A Community Based Epidemiological and Clinical Study of Hospitalization of Patients With Congestive Heart Failure in Northern Iwate, Japan

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Background Community based studies of congestive heart failure (HF) are lacking in the Japanese population. **Methods and Results** To delineate the epidemiological and clinical features of advanced HF in the general Japanese population, hospitalized adult cases of HF in all hospitals within the Ninohe district were registered for 3 years. During the survey period, 190 new onset cases (males n=93; females n=97) and a total of 391 hospitalizations (including repeat admissions) were registered. The prevalence of atrial fibrillation in new HF cases was 56% in males and 45% in females. On the basis of the population of the district, the incidence of hospitalized HF was 96 in males and 92 in females per 100,000 person-years. The percentage of HF patients who were ≥ 65 years of age was 82% in males and 94% in females. In cases undergoing echocardiography, preserved left ventricular systolic function (left ventricular ejection fraction $\geq 50\%$) was observed in 29% of males and 41% of females. There was a significant seasonal variation in HF admissions (Spring 32%; Summer 20%; Autumn 20%; Winter 28%; $p < 0.01$). **Conclusions** In comparison with published results of USA and European community based studies of HF, the present HF cohort showed that: (1) mean age, prevalence of preserved ejection fraction, and trends in seasonal variation were comparable; however (2) the incidence of HF was obviously lower. These epidemiological and clinical characteristics should be taken into consideration when establishing a therapeutic and preventive approach for HF. (Circ J 2007; 71: 455–459)

Key Words: Community; Epidemiology; Heart failure; Incidence; Population; Prevalence

Congestive heart failure (HF) is one of the most common reasons for hospital admission among the elderly in US and European populations^{1,2}. This increase in prevalence might be caused by rising mean age and improved survival of patients with cardiovascular disease because of therapeutic advances.^{3,4} Moreover, patients with HF are at high risk of readmission to hospital. In fact, surveys in the USA and Europe have reported that 16–50% of elderly HF patients are readmitted within 6 months of their first admission.^{2,5–7} As a consequence, HF has become an important public health problem, with increasing prevalence placing a growing burden on health-care systems in these countries.⁸

The mean age of the Japanese population is increasing steeply and it is estimated that by the year 2020 25% of the population will be ≥ 65 years of age. As observed in the USA and Europe, the HF epidemic might become evident in our population. However, there has been a deficiency of population or community based epidemiological studies in the Japanese population to date, leaving a gap in epidemiological data such as incidence, prevalence and prognosis of HF in this country. These data are not simply a matter of curiosity but will be essential for physicians, policy makers, economists, health-care administrators, and pharmaceutical manufacturers.

Although several epidemiological and clinical studies of HF in teaching hospitals have been published or are ongoing in this country,⁹ no adequate community based data have been reported. We have therefore collected prospective data on all registered hospitalized adult patients with HF over a 3-year period in the Ninohe district, a rural community in northern Iwate where medical facilities are limited and the population is relatively stable. On the basis of this registration survey, we have calculated hospitalization and readmission rates, seasonal variations, and the incidence of preserved left ventricular systolic function and atrial fibrillation in HF patients.

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Methods

Study Population

The Ninohe district is a rural area situated in the Iwate prefecture, northeast of Honsyu, Japan (Fig 1). The Ninohe district comprises the city of Ninohe, the towns of Ichinohe, Karumai and Jouboji, and the village of Kunohe. According to annual statistical data for 2003 issued by the Iwate prefecture government, this region had a resident population of 67,307 (32,257 males; 35,050 females). The percentage of the population aged ≥ 65 years was 26%. Following an in-

(Received October 10, 2006; revised manuscript received December 4, 2006; accepted December 21, 2006)

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Fig 1. Study area. Ninohe district of Iwate, northern Honshu, Japan.

tensive briefing on the rationale for the study and discussion of ethical issues, physicians representing all primary care and referral centers in the Ninohe district community agreed to participate. The district contains only 4 public hospitals (Ninohe, Ichinohe, Karumai and Ibonai Hospitals) and 7 private clinics with admission facilities. In addition, to ensure almost complete capture of all HF hospitalizations within the Ninohe district during the study period, registration was extended to include medical centers located in Morioka city (60 km south of Ninohe) including our University hospital and 3 referral medical centers located in Hachinohe city (50 km north of Ninohe). Approval was obtained from the ethics review board of each participating hospital prior to commencement of the study. Because the study protocol involved a review of charts obtained as part of routine medical care only, patient consent was not required.

Inclusion Criteria and Enrolment

Inclusion criteria were based on the Framingham definition of HF;¹⁰ with subjects assigned a diagnosis of HF if either 2 major criteria or 1 major and 2 minor criteria were present concurrently. The major criteria were: paroxysmal nocturnal dyspnea, orthopnea, abnormal jugular venous distention, rales, cardiomegaly, pulmonary edema, presence of a third heart sound, elevated central venous pressure, and weight loss of 4.5 kg or more in 5 days. The minor criteria included: edema, night cough, dyspnea on exertion, hepatomegaly, pleural effusion, tachycardia, and weight loss of 4.5 kg or more in 5 days.

Subjects were enrolled only if they had been hospitalized and fulfilled the following conditions: (1) were established residents of the Ninohe district; (2) were aged ≥ 20 years; and (3) were admitted between 1 April 2002 and 31 March 2005. Registration was initially performed by attending physicians at each hospital. Patients compatible with the diagnosis of HF in terms of symptoms, physical examination, chest X-rays, and response to treatment were checked by using a registration card after admission. Patients were excluded if they had been hospitalized: (1) to undergo invasive cardiac examination such as cardiac catheterization; (2) for the introduction of β -blocker therapy; (3) with an advanced stage malignant tumor and/or preceding apparent pneumonia; (4) within 4 weeks after onset of acute myocar-

Table 1 Comparison of Clinical Characteristics of Patients With Heart Failure Divided by Sex

	Male	Female	All
<i>No. (n)</i>			
New onset	93	97	190
Readmission	99	102	201
Total	192	199	391
<i>Mean age (years)</i>			
New onset	73.2 $\pm$ 12.7	80.1 $\pm$ 11.4	76.3 $\pm$ 13.3
Readmission	78.6 $\pm$ 10.4	82.0 $\pm$ 9.7	79.9 $\pm$ 10.7
Total	75.3 $\pm$ 12.2	81.0 $\pm$ 10.7	78.1 $\pm$ 12.3
<i>% of age ≥ 65 years</i>			
New onset	74	92	83
Readmission	90	95	92
Total	82	94	88
<i>% of age ≥ 80 years</i>			
New onset	32	63	48
Readmission	56	65	60
Total	42	64	53
<i>% of atrial fibrillation</i>			
New onset	56	45	50
Readmission	44	37	40
Total	53	44	48
<i>% of ejection fraction $\geq 50\%$</i>			
New onset	26	40	33
Readmission	33	46	32
Total	29	41	34

dial infarction; or (5) with end-stage renal failure and without apparent cardiac dysfunction.

To ensure that nearly all appropriate cases had been identified, we periodically retrieved and reviewed medical charts and/or discharge summaries for nearly all patients ($>99\%$) admitted to the cardiology and internal medicine wards of all hospitals within the study district. This was carried out by 2 or more members of the study steering committee, which comprised 3 cardiologists, 3 trained research nurses, and 2 epidemiologists. Patients who had been transferred to another hospital were counted on the index admission only. Echocardiographic evaluation such as left ventricular ejection fraction assessment (Simpson or Teichholtz method) was performed for all patients with HF at 1 hospital (Ninohe Hospital) by full-time attending cardiologists, whereas in the remaining hospitals, evaluation was performed by part-time cardiologists in a small percentage of patients only. The percentage of patients who underwent echocardiographic examination was 65%.

Data Analysis

Continuous variables are expressed as mean $\pm$ SD. Group comparisons were based on the Student's t-test or chi-square test, as appropriate. Incidence rates were calculated as the observed number of new cases of HF divided by the age- and sex-specific person-years of observation. An estimation of residents in the Ninohe district aged ≥ 20 years was derived from published census data at October 2003. In addition, the incidence rate was adjusted by using the standard Japanese population. Seasons were defined as follows: Spring=20 March to 19 June; Summer=20 June to 21 September; Autumn=20 September to 20 December; Winter=21 December to 19 March. The significance of seasonal variation was tested by the Roger's method.¹¹

Fig2. Incidence of heart failure according to the sex and 10-year age group.

Results

Registered Number of Patients

During the 3-year study period, the total number of HF patients including readmission cases was 391 (192 males; 199 females). This total included 190 cases of new onset (93 males; 97 females), yielding a readmission case of 51% in both sexes. There were no significant differences in the number of registered cases by year (2002, $n=118$; 2003, $n=149$; 2004, $n=124$; NS).

Patient Characteristics

The age range for new onset cases was 35–96 years in males and 28–98 years in females. As shown in Table 1, the mean age was significantly higher in females (81.0 ± 10.7 years vs males 75.3 ± 12.2 years; $p < 0.001$). Within the new onset cohort, 83% were ≥ 65 years of age (74% males; 92% females; $p < 0.01$), and 48% were ≥ 80 years of age (32% males; 63% females; $p < 0.01$).

Atrial Fibrillation

Atrial fibrillation was observed in approximately half of new onset cases (Table 1), with no significant difference between the sexes (56% males; 45% females; NS). Readmission cases showed a comparable trend (44% males; 37% females; NS).

Preserved Ejection Fraction

After exclusion of patients with significant valvular abnormalities, the percentage with a preserved left ventricular ejection fraction of $\geq 50\%$ was higher in females than in males (41 vs 29%). Thirty-four percent of registered cases were therefore classified as having HF with preserved ejection fraction. Among the new onset HF cases, the ejection fraction was preserved in 40% of females and 26% of males. A similar trend was observed in readmission cases (46% females, 33% males). The mean age of patients who underwent echocardiography was significantly younger than that of patients who did not (76.3 ± 12.5 vs 81.7 ± 10.0 years of age; $p < 0.01$).

Incidence

During the 3-year study period, 190 new cases of HF (93 male, 97 female) were diagnosed in the Ninohe district. The crude overall incidence rate was 94 per 100,000 person-years. Male subjects had a slightly higher crude incidence rate at 96 compared to female subjects at 92 per

Fig3. Incidence of heart failure according to sex and age below 65 years, ≥ 65 years, and ≥ 80 years.

Fig4. Seasonal variation in the accumulated number of hospitalizations for heart failure during the 3-year study period.

100,000 person-years. The age- and sex-adjusted incidence rate for the standard Japanese population was 39 per 100,000 person-years. Analysis of incidence rates by age and sex showed a general age-associated increase with male predominance (Fig 2). The incidence rate varied from less than 0.5 per 1,000 person-years in females aged under 65 years to 15 per 1,000 person-years in males aged ≥ 85 years. As shown in Fig 3, the incidence rates for elderly subjects (≥ 65 years old) were 3.05 per 1,000 person-years for males and 2.65 per 1,000 person-years for females. In the very elderly (≥ 80 years), rates were higher at 7.24 per 1,000 person-years for males and 6.76 per 1,000 person-years for females.

Seasonal Variation

The cumulative number of new hospitalized cases during the 3-year study period is shown in Fig 4. There was significant variation by season (Spring 37%; Summer 17%; Autumn 19%; Winter 27%; $p < 0.01$). Hospitalization rates in Spring and Winter were greater than 50% higher than in Summer and Autumn. This seasonal variation remained evident when the analysis was performed on all admission cases (including readmissions) (Spring 32%; Summer 20%; Autumn 20%; Winter 28%; $p < 0.01$).

Discussion

The present study was conducted in a rural Japanese community where the proportion of the population aged ≥ 65 years is similar to that predicted for the future Japanese population. We have demonstrated the following new observations: (1) a significant proportion of HF patients

were elderly (aged ≥ 65 years); (2) approximately half of HF cases showed atrial fibrillation at admission; (3) the prevalence of preserved ejection fraction was significantly higher in females than in males; (4) the incidence of HF was less than 100 per 100,000 person-years; and (5) there was seasonal variation with the onset of HF.

The median age of HF cases as a whole was just under 80 years, with a significantly higher mean age in females than in males. This is comparable to reports in other racial populations.^{12–14} Approximately half of the HF patients captured by the present study showed atrial fibrillation at admission. No previous community based study in Japan has reported the prevalence of atrial fibrillation in patients with HF. However, a similar rate has been reported in hospital-based studies.^{15,16} There is also evidence of racial variation in the prevalence of atrial fibrillation among patients with HF. Ruo et al have demonstrated that African-Americans had a 50% lower incidence of atrial fibrillation than Caucasians.¹⁷ As incidence rates of atrial fibrillation among Caucasian HF patients have been reported to range from 28 to 42%,^{18,19} the prevalence of atrial fibrillation in our patients with HF was somewhat higher than that in other racial populations. However, as atrial fibrillation was prevalent in males and the elderly,²⁰ sex- and age-adjusted analysis would be essential to determine the racial difference.

Of patients with HF who underwent echocardiography, half of the female cohort showed preserved ejection fraction while only a quarter of males did so. Although there are no previous reports of the incidence of preserved ejection fraction among HF patients in community based Japanese populations, the present value is comparable to that reported from other ethnic populations using the same partition value for left ventricular ejection fraction.^{21,22} However, of the potentially eligible patients in the present study, only 65 percent had a documented assessment of left ventricular ejection fraction. This might have resulted in a selection bias. The mean age of patients not undergoing echocardiography was higher than those who did undergo echo examination. As the incidence of preserved ejection fraction is greater in the elderly, this might have been underestimated in the present study.

The incidence of HF in our study community was less than 100 per 100,000 person-years for patients aged 20–65 years. The value rose to approximately 300 per 100,000 person-years in those aged ≥ 65 years, and approximately 700 per 100,000 person-year in those aged ≥ 80 years. However, these values are clearly lower than that of published data from the USA and European countries using the same definition of HF.^{23–26} The reasons for the low incidence of HF in our population remain unknown on the basis of the present study. However, as the main etiology of HF was recognized as coronary artery disease, 1 reason might be the low prevalence of coronary artery disease in the Japanese population.^{27–29} Alternatively, health-care systems differ between countries. Specifically, Japan has a universal health insurance system and most Japanese could visit medical facilities at relatively low cost. In contrast, in the USA, 15% of persons aged under 65 years are uninsured.³⁰ One may argue, however, that the system for capturing HF cases in the present study might have been incomplete, resulting in the underestimation of incidence. However, we did attempt to retrieve and review all medical charts or discharge summaries from cardiology and internal medicine wards of all hospitals located within the survey district. Moreover, to

further reduce the potential for missing cases, the study included several remote teaching hospitals and tertiary referral medical centers located within 100 km of the survey area. This makes it unlikely that a significant number of HF cases would have been lost to the present registry.

Our community based study revealed significant seasonal variation in the onset of new HF as well as acute worsening of the condition. The peak in variation was seen in Winter-Spring compared to Summer-Autumn. A similar seasonal variation has been reported from European countries.^{31–33} Although the precise reasons for this variation remain unknown, a potential explanation might be the presence of some other condition with a well-known seasonal variation such as respiratory tract infection, myocardial infarction and ischemia, or high blood pressure. Heart rate and systemic blood pressure have been reported to rise in cold environments, thus increasing cardiac oxygen consumption and cardiac afterload. This, in turn, might increase the onset of HF during the Winter-Spring season in a cold climate.

Despite the advantages afforded by our community based study, several limitations must be considered when the results are interpreted. First, registration was restricted to hospitalized patients so that HF patients treated at an out-patient clinic only might be missing from the registry, resulting in an underestimation of the incidence of HF. However, physicians are less likely to treat a severe HF patient without hospitalization as the Framingham criteria used in this study tended to capture relatively advanced HF. Second, this community based study was limited to the Ninohe district, a rural area in Northeast Japan, and might therefore be restricted in its generalizability to other areas in Japan. However, other ethnicities are very rare in the Japanese population (less than 2%), making the genetic background relatively homogeneous. Moreover, the percentage of the population aged ≥ 65 years in the survey area is identical to the value predicted for the Japanese population in 2020. In light of this, the present study results might assist our understanding of the future epidemiological setting of HF in this country. Third, as the determination of exact etiology of HF (ie, coronary artery disease, hypertensive heart disease, valvular heart disease, cardiomyopathy, myocarditis) by non-invasive examination in an epidemiological setting has been reported to be difficult,³⁴ we did not attempt to classify the etiology of HF in this study. Specifically, a predominantly elderly population is unlikely to be systematically examined in detail for possible coronary artery disease by coronary angiography or stress myocardial perfusion imaging. Finally, the present study did not evaluate the prognosis of HF, and thus could not compare the prognosis for Japanese patients with HF to that of other racial populations. Further community based studies using a follow-up design would be needed to answer this question.

In conclusion, when compared with USA and European community based studies of HF, the present HF cohort has shown that: (1) mean age, prevalence of preserved ejection fraction, and seasonal variability were comparable; however, (2) the incidence rate was obviously lower. These epidemiological and clinical characteristics should be taken into consideration when establishing therapeutic and preventive strategies for HF.

Acknowledgments

This study was supported, in part, by grant-in-aid no. 18590786 for the scientific research fund of the Ministry of Education, Science, and Culture of Japan, the Japan Arteriosclerosis Prevention Fund, and Open

Translational Research Center Project for our University.

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