Characterization of Outpatients With Systolic Dysfunction in a Japanese Community by Total Enumeration

— Sado Heart Failure Study —

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Background The prevalence of congestive heart failure (CHF) is increasing with the aging of the community. Management of patients with systolic dysfunction (SD) is important for prevention of CHF, but there is little information regarding the burden of SD on Japanese communities.

Methods and Results In order to delineate the epidemiological and clinical characteristics of SD patients, the medical records of patients from Sado Island were collected and summarized in 2003. From the 5 years prior to 2003, data for 497 patients were extracted. The mortality rate was significantly higher compared with the general population; and the total number of survivors had decreased to 410 by 2003. The proportion of SD patients in the general population increased sharply after the age of 65 years in males and 70 years in females, reaching 3.3% and 1.7% for men and women, respectively, in their 80s. In 49% of the patients, the Charlson comorbidity index was ≥ 2 , whereas 24% of females led a solitary life.

Conclusions The total count of outpatients with SD is progressively increasing with age. These patients have multiple comorbidities, making the outcome of SD a poor one. The gender difference in disease characteristics and living conditions should be taken into consideration when establishing preventive strategies for CHF in Japanese communities. (Circ J 2007; 71: 1004–1012)

Key Words: Charlson comorbidity index; Heart failure; Systolic dysfunction

In developed countries, the number of patients with heart failure (HF) is increasing progressively with the aging of the population, and the “New Epidemic” which Braunwald predicted at the end of the 20th century has now come true.¹ Population-based studies in the United States and Europe have indicated that a large number of individuals with left ventricular (LV) systolic dysfunction (SD) are “hidden” behind those with symptomatic chronic HF.^{2–4} Therefore, guidelines for the management of HF emphasize the early detection and treatment of patients with SD as an important step in the strategy to reduce this burden in the future.^{5,6} Management of SD may also be important for reducing the future burden in Asian communities, where aging of the population is rapidly advancing.⁷

Japan has a universal health insurance system for treatment of diseases and local governments provide financial support for medical check-ups aimed at early detection of diseases. Because of good accessibility to medical services,

a considerable percentage of residents have been screened for heart disease, so much information has accumulated in the local medical centers. Not a few patients are presumed to be under treatment for SD; however, scarce information is available. Therefore, in order to delineate the epidemiological and clinical characteristics of patients with SD in January 2003, we carried out a complete enumeration of the patients in Sado City (an island city in Japan) via cooperation with the local core hospitals and medical societies.

Methods

Study Design and Participants

The Niigata-Sado Heart Failure Study was a complete enumeration survey for outpatients with SD at hospitals and clinics in 2 cities in Japan: Niigata and Sado (Fig 1). Sado City is an island with a surface area of 855 km² (about 1.4-fold the size of Tokyo metropolis), having a total population of 70,000 (almost all Japanese). This study was carried out at 4 core hospitals with hospitalization capacity, in collaboration with the local medical society. SD was defined as LV ejection fraction (LVEF) $\leq 50\%$. Within a total period of 6 years (extending from January 1st 1997 to December 31st 2002), data for patients with SD were extracted from the records of approximately 7,982 consecutive individuals who had their echocardiographic (Echo) examinations performed at 3 of the core hospitals in Sado City.

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Fig 1. Map of the location and population of Niigata City and Sado Island in Japan on January 1st 2003; with details of the study area and its administrative divisions.

Niigata City is the nearest port to Sado City and has a population of 518,233 persons (Fig 1). Similarly, we examined all records of patients who underwent Echo examination in 14 hospitals in Niigata City to extract the total number of SD patients there.

Determination of Recruitment Period

The extraction of SD patients was begun on January 1st for 6 consecutive years (such as 2002, 2001, 2000, 1999, 1998, and 1997), and continued until December 31st 2002. Thus, SD patients were extracted from the Echo logs by tentatively setting the recruitment periods at 1, 2, 3, 4, 5, and 6 years. We noticed that the number of extracted patients increased with the extension of the recruitment period. However, the earlier the patients were identified, the more information was lost before 2003 because of death or missing data. Therefore, we compared the total counts of recruited patients in these 6 intervals to find the optimal period for identifying the proportion of SD patients in the general population in 2003. In case the same patient was extracted twice or more during the recruitment period, only data from the first extraction was considered.

Review of Cases

All medical records of the extracted patients were reviewed, and their clinical data were collected and summarized according to a predetermined protocol. If a patient consulted 2 or more institutions during the recruitment period, all the records at these institutions were reviewed.

Extraction of Patients' Data

The available clinical records were reviewed with regard to demography, medical history, SD etiology, associated comorbidities or complications, medical therapies, laboratory investigations, ECG and Echo examinations. For the patients who survived until 2003, the information was collected up to January 1st 2003. Present or past history of congestive HF (CHF) was confirmed using the Framingham

criteria⁸

Determination of SD Etiology

Three cardiologists (Y Okura, K Suzuki, K Taneda) collaboratively consulted and diagnosed the etiology of SD. Ischemic heart disease (IHD) was considered as an etiology if the patient had 1 of the following: (1) documented history of myocardial infarction (MI), angina or prior coronary revascularization; (2) pathologic Q waves on ECG; or (3) >75% stenosis in 1 or more coronary arteries on coronary angiograms. Dilated cardiomyopathy (DCM) was diagnosed by the presence of global LV dilatation with impaired systolic function occurring in the absence of known cardiac or systemic causes. Valvular heart disease (VHD) was considered as an etiology of SD if mitral or aortic valve involvement was documented by Echo in the absence of IHD or DCM. Hypertensive heart disease was considered present if there was a history of hypertension and LV hypertrophy confirmed by Echo.

Confirmation of Survival

The survival of SD patients up to or beyond January 1st 2003 was confirmed by medical records. For those lacking records up to that date, direct phone calls to the family or attending physician were undertaken.

Determination of the Proportion of SD Patients in the General Population

This was done using the following equation:

$$\frac{\text{No. of SD survivors up to January 1st 2003}}{\text{Estimated population of Sado City on January 1st 2003}} \times 100$$

The numerator represents the Echo-documented SD patients extracted within the 5-year period after excluding those for whom survival status was impossible to determine. The denominator estimate was obtained from the Niigata Prefectural Department of Policy and Planning, Niigata,

Fig 2. Cumulative frequency plot showing the yearly-partitioned recruitment period and the corresponding numbers of patients with systolic dysfunction extracted from the echocardiography files up to January 1st 2003. The increase in the number of patients was negligible when the recruitment period exceeded 5 years (dotted line). The number of patients missed because of a lack of medical records also increased with prolongation of the recruitment period (not shown). *January 1st of each year.

Fig 3. Flow chart of Sado Heart Failure study, showing the process of extraction and follow-up of patients with systolic dysfunction. When the starting date of the recruitment period was set at 5 years (from January 1st 1998 until December 31st 2002), 578 patients were extracted. Of them, 168 patients were excluded because of a lack of medical records, in-hospital (pre-discharge) mortality, or death during follow-up. Thus, 410 patients finally survived until January 1st 2003 and were included in the analysis. *Residents of Sado City with expected age range 45–84 years at January 1st 2003.

Japan.⁹ The obtained proportion was compared after stratification by gender and 5-year age intervals.

Survival Analysis

Survival curves of the general population of Sado City were prepared for both genders on the basis of the Niigata Prefecture Life Table (2000) using actuarial analysis.^{10,11} The latter table was made according to the National Life Table, which is based on the results of the Japan Population Census (2000). Similarly; survival curves of patients with LVEF ≤40% and those with LVEF 41–50% at the time of diagnosis were prepared, stratified by gender, and compared with the general population curves by log-rank test. Each of these curves was drawn by linking the points representing the average survival rate of each 5-year age group.

In addition, we evaluated the effects of associated comorbidities (included or not in the Charlson comorbidity index (CCI))^{12,13} on patient's survival. Although CCI is a survival index, it has also been validated to correlate with physical disabilities and the re-admission rate in patients with chronic HF.^{13,14}

Statistical Analysis

Data analyses were performed using SPSS for Windows Version 13 (SPSS Inc, Chicago, IL, USA). Results for continuous normal data were expressed as mean ± standard deviation. Comparison of means of continuous normal variables across a grouping variable with 2 was undertaken using Student's t-test. Comparison of proportions was made by ² test with Yates's correction. A 2-sided significance level of 0.05 was used for all analyses.

Ethical Considerations

The study protocol was reviewed and accepted by the local ethical review board of each medical institution participating in this study, including the Niigata University Graduate School of Medical and Dental Sciences, and written consent was given by all patients.

Results

Evaluating the Cumulative Counts of SD Patients

The cumulative counts of SD patients recruited during the periods of varying length (ie, from 1 to 6 years) are shown in Fig 2. In order to determine the appropriate re-

Fig4. Bar graphs showing the proportion of patients with systolic dysfunction (SD) in the general population on January 1st 2003. The number shown at the upper end of each bar represents the SD patients' count, while the numbers below each age range along the horizontal axis represent the male and female populations for that range.

Fig5. Bar graphs showing the regional proportions of patients with systolic dysfunction (SD) in the general population in Sado City on January 1st 2003. there is no significant difference regarding these proportions among the 4 regions. *The letters A to D represent the 4 divisions of Sado City (Island).

cruitment period for counting surviving patients in 2003, we evaluated the relationship between recruitment period and the cumulative counts of SD patients. Because some of the recruited patients died before 2003, the number of SD patients who were alive was somewhat fewer than those who were recruited. As shown in Fig2, solid lines connect the total counts of recruited patients, including those who died before 2003 (Deaths included) and the dotted lines connect the counts of recruited patients who survived until 2003 (Deaths excluded). Considering the yearly intervals as a continuum, a significant positive trend was found for the cumulative counts of SD patients in all patients and in both genders (Deaths included). Nevertheless, such an estimate showed a weak trend relative to the increment of the recruitment period when considering only the cumulative numbers of survivors; that is, the patients' cumulative count curve became nearly flat on moving from 2002–2003 to 1997–2003 (Deaths excluded).

Follow-up of Extracted Patients

A total of 578 patients were extracted within the 5-year recruitment period (from January 1st 1998 till December 31st 2002) (Fig2) and of them 28 (5%) were excluded because of either the absence of medical records or inability to confirm survival (Fig3). Moreover, 53 in-hospital deaths (before discharge) were excluded, as well as 87 deaths that were ascertained to have taken place before January 1st 2003 on careful follow-up. Thus, 410 patients were confirmed to have survived up to that date and were eventually included in our study. We found 18 Sado residents with SD in the Echo logs of the Niigata hospitals, but they had already been diagnosed as SD in Sado.

Proportion of SD Patients in the General Population in Relation to Age, Gender, and Region

The proportion of SD patients in the general population sector aged 45–84 years was 1.5% for males and 0.6% for

Fig 6. Comparative analysis of survival between patients with systolic dysfunction (SD) and the general population. Survival curves of the general population (on the basis of the Niigata Prefecture Life Table [2000]), and those of patients with mild (left ventricular ejection fraction (LVEF) 41–50%) and severe (LVEF $\leq$ 40%) SD were prepared using actuarial methods; and comparisons were made by log-rank test. Compared with the general population, the survival rate was significantly lower in both the mild and severe SD patient groups. On the other hand, this rate did not significantly differ between the 2 groups.

females (Fig 4). This proportion increased sharply after the age of 65 years in males and 70 years in females; reaching 3.3% in males and 1.7% in females in their 80s. The proportion in the 4 zones of Sado Island (labeled A–D in Fig 1) was compared after stratification by gender and age decades (Fig 5) and no significant difference in that proportion was found in either gender within any age group among the 4 areas.

Comparison of Patients' Survival Rates Relative to the General Population

We followed 497 outpatients with SD from diagnosis. The duration of follow-up was 4.5 ± 2.3 years. Fig 6 shows survival curves of the general population (based on the life table), compared with those of SD patients, before and after stratification by gender. In comparison with the general population, the cumulative survival was significantly lower in patients with mild SD (LVEF 41–50%) as well as in those with severe SD (LVEF $\leq$ 40%). However, this rate was not significantly different between the 2 groups.

Characteristics of SD Patients

Demographic Characteristics We included 410 patients with SD whose survival until January 1st 2003 was correctly confirmed. Approximately two-thirds of them (68%) were males, who were significantly younger than the females (70.2 ± 8.2 vs 73.9 ± 8.6 years; $p < 0.01$).

Primary Etiologies of SD Two hundred and three patients (50%) underwent diagnostic coronary angiography. As shown in Table 1, IHD was the most frequent etiology of SD in all cases (34%) and in males (41%), whereas VHD was the most prevalent in females (24%). Hypertensive heart disease was the second important cause of in all cases (21%). The primary disease could not be determined in 10% of cases, particularly in those with mild SD.

Associated Comorbidities Adequately documented present or past histories of comorbidities are shown for both genders in Table 2. Hypertension was the most prevalent comorbidity found in all cases ($\approx$ 41%) and males (42%). CHF was significantly associated with SD and was the second most prevalent comorbidity in all cases (29%) and the first one in females (42%). MI occurred more often in males (32%) than did CHF (23%) which came next in importance. Notably, cerebral stroke was markedly prevalent in SD patients (20% of all cases), especially males (23% compared with 14% in females); as well as psychiatric disorders, such as depression and dementia, which were found in 13% of patients.

Level of Daily Activities and Lifestyle As can be ascertained from Table 2, the majority of patients (92%) were independently mobile and wheel-chair-dependents constituted the minority (3%). Notably, women tended to lead a more solitary life than men who tended to live in families.

CCI In this index, a score of 1 point is given for each of the following conditions: CHF, MI, and diabetes. Thus, nearly one-quarter (24%) of patients were free of comorbidities (a score of 0), and similar proportions (27% and 25%) had scores of 1 and 2, respectively. Half of the patients had a CCI score $\geq$ 2, which was considered to indicate a poor prognosis. Approximately 12% of patients had a score $\geq$ 4, indicating a low possibility of survival.¹⁴

Table 1 Primary Etiologies of SD in the Study Patients

Primary etiology of SD	Male (n=278)	Female (n=132)	p value
Ischemic heart disease	113 (40.6%)	26 (19.7%)	<0.01
Hypertensive heart disease	60 (21.6%)	27 (20.5%)	NS
Valvular heart disease	26 (9.4%)	32 (24.2%)	<0.01
Dilated cardiomyopathy	39 (14%)	14 (10.6%)	NS
Chronic renal failure	8 (2.9%)	4 (3.0%)	NS
Tachyarrhythmias	6 (2.2%)	8 (6.1%)	<0.01
Congenital cardiac malformations	5 (1.8%)	0 (0%)	NS

SD, systolic dysfunction.

Table 2 Clinical and Other Characteristics of Surviving Patients With SD*

	Male (n=278)	Female (n=132)	p value
<i>Associated comorbidities and their management</i>			
<i>Cardiovascular risk factors/chronic medical illnesses</i>			
Age (years)	70.2±8.9	73.9±8.6	<0.01
Hypertension	117 (42.1%)	49 (37.1%)	NS
Diabetes mellitus	82 (29.5%)	18 (13.6%)	<0.01
Dyslipidemia	54 (19.4%)	25 (18.9%)	NS
Body mass index			
≥25 to <30 kg/m ² (overweight)	47 (16.9%)	13 (9.6%)	<0.05
≥30 kg/m ² (obesity)	5 (1.7%)	4 (2.7%)	NS
<i>Cardiac disorders</i>			
CHF hospital admission	65 (23.4%)	55 (41.7%)	<0.01
Angina pectoris	34 (12.2%)	4 (3%)	<0.01
Myocardial infarction	89 (32.0%)	24 (18.2%)	<0.01
Arrhythmias			
Atrial fibrillation			
Paroxysmal	31 (11.2%)	9 (6.8%)	NS
Chronic	55 (19.8%)	33 (25.0%)	NS
Sustained ventricular tachyarrhythmia	5 (1.8%)	2 (1.5%)	NS
Permanent cardiac pacemaker	8 (2.9%)	0 (0%)	<0.05
Intraventricular cardioverter defibrillator	0 (0%)	1 (0.8%)	NS
<i>Cardiac surgery/intervention</i>			
Cardiac valve replacement	12 (4.3%)	10 (7.6%)	NS
Diagnostic coronary angiography	151 (54.3%)	52 (39.4%)	NS
Percutaneous coronary intervention	45 (16.2%)	12 (9.1%)	NS
Coronary artery bypass graft operation	23 (8.3%)	3 (2.3%)	<0.05
<i>Neuropsychiatric disorders</i>			
Stroke	63 (22.7%)	18 (13.6%)	<0.05
Psychiatric illness	31 (11.2%)	22 (16.7%)	NS
<i>Chronic kidney disease</i>			
CRI (serum creatinine ≥2 mg/dl)	10 (3.6%)	6 (4.5%)	NS
CRF (on regular hemodialysis)	16 (5.8%)	4 (3.0%)	NS
<i>Pulmonary disorders</i>			
Bronchial asthma	16 (5.8%)	1 (0.8%)	<0.05
Chronic obstructive pulmonary disease	18 (6.5%)	2 (1.5%)	<0.05
Home oxygen therapy	6 (2.2%)	1 (0.8%)	NS
<i>Malignancy</i>			
Nonmetastatic	23 (8.3%)	14 (10.6%)	
Advanced	10 (3.5%)	3 (2.3%)	NS
<i>Level of daily activities and lifestyle</i>			
Independently mobile	263 (94.6%)	115 (87.2%)	
Wheel chair-dependent	6 (2.0%)	6 (4.3%)	<0.05
Bedridden	9 (3.4%)	11 (8.5%)	
Solitary life	35 (12.7%)	31 (23.6%)	<0.01
<i>Educational background</i>			
≤12 years	241 (86.7%)	119 (90.3%)	
>12 years	37 (13.3%)	13 (9.7%)	NS
<i>Medications</i>			
ACEIs	98 (35.3%)	42 (31.8%)	NS
Angiotensin-II receptor blockers	32 (11.5%)	6 (4.5%)	<0.05
-adrenergic receptor blockers	51 (18.3%)	12 (9.1%)	<0.05
Calcium-channel blockers	92 (33.1%)	46 (34.8%)	NS
Loop diuretics	120 (43.2%)	74 (56.1%)	<0.05
K ⁺ -sparing diuretics	42 (15.1%)	23 (17.4%)	NS
Digitalis glycosides	49 (17.6%)	38 (28.8%)	<0.01
Aspirin	87 (31.3%)	32 (24.2%)	NS
Ticlopidine	30 (10.8%)	8 (6.1%)	NS
Oral anticoagulants	98 (35.3%)	32 (24.2%)	<0.05
Nitrates	59 (21.2%)	26 (19.7%)	NS
Statins	55 (19.8%)	20 (15.2%)	NS
<i>Electrocardiographic data</i>			
LV hypertrophy	50 (18.0%)	27 (20.5%)	NS
Left bundle branch block	17 (6.1%)	6 (4.5%)	NS
Right bundle branch block	18 (6.5%)	7 (5.3%)	NS
Pathologic Q-wave	60 (21.6%)	11 (8.3%)	<0.01
<i>Echocardiographic data</i>			
Ejection fraction (%)	39.4±8.8	41.2±8.1	<0.05
Fractional shortening (%)	19.8±5.1	20.5±4.3	NS
LVDd (mm)	56.4±9	54.3±8.2	<0.05
LVDs (mm)	45.7±7.6	43.3±7.6	<0.01
IVST (mm)	10.5±3.0	9.6±2.7	<0.01
PWT (mm)	10.4±2.4	9.8±2.1	<0.05
LV mass index (g/m ²)	149.5±52.0	145.9±46.9	NS

Left atrial diameter (mm)	41.9±8.8	43.3±9.7	NS
Tricuspid valve regurgitation	45 (16.2%)	27 (20.5%)	NS
Mitral valve regurgitation	28 (10.1%)	20 (15.2%)	NS
Aortic valve regurgitation	12 (4.3%)	7 (5.3%)	NS
Functional and prognostic indices			
New York Hear Association functional class			
Class I	74 (26.5%)	25 (19.0%)	<0.05
Class II-III	193 (69.5%)	107 (81.0%)	
Class IV	11 (4.0%)	0 (0%)	
Charlson comorbidity index			
0 point	57 (20.5%)	41 (31.1%)	NS
1 point	76 (27.3%)	34 (25.8%)	
2 points	69 (24.8%)	32 (24.2%)	
3 points	43 (15.5%)	11 (8.3%)	
≥4 points	33 (11.9%)	14 (10.6%)	

*Survived until January 1st 2003.

Echocardiography data shown are those obtained on the initial diagnosis of SD. LV mass (g) was calculated according to the method recommended by the American Society of Echocardiography [$LV\ mass = 0.8 \times (1.04 \times [LVDd + IVST + PWT]^3 - LVDd^3) + 0.6$] then was indexed to body surface area (m^2).

CHF, congestive heart failure; CRI, chronic renal impairment; CRF, chronic renal failure; ACEIs, angiotensin-converting enzyme inhibitors; LV, left ventricular; LVDd, left ventricular diastolic dimension; LVDs, left ventricular systolic dimension; IVST, interventricular septal thickness; PWT, posterior wall thickness.

Values are mean ± SD or number of subjects (%).

Table 3 Variables Independently Associated With Mortality*

	-coefficient	OR	95%CI of OR	p value
Body mass index (kg/m^2)	-0.168	0.845	0.796–0.898	<0.001
Age at diagnosis	0.033	1.034	1.012–1.055	0.002
LVDd×LVDs interaction (cm^2)	0.039	1.040	1.020–1.060	<0.001
CHF history	0.525	1.690	1.218–2.346	0.002
Malignancy	0.788	2.199	1.492–3.242	<0.001
Stroke	0.798	2.221	1.591–3.101	<0.001
Chronic kidney disease	0.921	2.511	1.655–3.808	<0.001

*Using stepwise Cox proportionate hazard regression model, with the corresponding ORs.

OR, odds ratio; CI, confidence interval. Other abbreviations see in Table 2.

Predictors of Mortality

A Cox proportionate hazard regression model was constructed for identifying the prognostic predictors of death. Simple univariate analysis was done first for each of the input variables against positive death outcome, and all the variables (except for gender) associated with it at $p \leq 0.1$ were finally entered in a multivariate backward stepwise Cox regression model. Owing to the high correlation between LV systolic dimension (LVDs) and LV diastolic dimension (LVDd), as well as LVEF and fraction shortening (FS), these 2 pairs of variables were entered into the model as interaction terms (ie, LVDd×LVDs in cm^2 and LVEF×FS) to avoid collinearity. Thus, the following variables were included in the final model: age at diagnosis, gender, body mass index (BMI), presence of dyslipidemia, history of CHF, chronic kidney disease (CKD) (serum creatinine ≥ 2 mg/dl or regular hemodialysis), stroke, malignancy, treatment with angiotensin-converting enzyme inhibitors or diuretics, and the interactions of LVDd/LVDs and EF/FS. The model was proven to be highly significant (p -value for the omnibus tests of model coefficients <0.001). Eventually, age at primary diagnosis, LVDd×LVDs interaction, history of CHF, presence of stroke, CKD, and malignancy were found to be significantly and independently associated with death, and BMI was an independent inverse correlate of that event (Table 3).

Discussion

Evaluating the burden of cardiovascular disease on society has become an urgent requirement because disease profiles have changed rapidly in accordance with aging of the general population. The Niigata-Sado Heart Failure Study was conducted to provide such information. The demo-geographic characteristics of the study area (ie, an island) facilitated follow-up of the study cohort and improved subject inclusiveness and the sequentiality of enrollment, giving the advantage of reducing bias in patient selection. From this study, we have the following new observations: (1) the number of outpatients with SD amount to 2–3% of the population; (2) there is a gender difference in the characteristics of patients with SD; (3) patients with SD have several comorbidities that affect prognosis; and (4) the prognosis of patients with SD, even with favorable LVEF (41–50%), is worse than that of the general population.

The aim of this study was to count the number of outpatients with SD in 2003 and clarify their characteristics. Before doing so, we verified whether recruitment period was appropriate (Fig 2), and SD patients were collected without regional difference on the island (Fig 5). The dates when the patients were diagnosed to have SD varied; for example, when considering 2 patients who were diagnosed in 2002 and in 1999, the recruitment from 2002 to 2003 could identify the former but not the latter, whereas recruitment from 1999 to 2003 could identify both. Because there

was a directly proportional relationship between the number of identified patients and the length of the recruitment period; high inclusiveness was expected by setting the starting point of the period as early as possible (even more than 5 years) as shown in Fig 2. However, some SD patients died before 2003, and there was also an incremental relationship between the number of SD patients who died before 2003 and the length of the recruitment period. Therefore, the net increase in SD survivors by 2003 was suppressed by extending the recruitment period (Fig 2). Thus, we believe that the 5-year recruitment period (from 1998 to 2002) was efficient and appropriate for counting SD survivors in 2003.

The proportion of SD patients in the general population sector aged 45–84 years was 1.5% for males and 0.6% for females (Fig 4). This proportion increased after the age of 65 years in males and 70 years in females, reaching 3.3% in males and 1.7% in females in their 80s. These estimates were only based on the number of patients who were confirmed to have SD, and those in the general population with latent cardiac dysfunction who did not undergo Echo examinations were not included. Therefore, the estimates presented here are virtually lower than the true counts, and more residents may have untreated SD. These estimates differ considerably from the prevalence rates reported by population-based studies in the United States and Europe (6.9–10.2% for males and 3.4–3.8% for females; 11.2% for males and 8.3% for females in their 80s)^{2,3} In fact, detailed comparison would be impossible for many reasons (eg, geo-demographic, ethnic and methodological differences); however, the lower incidence of MI in the Japanese population compared with those of Western countries may be the reason for the lower prevalence of SD in Japan.^{15,16}

Our results highlighted the average characteristics of patients who were often clinically observed with the least possible selection bias, unlike the data derived from large-scale clinical studies conducted on subjects who have passed multiple exclusion criteria. Tsutsui et al¹⁷ and Shiba et al¹⁸ reported the clinical characteristics of Japanese patients with CHF in Fukuoka and Tohoku, respectively. The prevalence of hypertension, IHD, and atrial fibrillation (AF) was 39–41%, 25–44%, and 31–41%, respectively. Compared with their cohorts in which most patients had a history of hospital admission for CHF, the majority (71%) of our SD cohort did not have such a history. However, the prevalences of hypertension (40%), IHD (34%), and AF (31%) were consistent with these previous reports. Senni et al¹⁹ reported the clinical characteristics of white patients who were admitted with new-onset CHF in Olmsted County. They categorized 137 patients into CHF with reduced LVEF (<50%) group and that with preserved LVEF (≥50%). Seventy-eight patients (57%) showed reduced LVEF, males were dominant (59%), and the average age was 74.2 years. The prevalences of hypertension, IHD, AF and DCM were 50%, 53%, 24%, and 3% respectively. Hypertension and IHD prevailed more in the white cohorts than in ours, whereas AF and DCM were more prevalent in our cohort.

Comorbidity was a significant health problem for the patients with SD in this study. Half of them had a CCI score ≥2 (Table 2), and were thus considered as a poor prognosis group.^{20,21} Compared with the reports from North America,^{20,21} our cohort had a higher CCI score; for example, the proportion of patients (or residents) with CCI score ≥2 in the Duke databank of IHD (1,471 patients, 61 years old on average)²⁰ the population-based cohort of Olmsted

county (2,037 people, average age of 61 years)²² and in the HF registry of Ontario (38,702 patients, 85% of the patients were over 65 years old)²¹ was only 19%, 32%, and 29%, respectively. The reasons for the higher CCI score in our cohort are not clear, but we hypothesize higher age, the hospital-based study design, and the meticulous archiving of patients data, which maximized the diagnosis of associated comorbidities.

Additionally, some of the comorbidities (CHF, stroke, CKD, and malignancy), which were also scored by CCI, were shown to be independently and significantly associated with death in our cohort. In general, the high prevalence of poor prognostic comorbidities worsens the survival of the cohort. Therefore, the survival of these patients was poorer than that of the general population, in either those with relatively favorable systolic function (LVEF 41–50%) or those with significantly impaired LVEF (≤40%) (Fig 6).

Study Limitations

First, because this study was hospital-based and not population-based, it might have missed the latent SD patients in the community. In Sado City, 43% of residents over 45 years annually undergo medical check-up for early detection of disease, which is supported by the local government. However, we cannot exactly define the proportion of residents who proceeded to Echo examinations out of the total number examined clinically. Accordingly, estimation of the precise prevalence of SD in the general population was not possible, so instead we have shown the proportion of Echo-documented SD. Also, the literature has indicated a gender difference regarding consultation, examination, and treatment of cardiac patients;²³ which our study could not avoid. Moreover, the limitation of the study area to Sado Island may restrict the generalization of our results to other areas in Japan. In addition, half of the patients, especially asymptomatic ones with mild SD, did not undergo diagnostic coronary angiography. In this respect, it is known whether noninvasive diagnostic processes have limitations in classifying disease etiology precisely.

Conclusions

We carried out the first complete enumeration survey of SD in a Japanese community. The Sado Heart Failure Study is a highly inclusive hospital-based study that may be able to characterize patients with SD in the community. The proportion of patients with SD in the general population increases progressively with age. These patients often have multiple comorbidities, making the outcome of even mild SD a poor one. The gender difference in disease characteristics and living conditions of patients should be taken into consideration when establishing preventive strategies for HF in Japanese communities.

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