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Systolic Dysfunction in Urban Japan
—— Niigata-Sado Heart Failure Study ——

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Background Heart failure (HF), which can be caused by left ventricular systolic dysfunction (LVSD), is a growing problem in developed countries with a large aging population. The aim of the present study was to characterize outpatients with LVSD in the adult population (45–84 years) in an urban Japanese community (Niigata City), and delineate their characteristics in comparison with those in a rural one (Sado).

Methods and Results Over a 5-year period, 1,297 patients (67% males) with LVSD (defined as ejection fraction ≤50%) were extracted from 87,953 echocardiography records available in 15 hospitals in Niigata City. The proportion of LVSD increased progressively with age (p-for-trend <0.0001), reaching 1–2% in those aged ≥75 years. The prevalence of comorbidities was noticeable (47% had hypertension, 41% myocardial ischemia, 34% atrial fibrillation, 33% previous hospitalization because of congestive HF, 27% cerebral stroke). In comparison with Sado, Niigata patients were younger, with a higher prevalence of comorbidities (hypertension, diabetes, dyslipidemia, and cerebral stroke).

Conclusions As the proportion of LVSD cases increases progressively with age, it is expected to simulate a future epidemic. The differences between patients' characteristics and disease patterns in urban and rural communities may favor individually tailoring preventive strategies for HF in these areas. (*Circ J* 2008; **72:** 349–357)

Key Words: Echocardiography; Heart failure; Niigata-Sado Heart Failure Study; Systolic dysfunction

Heart failure (HF), which can be caused by left ventricular systolic dysfunction (LVSD), is a growing problem in developed countries with a large aging population.[1,2] Guidelines for the management of HF emphasize early detection and treatment of patients with LVSD as an important strategy to reduce the future burden of HF.[3,4] To achieve the latter goal, we proceeded to delineate the epidemiological and clinical characteristics of outpatients with LVSD (both symptomatic and asymptomatic) in the adult population (45–84 years) in an urban Japanese community (Niigata City). We aimed to include as many LVSD outpatients as possible rather than only those with definite HF symptoms, to avoid missing the asymptomatic patients with resultant underestimation of the burden of LVSD and deviation from the aforementioned guidelines. We also compared these results with our previously reported findings[5] in a rural Japanese community (Sado City). The reasons for this comparison include the recommended determination of the burden of HF at each local level in a country.[6] In addition, a number of differences exist between Niigata and Sado cities (Table 1), such as the higher proportion of elderly (≥65 years, who are more vulnerable to LVSD) in Sado and the more pronounced Westernized lifestyle, including dietary habits, in Niigata City. Whether these differences influence the proportion and/or clinical characteristics of LVSD patients in the 2 areas is an important issue that has not been investigated previously.

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Methods

Study Design and Selection of Participants

The present arm of the Niigata-Sado Heart Failure Study is a multicenter research project designed to characterize outpatients with cardiac dysfunction in an urban Japanese community, via the cooperation and integration of 15 hospitals representing all the echocardiography (Echo)-

Table 1 Comparison of Geo-Demographic Characteristics of Niigata and Sado Cities

Parameter[a]	*Niigata City*	*Sado City*
Population	*501,325*	*72,187*
Elderly (≥65 years)	*85,016 (17%)*	*23,149 (32%)*
Surface area (km²)	*205.9*	*855.3*
Population density (persons/km²)[b]	*2,434.8*	*84.4*
Residents engaged in industry	*244,248 (48.7%)*	*39,410 (54.6%)*
Primary industries	*5,318 (1.1%)*	*8,803 (12.2%)*
Secondary industries	*55,089 (10.9%)*	*9,911 (13.7%)*
Tertiary industries	*183,841 (36.7%)*	*20,696 (28.7%)*

[a]*Data obtained from the national population census (2000) in Japan.*[7]
[b]*Average for Japanese cities is 340 persons/km², thus Niigata City is ranked as the 23rd largest city in Japan.*

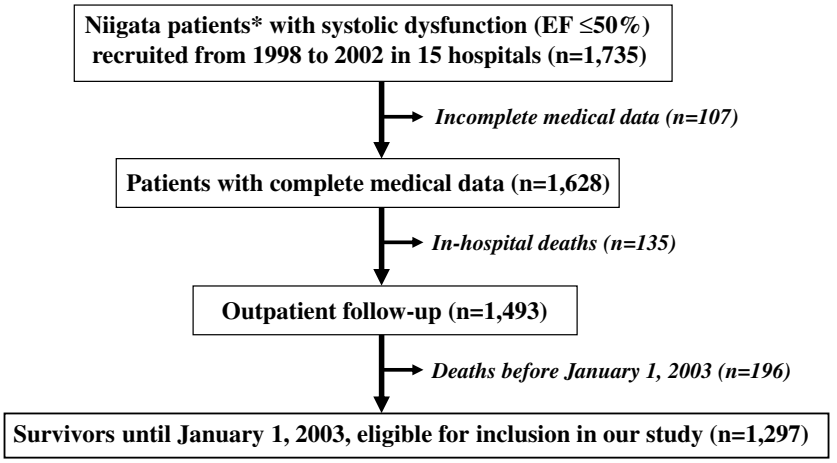

Fig 1. Flow chart of the Niigata-Sado Heart Failure Study, showing the process of extraction and follow-up of patients with left ventricular systolic dysfunction in Niigata City. EF, ejection fraction. *Patients with expected age range 45-84 years on January 1, 2003.

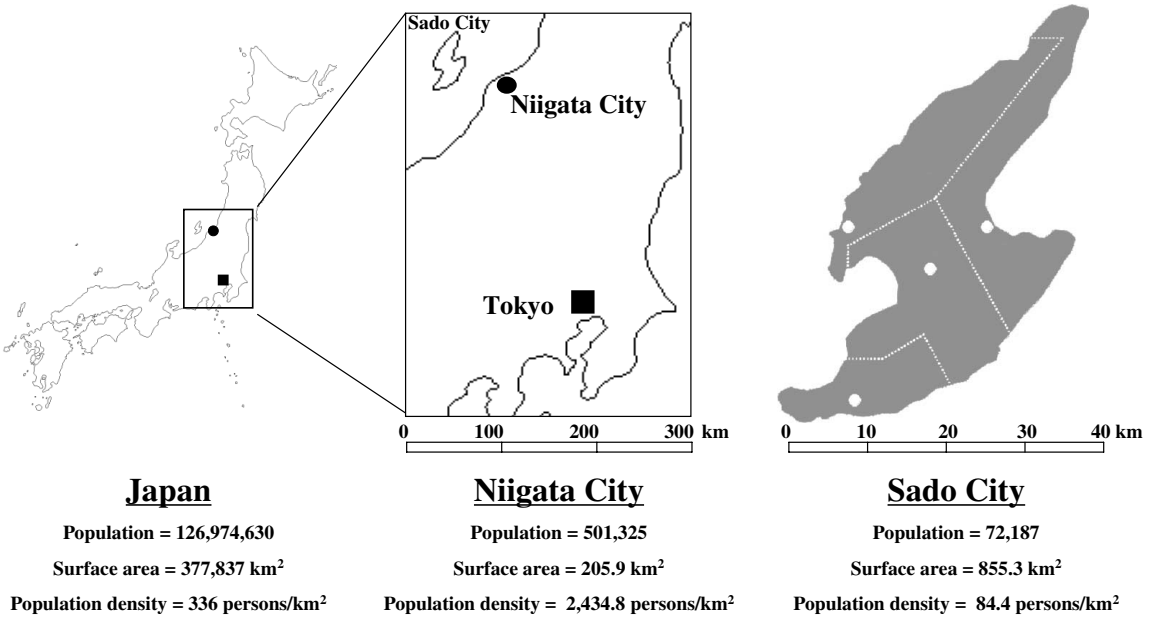

Fig 2. Map showing the locations and populations of Niigata City and Sado Island in Japan.

equipped centers in Niigata City. Over a period of 5 years (from January 1, 1998 through December 31, 2002), residents of Niigata City with LVSD (defined as ejection fraction (EF) ≤50% by 2-dimensionally guided M-mode measurements) were extracted from 87,953 Echo records available in these hospitals. The main indications for performing Echo in the study population included the following: the presence of symptoms suggestive of cardiac disease; after cerebrovascular or peripheral vascular emboli; to confirm signs found on physical examination (murmurs etc); to confirm electrocardiographic (ECG) abnormalities (ie, LV hypertrophy criteria, ST–T wave changes, abnormal Q-waves, bundle branch blocks, dysrhythmias etc); presence of cardiomegaly on chest X-ray; and any past or therapeu-

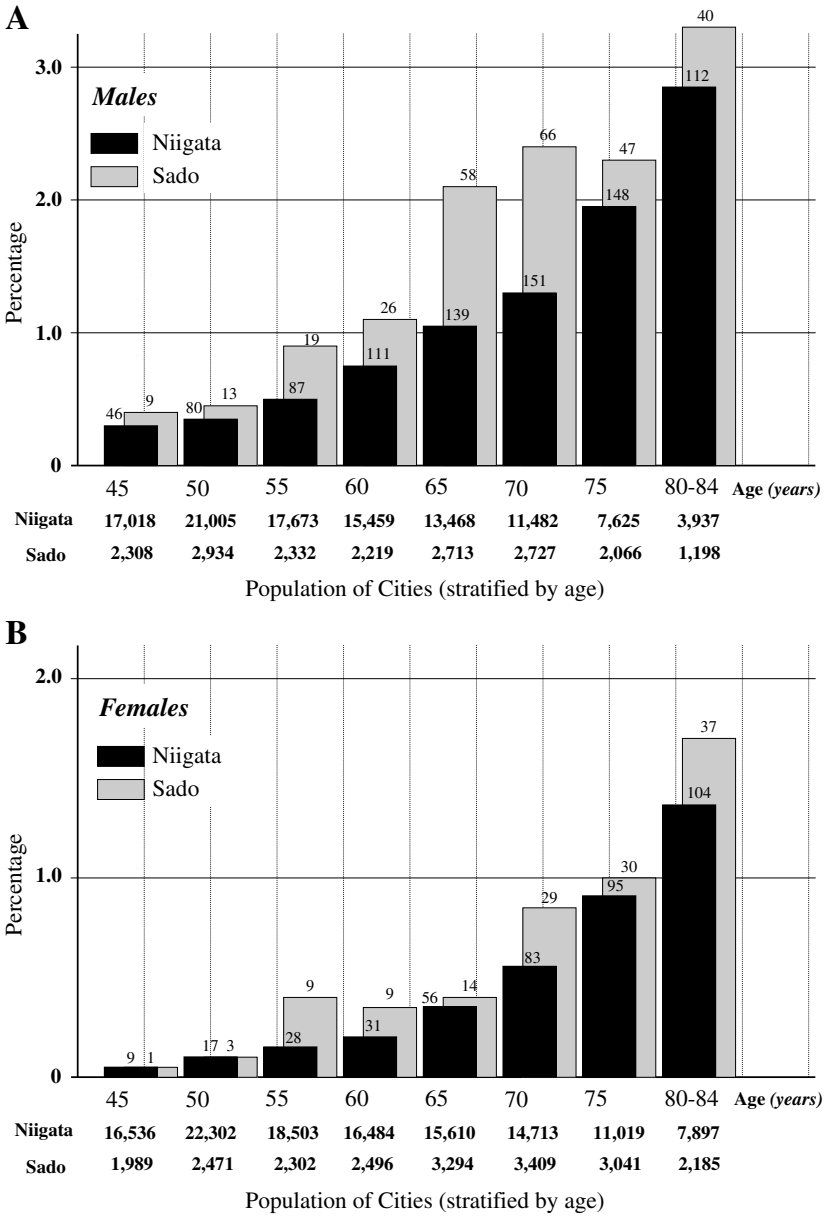

Fig 3. Bar graphs showing the distribution of cases of left ventricular systolic dysfunction in relation to ascending age groups (45–84 years) and the corresponding proportions of the population in each age interval, for males (A) and females (B), in Niigata City and Sado City on January 1, 2003.

tic history suggestive of cardiac dysfunction.

Initially, 1,735 participants with EF ≤50% were recruited, but we excluded some patients because of incomplete medical records (107), in-hospital death (135), or death before January 1, 2003 (196). Thus, 1,297 outpatients with LVSD were eligible for inclusion in this study (Fig 1).

Definition of Urban and Rural Areas

An urban area requires a minimum population density of 400 persons/km^2, in agreement with the data[7] shown in Table 1. In 1996, Niigata City was nominated as a core city by the Japanese Ministry of Internal Affairs and Communications. On the other hand, rural areas are sparsely settled places away from the influence of large cities; a typical case is Sado City, an isolated island that lies approximately 60 km off the nearest (Niigata) harbor (Fig 2).

Review of Cases and Collection of Data

All available medical records of the extracted LVSD patients were reviewed by 2 cardiologists. This information included data on demography, medical history, associated comorbidities, ECG and Echo data. Diagnosis of validated congestive HF (CHF) according to the Framingham criteria was also checked. If a patient consulted 2 or more institutions, all records at these institutions were reviewed. If the same patient was extracted twice or more in the Echo logs during the recruitment period, only the data on the first extraction was considered.

Determination of the Proportion of LVSD

We determined the proportion of LVSD in the general population of Niigata City using the following equation:[5]

$$\frac{\text{No. of LVSD survivors (45–84 years) up to January 1, 2003}}{\text{Estimated population of Niigata City (45–84 years) on January 1, 2003}} \times 100$$

The numerator represents the Echo-documented LVSD survivors extracted for the 5-year period as described. The

Table 2 Primary Etiologies of LV Systolic Dysfunction in the Study Patients, Stratified by Residence and Gender

Primary etiology	Niigata											
	Male (n=874)	Female (n=423)	p value (non-adjusted)	Adjusted for age			Niigata (n=1,297)	Sado (n=410)	p value (non-adjusted)	Adjusted for age and gender		
				OR (M/F)	95%CI	p value				OR (Niigata/Sado)	95%CI	p value
Ischemic heart disease	405 (46.3%)	123 (29.1%)	<0.001*	2.423	1.932–3.039	<0.001*	528 (40.7%)	139 (33.9%)	0.016*	1.414	1.115–1.794	0.004*
Hypertensive heart disease	201 (23.0%)	69 (16.3%)	0.007*	1.444	1.108–1.881	0.006*	270 (20.8%)	89 (21.7%)	0.752	0.964	0.734–1.265	0.792
Valvular heart disease	81 (9.3%)	80 (18.9%)	<0.001*	0.414	0.308–0.557	<0.001*	161 (12.4%)	56 (13.7%)	0.565	0.906	0.650–1.263	0.560
Dilated cardiomyopathy	108 (12.4%)	41 (9.7%)	0.188	1.144	0.817–1.602	0.433	149 (11.5%)	53 (12.9%)	0.485	0.815	0.580–1.144	0.236
Other	79 (9.0%)	110 (26.0%)	<0.001*	–	–	–	189 (14.6%)	73 (17.8%)	0.137	–	–	–

LV, left ventricular; CI, confidence interval; OR, odds ratio.

survivorship of patients up to January 1, 2003, was confirmed from their medical records. For those without records, we made direct phone calls to the patients' families or attending physicians. The denominator estimate was obtained from the Niigata Prefecture Department of Policy and Planning.[8]

Statistical Analyses

Data analyses were performed with SPSS for Windows version 15 (SPSS Inc, Chicago, IL, USA). Results for continuous data are expressed as mean ± standard deviation. Comparison of means of continuous variables across a variable with 2 levels was done by Student's t-test. Comparison of proportions was made by χ^2 or Fischer's exact test with the relevant test-for-trend. A 2-tailed significance level of 0.05 was used.

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

Proportion of LVSD in the Adult Population

We included 1,297 patients with LVSD (874 males, 67%) whose survivorship until January 1, 2003 was confirmed. Thus the proportion of LVSD in the population sector aged 45–84 years was 0.82% for males and 0.34% for females, a low estimate that is explained by the inclusion of relatively younger adults. However, the proportion in the elderly rose markedly to 1–2% of those aged ≥75 years. We found a significant positive increment trend for absolute counts and proportions of LVSD with increasing age (p-for-trend <0.0001) in both males (Fig 3A) and females (Fig 3B).

Primary Etiologies of LVSD

As shown in Table 2, ischemic heart disease (IHD) was the most prevalent etiology of LVSD in all cases (41%) and in both genders, followed by hypertensive (21%) and then valvular (12%) etiologies. The same order of frequency was found in Sado patients, but the ischemic etiology was significantly more frequent in the Niigata LVSD group (41% vs 34% for Sado). Ischemic and hypertensive etiologies prevailed more in males than in females, whereas the reverse was found for valvular causes.

Characteristics of LVSD Patients

The characteristics of the Niigata LVSD patients are shown after stratification by gender in Table 3, and in comparison with Sado patients in Table 4. Hypertension was the most prevalent comorbidity found in all cases (47%) and in both genders, followed by IHD (41%). On the other hand, previous hospitalization because of CHF was the second most prevalent comorbidity in females (37%) and the third most prevalent 1 in all cases (33%). Chronic atrial fibrillation was the most frequent arrhythmia and a prominent finding in these patients (34% of all cases; 34% of males, 32% of females). The prevalence of cerebral stroke was remarkable in LVSD patients (27% of all cases; 26% of males and 28% of females), as well as other psychiatric disorders such as depression and dementia (13% of patients). Approximately 1 in 2 patients had undergone coronary angiography, and 1 in 5 had undergone percutaneous

Table 3 Clinical Characteristics of Niigata LVSD Survivors (Until January 1, 2003) Stratified by Gender, Before and After Adjustment for Age

	Males (n=874)	*Females (n=423)*	*p value*	*Adjusted for age*		
				OR (M/F)	*95%CI*	*p value*
Demographic data						
Age (years)	*67.9±10.2*	*72.5±9.5*	*<0.001**	–	–	–
≥70	*411 (47.0%)*	*282 (66.7%)*	*<0.001**	–	–	–
≥65	*476 (54.5%)*	*307 (72.6%)*	*<0.001**	–	–	–
Anthropometric/medical measurements						
Body mass index (kg/m²)	*23.3±3.2*	*21.8±3.6*	*0.004**	*1.117*	*1.075–1.161*	*<0.001**
Systolic blood pressure (mmHg)	*128.7±16.7*	*130.8±15.3*	*0.023**	*0.994*	*0.986–1.001*	*0.089*
Diastolic blood pressure (mmHg)	*75.1±10.2*	*73.5±9.4*	*0.006**	*1.010*	*0.997–1.022*	*0.124*
Associated comorbidities and their management						
Cardiovascular risk factors/chronic medical illnesses						
Hypertension	*423 (48.4%)*	*182 (43.0%)*	*0.079*	*1.307*	*1.028–1.660*	*0.029**
Diabetes mellitus	*301 (34.4%)*	*99 (23.4%)*	*<0.001**	*1.680*	*1.283–2.201*	*<0.001**
Dyslipidemia	*227 (26.0%)*	*117 (27.7%)*	*0.563*	*0.807*	*0.616–1.057*	*0.120*
Cardiac disorders						
Previous hospitalization because of HF	*266 (30.4%)*	*156 (36.9%)*	*0.024**	*0.821*	*0.639–1.056*	*0.125*
Angina pectoris	*91 (10.4%)*	*27 (6.4%)*	*0.024**	*1.752*	*1.114–2.755*	*0.015**
Myocardial infarction	*316 (36.2%)*	*94 (22.2%)*	*<0.001**	*2.140*	*1.628–2.814*	*<0.001**
Arrhythmias						
Atrial fibrillation	*301 (34.4%)*	*134 (31.7%)*	*0.355*	*1.223*	*0.949–1.577*	*0.120*
Ventricular tachyarrhythmia	*17 (1.9%)*	*14 (3.3%)*	*0.189*	*0.573*	*0.275–1.195*	*0.138*
Cardiac surgery/intervention						
Cardiac valve replacement	*22 (2.5%)*	*16 (3.8%)*	*0.275*	*0.564*	*0.288–1.107*	*0.096*
Diagnostic coronary angiography	*520 (59.5%)*	*169 (40.0%)*	*<0.001**	*2.091*	*1.642–2.663*	*<0.001**
Percutaneous coronary intervention	*196 (22.4%)*	*49 (11.6%)*	*<0.001**	*2.147*	*1.524–3.023*	*<0.001**
Coronary artery bypass graft operation	*101 (11.6%)*	*25 (5.9%)*	*0.002**	*2.143*	*1.352–3.395*	*0.001**
Neuropsychiatric disorders						
Cerebral stroke	*229 (26.2%)*	*119 (28.1%)*	*0.504*	*1.073*	*0.820–1.405*	*0.608*
Psychiatric illness	*89 (10.2%)*	*73 (17.3%)*	*<0.001**	*0.707*	*0.500–0.950*	*0.045**
Chronic kidney disease	*78 (8.9%)*	*30 (7.1%)*	*0.311*	*1.147*	*0.732–1.797*	*0.550*
Chronic obstructive lung disease	*49 (5.6%)*	*22 (5.2%)*	*0.868*	*0.680*	*0.411–1.126*	*0.134*
Malignancy	*124 (14.2%)*	*44 (10.4%)*	*0.069*	*1.811*	*1.244–2.638*	*0.002**
NYHA class						
I	*105 (12.0%)*	*68 (16.1%)*				
II	*460 (52.6%)*	*245 (57.9%)*	*0.004**	–	–	–
III	*304 (34.8%)*	*107 (25.3%)*				
IV	*5 (0.6%)*	*3 (0.7%)*				
Electrocardiographic data						
LV hypertrophy	*150 (17.2%)*	*73 (17.3%)*	*0.966*	*0.978*	*0.714–1.341*	*0.892*
Left bundle branch block	*32 (3.7%)*	*27 (6.4%)*	*0.039**	*0.635*	*0.371–1.087*	*0.098*
Right bundle branch block	*80 (9.2%)*	*30 (7.1%)*	*0.253*	*1.534*	*0.983–2.393*	*0.059*
Echocardiographic data						
Ejection fraction (%)	*41.6±8.2*	*41.5±8.3*	*0.907*	*1.002*	*0.987–1.016*	*0.828*
Fractional shortening (%)	*20.8±5.2*	*20.6±5.1*	*0.574*	*1.007*	*0.984–1.030*	*0.580*
LVDd (mm)	*55.7±8.2*	*51.8±8.1*	*<0.001**	*1.055*	*1.039–1.072*	*<0.001**
LV systolic dimension (mm)	*44.2±7.8*	*41.2±7.6*	*<0.001**	*1.048*	*1.031–1.065*	*<0.001**
IVST (mm)	*10.3±2.9*	*9.8±3.1*	*0.004**	*1.074*	*1.023–1.127*	*0.004**
PWT (mm)	*10.2±2.5*	*9.6±2.1*	*<0.001**	*1.129*	*1.062–1.200*	*<0.001**
LV mass index (g/m²)§	*137.3±54.6*	*132.9±64.6*	*0.202*	*1.001*	*0.999–1.004*	*0.224*
Left atrial diameter (mm)	*41.1±7.9*	*40.7±8.9*	*0.437*	*1.006*	*0.991–1.020*	*0.444*

The echocardiographic data were obtained upon initial diagnosis of LVSD. Values are expressed as mean ± standard deviation or number of subjects (%).
§LV mass (g) was calculated according to the method recommended by the American Society of Echocardiography [LV mass = 0.8×(1.04×[LVDd + IVST + PWT]³ –LVDd³) + 0.6] then was indexed to body surface area (m²); where LVDd = LV diastolic dimension (mm), IVST = interventricular septum thickness (mm), and PWT = posterior wall thickness (mm).
LVSD, LV systolic dysfunction; HF, heart failure; NYHA, New York Heart Association. Other abbreviations see in Table 2.

coronary intervention (PCI), whereas 1 in 10 proceeded to coronary artery bypass graft (CABG) operation.

Gender Comparisons

The proportion of LVSD in men was always greater than that in women of the same age group (Fig 3). However, the male/female odds for LVSD begin to converge from the lowest to the highest age group. As shown in Table 3, men acquired LVSD at younger ages than women (67.9±10.2 vs 72.5±9.5 years for women; p<0.001); approximately half (53%) of the men were aged under 70 years, and had a higher prevalence of diabetes than females (34% vs 23%; p<0.001). Also, IHD and consequently its management procedures, such as coronary angiography, PCI, and CABG, were more prevalent in men. On the other hand, previous CHF hospitalization and psychiatric illness were more common in women.

Urban (Niigata) vs Rural (Sado) Findings

The proportion of LVSD in Niigata was half that in Sado for all cases (0.56% vs 1.03%) and for each gender (0.82% vs 1.50% in males; 0.34% vs 0.62% in females). However, the proportion in the elderly ≥75 years was similar (1.5% for Niigata vs 1.8% for Sado in all patients: p=0.060; 2.3%

Table 4 Clinical Characteristics and Comparisons of LVSD Survivors (Until January 1, 2003) Stratified by Residence, Before and After Adjustment for Age and Gender

	Niigata (n=1,297)	Sado (n=410)	p value (non-adjusted)	Adjusted for age and gender		
				OR (Niigata/Sado)	95%CI	p value
Demographic data						
Age (years)	69.4±10.2	71.3±8.9	<0.001*	–	–	–
≥70	693 (53.4%)	294 (60.7%)	0.011*	–	–	–
≥65	783 (60.4%)	320 (78.0%)	<0.001*	–	–	–
Gender						
Male	874 (67.4%)	278 (67.8%)	0.923	–	–	–
Female	423 (32.6%)	132 (32.2%)		–	–	
Anthropometric/medical measurements						
Body mass index (kg/m²)	22.8±3.4	22.3±3.2	0.005*	1.040	1.004–1.077	0.028*
Systolic blood pressure (mmHg)	129.4±16.3	131.7±14.8	0.007*	0.991	0.984–0.998	0.014*
Diastolic blood pressure (mmHg)	74.6±9.9	75.5±7.8	0.041*	0.986	0.974–0.997	0.017*
Associated comorbidities and their management						
Cardiovascular risk factors/chronic medical illnesses						
Hypertension	605 (46.6%)	166 (40.5%)	0.033*	1.321	1.053–1.658	0.016*
Diabetes mellitus	400 (30.8%)	100 (24.4%)	0.015*	1.387	1.073–1.794	0.013*
Dyslipidemia	344 (26.5%)	79 (19.3%)	0.004*	1.440	1.092–1.899	0.010*
Cardiac disorders						
Previous hospitalization because of HF	422 (32.5%)	120 (29.3%)	0.239	1.219	0.954–1.559	0.114
Angina pectoris	118 (9.1%)	38 (9.3%)	0.995	0.994	0.676–1.463	0.978
Myocardial infarction	410 (31.6%)	113 (27.6%)	0.136	1.271	0.990–1.633	0.060
Arrhythmias						
Atrial fibrillation	435 (33.5%)	128 (31.2%)	0.418	1.147	0.902–1.458	0.263
Ventricular tachyarrhythmia	31 (2.4%)	7 (1.7%)	0.532	1.401	0.610–3.215	0.426
Cardiac surgery/intervention						
Cardiac valve replacement	38 (2.9%)	22 (5.4%)	0.029*	0.485	0.282–0.853	0.009*
Diagnostic coronary angiography	689 (53.1%)	203 (49.5%)	0.223	1.138	0.907–1.428	0.262
Percutaneous coronary intervention	245 (18.9%)	57 (13.9%)	0.026*	1.452	1.060–1.991	0.020*
Coronary artery bypass grafting	126 (9.7%)	26 (6.3%)	0.046*	1.616	1.040–2.509	0.033*
Neuropsychiatric disorders						
Cerebral stroke	348 (26.8%)	81 (19.8%)	0.005*	1.614	1.224–2.128	0.001*
Psychic illness	162 (12.5%)	53 (12.9%)	0.883	1.057	0.753–1.484	0.748
Chronic kidney disease	108 (8.3%)	36 (8.8%)	0.852	0.904	0.607–1.345	0.618
Chronic obstructive lung disease	71 (5.5%)	21 (5.1%)	0.879	1.171	0.707–1.942	0.540
Malignancy	168 (13.0%)	50 (12.2%)	0.752	1.180	0.838–1.662	0.343
Electrocardiographic data						
LV hypertrophy	223 (17.2%)	77 (18.8%)	0.508	0.898	0.674–1.198	0.465
Left bundle branch block	59 (4.5%)	23 (5.6%)	0.457	0.848	0.516–1.396	0.518
Right bundle branch block	110 (8.5%)	25 (6.1%)	0.146	1.509	0.960–2.369	0.074
Echocardiographic data						
Ejection fraction (%)	41.5±8.2	39.9±8.5	0.001*	1.022	1.009–1.035	0.001*
Fractional shortening (%)	20.8±5.2	20.7±6.5	0.801	1.003	0.983–1.023	0.758
LVDd (mm)	54.4±8.3	55.6±8.3	0.010*	0.979	0.966–0.993	0.003*
LV systolic dimension (mm)	43.2±7.9	44.2±8.2	0.022*	0.981	0.967–0.995	0.008*
IVST (mm)	10.1±3.0	10.2±2.9	0.557	0.990	0.954–1.026	0.576
PWT (mm)	9.9±2.4	10.2±2.3	0.060	0.995	0.912–1.001	0.048*
LV mass index (g/m²)	135.9±58.0	146.5±51.2	0.001*	0.997	0.995–0.999	0.002*
Left atrial diameter (mm)	40.9±8.3	42.3±8.9	0.008*	0.981	0.969–0.994	0.005*

Abbreviations see in Tables 2,3.

for Niigata vs 2.7% for Sado men: p=0.193; and 1.1% for Niigata vs 1.3% for Sado women: p=0.182). In comparison with Niigata, Sado patients were older, with lower body mass index (Table 4). They had a lower prevalence of comorbidities (hypertension, diabetes, dyslipidemia, and cerebral stroke) and a lower rate of undergoing advanced coronary procedures (PCI and CABG), but more frequent cardiac valve replacement. We found no significant difference between Niigata and Sado in the proportion of patients with previous CHF hospitalization. On multivariate logistic regression analysis, a higher prevalence of diabetes, dyslipidemia, and cerebral stroke was independently associated with Niigata residency, whereas a higher frequency of cardiac valve replacement was independently associated with Sado (Table 5).

Discussion

The key observations of this study are: (1) the frequency of LVSD increased proportionally with age; (2) LVSD was more common in males; (3) more frequent comorbidities were observed in LVSD patients in comparison with the general population; (4) differences in the characteristics of LVSD patients existed between urban and rural areas.

In the present study the proportion of patients with LVSD in the adult population sector aged 45–84 years was 0.82% for males and 0.34% for females (Fig 3). This proportion increased considerably in the elderly, reaching 2.3% of males and 1.1% of females aged ≥75 years. Prospectively, these figures are quite ominous, predicting an epidemic in those ≥75 years who will constitute >20% of the population

Table 5 Final Results of the Multivariate Stepwise Logistic Regression Model Used to Test the Independent Association of Comorbidities With the Type of Residency

	Association with Niigata			Association with Sado			p value
	β-coefficient	OR	95%CI	β-coefficient	OR	95%CI	
Diabetes	*0.318*	*1.374*	*1.033–1.827*	*–0.318*	*0.728*	*0.547–0.968*	*0.029**
Dyslipidemia	*0.356*	*1.428*	*1.079–1.890*	*–0.356*	*0.700*	*0.529–0.926*	*0.013**
Cerebral stroke	*0.417*	*1.518*	*1.153–1.999*	*–0.417*	*0.659*	*0.500–0.867*	*0.003**
Cardiac valve replacement	*–0.611*	*0.543*	*0.315–0.936*	*0.611*	*1.842*	*1.842–3.175*	*0.028**
Percutaneous coronary intervention	*0.301*	*1.351*	*1.014–1.798*	*–0.301*	*0.740*	*0.556–0.986*	*0.040**

Besides adjusting for age, gender, and body mass index, the initial variables entered included hypertension, diabetes, dyslipidemia, percutaneous coronary intervention, coronary artery bypass grafting, cerebral stroke, and cardiac valve replacement.
Abbreviations see in Table 2.

Table 6 Prevalence of Common Comorbidities in the General Population of Japan

Comorbidity	Males		Females	
	General population[a]	Present study	General population[a]	Present study
Hypertension[b]	*56.0%[22]*	*48.4%*	*60.0%*	*43.0%*
Diabetes[c]	*21.0%[23]*	*34.4%*	*12.0%*	*23.4%*
Dyslipidemia[d]	*17.0%[22]*	*26.0%*	*39.0%*	*27.7%*
Myocardial infarction[e]	*4.7%[22]*	*36.2%*	*3.0%*	*22.2%*
Atrial fibrillation[f]	*3.5%[22]*	*34.4%*	*2.1%*	*31.7%*
Cerebral stroke[g]	*12.0%[22]*	*26.2%*	*7.0%*	*28.1%*
Chronic kidney disease[h]	*2.0%[22]*	*8.9%*	*0.5%*	*7.1%*

[a]Population-based studies of subjects aged ≥70 years. [b]Arterial blood pressure ≥160/95 mmHg or drug therapy. [c]Hemoglobin A_{1c} ≥6.1% or drug therapy. [d]Total cholesterol >220 mg/dl or drug therapy. [e]Documented diagnosis. [f]Documented diagnosis by electrocardiography. [g]Self-reported (diagnosed by computed tomography or magnetic resonance imaging in our study). [h]Serum creatinine ≥2.0 mg/dl.

in Japan by 2050? Our estimate varies considerably from those for the USA 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)[10,11] Nevertheless, our estimate should be regarded as a minimum value, essentially lower than the true LVSD count, as it was based only on the number of outpatients who were confirmed by Echo to have LVSD. In fact, detailed comparison with other studies is difficult because of many factors (eg, geo-demographic, ethnic and methodological differences). However, the lower prevalence of myocardial infarction in the Japanese than in Western populations[12–14] may explain this low estimate.

The most frequent etiologies of LVSD in this study were myocardial ischemia, hypertension, and valvular lesions (Table 2). IHD has been identified as the etiological factor conferring the greatest relative risk for LVSD![15] Data from the SOLVD registry[16] indicates that IHD is the primary cause of HF (in 69% of patients), followed by hypertension (43%). In line with our results, it has been reported that the leading causes of HF are IHD and hypertension, whereas valvular lesions have become a less frequent cause![17,18]

In agreement with previous studies![15,19–21] our results confirm that LVSD is more common (at least double) in men than in women for all ages, consistent with the gender difference in the prevalence of IHD![19] This result may have practical importance, as it has been supposed that targeting individuals for more detailed assessment on the basis of gender, age, and history of IHD would detect a substantial proportion of the currently unrecognized cases of LVSD![19]

Comorbidity was a significant issue in LVSD patients in this study. The prevalence of the common comorbidities (apart from hypertension) was higher in the LVSD patients compared with the average prevalence in the general population in Japan[22,23] (Table 6). The impact of comorbidities on LVSD patients derives from the following facts: (1) HF in elderly patients may have more nonspecific symptoms and signs because they are masked by the presence of comorbidities;[24] leading to diagnostic difficulties; (2) polypharmacy and more frequent drug side-effects;[25] (3) comorbidities that may be overlooked during routine management of HF have a great impact on hospital admissions;[26] which is significantly related to a number of these chronic conditions.[27] Therefore, if these comorbidities could be better recognized and managed, outcomes for LVSD patients may be greatly improved.

We previously reported the proportion and characteristics of LVSD patients in Sado City,[5] a rural Japanese community; however, those results may not directly translate to other communities in Japan, because of variations in population structure, dietary habits, lifestyle, and the quality of medical care. The proportion of LVSD in the general population (45–84 years) of Sado was found to double that of Niigata, in males and in females, which may be explained by the higher rate of performing advanced coronary procedures (PCI and CABG) in Niigata. However, we cannot exclude the possibility of referral bias in this setting, as the Sado estimates look more compact, which is because of the unique geo-demographic characteristics of Sado City, being an isolated island with healthcare resources limited to the hospitals from which the data were recruited (in contrast to Niigata City). Nevertheless, the similar proportion of LVSD in outpatients aged ≥70 years was a consistent finding in both areas.

The impact of urbanization and Westernized lifestyle on patients with LVSD could be deduced from the results, such as the higher prevalence of hypertension, diabetes, dyslipidemia, and cerebral stroke in the Niigata patients. Also, the availability of advanced medical care (PCI and CABG) was more pronounced in Niigata compared with rural Sado, but the rate of occurrence of CHF did not differ between

the 2 locations, reflecting the equality of basic health care. In accordance with our findings, it has been reported that the incidence of IHD is increasing more in urban than in rural areas of Japan;[28,29] because of the Westernization of diet in the former[28] and relatively higher fish consumption in the latter.[29] Moreover, Shiba et al reported differences in patient characteristics and comorbidities between urban and rural Japanese patients with CHF in the Tohoku District.[30] Finally, significant differences in plasma fatty acid composition and platelet aggregability have been reported between Japanese residents of a fishing village and a farming area;[31] presumably because of differences in long-term dietary habits between the people in these locations.

Study Limitations

First, and in addition to its cross-sectional design, this study was not population-based, but rather hospital-based, so we might have missed community dwellers with latent LVSD who had not been referred for Echo. However, we recruited the patients from all Echo-equipped centers in Niigata City in an attempt to maximize the inclusion of LVSD patients. Second, the literature has indicated gender differences in cardiac patients regarding consultation, examination, and treatment;[32] which our study could not reconcile.

Conclusions

The Niigata-Sado Heart Failure Study is a hospital-based project that aims to characterize patients with LVSD, and is considered to be the first complete enumeration survey of LVSD in urban Japanese community hospitals. As the proportion of LVSD increases with age, the public health burden of this condition is expected to inflate in progressively aging populations such as that of Japan. Comorbidities are common in patients with LVSD, so it is important to recognize these conditions and take them into consideration when selecting treatment for these patients. The differences in patient characteristics and disease patterns observed between urban and rural areas in this study suggest a more comprehensive strategy for HF management, tailored to urban and rural residencies.

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