

## CARDIOVASCULAR MEDICINE

# Epidemiology of idiopathic cardiomyopathy in Japan: results from a nationwide survey

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**Objective:** To estimate the total number of patients with idiopathic cardiomyopathy in Japan and the prevalence of the disorder.

**Design:** A nationwide epidemiological survey.

**Setting:** Hospitals selected randomly from among all hospitals in Japan.

**Patients:** Patients presenting with any of the three types of idiopathic cardiomyopathy: dilated cardiomyopathy, hypertrophic cardiomyopathy, and restrictive cardiomyopathy.

**Main outcome measures:** The total number of patients in Japan was estimated using the sampling and response rates in each stratum with respect to hospital size. The second survey was conducted for patients reported in the first survey in order to obtain detailed information, including age, sex, and specific clinical data.

**Results:** Estimated patient totals and 95% confidence intervals (CI) were 17 700 (95% CI 16 500 to 18 800) for dilated cardiomyopathy, 21 900 (95% CI 20 600 to 23 200) for hypertrophic cardiomyopathy, and 300 (95% CI 250 to 350) for restrictive cardiomyopathy. Crude prevalence per 100 000 population was estimated as 14.0 for dilated cardiomyopathy, 17.3 for hypertrophic cardiomyopathy, and 0.2 for restrictive cardiomyopathy; crude incidence per 100 000 person-years was estimated as 3.58, 4.14, and 0.06, respectively.

**Conclusions:** The total number and prevalence of patients with idiopathic cardiomyopathy in Japan are estimated for the first time in a nationwide survey. The prevalence of dilated cardiomyopathy in Japan appears to be about half that of Western populations, while that of hypertrophic cardiomyopathy is about the same.

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Investigation of the prevalence of specific diseases and estimation of the total number of patients affected are important in planning public health policy. Idiopathic cardiomyopathy is a heart muscle disease of unknown aetiology. Patients presenting with this disease tend to have a poor prognosis and may require heart transplantation.<sup>1</sup> The prevalence of the disease in a general population has been investigated in several epidemiological studies in Western countries.<sup>2–4</sup> However, few such studies have been conducted in Asian populations.<sup>5</sup> Thus the total number of patients with idiopathic cardiomyopathy in Japan has not been estimated to date in any nationwide survey employing appropriate epidemiological methods.

In 1999, the Japanese research committees on epidemiology of intractable diseases and idiopathic cardiomyopathy undertook a nationwide epidemiological survey of idiopathic cardiomyopathy in Japan. The objectives of the survey were to estimate total numbers of patients involved and the prevalence of the disease, to describe the detailed clinico-epidemiological features, and to provide this information for appropriate health service planning. In this paper we report the estimated total numbers of patients with idiopathic cardiomyopathy in Japan, and the prevalence and incidence of the disease, as well as the distribution of patients by age and sex. A detailed description of the clinico-epidemiological features will be presented elsewhere.

## METHODS

A nationwide survey was conducted for the three types of idiopathic cardiomyopathy: dilated cardiomyopathy, hypertrophic cardiomyopathy, and restrictive cardiomyopathy. Classification criteria, which are based on the report of the

World Health Organization/International Society and Federation of Cardiology (WHO/ISFC) task force on the definition and classification of cardiomyopathies,<sup>6</sup> were prepared by the research committee on idiopathic cardiomyopathy, Japan.<sup>7</sup> Specific heart muscle disease, which was defined as heart muscle disease of known aetiology or associated with disorders of other systems, was excluded from the survey.

A list of all hospitals with 20 or more beds was obtained—including name, address, number of beds, and departments within the hospital—from the Ministry of Health and Welfare, Japan. Departments surveyed were randomly selected by stratified sampling from all departments of internal medicine, circulatory diseases, and paediatrics in hospitals throughout Japan, as most patients with cardiomyopathy in Japan are treated in such institutions. Sampling rates were approximately 5%, 10%, 20%, 40%, 80%, and 100% for the stratum of general hospitals with 20 to 99 beds, 100 to 199 beds, 200 to 299 beds, 300 to 399 beds, 400 to 499 beds, and 500+ beds, respectively (table 1). All university hospitals in Japan were also surveyed.

The study consisted of two surveys, as in previous nationwide surveys of intractable diseases.<sup>8–11</sup> In the first survey, a simple questionnaire was used to inquire about the number of patients presenting with the three types of idiopathic cardiomyopathy who visited the specific departments and received treatment in 1998. Both inpatients and outpatients were surveyed, and asymptomatic patients in whom the disease was found incidentally were included. This

**Abbreviations:** ISFC, International Society and Federation of Cardiology; WHO, World Health Organization

**Table 1** Departments surveyed and numbers of patients reported in the first survey (1998)

Department	Hospital type	Number of beds	Total number of departments	Number of surveyed departments	Sampling rate (%)	Number of departments responding	Response rate (%)	Number of patients reported		
								DCM	HCM	RCM
Internal medicine and circulatory diseases	General	20-99	3493	172	4.9	86	50.0	20	40	0
		100-199	2165	214	9.9	108	50.5	97	173	0
		200-299	852	170	20.0	80	47.1	217	290	5
		300-399	497	199	40.0	90	45.2	571	709	13
		400-499	211	168	79.6	81	48.2	954	913	12
		≥500	254	254	100	114	44.9	1968	1974	29
Circulatory diseases	University	Any	24	24	100	23	95.8	861	906	7
Internal medicine	University	Any	295	295	100	194	65.8	1507	1945	20
Paediatrics	General	20-99	1368	66	4.8	30	45.5	2	1	1
		100-199	1010	99	9.8	56	56.6	2	2	0
		200-299	544	109	20.0	74	67.9	4	16	0
		300-399	397	158	39.8	122	77.2	7	14	0
		400-499	184	146	79.3	119	81.5	19	32	1
		≥500	221	221	100	149	67.4	50	101	9
	University	Any	119	119	100	83	69.7	62	146	5
Total			11634	2414	20.7	1409	58.4	6341	7262	102

DCM, idiopathic dilated cardiomyopathy; HCM, idiopathic hypertrophic cardiomyopathy; RCM, idiopathic restrictive cardiomyopathy.

questionnaire was mailed directly to the heads of 2414 departments, randomly selected in January 1999.

Following the collection of the first questionnaire, a second questionnaire was forwarded to those departments reporting patients in the first survey. This questionnaire requested detailed clinico-epidemiological information on individual patients receiving treatment, including age and sex, symptoms, complications, examination results, treatment, prognosis, and current medical care. Patients reported by more than one hospital or department were treated as "duplicate". Patients who died before 1998 or whose initial hospital visit was after 1999 were excluded from the study; these were called "inappropriate cases".

The number of patients treated for a given intractable disease in a specified year was estimated by a method described elsewhere in detail.<sup>8-12</sup> In brief, estimation was based on the assumption that the mean number of patients among departments responding to the survey is equal to that among departments not responding.<sup>13</sup> Formulas used to estimate the total number of patients and the 95% confidence intervals are described in these reports. The computed total number of patients was then corrected, employing the proportions of duplicate cases (D) and inappropriate cases (I) among those patients reported in the second survey—that is, the number was multiplied by  $1 - (D + I)$ .

The crude prevalence rate per 100 000 population was determined from the population of Japan in 1998. Prevalence was multiplied by the proportion of patients newly diagnosed in 1998 as having the disease, in order to estimate the crude incidence rate per 100 000 person-years. This proportion was

obtained from the second survey. Age and sex specific prevalence rates were estimated for dilated cardiomyopathy and hypertrophic cardiomyopathy, using the age distribution of patients by sex, which was obtained from the second survey. Age and sex specific prevalence is not shown for restrictive cardiomyopathy, as the number of patients in the second survey was too small for a reliable estimate.

## RESULTS

Table 1 presents the results of the first survey. Of 2414 departments sampled, 1409 replies were received to the first questionnaire (response rate 58.4%), reporting a total of 13 675 patients treated for the three types of cardiomyopathy in 1998. In the second survey, detailed data were collected from 4348 patients (31.8% of the patients in the first survey). Data in the second survey showed rates of duplicated and inappropriate cases of 5.2% for dilated cardiomyopathy, 6.5% for hypertrophic cardiomyopathy, and 7.4% for restrictive cardiomyopathy. Following exclusion of those cases ( $n = 256$ ), 4092 cases from the second survey were analysed. Accounting for the rates of duplicated and inappropriate cases, the total number of patients treated for idiopathic cardiomyopathy in 1998 was estimated. The results are given in table 2. The estimated prevalences per 100 000 Japanese population were 14.0 for dilated cardiomyopathy, 17.3 for hypertrophic cardiomyopathy, and 0.2 for restrictive cardiomyopathy (table 2). The overall prevalence of idiopathic cardiomyopathy was 31.5 per 100 000. From the second survey, the proportions of patients newly diagnosed in 1998 were 25.6% for dilated cardiomyopathy, 23.9% for hypertrophic cardiomyopathy, and 24.0% for

**Table 2** Estimated total numbers of cases, prevalence, and incidence of idiopathic cardiomyopathy in Japan (1998)

Classification	Estimated total number in Japan	95% CI	Estimated crude prevalence (per 100000 population)	Estimated crude incidence (per 100000 person-years)
DCM	17700	16500 to 18800	14.0	3.58
HCM	21900	20000 to 23200	17.3	4.14
RCM	300	250 to 350	0.2	0.06

CI, confidence interval; DCM, idiopathic dilated cardiomyopathy; HCM, idiopathic hypertrophic cardiomyopathy; RCM, idiopathic restrictive cardiomyopathy.

**Table 3** Age distribution of patients with idiopathic cardiomyopathy reported in the second survey, by sex

Age group (years)	Male		Female		Total	
	n	%	n	%	n	%
<i>Idiopathic dilated cardiomyopathy</i>						
0-9	12	0.9	16	3.0	28	1.4
10-19	12	0.9	10	1.9	22	1.1
20-29	38	2.7	16	3.0	54	2.8
30-39	100	7.1	13	2.4	113	5.8
40-49	204	14.6	55	10.3	259	13.4
50-59	360	25.7	85	16.0	445	23.0
60-69	417	29.8	178	33.5	595	30.8
70-79	201	14.4	128	24.1	329	17.0
≥80	56	4.0	31	5.8	87	4.5
Total	1400	100.0	532	100.0	1932	100.0
<i>Idiopathic hypertrophic cardiomyopathy</i>						
0-9	11	0.7	14	2.2	25	1.2
10-19	55	3.7	31	4.8	86	4.0
20-29	39	2.6	31	4.8	70	3.3
30-39	61	4.1	20	3.1	81	3.8
40-49	152	10.2	50	7.8	202	9.5
50-59	348	23.4	101	15.7	449	21.0
60-69	506	34.0	184	28.6	690	32.3
70-79	267	17.9	163	25.3	430	20.1
≥80	51	3.4	50	7.8	101	4.7
Total	1490	100.0	644	100.0	2134	100.0
<i>Idiopathic restrictive cardiomyopathy</i>						
0-9	1	7.1	1	8.3	2	7.7
10-19	2	14.3	2	16.7	4	15.4
20-29	3	21.4	0	0.0	3	11.5
30-39	1	7.1	0	0.0	1	3.8
40-49	0	0.0	0	0.0	0	0.0
50-59	1	7.1	1	8.3	2	7.7
60-69	5	35.7	3	25.0	8	30.8
70-79	1	7.1	4	33.3	5	19.2
≥80	0	0.0	1	8.3	1	3.8
Total	14	100.0	12	100.0	26	100.0

restrictive cardiomyopathy. These values yielded the estimated crude incidence rates shown in table 2. The overall incidence of idiopathic cardiomyopathy in Japan was estimated as 7.78 per 100 000 person-years.

Table 3 shows the age distribution of the 4092 patients reported in the second survey by sex. For both dilated and hypertrophic cardiomyopathy, a single peaked distribution was observed. Both male and female patients were most likely to be between the ages of 60 and 69 years. Although the number of patients was smaller, the distribution of restrictive cardiomyopathy appeared to show two peaks, one occurring in individuals younger than 40 years of age and the second occurring in individuals older than 50. The mean (SD) age of the patients in the three categories of cardiomyopathy was 57.8 (15.4) years for those with dilated cardiomyopathy, 58.4 (16.8) years for those with hypertrophic cardiomyopathy, and 47.7 (25.8) years for those with restrictive cardiomyopathy. The male/female sex ratios were 2.6 for dilated cardiomyopathy, 2.3 for hypertrophic cardiomyopathy, and 1.2 for restrictive cardiomyopathy. The second survey also showed that 97.7% of patients with dilated cardiomyopathy and 96.2% of those with hypertrophic cardiomyopathy underwent echocardiography, while 70.5% of patients with dilated cardiomyopathy and 49.1% of those with hypertrophic cardiomyopathy patients had angiography. Over 97% of these patients had ECGs.

The estimated prevalence rates of dilated cardiomyopathy and hypertrophic cardiomyopathy by age group are presented in table 4 for each sex and for the total population of Japan. For dilated cardiomyopathy, the prevalence in men was highest at ages 60-69 (54.7 per 100 000), whereas in women it was highest at ages 70-79 (21.8 per 100 000). The prevalence in

**Table 4** Estimated prevalence rate of idiopathic cardiomyopathies in Japan by sex and age per 100000 population (1998)

Age group (years)	Prevalence rate		
	Male	Female	Total
<i>Idiopathic dilated cardiomyopathy</i>			
0-9	1.8	2.5	2.1
10-19	1.5	1.3	1.4
20-29	3.6	1.6	2.6
30-39	11.1	1.5	6.3
40-49	20.5	5.6	13.1
50-59	37.2	8.6	22.8
60-69	54.9	21.4	37.4
70-79	48.1	21.8	32.7
≥80	35.4	9.5	17.9
All ages	20.7	7.5	14.0
<i>Idiopathic hypertrophic cardiomyopathy</i>			
0-9	1.8	2.4	2.1
10-19	7.4	4.4	6.0
20-29	4.1	3.4	3.8
30-39	7.6	2.5	5.1
40-49	17.1	5.7	11.4
50-59	40.3	11.5	25.7
60-69	74.6	24.8	48.6
70-79	71.5	31.1	47.9
≥80	36.1	17.1	23.3
All ages	24.7	10.2	17.3

men was highest at ages 60–69 (74.6 per 100 000) for hypertrophic cardiomyopathy, whereas in women it was highest at ages 70–79 (31.1 per 100 000). For both dilated and hypertrophic cardiomyopathy, the prevalence in women was higher than in men only between the ages of 0–9 years.

## DISCUSSION

In this paper we report the total number of patients with idiopathic cardiomyopathy in Japan. To our knowledge, this is the first survey of its kind in Japan employing reliable epidemiological methods. We also report the prevalence and incidence of this disease in an Asian population.

One methodological issue in the present survey involves the diagnostic criteria used. In 1995, the WHO/ISFC task force reported a new definition and classification of cardiomyopathy in which the cardiomyopathies were defined simply as diseases of the myocardium associated with cardiac dysfunction.<sup>14</sup> However, we employed the definition and classification provided by the earlier task force of 1980,<sup>7</sup> in which idiopathic cardiomyopathy was distinguished from other specific heart muscle diseases. Our reasons for doing this were: firstly, that nearly all cardiologists and specialists in general medicine in Japan have been applying this definition to their diagnosis of cardiomyopathies for a long time; and secondly, that numerous previous reports on the prevalence of cardiomyopathies have also used the same definition of idiopathic cardiomyopathy, so we could compare our data with those reports.

It is of the greatest importance to use appropriate diagnostic tests to diagnose this disease and to exclude other heart muscle disorders. In the present study, the second survey showed that nearly all patients with dilated and hypertrophic cardiomyopathy had echocardiography, while approximately 70% of patients with dilated cardiomyopathy and 50% of those with hypertrophic cardiomyopathy underwent angiography. Over 97% of these patients had ECGs. These figures suggest a high specificity in the diagnosis. In addition, because echocardiography is currently a very popular form of examination in Japan, and nearly all patients with cardiac symptoms who consult a cardiologist undergo echocardiographic screening, the sensitivity of the diagnosis of cardiomyopathy can be expected to be higher than observed previously. Thus the accuracy of our survey is likely to be greater than that of the previous reports from the 1970s and 1980s.

The most comparable data on the prevalence of this disease in Western countries were obtained in Olmsted County, Minnesota in 1985; the investigators assessed diagnostic data on the entire population of this county.<sup>2</sup> Prevalence rates were shown to be 36.5 per 100 000 population for dilated cardiomyopathy and 19.7 for hypertrophic cardiomyopathy. The prevalence of dilated cardiomyopathy was over twofold greater than observed in the present study, while the prevalence of hypertrophic cardiomyopathy was similar in the two surveys. One possible explanation for the large difference in dilated cardiomyopathy prevalence could be a higher coexisting rate of coronary artery disease in the Minnesota data. However, this explanation is unlikely because considerable steps were taken to exclude underlying coronary artery disease in that study, although not every patient underwent angiography. Another explanation would be a genetic difference between the Japanese and the US populations, as there is increasing evidence that dilated cardiomyopathy has a strong genetic component.<sup>15, 16</sup> Another factor is that some of the patients in the Olmsted County study were diagnosed initially at necropsy, which means that our results could have underestimated the prevalence.

With respect to incidence, the Olmsted County data showed incidence figures of 6.0 per 100 000 for dilated cardiomyopathy and 2.5 per 100 000 for hypertrophic cardiomyopathy.<sup>2</sup> A study conducted in Malmö, Sweden, showed that the incidence of established dilated cardiomyopathy was 3.6 per 100 000.<sup>17, 18</sup> A study undertaken in the USA between 1985 and

1991 found an annual incidence of dilated cardiomyopathy of 3.5 per 100 000 men and 2.5 per 100 000 women.<sup>19</sup> These figures suggest that the incidence of idiopathic cardiomyopathies in Japan is somewhat lower than or similar to those in Western populations. Neither prevalence nor incidence rates have been given for restrictive cardiomyopathy in previous reports.

To our knowledge, there are very few studies giving the estimated total number of cases of idiopathic cardiomyopathy in Japan, or the prevalence rates of this disorder. Hada and colleagues showed that the prevalence of hypertrophic cardiomyopathy among 12 841 adult Japanese workers was 170 per 100 000, based on results of echocardiographic screening.<sup>5</sup> The research committee on the epidemiology of intractable diseases in Japan at one time estimated the total number of patients with idiopathic cardiomyopathy in the country to be just in excess of 33 000, employing data from the national one day patient survey.<sup>20</sup> Our estimate (39 900) is similar to that figure. In addition, the overall prevalence of cardiomyopathies was estimated to be 26.5 per 100 000 (34.5 for men and 18.6 for women). We found the overall prevalence to be 31.5 per 100 000 (table 2). These figures are reasonably comparable, despite the small number of patients presenting with the disease in the one day patient survey.

The number of patients was estimated on the assumption that the response from hospital departments was independent of the frequency of the patients.<sup>13</sup> This assumption requires validation, as the response rate (58.4%) was relatively low; however, rates were comparable with those of the six nationwide surveys conducted in 1992 (53.0–62.1%).<sup>21</sup> Hashimoto and colleagues compared the mean number of patients presenting with an intractable disease financially subsidised for treatment among responding departments with those among non-responding departments; the ratio of the former to the latter was found to be between 1.0–1.1.<sup>22</sup> This suggests that the above assumption may be valid in nationwide epidemiological surveys of intractable diseases in Japan.

Another issue in our estimates may involve the inclusion of inpatients and outpatients treated solely in hospitals with 20 or more beds, ignoring those treated in clinics (with less than 20 beds or without beds). However, it is likely that most patients with cardiomyopathy in Japan are diagnosed and treated in hospitals and not clinics; thus any underestimation of the total number and the prevalence would be small and acceptable. A low response rate for the second survey could also be a limitation of our study. Our results are based on an assumption that the age–sex distribution in patients who were reported in the second survey is similar to that of patients who were not reported, although we have no evidence for this assumption.

It has been pointed out in some previous reports that there could be substantial numbers of undetected asymptomatic patients with dilated or hypertrophic cardiomyopathy in any population, some of whom may be diagnosed at necropsy after sudden death.<sup>23, 24</sup> In fact, studies screening an entire population by echocardiography have shown a much higher prevalence of hypertrophic cardiomyopathy (approximately 200 per 100 000).<sup>5, 25</sup> However, as population based screening using ECG and chest x ray examination is undertaken at school and in the community and workplace in Japan, some of the cases reported in our study were detected early on the basis of cardiomegaly or an abnormal ECG. Thus any underestimation of prevalence because of undetected asymptomatic patients is likely to be smaller in our study than in previous hospital based studies.

## Conclusions

An estimate of the prevalence, incidence, and total number of patients presenting with a disease is important in planning public health policies. Recently, heart transplantation has been shown to improve the quality of life and increase survival in end stage dilated cardiomyopathy. Detailed data from the

second survey may be valuable in assessing the potential contribution of heart transplantation to the management of dilated cardiomyopathy.

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## IMAGES IN CARDIOLOGY

### Inhibition of temporary pacing by a mobile phone

A patient with no underlying rhythm was receiving transvenous temporary pacing from an external pulse generator and bipolar temporary pacing wire on a coronary care unit. While examining the patient, the consultant cardiologist was telephoned on his mobile phone, carried in his jacket pocket. The electromagnetic interference generated by the ringing mobile phone caused inappropriate sensing by the pulse generator and inhibition of ventricular pacing. The image shows the

resultant 2.5 second pause. Pacing recommenced when the mobile phone was moved away from the bedside.

This case is a reminder that mobile phones may adversely affect electronic hospital equipment.

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