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ORIGINAL ARTICLE
Heart Failure

Clinical Characteristics and Contemporary Management of Patients With Cardiomyopathies in Japan

— Report From a National Registry of Clinical Personal Records —

Nobuyuki Enzan, MD; Shouji Matsushima, MD, PhD; Tomomi Ide, MD, PhD; Hidetaka Kaku, MD; Takeshi Tohyama, MD, PhD; Kouta Funakoshi, MD; Taiki Higo, MD; Hiroyuki Tsutsui, MD, PhD for the Research Group of Idiopathic Cardiomyopathy

Background: The clinical features of patients with cardiomyopathy, including dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), or restrictive cardiomyopathy (RCM), have not been recently elucidated in Japan.

Methods and Results: We collected individual patient data regarding demographics, echocardiogram, and treatment in DCM from 2003 to 2014 and in HCM and RCM from 2009 to 2014 from the national registry of clinical personal records organized by the Japanese Ministry of Health, Labour and Welfare. In all, 44,136 patients were included in this registry: 40,537 with DCM, 3,553 with HCM, and 46 with RCM. The median age at diagnosis was older for DCM and HCM than RCM (54 and 55 vs. 42 years, respectively). Male patients accounted for 74.6%, 58.7%, and 60.9% of the DCM, HCM, and RCM groups, respectively. NYHA functional Class III–IV was found in 26.9%, 11.3%, and 58.1% of patients in the DCM, HCM, and RCM groups, respectively. In the DCM group, the rates of β-blocker and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker prescription were 69% and 76%, respectively. In regional subgroup analysis, the median age at diagnosis of DCM and HCM was younger in the Kanto region. A family history of HCM was less frequent in the Hokkaido/Tohoku region.

Conclusions: The national registry of clinical personal records of cardiomyopathy could provide important information regarding the demographics, clinical characteristics, and management of cardiomyopathy throughout Japan.

Key Words: Clinical characteristics; Dilated cardiomyopathy; Hypertrophic cardiomyopathy; Registry; Restrictive cardiomyopathy

Cardiomyopathies are diverse diseases characterized by structural and functional abnormalities of the myocardium in the absence of coronary artery disease, hypertension, valvular disease, congenital heart disease, or other systemic diseases sufficient to explain the observed myocardial disorder. Dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), and restrictive cardiomyopathy (RCM) are representative cardiomyopathies that are associated with critical conditions such as sudden death,[1] lethal arrhythmia,[2] heart failure (HF),[3] and stroke.[4]

In 2002, a nationwide survey of cardiomyopathies demonstrated epidemiologic and clinical characteristics of cardiomyopathies in Japan.[5,6] In that survey, the crude prevalence per 100,000 population was estimated to be 14.0 for DCM, 17.3 for HCM, and 0.2 for RCM.[5] The prevalence of DCM and HCM was higher in males than females, and the 1-year mortality rates were 5.6% and 2.8% in DCM and HCM patients, respectively.[6] Later, several groups reported the features and prognosis of cardiomyopathies in Japan. With the implementation of evidence-based medication such as β-blockers, long-term prognosis of DCM patients has improved in past decades.[7,8] Characteristics of the HCM subtype and the significance of biomarkers, such as troponin, in HCM have been reported.[9–12] Unlike DCM, the prognosis of HCM patients has not improved.[13,14] In contrast, very little information is available in Japan regarding the clinical profiles and natural history of RCM because it is less common and an obscure disease.[15] Importantly, cardiomyopathy is a frequent etiology

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Department of Cardiovascular Medicine (N.E., S.M., T.H., H.T.), Department of Experimental and Clinical Cardiovascular Medicine (T.I.), Faculty of Medical Sciences, Kyushu University, Fukuoka; Department of Cardiology, Japan Community Healthcare Organization, Kyushu Hospital, Kitakyushu (H.K.); and Center for Clinical and Translational Research, Kyushu University Hospital, Fukuoka (T.T., K.F.), Japan

T.I. is a member of *Circulation Reports*' Editorial Team.

Mailing address: Shouji Matsushima, MD, PhD, Department of Cardiovascular Medicine, Faculty of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. E-mail: shouji-m@cardiol.med.kyushu-u.ac.jp

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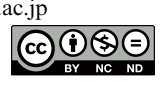

of HF in Japan compared with Europe and the US.[16,17] Despite recent advances in therapy, DCM remains the leading cause of heart transplantation in Japan.[18] HCM is a major risk factor for sudden cardiac death and death due to HF.[2,19]

Recently, the EURObservational Research Programme (EORP) Cardiomyopathy Registry was established by the European Society of Cardiology (ESC) Working Group on Myocardial and Pericardial Disease to provide a summary of contemporary features and the management of patients with cardiomyopathy across a large range of centers in Europe.[20,21] This registry is useful for clinical service provision and therapy. However, in Japan, most reports concerning cardiomyopathy are based on regional and small cohort studies after 2002. Furthermore, the distribution of cardiomyopathy patients in Japan has not been reported. For better management, information regarding the demographics, clinical characteristics, and treatment of cardiomyopathy patients throughout Japan is needed. These findings become basic data for comparisons with future studies and medical administration to improve pharmacological and non-pharmacological therapies for the treatment of cardiomyopathy.

Clinical personal records are a nationwide administrative database of public expenditure for refractory disease maintained by the Japanese Ministry of Health, Labour and Welfare to register and certify intractable diseases, including cardiomyopathy, throughout Japan; this database started collecting records for DCM in 2003 and for HCM and RCM in 2009. The clinical personal records database is useful for investigating the clinical features of and routine practice for cardiomyopathy in Japan. The aim of this study was to describe the demographics, clinical characteristics, and management of adult DCM, HCM, and RCM in Japan by using the nationwide registry of clinical personal records.

Methods

Clinical Personal Records

As noted above, the clinical personal records is a nationwide administrative database of public expenditure for refractory diseases, including cardiomyopathies, throughout Japan. The records prospectively and annually collect demographic data (age, sex, duration of HF, and New York Heart Association [NYHA] functional class), vital signs, electrocardiographic, echocardiographic, and laboratory data, and medication use. The database does not contain information about clinical outcomes, such as hospitalization and death. All clinical personal records are registered after being reviewed by certified cardiologists. In the present study, we analyzed the baseline data of each registered patient.

Diagnostic Criteria

DCM was diagnosed on the basis of a dilated left ventricle (LV) and reduced left ventricular ejection fraction (LVEF) in the absence of any specific cardiac or systemic diseases, such as hypertensive heart disease, valvular heart disease, congenital heart disease, coronary artery disease, alcoholic cardiomyopathy, cardiomyopathy caused by toxins or medications, amyloidosis, sarcoidosis, connective tissue disease, dystrophy, or metabolic disease, such as Pompe disease or Fabry disease.

HCM was diagnosed on the basis of asymmetric or diffuse LV hypertrophy with reduced diastolic function in the absence of any specific cardiac or systemic diseases as listed above.

RCM was diagnosed on the basis of a lack of LV dilatation, a lack of LV hypertrophy, normal LV systolic function, and LV diastolic dysfunction.

Study Population

The present study used clinical personal records of DCM from 2003 to 2014 and HCM and RCM from 2009 to 2014. Patients aged >18 years were included in the study.

Characteristics and Management of Cardiomyopathies

The characteristics and management of each cardiomyopathy in this registry were determined. In addition, regional differences (Hokkaido/Tohoku, Kanto, Chubu, Kinki, Chugoku/Shikoku, and Kyushu regions) in DCM, HCM, and RCM were investigated. Data from the clinical personal records registry were compared with those from the EORP Cardiomyopathy Registry of the ESC.[20]

Statistical Analysis

Patient characteristics and management were compared between cardiomyopathy types or regions using χ^2 tests for categorical variables and analysis of variance (ANOVA) for continuous variables. Data are presented as the mean±SD or as the median with interquartile range (IQR). All tests were 2-tailed and a $P<0.05$ was considered significant. Statistical analyses were performed using SAS®9.4 (SAS Institute, Cary, NC, USA).

Ethics Statement

This study was conducted according to the principles of the Declaration of Helsinki. The original study protocol was approved by the Institutional Review Board at Kyushu University (No. 29-48). Because this study analyzed a nationwide administrative database, the "opt-out" principle was applied: patients could choose to have their information excluded. The authors had full access to the data and take full responsibility for their integrity.

Results

Age and Sex

There were number of 40,537, 3,553, and 46 patients with DCM, HCM, and RCM, respectively (**Table 1**). The median (IQR) age at enrollment was younger for RCM than for DCM and HCM (54 [41–68] vs. 59 [49–68] and 64 [53–73] years, respectively; $P<0.001$). The median (IQR) age at diagnosis was also younger for RCM than DCM and HCM (42 [28–63] vs. 54 [44–63] and 55 [42–64] years, respectively; $P=0.044$; **Table 1**). DCM and HCM were diagnosed at the same frequency among all age quartiles. RCM was diagnosed most frequently in the younger age quartile (**Figure**). There was a male predominance for all cardiomyopathy subtypes.

Symptoms, Family History, and Laboratory Data

NYHA functional class III–IV was more frequent in RCM (58.1%) than in DCM or HCM (26.9% and 11.3%, respectively; $P<0.001$; **Table 1**). The frequency of a family history of any cardiomyopathies was 20.0% in HCM, 17.1% in RCM, and 3.5% in DCM ($P<0.001$). A family history of sudden cardiac death was most frequent in HCM (6.5%), followed by DCM (2.5%; $P<0.001$; **Table 1**). B-type natriuretic peptide (BNP) concentrations were higher in RCM,

Table 1. Patient Characteristics

Variables	DCM (n=40,537)	HCM (n=3,553)	RCM (n=46)	P value
Demographics				
Age at enrollment (years)	59 [49–68]	64 [53–73]	54 [41–68]	<0.001
Age at diagnosis (years)	54 [44–63]	55 [42–64]	42 [28–63]	0.044
Male sex	30,230 (74.6)	2,087 (58.7)	28 (60.9)	<0.001
NYHA functional class				
I	9,084 (23.8)	873 (27.1)	2 (4.7)	<0.001
II	18,845 (49.3)	1,986 (61.6)	16 (37.2)	<0.001
III	7,649 (20.0)	319 (9.9)	17 (39.5)	<0.001
IV	2,628 (6.9)	45 (1.4)	8 (18.6)	<0.001
Family history				
Cardiomyopathy	568 (3.5)	709 (20.0)	6 (17.1)	<0.001
Sudden cardiac death	405 (2.5)	231 (6.5)	0 (0.0)	<0.001
Vital signs				
SBP (mmHg)	120.6±20.7	121.3±20.0	104.5±16.1	<0.001
DBP (mmHg)	73.8±15.2	70.7±13.9	62.7±11.3	<0.001
Heart rate (beats/min)	78.4±19.4	68.4±25.0	74.4±13.7	<0.001
Laboratory data				
Hemoglobin (g/dL)	13.9±1.9	13.7±1.8	12.7±2.3	<0.001
Albumin (g/dL)	4.1±0.5	4.1±0.5	4.0±0.5	0.010
AST (U/L)	24.0 [19.0–32.0]	25.0 [20.0–31.0]	27.0 [22.0–34.0]	<0.001
ALT (U/L)	23.0 [16.0–36.0]	21.0 [15.0–31.0]	21.0 [14.0–25.0]	<0.001
BUN (mg/dL)	19.8±15.0	20.0±17.6	25.5±15.1	0.040
Creatinine (mg/dL)	0.90 [0.74–1.09]	0.87 [0.71–1.05]	1.00 [0.83–1.30]	<0.001
eGFR (mL/min/1.73 m^2)	69.1±95.4	64.0±21.2	58.7±25.2	0.007
Uric acid (mg/dL)	6.7±2.0	6.1±1.7	7.8±2.3	<0.001
Sodium (mEq/L)	140.3±3.2	140.6±3.0	137.1±5.5	<0.001
BNP (pg/mL)	143.0 [39.1–486.0]	241.8 [106.0–511.0]	416.0 [184.8–826.0]	<0.001
Electrocardiographic findings				
Atrial fibrillation	9,218 (22.7)	971 (27.3)	23 (50.0)	<0.001
Pacing	1,012 (2.5)	180 (5.1)	3 (6.5)	<0.001
Biventricular pacing	173 (0.4)	26 (0.7)	0 (0.0)	<0.001
Echocardiographic findings				
LVEF (%)	38.0±15.0	62.5±15.6	55.2±15.4	<0.001
LVDd (mm)	60.2±9.6	46.1±8.8	47.4±9.4	<0.001
LVDs (mm)	49.0±11.6	29.8±9.8	33.8±10.3	<0.001
IVS (mm)	9.3±2.2	16.0±5.3	10.4±5.0	<0.001
LVPW (mm)	9.5±2.1	11.7±3.3	10.3±3.2	<0.001
MR Grade III–IV	4,088 (13.9)	225 (8.9)	0 (0.0)	<0.001
Medication				
β-blockers	28,069 (69.2)	1,989 (56.8)	27 (64.3)	<0.001
ACEi/ARB	30,712 (75.8)	1,761 (49.6)	27 (58.7)	<0.001
MRA	12,734 (31.4)	554 (15.6)	10 (21.7)	<0.001
Loop diuretics	27,383 (70.3)	956 (26.9)	13 (28.3)	<0.001
Thiazides	899 (2.3)	150 (4.2)	1 (2.2)	<0.001
Digitalis	11,728 (28.9)	139 (3.9)	8 (17.4)	<0.001
Amiodarone	4,217 (10.5)	431 (12.2)	5 (10.9)	<0.001
Oral inotropes	1,950 (4.8)	42 (4.0)	6 (13.0)	<0.001

Unless specified otherwise, data are given as n (%), the mean±SD, or as the median [interquartile range]. ACEi, angiotensin-converting enzyme inhibitors; ALT, alanine aminotransferase; ARB, angiotensin receptor blockers; AST, aspartate aminotransferase; BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; DBP, diastolic blood pressure; DCM, dilated cardiomyopathy; eGFR, estimated glomerular filtration rate; HCM, hypertrophic cardiomyopathy; IVS, interventricular septal thickness; LVDd, left ventricular diastolic diameter; LVDs, left ventricular systolic diameter; LVEF, left ventricular ejection fraction; LVPW, left ventricular posterior wall thickness; MR, mitral regurgitation; MRA, mineralocorticoid receptor antagonists; NYHA, New York Heart Association; RCM, restrictive cardiomyopathy; SBP, systolic blood pressure.

followed by HCM and DCM (416, 242, and 143 pg/mL, respectively; P<0.001; **Table 1**).

Electrocardiography and Echocardiography

Electrocardiographic and echocardiographic findings are summarized in **Table 1**. Atrial fibrillation was most frequent in RCM (50.0%; P<0.001). The mean LVEF of DCM, HCM, and RCM was 38.0%, 62.5%, and 55.2%, respectively. LV diastolic diameter (LVDd) and LV systolic diameter were larger in DCM, whereas interventricular septal thickness and LV posterior wall thickness were greater in HCM. Mitral regurgitation (MR) Grade III–IV was more frequent in DCM (13.9%; P<0.001).

Medications

In each type of cardiomyopathy, most patients were receiving β-blockers. Angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), and mineralocorticoid receptor antagonists (MRA) were used in all 3 types of cardiomyopathies. The highest use of all 4 classes of drug was in patients with DCM (**Table 1**).

Regional Differences

The clinical characteristics and management of DCM in each region are summarized in **Table 2**. The median age at enrollment and diagnosis for DCM was youngest (57 and 52 years, respectively; P<0.001) and a family history of DCM was lowest (2.9%; P=0.046) in the Kanto region. NYHA functional class III–IV was less frequent in the Hokkaido/Tohoku region (21.3%; P<0.001). LVEF was lowest (36.2%; P<0.001) and MR Grade III–IV was more frequent (13.9%; P<0.001) in the Kanto region.

The clinical characteristics and management of HCM in each region are summarized in **Table 3**. The median age at enrollment and diagnosis for HCM was youngest in Kanto region (62 and 52 years, respectively) and oldest in the Hokkaido/Tohoku region (67 and 56 years, respectively; P<0.001). NYHA functional class III–IV and syncope were less frequent in the Hokkaido/Tohoku region (6.6% and 13.4%, respectively; P<0.001). A family history of HCM and sudden cardiac death were also less frequent in the Hokkaido/Tohoku region (13.7% and 3.4%, respectively; P<0.001). LVEF and maximum wall thickness were comparable among regions. However, LV outflow gradient >50 mmHg was less frequent in the Hokkaido/Tohoku region (13.1%; P<0.001).

The clinical characteristics and management of RCM in each region are summarized in **Table 4**. The median age at enrollment and diagnosis for RCM tended to be higher in the Kyushu region (71 and 65 years, respectively), but the difference was not statistically significant. Atrial fibrillation was most frequent in the Hokkaido/Tohoku region (100%; P=0.036). Pericardial effusion was most frequently observed in the Kinki region (62.5%; P=0.020).

Comparison With the European Registry

The clinical characteristics and management of DCM, HCM, and RCM in the Japanese clinical personal records database and the EORP Cardiomyopathy Registry are shown in the **Supplementary Table**. Compared with European countries, the median age at enrollment (59 vs. 55 years) and diagnosis (54 vs. 49 years) for patients with DCM was higher in Japan. A family history of sudden cardiac death (2.5% vs. 11.9%) and NYHA functional class III–IV (26.9% vs. 38.4%) in patients with DCM were lower in Japan. LVDd was smaller (60.2±9.6 vs. 64.2±9.8 mm) and LVEF was higher (38.0±15.0 vs. 32.5±11.8%) in Japanese DCM patients. The prescription of β-blockers (69.2% vs. 89.7%), ACEi (38.7% vs. 72.8%), MRA (31.4% vs. 63.1%), and antiarrhythmic drugs (19.3% vs. 28.7%) was lower, whereas the prescription of ARB (38.7% vs. 16.7%) was higher, in Japan. Pacemakers were more frequently implanted in Europe (2.5% vs. 14.3%).

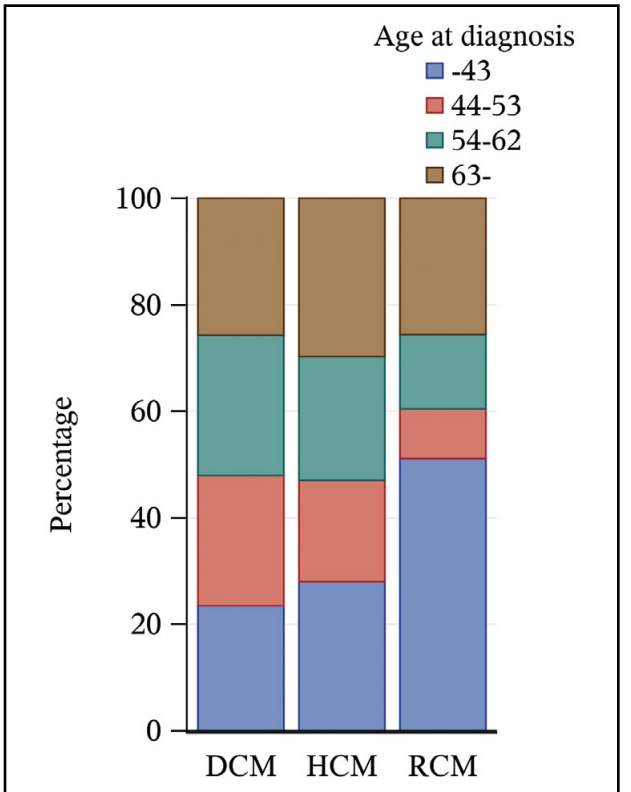

Figure. Distribution of age at diagnosis for each cardiomyopathy subtype according to age quartiles (years). DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy.

The median age at enrollment (64 vs. 55 years) and diagnosis (55 vs. 47 years) in patients with HCM was higher in Japan than in Europe. A family history of sudden cardiac death (6.5% vs. 21.1%) and NYHA functional class III–IV (11.3 vs. 17.4%) in HCM were lower in Japan. In the ESC EORP Cardiomyopathy Registry, the frequency of "resuscitated" ventricular fibrillation/cardiac arrest was 2.8%. Conversely, in the clinical personal records, the frequency of ventricular tachycardia/ventricular fibrillation/cardiac arrest that was not necessarily resuscitated was 23.0%. Echocardiographic findings were similar between Japan and Europe. In HCM patients, the use of β-blockers (56.8% vs. 74.4%) and ACEi (14.9% vs. 19.7%) was lower and the use of ARB (36.8% vs. 15.2%) and antiarrhythmic drugs (41.4% vs. 15.2%) was higher in Japan.

As in Europe, the number of patients with RCM in the clinical personal records database was small in Japan (46 patients registered over 6 years in Japan; 66 patients registered over 5 years in the ESC registry). The median age at enrollment (54 vs. 60 years) and diagnosis (42 vs. 57 years) of RCM was younger in Japan. NYHA functional class IV

Table 2. Characteristics of DCM Patients in Different Regions in Japan

Variables	Hokkaido/ Tohoku (n=5,478)	Kanto (n=10,617)	Chubu (n=6,126)	Kinki (n=9,011)	Chugoku/ Shikoku (n=4,609)	Kyushu (n=4,696)	P value
Demographics							
Age at enrollment (years)	59 [49–68]	57 [46–66]	60 [49–68]	59 [49–68]	59 [50–68]	60 [50–69]	<0.001
Age at diagnosis (years)	54 [45–63]	52 [42–61]	55 [45–63]	55 [45–63]	55 [46–64]	55 [45–64]	<0.001
Male sex	3,991 (72.9)	8,158 (76.8)	4,580 (74.8)	6,771 (75.1)	3,386 (73.5)	3,344 (71.2)	<0.001
NYHA functional class							
I	1,413 (27.5)	2,328 (23.7)	1,515 (25.8)	2,069 (24.2)	975 (22.4)	784 (17.5)	<0.001
II	2,627 (51.2)	4,710 (47.9)	2,909 (49.6)	4,184 (49.0)	2,050 (47.0)	2,365 (52.9)	<0.001
III	832 (16.2)	2,024 (20.6)	1,076 (18.3)	1,683 (19.7)	991 (22.7)	1,043 (23.3)	<0.001
IV	261 (5.1)	762 (7.8)	369 (6.3)	607 (7.1)	346 (7.9)	283 (6.3)	<0.001
Family history							
Dilated cardiomyopathy	88 (4.3)	137 (2.9)	84 (3.5)	139 (3.6)	71 (3.5)	49 (4.2)	0.046
Sudden cardiac death	51 (2.5)	101 (2.1)	75 (3.1)	85 (2.2)	52 (2.6)	41 (3.5)	0.025
Vital signs							
SBP (mmHg)	120.4±19.8	119.9±20.4	120.4±20.6	122.5±21.2	121.1±21.3	119.0±20.7	<0.001
DBP (mmHg)	73.9±14.9	74.4±15.6	73.3±15.0	74.5±15.5	74.2±15.6	71.8±14.1	<0.001
Heart rate (beats/min)	76.1±18.8	80.6±20.3	77.6±18.8	78.6±19.7	78.6±19.6	76.2±17.7	<0.001
Laboratory data							
Hemoglobin (g/dL)	13.9±2.0	14.1±1.9	13.9±1.9	13.9±1.9	13.8±1.9	13.8±1.9	<0.001
Albumin (g/dL)	4.1±0.5	4.1±0.5	4.1±0.5	4.1±0.5	4.1±0.5	4.1±0.5	<0.001
AST (U/L)	25.0 [19.0–33.0]	24.0 [19.0–33.0]	24.0 [19.0–32.0]	24.0 [19.0–32.0]	24.0 [19.0–33.0]	23.0 [19.0–31.0]	<0.001
ALT (U/L)	23.0 [16.0–37.0]	23.0 [16.0–37.0]	22.0 [15.0–35.0]	22.0 [15.0–35.0]	23.0 [16.0–36.0]	21.0 [15.0–33.0]	<0.001
BUN (mg/dL)	19.5±14.8	19.9±16.0	19.5±13.7	20.1±15.7	19.6±13.9	20.1±14.2	0.1
Creatinine (mg/dL)	0.88 [0.72–1.04]	0.90 [0.75–1.08]	0.90 [0.73–1.09]	0.90 [0.75–1.10]	0.89 [0.72–1.06]	0.90 [0.73–1.10]	<0.001
eGFR (mL/min/1.73 m^2)	71.2±138.2	71.8±122.8	67.7±37.9	68.3±97.7	68.1±34.4	65.5±37.6	0.001
Uric acid (mg/dL)	6.6±2.0	6.8±2.0	6.7±2.0	6.8±2.0	6.7±2.0	6.7±1.9	<0.001
Sodium (mEq/L)	140.4±3.2	140.2±3.3	140.3±3.0	140.4±3.3	140.2±3.3	140.2±3.3	<0.001
BNP (pg/mL)	130.0 [38.3–405.8]	157.0 [41.4–531.0]	142.4 [38.8–466.0]	141.0 [39.4–497.0]	163.6 [41.9–530.0]	120.2 [33.9–420.0]	<0.001
Electrocardiographic findings							
Atrial fibrillation	1,398 (25.5)	2,272 (21.4)	1,503 (24.5)	2,006 (22.3)	986 (21.4)	1,053 (22.4)	<0.001
Pacing	55 (2.8)	228 (2.2)	131 (2.1)	207 (2.3)	128 (2.8)	163 (3.5)	<0.001
Biventricular pacing	25 (0.5)	43 (0.4)	24 (0.4)	33 (0.4)	25 (0.5)	23 (0.5)	0.68
Echocardiographic data							
LVEF (%)	40.5±15.9	36.2±14.8	38.6±15.1	37.7±14.9	37.3±14.5	39.4±14.5	<0.001
LVDd (mm)	59.0±10.0	61.4±9.7	60.2±9.6	59.9±9.1	60.0±9.1	59.3±9.7	<0.001
LVDs (mm)	47.5±11.9	50.7±11.8	49.0±11.6	48.4±11.3	48.9±11.1	47.8±11.5	<0.001
IVS (mm)	9.5±2.4	9.1±2.1	9.5±2.3	9.3±2.2	9.2±2.1	9.4±2.2	<0.001
LVPW (mm)	9.8±2.3	9.4±2.1	9.7±2.4	9.5±2.0	9.4±2.1	9.6±2.1	<0.001
MR Grade III–IV	468 (12.1)	1,019 (13.9)	591 (12.9)	1,047 (16.1)	522 (14.7)	441 (12.2)	<0.001
Medication							
β-blockers	3,742 (68.3)	7,257 (68.4)	4,343 (70.9)	6,566 (72.9)	2,966 (64.4)	3,195 (68.0)	<0.001
ACEi/ARB	3,947 (72.1)	7,963 (75.0)	4,820 (78.7)	6,929 (76.9)	3,369 (73.1)	3,684 (78.5)	<0.001
MRA	1,404 (25.6)	3,491 (32.9)	2,051 (33.5)	2,693 (29.9)	1,500 (32.6)	1,595 (34.0)	<0.001
Loop diuretics	3,639 (69.4)	7,324 (72.5)	4,434 (74.0)	5,814 (66.4)	2,957 (69.9)	3,215 (69.6)	<0.001
Thiazides	105 (2.0)	197 (2.0)	149 (2.5)	225 (2.6)	64 (1.5)	159 (3.4)	<0.001
Digitalis	1,690 (30.9)	2,904 (27.4)	1,927 (31.5)	2,505 (27.8)	1,275 (27.7)	1,427 (30.4)	<0.001
Amiodarone	560 (10.4)	1,441 (13.8)	638 (10.5)	770 (8.6)	328 (7.3)	480 (10.3)	<0.001
Oral inotropes	398 (7.3)	495 (4.7)	297 (4.9)	366 (4.1)	215 (4.7)	179 (3.8)	<0.001

Unless specified otherwise, data are given as n (%), the mean±SD, or as the median [interquartile range]. Abbreviations as in Table 1.

was more frequent in Japan (18.6% vs. 1.6%). Although LVDd and LVEF in RCM patients were similar between Japan and Europe, maximum LV wall thickness was greater in Europe (11.3±4.9 vs. 15.1±4.4 mm). The use of ACEi (28.3% vs. 22.7%) and ARB (32.6% vs. 10.6%) was greater and the use of diuretics (32.6% vs. 85.5%), MRA (21.7% vs. 45.5%), and antiarrhythmic drugs (13.0% vs. 18.2%) was lower in Japan.

Discussion

The clinical personal records is the largest national database of more than 40,000 patients with cardiomyopathies in Japan. This study provides information on important clinical features of patients with DCM, HCM, and RCM throughout Japan.

A previous Japanese nationwide survey on cardiomyopathies was reported in 2002.[5,6] Even though that study did report the age at enrollment and diagnosis of each cardiomyopathy, the peak age of DCM and HCM was in the those aged in their 50–60s. The present study found that the median age at enrollment in DCM and HCM was 59 and 64 years, respectively, which seems to be compatible with the findings of the previous study. In addition, the male predominance for all cardiomyopathy subtypes in the present study is similar to the previous findings.[6] The rate of a family history in DCM, HCM, and RCM was reported as 6.2%, 17.6%, and 28.6%, respectively, in the previous study.[5,6] In the present study, the frequency of a family history for each cardiomyopathy (3.5%, 20.0%, and 17.1%, respectively) was almost the same. Compared with the previous study,[5,6] NYHA functional class III–IV was less frequent in DCM patients in the present study (26.9% vs. 37.7%), whereas it was more frequent in HCM (11.3% vs. 5.2%) and RCM (59.1% vs. 39.1%) patients. Atrial fibrillation in HCM (27.3 vs. 7.5%) and RCM (50.0 vs. 20.0%) was more frequently observed in the present study than in the previous study, which may be due to differences in disease severity in HCM and RCM. Compared with the previous study,[5,6] the prescription rate of β-blockers (69.2%

Table 3. Characteristics of HCM Patients in Different Regions in Japan

Variables	Hokkaido/ Tohoku (n=1,049)	Kanto (n=894)	Chubu (n=372)	Kinki (n=555)	Chugoku/ Shikoku (n=277)	Kyushu (n=406)	P value
Demographics							
Age at enrollment (years)	67 [58–75]	62 [47–71]	64 [53–73]	64 [53–73]	62 [54–72]	63 [54–73]	<0.001
Age at diagnosis (years)	56 [45–64]	52 [38–63]	56 [40–65]	53 [40–65]	55 [43–65]	56 [43–65]	0.001
Male sex	663 (63.2)	527 (59.0)	204 (54.8)	291 (52.4)	164 (59.2)	238 (58.6)	0.001
NYHA functional class							
I	346 (35.7)	220 (27.8)	69 (20.1)	104 (20.6)	60 (23.9)	74 (20.4)	<0.001
II	558 (57.6)	493 (62.3)	214 (62.2)	317 (62.7)	155 (61.8)	249 (68.6)	<0.001
III	59 (6.1)	69 (8.7)	50 (14.5)	74 (14.6)	33 (13.2)	34 (9.4)	<0.001
IV	5 (0.5)	9 (1.1)	11 (3.2)	11 (2.2)	3 (1.2)	6 (1.7)	<0.001
Syncope	141 (13.4)	193 (21.6)	80 (21.5)	125 (22.5)	51 (18.4)	66 (16.3)	<0.001
Family history							
HCM	144 (13.7)	199 (22.3)	95 (25.5)	135 (24.3)	59 (21.3)	77 (19.0)	<0.001
Sudden cardiac death	36 (3.4)	67 (7.5)	33 (8.9)	44 (7.9)	26 (9.4)	25 (6.2)	<0.001
Vital signs							
SBP (mmHg)	122.6±18.5	121.0±20.4	119.5±20.3	120.5±21.2	122.0±19.9	121.0±20.4	0.11
DBP (mmHg)	70.5±12.3	71.6±15.3	69.9±13.0	70.5±15.2	70.0±12.3	70.5±14.7	0.33
Abnormal BP response	11 (1.1)	28 (3.1)	5 (1.3)	12 (2.2)	3 (1.1)	17 (4.2)	<0.001
Heart rate (beats/min)	68.0±32.3	68.3±14.1	67.2±15.9	69.4±14.3	69.0±15.9	69.0±41.2	0.80
Laboratory data							
Hemoglobin (g/dL)	13.7±1.9	13.9±1.8	13.5±2.0	13.7±1.9	13.7±1.8	13.8±1.7	0.029
Albumin (g/dL)	4.1±0.5	4.1±0.5	4.1±0.5	4.1±0.5	4.2±0.5	4.1±0.4	0.52
AST (U/L)	25.0 [21.0–32.0]	24.0 [20.0–31.0]	25.0 [20.0–32.0]	24.0 [21.0–32.0]	25.0 [21.0–32.0]	25.0 [20.0–30.0]	0.39
ALT (U/L)	21.0 [15.0–31.0]	21.0 [15.0–31.0]	21.0 [15.0–30.0]	21.0 [15.0–31.0]	22.0 [16.0–32.0]	20.0 [15.0–29.0]	0.55
BUN (mg/dL)	22.7±24.3	18.7±15.8	18.4±7.8	19.2±13.4	17.7±9.4	19.7±15.2	<0.001
Creatinine (mg/dL)	0.88 [0.73–1.07]	0.86 [0.71–1.04]	0.87 [0.71–1.08]	0.84 [0.70–1.00]	0.83 [0.68–1.00]	0.88 [0.72–1.05]	0.025
eGFR (mL/min/1.73 m^2)	62.6±21.5	65.7±21.2	62.4±20.2	65.0±21.0	66.6±20.8	62.6±21.6	0.002
Uric acid (mg/dL)	6.1±1.8	6.2±1.8	6.1±1.5	6.2±1.8	6.0±1.6	6.3±1.6	0.19
Sodium (mEq/L)	141.0±2.8	140.6±2.8	140.7±3.7	140.6±3.1	140.0±3.4	140.3±2.9	<0.001
BNP (pg/mL)	194.1 [84.0–407.0]	227.9 [100.8–511.0]	320.0 [146.6–669.0]	317.4 [120.0–626.0]	297.7 [144.0–563.4]	247.2 [100.5–480.2]	<0.001

(**Table 3** continued the next page.)

Variables	Hokkaido/ Tohoku (n=1,049)	Kanto (n=894)	Chubu (n=372)	Kinki (n=555)	Chugoku/ Shikoku (n=277)	Kyushu (n=406)	P value
Electrocardiographic findings							
Atrial fibrillation	264 (25.2)	203 (22.7)	121 (32.5)	172 (31.0)	81 (29.2)	130 (32.0)	<0.001
VF/VT	208 (19.8)	228 (25.5)	101 (27.2)	125 (22.5)	72 (26.0)	82 (20.2)	0.006
Pacing	75 (7.2)	42 (4.7)	17 (4.6)	15 (2.7)	13 (4.7)	18 (4.4)	0.004
Biventricular pacing	9 (0.9)	8 (0.9)	2 (0.5)	2 (0.4)	3 (1.1)	2 (0.5)	0.76
Echocardiographic findings							
LVEF (%)	62.7±14.8	62.1±16.9	63.8±15.0	61.1±16.1	62.7±14.9	63.6±15.0	0.14
LVDd (mm)	47.1±8.7	45.7±9.4	45.4±8.2	46.1±9.0	46.4±8.2	44.7±8.1	<0.001
LVDs (mm)	30.4±9.6	30.0±10.6	29.4±9.7	29.8±9.9	29.6±8.9	28.5±9.4	0.054
IVS (mm)	16.2±5.4	15.7±5.5	16.7±5.8	15.4±4.6	16.6±5.1	16.5±5.2	<0.001
LVPW (mm)	11.6±3.0	11.6±3.5	12.2±3.4	11.3±2.9	12.0±3.4	12.5±3.5	<0.001
Maximum LVWT (mm)	18.9±5.7	19.0±6.5	19.7±6.5	18.4±4.9	18.6±5.5	18.8±5.2	0.11
LVWT >30 mm	66 (6.3)	73 (8.2)	42 (11.3)	33 (6.0)	24 (8.7)	37 (9.1)	0.017
Left atrial diameter (mm)	44.1±8.2	43.1±9.7	44.1±9.4	44.2±8.8	43.7±10.2	43.7±9.0	0.26
MR Grade III–IV	68 (10.0)	38 (6.3)	32 (10.8)	39 (8.9)	20 (9.0)	28 (9.5)	0.17
LV obstruction	174 (16.6)	228 (25.5)	101 (27.2)	152 (27.4)	77 (27.8)	107 (26.4)	<0.001
LVOT gradient >50 mmHg	137 (13.1)	203 (22.7)	88 (23.7)	128 (23.1)	57 (20.6)	77 (19.0)	<0.001
LV mid-obstruction	74 (7.1)	102 (11.4)	45 (12.1)	59 (10.6)	28 (10.1)	46 (11.3)	0.01
Systolic anterior movement	2 (0.2)	7 (0.8)	3 (0.8)	4 (0.7)	3 (1.1)	1 (0.3)	0.29
Pericardial effusion	20 (1.9)	58 (6.5)	33 (8.9)	39 (7.0)	26 (9.4)	22 (5.4)	<0.001
Apical hypertrophy	7 (0.7)	13 (1.5)	1 (0.3)	5 (0.9)	4 (1.4)	1 (0.3)	0.13
Medication							
β-blockers	558 (53.8)	461 (52.9)	214 (58.5)	337 (60.9)	153 (56.5)	266 (65.7)	<0.001
ACEi/ARB	562 (53.6)	430 (48.1)	186 (50.0)	251 (45.2)	136 (49.1)	196 (48.3)	0.034
MRA	155 (14.8)	137 (15.3)	58 (15.6)	95 (17.1)	53 (19.1)	56 (13.8)	0.39
Dihydropyridine CCB	172 (16.4)	94 (10.5)	48 (12.9)	58 (10.5)	31 (11.2)	60 (14.8)	<0.001
Verapamil	81 (7.7)	48 (5.4)	25 (6.7)	56 (10.1)	11 (4.0)	33 (8.1)	0.004
Diltiazem	55 (5.2)	25 (2.8)	19 (5.1)	23 (4.1)	2 (0.7)	32 (7.9)	<0.001
Loop diuretics	314 (29.9)	203 (22.7)	119 (32.0)	144 (26.0)	72 (26.0)	104 (25.6)	0.002
Thiazides	47 (4.5)	30 (3.4)	23 (6.2)	21 (3.8)	10 (3.6)	19 (4.7)	0.29
Digitalis	46 (4.4)	35 (3.9)	14 (3.8)	22 (4.0)	13 (4.7)	9 (2.2)	0.52
Amiodarone	117 (11.3)	102 (11.6)	71 (19.1)	64 (11.6)	37 (13.6)	40 (9.9)	0.001
Disopyramide	61 (5.9)	27 (3.1)	11 (3.0)	14 (2.5)	16 (5.9)	22 (5.4)	0.002
Cibenzoline	157 (15.1)	165 (18.8)	64 (17.2)	103 (18.7)	43 (15.8)	60 (14.8)	0.2
Oral inotropes	13 (12.4)	6 (1.5)	6 (6.4)	8 (3.3)	5 (6.4)	4 (3.2)	<0.001

Unless specified otherwise, data are given as n (%), the mean±SD, or as the median [interquartile range]. CCB, calcium channel blockers; LV, left ventricular; LVOT, left ventricular outflow tract; LVWT, left ventricular wall thickness; VF, ventricular fibrillation; VT, ventricular tachycardia. Other abbreviations as in Table 1.

vs. 40.9%) and ACEi/ARB (75.8% vs. 64.6%) was increased in DCM in the present study. These findings are consistent with recent studies demonstrating the implementation of evidence-based medication in DCM.[7,8] These drugs were also more frequently prescribed in HCM and RCM in the present study than in the previous study. In general, β-blockers are administered to patients with hypertrophic obstructive cardiomyopathy. However, the prevalence of LV outflow tract obstruction was similar between the present study and the previous nationwide survey (21% vs. 19%, respectively).[6] The Japanese Circulation Society (JCS) Guideline on Diagnosis and Treatment of Cardiomyopathies (https://www.j-circ.or.jp/old/guideline/pdf/JCS2018_tsutsui_kitaoka.pdf) recommends that patients with hypertrophic non-obstructive cardiomyopathy should be administered β-blockers to relieve symptoms caused by diastolic dysfunction. The clinical personal records database was originally established to certify intractable diseases. Therefore, the higher prescription rate of β-blockers in HCM in the present study may be due to the exclusion of asymptomatic patients because of the administrative nature of this record.

To date, the clinical characteristics and management of cardiomyopathies in each region in Japan have not been elucidated. This study identified several notable regional differences in DCM and HCM. DCM and HCM patients were youngest in the Kanto region, which may be due to a difference in the aging population in each region. A family history of DCM and HCM was less frequent in the Hokkaido/Tohoku region. A family history of DCM and HCM is known to be present in 20–50% of all cases.[22–24] Several specific mutations in HCM were reported to be found in the Kyushu and Kansai regions.[25] Thus, the regional differences in family history identified in the present study suggest a novel finding regarding the distribution of familial cardiomyopathy in Japan. In DCM, LVEF was

Table 4. Characteristics of RCM Patients in Different Regions in Japan

Variables	Hokkaido/ Tohoku (n=3)	Kanto (n=17)	Chubu (n=4)	Kinki (n=8)	Chugoku/ Shikoku (n=7)	Kyushu (n=7)	P value
Demographics							
Age at enrollment (years)	51 [42–68]	49 [39–58]	54 [30–71]	54 [44–62]	53 [22–73]	71 [67–76]	0.10
Age at diagnosis (years)	42 [31–62]	37 [17–52]	50 [20–67]	38 [28–52]	52 [21–72]	65 [56–76]	0.16
Male sex	3 (100.0)	10 (58.8)	3 (75.0)	7 (87.5)	3 (42.9)	2 (28.6)	0.12
NYHA functional class							
I	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0.33
II	1 (33.3)	7 (50.0)	2 (50.0)	3 (37.5)	3 (42.9)	0 (0.0)	0.33
III	1 (33.3)	3 (21.4)	0 (0.0)	5 (62.5)	4 (57.1)	4 (57.1)	0.33
IV	1 (33.3)	3 (21.4)	2 (50.0)	0 (0.0)	0 (0.0)	2 (28.6)	0.33
Cause of RCM							
Primary	–	10 (83.3)	3 (100.0)	5 (62.5)	7 (100.0)	5 (83.3)	0.34
Secondary	–	2 (16.7)	0 (0.0)	3 (37.5)	0 (0.0)	1 (16.7)	0.34
Other cardiomyopathy	–	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0.68
Amyloidosis	–	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (16.7)	0.68
Eosinophilic	–	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.68
Other	–	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0.68
Vital signs							
SBP (mmHg)	100.0±14.1	98.1±13.4	96.0±12.7	106.4±10.8	112.9±23.8	115.7±14.2	0.12
DBP (mmHg)	60.0±14.1	58.4±9.0	62.0±11.2	66.3±9.1	67.1±17.6	65.0±10.0	0.50
Heart rate (beats/min)	77.5±17.7	69.2±13.8	74.0±11.8	81.4±15.5	80.4±14.5	68.5±4.3	0.25
Laboratory data							
Hemoglobin (g/dL)	11.2±3.5	13.1±2.0	14.0±3.0	13.3±2.1	12.9±2.5	11.0±1.6	0.25
Albumin (g/dL)	3.6±0.1	4.2±0.4	4.1±0.7	4.0±0.6	3.8±0.6	3.8±0.3	0.33
AST (U/L)	24.0 [8.0–45.0]	24.0 [23.0–28.0]	20.0 [10.0–26.0]	31.5 [26.5–38.0]	27.0 [23.0–42.0]	29.0 [18.0–37.0]	0.31
ALT (U/L)	11.0 [4.0–11.0]	21.0 [15.0–25.0]	19.5 [10.5–27.5]	21.0 [18.5–24.0]	26.0 [14.0–30.0]	17.0 [12.0–22.0]	0.054
BUN (mg/dL)	32.3±20.0	25.7±16.6	26.8±9.4	21.3±6.4	18.5±5.6	34.4±24.3	0.45
Creatinine (mg/dL)	1.34 [1.03–1.66]	0.99 [0.87–1.28]	1.00 [0.73–1.09]	0.92 [0.65–1.02]	1.00 [0.54–1.34]	1.46 [0.93–2.00]	0.20
eGFR (mL/min/1.73 m^2)	47.7±15.7	63.9±24.8	63.8±29.3	69.0±21.8	59.3±31.0	34.5±15.5	0.14
Uric acid (mg/dL)	7.3±2.2	7.3±1.6	9.7±3.8	7.5±2.6	7.8±2.9	8.6±1.8	0.62
Sodium (mEq/L)	132.0±2.6	136.9±5.8	136.0±7.0	138.0±5.2	139.4±4.6	137.3±5.6	0.53
BNP (pg/mL)	357.9 [190.5–607.0]	448.8 [293.8–637.0]	353.0 [236.8–991.7]	179.0 [149.0–985.0]	262.0 [217.6–1,493.0]	1,076.0 [449.1–1,151.0]	0.80
Electrocardiographic findings							
Atrial fibrillation	3 (100.0)	8 (47.1)	2 (50.0)	5 (62.5)	0 (0.0)	5 (71.4)	0.036
Pacing	0 (0.0)	1 (5.9)	1 (25.0)	0 (0.0)	0 (0.0)	1 (14.3)	0.52
Echocardiographic findings							
LVEF (%)	56.3±13.7	55.9±12.4	45.6±16.7	58.7±16.6	60.6±22.2	49.6±14.3	0.60
LVDd (mm)	44.7±10.8	47.2±7.5	46.7±7.9	43.2±7.1	47.6±14.0	53.9±10.5	0.41
LVDs (mm)	32.0±11.8	33.4±6.8	36.6±10.5	29.9±6.3	32.1±17.3	40.0±12.1	0.53
IVS (mm)	7.0±3.6	10.9±6.8	12.7±5.8	9.7±3.5	8.2±1.4	12.3±3.4	0.44
LVPW (mm)	11.7±3.1	9.7±1.8	13.0±8.4	10.1±3.3	8.9±2.0	10.9±1.6	0.36
Hypertrophied pericardium	1 (33.3)	1 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.19
Pericardial effusion	1 (33.3)	1 (5.9)	1 (25.0)	5 (62.5)	3 (42.9)	0 (0.0)	0.020
Medication							
β-blockers	1 (33.3)	12 (75.0)	3 (75.0)	3 (42.9)	4 (66.7)	4 (66.7)	0.59
ACEi/ARB	1 (33.3)	11 (64.7)	1 (25.0)	3 (37.5)	6 (85.7)	5 (71.4)	0.22
MRA	2 (66.7)	3 (17.7)	1 (25.0)	1 (12.5)	3 (42.9)	0 (0.0)	0.16
Calcium channel blocker	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	2 (28.6)	1 (14.3)	0.28
Loop diuretics	2 (66.7)	4 (23.5)	1 (25.0)	2 (25.0)	3 (42.9)	1 (14.3)	0.57
Thiazides	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.011
Digitalis	0 (0.0)	3 (17.7)	1 (25.0)	2 (25.0)	1 (14.3)	1 (14.3)	0.94
Amiodarone	0 (0.0)	2 (11.8)	1 (25.0)	1 (12.5)	0 (0.0)	1 (14.3)	0.82
Oral inotropes	0 (0.0)	1 (5.9)	2 (50.0)	1 (12.5)	0 (0.0)	2 (28.6)	0.12

Unless specified otherwise, data are given as n (%), the mean±SD, or as the median [interquartile range]. Abbreviations as in Table 1.

lowest and MR Grade III–IV was more frequent in the Kanto region, indicating that DCM patients in this region may have severe LV dysfunction.

We also compared the results of the present study with those of the EORP Cardiomyopathy Registry. The major findings of the comparison were that: (1) Japanese patients with DCM and HCM were older and were diagnosed at an older age than European patients; (2) Japanese patients with DCM less frequently received optimal medical therapy for HF; (3) Japanese patients with HCM had a higher rate of ventricular fibrillation/cardiac arrest and more frequently received antiarrhythmic drugs; and (4) the number of RCM patients was small in both the Japanese and European registries.

In Japan, life expectancy at birth has increased from 79.0 years in 1990 to 83.2 years in 2015.[24] Hospitalized HF patients are older in Japan than in European countries (75.0±13.0 vs. 69.4±13.0 years) and 1-year all-cause mortality is lower in Japan than in Europe (18.6 vs. 26.7%).[17,26,27] A longer life expectancy and better prognosis of HF patients could result in older DCM or HCM patients in Japan. Another possible explanation may be differences in the diagnostic criteria for cardiomyopathies. Body size is generally smaller for Japanese than European people, which may potentially affect the echocardiographic diagnostic criteria of DCM and HCM. According to the revised definition of DCM by the ESC working group, LVEF was defined as LVDd or LV diameter >2SD from normal corrected by body surface area (BSA) and age, or BSA and sex;[28] LV wall thickness ≥15 mm is the diagnostic criterion for HCM.[29,30] However, currently, the JCS Guideline on Diagnosis and Treatment of Cardiomyopathies (https://www.j-circ.or.jp/old/guideline/pdf/JCS2018_tsutsui_kitaoka.pdf) does not determine cut-off points for LVEF, LVDd, or LV wall thickness in the definition and diagnosis of DCM. In addition, this guideline recommends an LV wall thickness of ≥15 mm, without adjustment for BSA, as the criterion for HCM. Using diagnostic criteria without adjusting for BSA may delay the diagnosis in Japanese patients because of their smaller LVDd and LV wall thickness.[31,32] Diagnostic criteria considering BSA in patients with DCM or HCM need to be defined.

Despite the implementation of evidence-based medications in DCM in recent decades, optimal medical therapy was less frequently received by patients with DCM in Japan than in Europe (**Supplementary Table**). These findings are consistent with previous HF registries showing that Japanese patients with HF less frequently receive β-blockers or MRA.[16,26,33] In the present study, the prognosis of DCM in Japan could not be compared with that in Europe because data regarding outcomes such as death and hospitalization were not available. However, DCM is the leading cause of heart transplantation in Japan, and the optimal diagnosis and management of DCM are critical and emerging issues in Japan. Thus, further action is needed to recommend physicians to adhere to optimal medical therapy, including ACEi/ARB, β-blockers, and MRA, for patients with DCM.

In the present study, the rate of ventricular fibrillation/cardiac arrest in HCM patients was higher in Japan than Europe (**Supplementary Table**). Sudden death due to lethal arrhythmia is the most serious complication in HCM, and several risk stratifications for sudden death have been proposed.[34] Although the lower use of β-blockers in Japanese HCM patients may be related to the high prevalence of ventricular fibrillation/cardiac arrest, further studies are needed to establish a precise risk stratification for sudden death in HCM.

RCM is a rare disease compared with DCM and HCM. A previous cross-sectional survey showed that the estimated crude prevalence of RCM was 0.2 per 100,000 population.[5] In fact, only 46 patients were registered during the period 2009–2014 in the clinical personal records database, and only 66 RCM patients were registered in the ESC's EORP Cardiomyopathy Registry. Thus, it is difficult to compare RCM characteristics between Japan and Europe. However, the younger age at enrollment and diagnosis and a higher frequency of NYHA functional class IV in Japan may be due to etiologic differences.

Study Limitations

The present study has several potential limitations that need to be acknowledged. First, the clinical personal records database does not include information regarding complications (e.g., hypertension and diabetes), genetic testing, non-pharmacological therapy, and outcomes such as hospitalization and death.

Second, the number of HCM patients was relatively small compared with the number of DCM patients. This may be due to differences in the registration period (12 and 6 years, respectively). However, this study is the largest registry of HCM in Japan. Indeed, it is larger than that of a previous nationwide survey regarding HCM (n=2,134).[6] We believe that this study provides valuable information regarding the characteristics of HCM in Japan.

Third, the number of RCM patients was small and some of the statistical analyses may have been affected. It is hard to compare characteristics between a large sample size and a small one. Nevertheless, in the EORP Cardiomyopathy registry, RCM (n=66) was compared with DCM (n=1,260) and HCM (n=1,739) despite the lower sample size. To clarify the characteristics of the cardiomyopathies, we compared DCM, HCM, and RCM in the same manner as reported previously.

Fourth, data regarding arrhythmogenic right ventricular cardiomyopathy were not obtained because it has not been specified as an intractable disease in adult patients.

Fifth, the prescription rate of HF medications, including renin-angiotensin-aldosterone system inhibitors and β-blockers, could be associated with the severity of HF, including HF symptoms or signs, LVEF, and MR. However, it is difficult to standardize all factors in descriptive analyses.

Sixth, although some regional differences within Japan, such as LVEF and MR, may be down to chance, the incidence of a family history may have some clinical relevance. The present study could not identify the reasons for differences in the incidence of a family history, or its clinical significance, because of the descriptive nature of the study. Further investigations are needed to elucidate these issues.

Finally, we demonstrated the characteristics of cardiomyopathy throughout Japan using descriptive analysis. However, temporal trend analysis would provide more clinically relevant findings. Further investigations using temporal trend analysis are needed to reveal longitudinal changes in demographics and the rate of guideline-directed medical treatments.

Despite the limitations described above, we analyzed the largest database of more than 40,000 Japanese cardiomyopathy patients, which were validated by certified cardiologists. This database can reveal clinical characteristics and

provide important insights for the optimal management of patients with cardiomyopathy throughout Japan.

Conclusions

By analyzing a nationwide database of more than 40,000 patients with cardiomyopathy, this study revealed the clinical characteristics of DCM, HCM, and RCM in Japan and provides critical insights for the development of optimal management strategies for these cardiomyopathies. The gap between current clinical practice and guideline recommendations should be discussed, and further investigations are needed to improve therapeutic strategies against cardiomyopathy in Japan.

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Disclosures

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IRB Information

The original study protocol was approved by the Institutional Review Board at Kyushu University (No. 29-48).

One Sentence Summary

The national registry of clinical personal records of cardiomyopathy could provide important information regarding the demographics, clinical characteristics, and management of cardiomyopathy in Japan.

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Supplementary Files

Please find supplementary file(s);
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