. Current medical treatment for oHCM focuses on symptomatic relief with β-blockers, nondihydropyridine (DHP) calcium channel blockers, and sodium channel blockers [1,2,4]. In drug-refractory symptomatic patients, invasive septal reduction therapy, including percutaneous transluminal septal myocardial ablation (PTSMA), may be effective [5].

Patients with HCM are often symptomatic and may have heart failure, malignant ventricular arrhythmias, and atrial fibrillation (AF) [6,7]. AF is the most common arrhythmia in patients with HCM [6–9] and is regarded as having a major impact on clinical outcomes, including heart failure and embolic stroke [6–10].

The prevalence in the general population has been previously estimated to be approximately 1 in 500 [1,2,11]. In contrast, in the US claims database, the prevalence of clinically established HCM was approximately 1 in 3000 [12]. In Japan in 1999, nationwide clinico-epidemiological surveys estimated the prevalence of HCM as approximately 1 in 5800 [13]. Furthermore, the number of HCM patients treated in a hospital setting appeared to be much lower than that diagnosed by using aggressive echocardiographic screening [14]. Unfortunately, no data are available since

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1999 on the epidemiology of HCM in Japan [13]. Therefore, this study aimed to examine the prevalence, patient characteristics, and treatment patterns of HCM using a hospital-based administrative claims database in Japan.

## Methods

### *Data source*

This retrospective observational cohort study used data extracted from a Japanese hospital-based administrative claims database provided by Medical Data Vision Co., Ltd. (MDV, Tokyo, Japan). The database contains healthcare claims data obtained from acute care hospitals using the Diagnosis Procedure Combination (DPC) system. As of June 2020, the database comprised approximately 32 million inpatients and outpatients in 438 acute care hospitals, covering 24–25 % of Japanese hospitals using the DPC system. Data recorded in the MDV database include International Classification of Diseases, 10th Revision (ICD-10) diagnosis codes, disease names coded using Japanese-specific disease codes, and procedures and drug prescriptions and administration coded using Japanese-specific receipt codes [15].

### *Study population*

The study eligibility period was from January 1, 2016, to December 31, 2020. Patients, irrespective of age, with ≥1 record of oHCM (defined as ICD-10 code I42.1) or other HCM (nHCM) (ICD-10 code: I42.2) between January 2016 and December 2020 in the MDV database were included in the analysis. The accuracy of definition of HCM with the ICD-10 code (ICD-10 code: I42.1 and I42.2) has been validated previously [16]. For these patients, their first diagnostic code in the whole period is referred to as index date. For oHCM, all patients were included in the prevalence analysis as well as the age and sex analysis. For nHCM, all patients were included in the prevalence analysis, but those with an oHCM diagnosis were excluded from the age and sex analysis and the clinical characteristics analysis. Data on demographics and clinical characteristics were extracted for patients meeting the selection criteria. Descriptive statistics were provided for each year (2016, 2017, 2018, 2019, and 2020) and for the whole period. For both populations, the look-back period was set to 12 months prior to the diagnosis date to ascertain the medical history of patients.

### *Prevalence of HCM*

The denominator for the whole period was defined as the number of patients with at least one outpatient or inpatient visit during January 2016 to December 2020 and the numerator was a diagnosis of HCM during the same period (Table 1). In the yearly analyses, patients from DPC hospitals that contributed data for the whole of each respective calendar year were included; similarly, the denominator for each calendar year was defined as the number of patients with at least one outpatient or inpatient visit during each respective calendar year and the numerator was a diagnosis code of oHCM or nHCM during the same period. The number of patients was standardized per 100,000 patients in the MDV database. The estimation of HCM prevalence assumed that most patients are treated at a DPC hospital and the mean number of patients in the MDV database is equal to that among DPC hospitals that are not currently covered by the MDV database, i.e. based on covering percentage of Japan DPC hospitals. The number of patients identified in the MDV database was multiplied by the total number of DPC hospitals in 2020.

### *Comorbidities and clinical manifestations*

Comorbidities and clinical manifestations in 12 months before index date were defined using the ICD-10 codes (Online Fig. 1). Medications and procedures were also extracted from the claims data.

### *Statistical analysis*

The demographic and clinical characteristics of the patients are expressed as mean and standard deviation (SD) for continuous variables and as count and percentage for categorical variables.

## Results

### *Prevalence of HCM*

A total of 3913 patients with oHCM and 21,714 patients with nHCM were identified over the whole period (January 2016 to December 2020; Fig. 1). Table 1 shows the number of patients with oHCM and nHCM for each year (2016, 2017, 2018, 2019, and 2020) and for the whole period. The prevalence of oHCM and nHCM steadily increased by 27 % (from 25.95 to 33.07 per 100,000) and 12 %, (from 152.46 to 170.40 per 100,000) respectively, from 2016 to 2020, with a 1:5.2 ratio of oHCM to nHCM in 2020. Furthermore, the estimated total number of patients with oHCM and nHCM based on the percentage of Japanese hospitals using the DPC system in 2020 was 8500 and 43,500, respectively.

### *Patient characteristics*

Fig. 2 shows the age distribution of patients with HCM (oHCM + nHCM) in 2020 compared with in 1999 [13]. In 2020, the highest prevalence was in the age group of 70–79 years, whereas in 1999, this was in the age group of 60–69 years.

The mean age of the oHCM and nHCM populations was 72.43 years and 69.80 years, respectively (Table 2). The proportion of patients in the older age group (≥70 years) was higher among women than men, and this was more pronounced in those with oHCM. In contrast, the proportion of patients aged <70 years was higher among men.

Overall, many patients with either oHCM or nHCM had multiple comorbidities (Table 3). Hypertension was the most common comorbidity in patients with HCM (oHCM, 72.6 %; nHCM, 66.9 %) followed by diabetes mellitus (oHCM, 57.4 %; nHCM, 58.5 %). A substantial number of patients had undergone hospitalization (oHCM, 45.0 %; nHCM, 37.7 %) in the previous year. Similar proportions of patients with oHCM and nHCM had AF (oHCM, 33.8 %; nHCM, 32.2 %), other arrythmia defined

**Table 1**
Estimated number of patients with oHCM and nHCM.

| | 2016 | 2017 | 2018 | 2019 | 2020 | Whole period |
|---|---|---|---|---|---|---|
| Patients treated in a hospital in the MDV database, n | 7,060,785 | 6,987,290 | 7,017,146 | 7,071,788 | 6,371,593 | 16,897,986 |
| oHCM | | | | | | |
| N | 1832 | 1926 | 2065 | 2144 | 2107 | 3913 |
| Per 100,000 | 25.95 | 27.56 | 29.43 | 30.32 | 33.07 | 23.16 |
| nHCM | | | | | | |
| N | 10,765 | 11,011 | 11,268 | 11,318 | 10,857 | 21,714 |
| Per 100,000 | 152.46 | 157.59 | 160.58 | 160.04 | 170.40 | 128.50 |

MDV, Medical Data Vision; nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy.

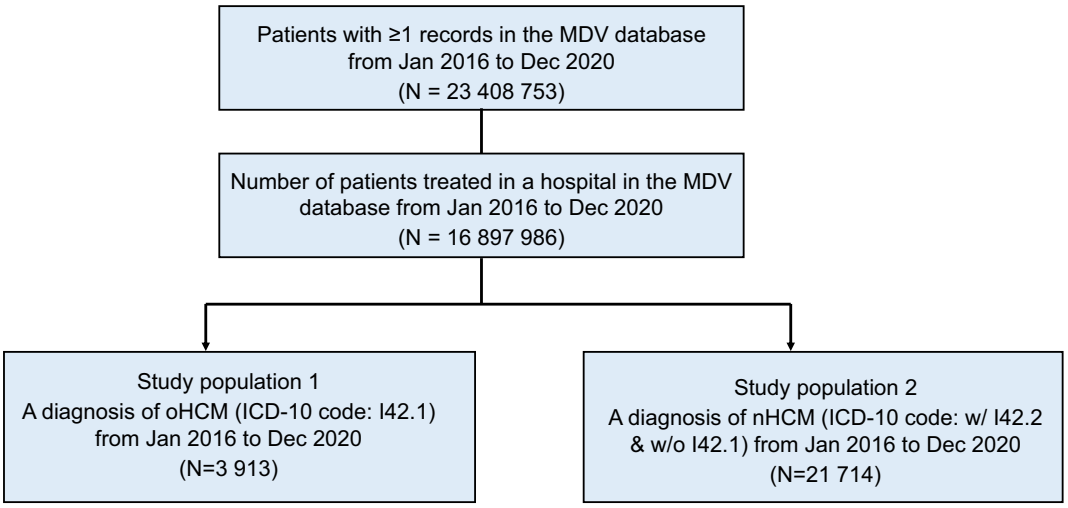


**Fig. 1.** Study population and patient identification.
ICD-10, International Classification of Diseases, 10th Revision; MDV, Medical Data Vision; nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy.

using the ICD-10 codes (Online Fig. 1) (oHCM, 30.1 %; nHCM, 27.6 %), and history of stroke (oHCM, 16.6 %; nHCM, 16.4 %).

We also investigated the age distribution of patients with HCM and comorbidities (Fig. 3). Among adult patients (≥20 years) with oHCM, the highest prevalence of other arrythmia (>50 %) was in the age group of 20–29 years followed by 30–39 years, and the rates decreased in an age-dependent manner. While a similar pattern was observed in patients with nHCM, the difference in prevalence across age groups was more pronounced in the oHCM population. In contrast, among patients with oHCM, the prevalence of AF was the lowest in the age group of 20–29 years (17 %), and the prevalence gradually increased to >30 % in those aged 50–59 years. Furthermore, in younger patients, the prevalence of AF was greater in those with oHCM than in those with nHCM, whereas in patients aged >60 years, the prevalence of AF was similar in both populations. History of stroke was reported even in younger patients with oHCM or nHCM aged between 30 and 39 years (10 % and 6 %, respectively). The prevalence of stroke increased steadily up to the age of 90 years.

*Treatment patterns*

Table 4 shows the treatment patterns in patients with oHCM and nHCM. β-blockers (oHCM, 64.0 %; nHCM, 42.1 %) were the most frequently prescribed treatment, followed by sodium channel blockers (oHCM, 29.5 %; nHCM, 5.7 %), non-DHP calcium channel blockers (oHCM, 25.4 %; nHCM, 25.6 %), direct oral anticoagulants (DOACs; oHCM, 14.5 %; nHCM, 15.2 %), warfarin (oHCM, 11.0 %; nHCM, 11.4 %), and potassium channel blockers (oHCM, 6.3 %; nHCM, 7.0 %). Approximately 30 % of patients with oHCM and nHCM received angiotensin-converting enzyme (ACE) inhibitors/angiotensin-II receptor blockers (ARBs) or DHP calcium channel blockers. The prescription ratio of diuretics in nHCM was similar with that in oHCM. Overall, 0.7 % of patients with oHCM compared with none with nHCM had undergone PTSMA. Cardiac resynchronization therapy (CRT; 0.02–0.04 %), implantable cardiac defibrillator (ICD; 0.1–0.4 %), and mitral valve replacement (MVR; 0.08–0.25 %) were less used.

## Discussion

This study analyzed data for 3913 patients with oHCM and 21,714 patients with nHCM between 2016 and 2020 from a large database of DPC hospitals in Japan. To our knowledge, this is the first nationwide medical claims database study in Japan and the largest survey for HCM in an Asian population.

*Prevalence of HCM*

We found that approximately 60 % of patients with oHCM and nHCM were aged ≥70 years. The highest prevalence shifted from the age group of 60–69 years in 1999 to 70–79 years in 2020 [13]. The total number of

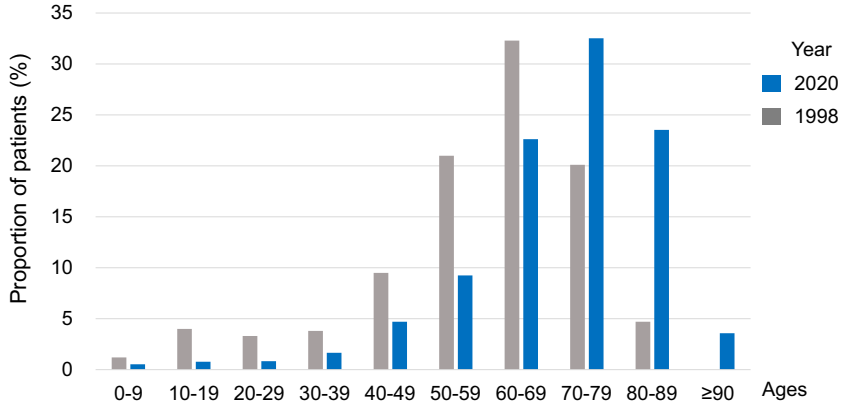


**Fig. 2.** Age distribution of patients with hypertrophic cardiomyopathy in Japan.
Year 2020: this study; 1999: Miura K et al. [13].

**Table 2**
Age distribution of patients with oHCM and nHCM in the whole period (from 2016 to 2020).

| | oHCM | | | | | | nHCM | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Total | | Male | | Female | | Total | |
| Mean age ± SD, years | 67.72 ± 13.40 | | 75.14 ± 11.92 | | 72.43 ± 12.98 | | 67.90 ± 14.71 | | 72.94 ± 14.71 | | 69.80 ± 14.91 | |
| Age group, years | n | % | n | % | n | % | n | % | n | % | n | % |
| 0–9 | 2 | 0.14 | 7 | 0.28 | 9 | 0.23 | 66 | 0.50 | 57 | 0.72 | 123 | 0.59 |
| 10–19 | 6 | 0.42 | 8 | 0.32 | 14 | 0.36 | 124 | 0.95 | 55 | 0.69 | 179 | 0.85 |
| 20–29 | 8 | 0.56 | 9 | 0.36 | 17 | 0.43 | 131 | 1.00 | 58 | 0.73 | 189 | 0.90 |
| 30–39 | 27 | 1.88 | 8 | 0.32 | 35 | 0.89 | 273 | 2.09 | 104 | 1.31 | 377 | 1.79 |
| 40–49 | 105 | 7.33 | 45 | 1.81 | 150 | 3.83 | 783 | 5.98 | 238 | 3.00 | 1021 | 4.86 |
| 50–59 | 170 | 11.86 | 118 | 4.76 | 288 | 7.36 | 1481 | 11.31 | 537 | 6.78 | 2018 | 9.60 |
| 60–69 | 424 | 29.59 | 446 | 17.98 | 870 | 22.23 | 3378 | 25.81 | 1391 | 17.56 | 4769 | 22.70 |
| 70–79 | 423 | 29.52 | 873 | 35.20 | 1296 | 33.12 | 4189 | 32.00 | 2622 | 33.10 | 6811 | 32.42 |
| 80–89 | 243 | 16.96 | 801 | 32.30 | 1044 | 26.68 | 2437 | 18.62 | 2385 | 30.11 | 4822 | 22.95 |
| ≥90 | 25 | 1.74 | 165 | 6.65 | 190 | 4.86 | 227 | 1.73 | 474 | 5.98 | 701 | 3.34 |
| Total | 1433 | 100.00 | 2480 | 100.00 | 3913 | 100.00 | 13,089 | 100.00 | 7921 | 100.00 | 21,010 | 100.00 |

nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy; SD, standard deviation.

patients with oHCM and nHCM in Japanese DPC hospitals in 2020 was estimated to be 8500 and 43,500, respectively, suggesting a >2-fold increase since 1999. Similarly, the absolute number of people in Japan aged ≥70 years increased approximately 2-fold between 2000 and 2020 [17]. Thus, the aging population may contribute to the increased incidence of HCM-related symptoms, providing more opportunity for diagnosis of HCM.

### *Multiple comorbidities in HCM*

The strong association of age with multiple comorbidities is well recognized, but our findings are new or less well described for HCM. The data showed that most patients with HCM had multiple comorbidities. In particular, the proportions of patients with hypertension (66.9–72.6 %) and diabetes mellitus (57.4–58.5 %) dramatically increased from 1999 (31 % and 9.1 %, respectively) [18]. In addition, 37.7–45.0 % of patients had undergone hospitalization. It is considered that patients with multiple comorbidities have poorer functional status, quality of life, and health outcomes than those without multiple comorbidities [19]. Unfortunately, current HCM guidelines do not well account for multiple comorbidities or help clinicians to prioritize recommendations [1,2,4]. As a result, patients with multiple comorbidities might be prescribed several drugs, each of which is recommended by a disease-specific guideline, making the overall drug burden difficult for patients to manage and potentially harmful [20]. The data also showed that >30 % of patients with oHCM received an ACE inhibitor/ARB, although the guidelines do not recommend these drugs as they may worsen LVOT obstruction by their vasodilator action [4]. Patients with HCM with multiple comorbidities may also have more difficulties with fragmentation of care and medical error because specialist care is usually focused on treatment of one disease [20].

**Table 3**
Patient characteristics.

| | oHCM N = 2450 | | nHCM N = 13,362 | |
|---|---|---|---|---|
| Comorbidities | n | % | n | % |
| Arrhythmia | 737 | 30.1 | 3688 | 27.6 |
| Atrial fibrillation or flutter | 828 | 33.8 | 4306 | 32.2 |
| Chronic kidney disease | 66 | 2.7 | 312 | 2.3 |
| Diabetes mellitus | 1406 | 57.4 | 7810 | 58.5 |
| Dyslipidemia | 1172 | 47.8 | 5716 | 42.8 |
| Hypertension | 1779 | 72.6 | 8941 | 66.9 |
| Malignant tumors | 880 | 35.9 | 5409 | 40.5 |
| Stroke | 406 | 16.6 | 2196 | 16.4 |
| ≥1 inpatient visit | 1103 | 45.0 | 5039 | 37.7 |

nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy.
Arrhythmia: except atrial fibrillation/flutter.

### *Prevalence of AF in HCM*

AF is an important factor responsible for a major impact on clinical outcomes in HCM, such as embolic stroke [8–10]. Indeed, we found that 16.4–16.6 % of patients with HCM had a history of stroke. The data also revealed that 32.2–33.8 % of patients had AF, similar to that in a previous report from the Kochi Prefecture in Japan [10]. However, the prevalence of AF in HCM populations reported from other countries was approximately 20 % [8,9]. The relatively high prevalence of AF is presumably due to current and previous [10] Japanese studies predominantly comprising aged patients. An additional major finding of the current study is that substantial numbers of younger patients with HCM, aged 20–59 years, had AF and a history of stroke, while in the general population, AF is more commonly reported in older people (e.g. mean age was 70.2 years in a study using pooled data from major Japanese AF registries) [21]. In HCM, structural abnormalities involving hypertrophies may play an important role in AF pathogenesis, as impaired diastolic function leads to left atrial pressure overload and enlargement, with subsequent atrial myopathy. Another important structural factor involved in AF development might be advanced myocardial fibrosis. These factors may contribute to the onset of AF in younger patients with HCM. It is recommended that all patients with AF receive lifelong treatment with an oral anticoagulant [1,2,4]. In this study, 25–26 % of patients with HCM received DOACs or warfarin, accounting for >70 % of patients with AF.

### *Prevalence of other arrythmia in HCM*

We also found that approximately 30 % of patients had other arrythmias. Importantly, the prevalence of these was greater in younger than in elderly patients, being more prominent in those with oHCM aged 20–29 years, with a prevalence of approximately 60 %. To our knowledge, this is the first study showed that other arrhythmias are more common in young patients and then decrease with age. Some studies have reported an association between malignant arrythmia, in particular non-sustained ventricular tachycardia, and the risk of sudden cardiac death (SCD) in patients with HCM [1,2]. In addition, HCM is a leading cause of SCD in young adults [1,2]. Our study obtained data from >200 young adult patients (aged 20–29 years) with HCM consistent with these findings and extends our knowledge of patient characteristics from earlier studies in Japan.

We observed that 6.3–7.0 % of patients with HCM received a potassium channel blocker (amiodarone), a class III antiarrhythmic agent. An observational study demonstrated that amiodarone therapy was

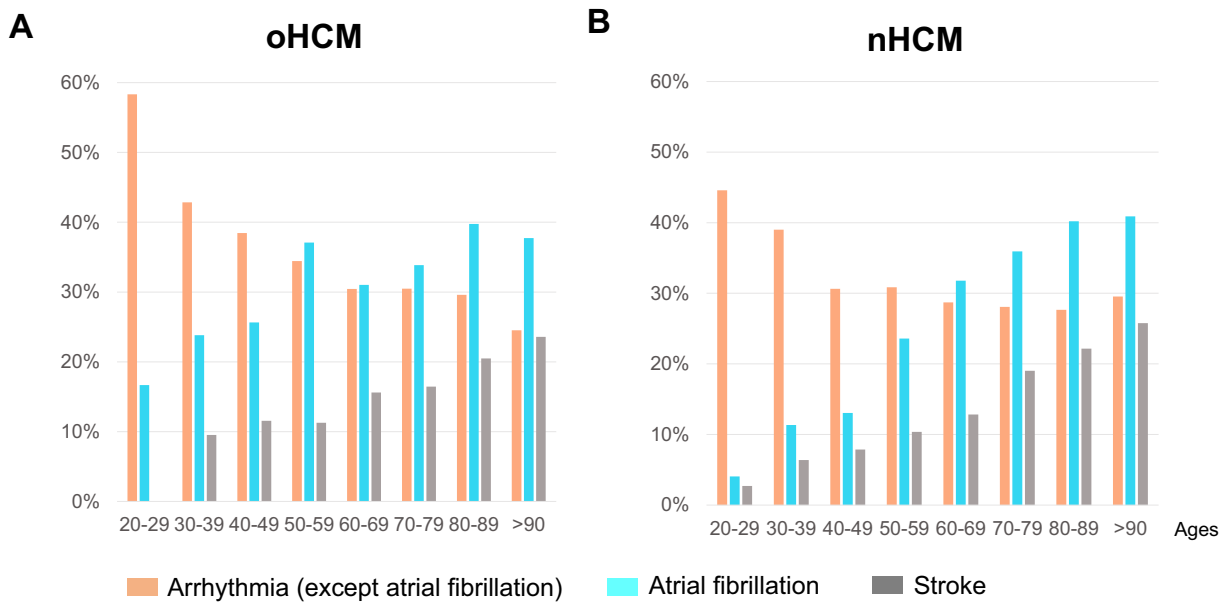


**Fig. 3.** Age distribution of patients with hypertrophic cardiomyopathy who had arrhythmia, atrial fibrillation, and stroke in Japan. (A) oHCM and (B) nHCM. nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy.

associated with maintenance of sinus rhythm [22]; however, the treatment appeared to have limited efficacy in the prevention of SCD [23].

*Medications in HCM*

According to current guidelines in Japan [4], symptomatic patients should be treated initially with a β-blocker. Indeed, for patients with oHCM and nHCM, β-blockers (64.0 % and 42.1 %, respectively) were the most frequently prescribed treatment, followed by sodium channel blockers (oHCM, 29.5 %; nHCM, 5.7 %) and non-DHP calcium channel blockers (oHCM, 25.4 %; nHCM, 25.6 %). Overall, these medications appear to be used more frequently in Japan than in other countries [24]. For oHCM, septal reduction therapy such as PTSMA should be considered for patients with drug-refractory symptoms. Our data showed that only 0.7 % of patients with oHCM underwent PTSMA, suggesting barriers in Japan for such invasive treatment in HCM. In addition, 0.08–0.25 % had MVR, however, the cause of clinical state could not be elucidated.

**Table 4**
Treatment patterns.

| | oHCM N = 2450 | | nHCM N = 13,362 | |
|---|---|---|---|---|
| | n | % | n | % |
| Medication | | | | |
| β-Blocker | 1568 | 64.0 | 5625 | 42.1 |
| Non-DHP Ca channel blocker | 622 | 25.4 | 3420 | 25.6 |
| Na channel blocker | 722 | 29.5 | 764 | 5.7 |
| K channel blocker | 154 | 6.3 | 931 | 7.0 |
| DOAC | 355 | 14.5 | 2025 | 15.2 |
| Warfarin | 270 | 11.0 | 1528 | 11.4 |
| ACEi or ARB | 762 | 31.1 | 4548 | 34.0 |
| DHP Ca channel blocker | 722 | 29.5 | 3882 | 29.1 |
| Diuretic | 608 | 24.8 | 3264 | 24.4 |
| MRA | 298 | 12.2 | 1625 | 12.2 |
| Procedure | | | | |
| PTSMA | 18 | 0.7 | 0 | 0 |
| ICD | 9 | 0.4 | 19 | 0.1 |
| CRT | 1 | 0.04 | 3 | 0.02 |
| MVR | 2 | 0.08 | 34 | 0.25 |

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; Ca, calcium; CRT, cardiac resynchronization therapy; DHP, dihydropyridine; DOAC, direct oral anticoagulant; K, potassium; ICD, implantable cardiac defibrillator; MRA, mineralocorticoid receptor antagonist; MVR, mitral valve replacement; Na, sodium; nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy; PTSMA, percutaneous transluminal septal myocardial ablation.

*Prevalence of oHCM and nHCM*

The data also demonstrated that the ratio of cases of oHCM to nHCM was approximately 1:5.2. While the prevalence of oHCM is consistent with earlier findings in Japan [10], this is markedly lower than in other countries [25–28]. The most likely explanation for the greater nHCM prevalence may be that, in Japan, routine health checkups, including electrocardiograms (ECGs), are required for all workers after the age of 40 years, even in the absence of recognized medical problems. Likewise, for students, an ECG test is mandatory at the time of admission to school, i.e. primary/middle/high school and university. If the ECG findings are abnormal, the individual is referred for further cardiovascular evaluation, including echocardiography, that may result in a diagnosis of HCM before the presentation of HCM-related symptoms. Indeed, a previous study in Japan reported that >50 % of patients with HCM were visiting hospitals to receive medical treatment despite having New York Heart Association functional class I heart failure (i.e. asymptomatic individuals) [10]. Another possible reason is anatomical racial differences—a higher percentage of patients had apical HCM compared with that reported in Western countries [10,29]. In addition, the use of provocation echocardiography with a low frequency rate if echocardiography at rest is inconclusive might partly affect the ratio, although alternative imaging tests, including cardiac magnetic resonance imaging, computed tomography, and catheter test, are often used for diagnosis instead of provocation echocardiography in Japan [30,31].

*Difference in prevalence of oHCM and nHCM by sex*

We also found that the number of female patients was higher than that of male patients for oHCM and lower than that of male patients for nHCM. As the prevalence of nHCM was greater than that of oHCM, the total number of women with HCM was lower than that of men with HCM, similar to an earlier observation in Japan [32].

HCM is often caused by mutations in the genes encoding sarcomere contractile proteins and is genetically transmitted in a Mendelian autosomal dominant pattern of inheritance. Thus, both sexes would be expected to be equally affected. Although routine health checkups are required for many workers in Japan, as described above, the working population of women is relatively small, which decreases the probability of a health checkup, thereby leading to fewer diagnoses of pre-symptomatic nHCM. Compared with patients with nHCM, more patients with oHCM are considered to be symptomatic [1,2,4]. Women who do not undergo routine health checkups might ultimately visit a hospital after the onset of symptoms. Furthermore, in the general population, there are more elderly women (>70 years) than men, similar to the age distribution of patients with HCM in this study [17]. In addition, it has previously been reported that women were more frequently diagnosed as having HCM at ≥65 years of age, although the mean age at diagnosis was similar between the two sexes. Several studies have shown that women with HCM had delayed onset of symptoms and clinical identification or diagnosis compared with men [32–34]. Thus, some endocrine association with female sex may also contribute to the delay in the development of overt HCM.

*Clinical implications*

This study provides information on the current situation of HCM in Japan, which is considered to be useful for better management of HCM patients. The aging population in Japan may lead to a growing proportion of older people with HCM, many of whom would have multiple comorbidities. Of which, AF is regarded as having a major impact on clinical outcomes, including heart failure and embolic stroke. AF may not be just comorbidity or a marker of disease stage but an important trigger of adverse events. Therefore, earlier diagnosis of AF, initiation of anticoagulant medication, and improved patient education are particularly important for younger patients with HCM, as AF is rarely found in the general population aged <60 years.

*Study limitations*

There are several limitations to be acknowledged in the present study. First, the inherent limitation of MDV, DPC hospital-based administrative claim database, did not allow for assessing clinical data such as echocardiography, electrocardiogram, or cardiac magnetic resonance imaging. Thus, information on the severity of the LVOT obstruction could not be obtained. Second, the diagnosis of HCM and other comorbidities were based on ICD-10 codes. Thus, the small possibility of misdiagnosis cannot be completely excluded. Patients with cardiac hypertrophy caused by hypertension, hypertensive heart disease with sigmoid septum, cardiac amyloidosis, and Fabry disease might be included in this cohort. The diagnosis of HCM by ICD-10 codes was verified by previous study [16], resulting in high reliability. Third, non-pharmacological therapeutic procedures for HCM include not only PTSMA and ICD implantation but include myectomy and radiofrequency catheter ablation (RCFA). However, myectomy and RCFA could not be defined in MDV database. Fourth, only patients with medical history available for the previous 12 months were included in the clinical characteristics analysis. Thus, the study population might include patients with more comorbidities and procedures. Fifth, the study population may not be similar to that in the previous study conducted in 1999, because of the difference in the survey methods (questionnaire vs. hospital-based administrative claim database).

## Conclusions

This nationwide claims-based database provides important insights on the current epidemiological and clinical characteristics of HCM in Japan. The number of elderly patients with HCM continues to increase, and these patients often have multiple comorbidities. AF was present in >30 % of patients with HCM. Substantial numbers of patients with HCM, even between the ages of 20 and 59 years had AF and a history of stroke. The prevalence of nHCM was greater than that of oHCM in Japan, with differences in prevalence by sex.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jjcc.2022.09.015.

## Declaration of competing interest

Naoki Terasaka, Dionysis Spanopoulos, and Hidetaka Miyagoshi are employees of Bristol Myers Squibb. Toru Kubo and Hiroaki Kitaoka have no conflict of interest.

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