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ORIGINAL ARTICLE
Epidemiology

Incidence Rate of Hospitalization for Heart Failure in a Japanese City

— An Updated Reference for Japan's Aging Society —

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Background: The prevalence of heart failure (HF) is increasing in aging societies, such as Japan. The current incidence rate (IR) of HF hospitalization in Japan is unknown.

Methods and Results: We conducted a regional population-based study assessing the IR of HF hospitalization in Nobeoka City. Data were collected over a period of 3 years from all patients with HF admitted for the first time to hospitals and clinics. 406 HF hospitalizations were registered (54% female; mean age 82 years). The IR of HF hospitalization was 129/100,000 person-years. The difference in the IR between women and men was not significant (131 vs. 127/100,000 person-years, respectively; P=0.767). The age-adjusted IR in the 2015 Japanese population was 105/100,000 person-years. According to 5-year age bands, the IR of HF hospitalization gradually increased up to 60–70 years of age, then increased rapidly in those aged ≥95 years for both sexes. The IR ratio compared with age <65 years was higher in women than men in each older age group.

Conclusions: In this population-based study, the current IR of HF hospitalization in a region of Japan was higher than the IR from another study conducted in a different region in early 2000. By presenting detailed age-related data, the research findings will contribute to estimating the number of HF hospitalizations in other areas of Japan.

Key Words: Heart failure; Hospitalization; Incidence rate; Japan

Heart failure (HF) is an emerging epidemic in aging societies.[1] HF is the primary cause of hospitalization in elderly people, and the prognosis of patients hospitalized with HF remains poor, with in-hospital mortality rate ranging from 4% to 7%, and 60- to 90-day mortality ranging from 7% to 11%.[2] Furthermore, in the US, hospitalizations account for 79% of lifetime costs of HF.[3] Therefore, hospitalization for HF is a major social problem in aging societies. To develop up-to-date healthcare strategies for the management of HF, a population-based study is needed to determine the epidemiological characteristics of hospitalization for HF, including its incidence rate.

Japan is at the forefront of aging societies and is facing an increase in hospitalization for HF. The Japanese Registry of All Cardiac and Vascular Diseases (JROAD) reported an increase in the number of patients hospitalized with HF.[4] In a different study, JROAD reported that 44% of the hospitalization costs for acute cardiovascular diseases were spent on patients with HF.[5]

However, more population studies of patients hospitalized with HF have been conducted in the US and Europe than in Japan.[6–12] A literature review identified a single Japanese population-based study[12] that reported the incidence rate of hospitalization for HF in 2002–2005. Considering Japan's increasingly aging population, the incidence rate may have changed since that study was conducted.

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Nobeoka Heart Study Investigators is presented in the **Appendix**.

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Table 1. List of all Public Hospitals or Private Clinics With Admission Facilities in the Study City

Hospital or clinic	No. beds	No. board-certified cardiologists	No. hospitalized HF patients
A (Miyazaki Prefectural Nobeoka Hospital)	410	4	181
B	72	0	117
C	108	0	70
D	76	0	13
E	195	0	9
F	125	0	6
G	76	1	5
H	17	0	2
I	19	0	2
J	7	0	1
K	80	0	0
L	19	0	0
M	54	0	0
N	57	0	0
O	93	0	0
P	52	0	0
Q	42	0	0
R	40	0	0
S	307	0	0
T	381	0	0
U	19	0	0
V	19	0	0
W	19	0	0
X	19	0	0
Y	19	0	0
Z	16	0	0

Nobeoka City, Japan, has a population of 120,000 and is relatively isolated from other urban centers, with medical care largely self-contained within the city. This provides a suitable environment to accurately estimate the incidence rate of diseases. In a previous study we reported the incidence rate of acute coronary syndrome in the city.[13] In the present study we collected data from all public hospitals and private clinics with admission facilities and conducted a population-based study to evaluate the incidence rate of hospitalization for HF in Nobeoka City.

Methods

Study Design

Nobeoka City is located in the east of Kyusyu Island and has a population of approximately 120,000 people (123,822 in 2015; 122,372 in 2016; 120,696 in 2017).[14] As of 2017, approximately 33% of the population of Nobeoka City was aged ≥65 years, which is greater than the percentage of Japan's population overall aged ≥65 years (28%).[15] Nobeoka City provides a highly suitable setting for epidemiological research because the city is relatively isolated from other urban centers and medical care is practically self-contained within the city. There is 1 public hospital (the Miyazaki Prefectural Nobeoka Hospital) and 25 private clinics with admission facilities in the city; all these hospitals were included in the present study (**Table 1**). Of the participating hospitals, only Miyazaki Prefectural Nobeoka Hospital and Hospital G employed board-certified cardiologists. Miyazaki Prefectural Nobeoka Hospital was registered as a certified hospital of the Japanese Circulation Society for the study period.

This study adhered to the principles of the Declaration of Helsinki and was approved by the institutional review boards of Miyazaki Prefectural Nobeoka Hospital (No. 20210628-4) and the National Cerebral and Cardiovascular Center (No. M30-007-6). Because patient data were anonymized, the requirement for consent was waived. However, we publicized the study by posting an easy-to-understand summary of the study on a board in Miyazaki Prefectural Nobeoka Hospital and on the hospital's website (https://nobeoka-kenbyo.jp/info/patient/20190215/1259/), thereby allowing patients to withdraw from the study.

Patient Identification

The study included consecutive adult patients (aged ≥20 years) with their first hospital admission for HF recorded between January 2015 and December 2017. Patients were enrolled in the study if they were established residents of Nobeoka City. In Miyazaki Prefectural Nobeoka Hospital, hospitalization for HF was identified using a 2-step process.[6,16] First, for case selection, the primary discharge diagnoses of the patients were reviewed using the International Classification of Diseases codes for HF (I50, I11.0, I13.0, I13.2).[17] Second, the complete records (including inpatient and outpatient records) of potential cases were manually reviewed to validate the diagnosis of HF using the Framingham criteria.[18] In the other hospitals and clinics,

Table 2. Incidence Rate of Hospitalization for HF in the Study City According to Age and Sex

	Men			Women			Men and women		
Age group (years)	Person-years (3 years)	Incident case	Incidence rate (per 100,000 person-years)	Person-years (3 years)	Incident case	Incidence rate (per 100,000 person-years)	Person-years (3 years)	Incident case	Incidence rate (per 100,000 person-years)
20–34	25,970	0	0 (0–14)	24,702	0	0 (0–15)	50,672	0	0 (0–7)
35–39	10,905	4	37 (10–94)	10,848	1	9 (0–51)	21,753	5	23 (8–54)
40–44	12,103	2	17 (2–60)	12,227	1	8 (0–46)	24,330	3	12 (3–36)
45–49	10,586	1	9 (0–60)	11,086	0	0 (0–33)	21,672	1	5 (0–26)
50–54	10,867	3	28 (6–81)	11,609	2	17 (2–62)	22,476	5	22 (7–52)
55–59	12,081	2	17 (2–60)	13,210	1	8 (0–42)	25,291	3	12 (2–35)
60–64	14,324	12	84 (43–146)	15,536	7	45 (18–93)	29,860	19	64 (38–99)
65–69	15,692	10	64 (31–117)	17,015	10	59 (28–108)	32,707	20	61 (37–94)
70–74	10,238	14	137 (75–229)	12,641	10	79 (38–146)	22,879	24	105 (67–156)
75–79	9,199	20	217 (133–336)	13,086	16	122 (70–199)	22,285	36	162 (113–224)
80–84	7,829	49	626 (463–827)	12,413	42	338 (244–457)	20,242	91	450 (362–552)
85–89	4,235	38	897 (635–1,231)	8,782	55	626 (472–815)	13,017	93	714 (577–875)
90–94	1,248	23	1,843 (1,168–2,765)	4,243	50	1,178 (875–1,554)	5,491	73	1,329 (1,042–1,671)
≥95	309	7	2,265 (911–4,668)	1,467	26	1,772 (1,158–2,597)	1,776	33	1,858 (1,279–2,610)
All ages (≥20 years)	145,586	185	127 (109–147)	168,865	221	131 (114–149)	314,451	406	129 (117–142)
Age-standardized incidence[A]	NA	NA	138 (84–227)	NA	NA	86 (55–142)	NA	NA	105 (75–148)

[A]Calculated using the Japanese model population in 2015. HF, heart failure.

all hospitalization records were checked to identify HF hospitalization cases using the Framingham criteria.

Elderly individuals were defined as those aged ≥65 years; these individuals were categorized into 3 groups as follows: young-old (aged 65–74 years), old-old (aged 75–84 years), and very old (aged ≥85 years).[5,19]

Echocardiographic evaluations were performed on patients diagnosed with HF at the Miyazaki Prefectural Nobeoka Hospital. The median duration between echocardiography and admission was 0.5 days (interquartile range [IQR] 0–2 days). Left ventricular ejection fraction (LVEF) was evaluated using standard procedures.[20]

Statistical Analysis

Continuous variables are expressed as the mean±SD, whereas variables with a skewed distribution are presented as the median with IQR. Categorical variables are expressed as numbers and percentages.

Using the annual population data of Nobeoka City, we calculated the crude incidence rate of hospitalization for HF according to age and sex distribution by dividing the number of cases admitted with HF for the first time by age- and sex-specific person-years of observation. In addition, the age-standardized incidence rate was obtained using a direct method based on the 2015 and 1985 Japanese standard populations.[21] The incidence rate ratio was estimated with Poisson regression.

Two-tailed $P<0.05$ was considered statistically significant. Statistical analyses were performed using SPSS version 24.0 (IBM, Armonk, NY, USA) and R statistical software version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

In all, 406 adults were admitted with HF for the first time during the 3-year study period. The mean patient age was 82±12 years, and 54% of the study participants were female. Of the 26 participating hospitals or clinics, 10 institutions had the capacity to provide inpatient treatment of HF, and more than half of all patients were admitted to institutions without board-certified cardiologists (**Table 1**). Among 166 (41%) who underwent echocardiographic examinations on admission, the mean LVEF was 44±14% and the proportion of HF with preserved ejection fraction (LVEF ≥50%), HF with mildly reduced

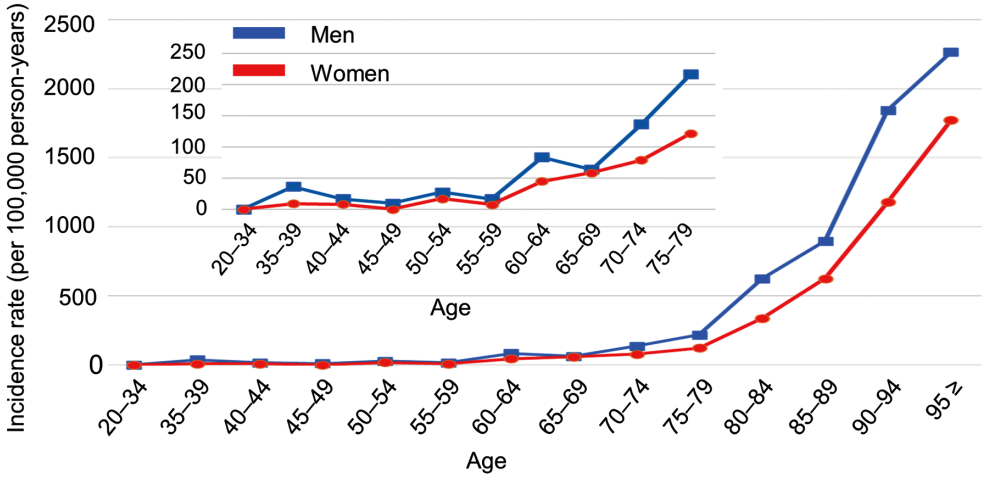

Figure 1. Incidence rate of hospitalization for heart failure (HF) in Nobeoka City according to age and sex. Inset, the incidence rate of hospitalization for HF in men and women aged <80 years.

ejection fraction (LVEF 40–50%), and HF with reduced ejection fraction (LVEF <40%) was 34%, 26%, and 40%, respectively.

The crude incidence rate of hospitalization for HF was 129/100,000 person-years (age ≥45 years, 183/100,000; age ≥65 years, 313/100,000; age ≥85 years, 981/100,000). Overall, the difference in the incidence rate between women (131/100,000 person-years) and men (127/100,000 person-years) was not significant (incidence rate ratio 1.03; 95% confidence interval [CI] 0.85–1.25; P=0.767). The age-adjusted incidence rate of hospitalization for HF for the standard Japanese population model of 2015 and 1985 was 105 (95% CI 75–148) and 39 (95% CI 26–65) per 100,000 person-years, respectively.

According to 5-year age bands, the incidence rate of hospitalization for HF increased gradually from 60 to 70 years of age and then increased rapidly, reaching an incidence rate of 2,265/100,000 person-years among those aged ≥95 years (**Table 2**; **Figure 1**). **Figure 2** shows the incidence rate ratios in older age groups compared with the non-elderly group (age <65 years) for both men and women. The 3 older age groups for both men and women had a significantly higher incidence rate of hospitalization for HF than the non-elderly group. The graph showing the incidence rate ratios for women is above that for men, suggesting that the effect of aging on the incidence rate of hospitalization for HF was more pronounced in women than in men (**Figure 2**).

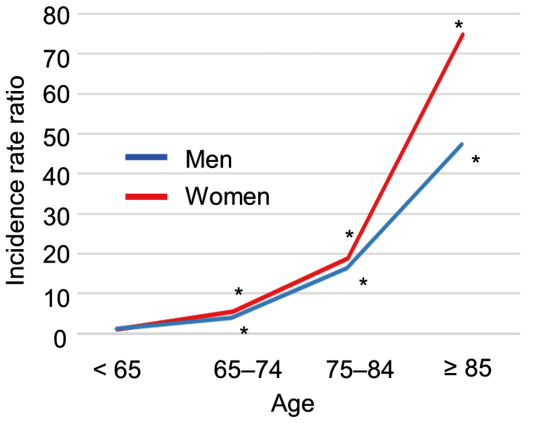

Figure 2. Incidence rate ratio based on the incidence rate of hospitalization for heart failure in a men and women according to age group. *P<0.001 compared with age <65 years.

Discussion

This study found that the incidence rate of hospitalization for HF in the study population was 129/100,000 person-years between 2015 and 2017. The incidence rates are provided in 5-year age bands by sex for reference to the current number of hospitalizations for HF in other regions of Japan.

Despite the differences in diagnostic criteria and population sources, the identified incidence rate of hospitalization for HF in this study is lower than in Western countries (**Table 3**). There are 2 possible reasons for this. The first factor to consider is ethnic differences. A population-based study that included individuals aged 45–65 years from 4 different communities in the US found that African Americans had a higher incidence rate of hospitalization for HF than Caucasians across most age groups.[7] Consistent with this, other studies have found that African Americans have a higher incidence rate of HF than Caucasians.[22,23] Furthermore, a multi-ethnic population-based cohort study of atherosclerosis, which included 6,814 Americans, found that Chinese Americans had a lower incidence of chronic HF (100/100,000 person-years) than African Americans (460/100,000 person-years), Hispanics (350/100,000 person-years), and Caucasians (240/100,000 person-years).[24] In the present study, the population was Japanese, and therefore racial differences between the present study and the studies conducted in Western countries need to be taken into consideration.

Table 3. Comparison of the Study Methods and Results Between Previous Population-Based Studies and the Present Study

Author(s)	Population source	Diagnostic criteria	Years	Incidence rate (per 100,000 person-years)		
				Total	Males	Females
Barker et al[6]	Individuals aged ≥65 years with health plan memberships for ≥2 years (9,272 people in 1970–1974; 31,399 people in 1990–1994), USA	Diagnostic codes (primary and secondary) confirmed by Framingham criteria	1970–1974	1,000	1,170	860
			1990–1994	1,130	1,270	1,180
Loehr et al[7]	Individuals aged 45–65 years from 4 communities without prevalent HF (population of 14,994), USA	Diagnostic codes (primary and secondary)	1987–1989	570		
Schaufelberger et al[8]	Residents of Sweden aged 45–84 years (population of 2,900,000)	Diagnostic codes (primary and secondary)	1988–2000		237–317	171–244
Jhund et al[9]	Residents of Scotland (population of 5,000,000)	Diagnostic codes (primary diagnosis)	1986–2003		105–162	101–160
Corrao et al[10]	Beneficiaries of the Italian National Health System from Lombardy (population of 10,000,000), Italy	Diagnostic codes (primary diagnosis)	2011	295	318	204
Goldberg et al[11]	Individuals aged ≥25 years who were residents of the Worcester, MA, metropolitan area (population of 478,000), USA	Diagnostic codes (primary and secondary) confirmed by Framingham criteria	2000	219	194	250
Ogawa et al[12]	Individuals aged ≥20 years who were residents of the Ninohe district (population of 67,307) Japan	Framingham criteria	2002–2005	94	96	92
Present study	Individuals aged ≥20 years who were residents of Nobeoka City (population of 120,000) Japan	Framingham criteria	2015–2017	127	131	129

The second factor is the lower prevalence of coronary artery disease in Japan than in Western countries.[25,26] Ischemic HF accounts for 33–57% of HF etiologies.[27] According to the MIYAGI-AMI Registry Study, the incidence rate of acute myocardial infarction is much lower in Japan (7.4 to 27.0/100,000 person-years) than in Western countries (Finland, 824/100,000 person-years; UK, 823/100,000 person-years; Canada, 605/100,000 person-years; US, 508/100,000 person-years; France, 314/100,000 person-years; Italy, 270/100,000 person-years).[25,28]

To the best of our knowledge, only 1 population study of patients hospitalized with HF has been conducted in Japan (**Table 3**). Ogawa et al investigated the incidence rate of hospitalization for HF in the Ninohe district, Japan, in 2002–2005.[12] The region had a resident population of 67,307, with 26% aged ≥65 years. The reported incidence rate of hospitalization for HF in that study (94/100,000 person-years) was lower than in the present study. However, the age-adjusted incidence rate for the standard Japanese population model of 1985 was 39/100,000 person-years, which is the same as our result of 39/100,000 person-years (95% CI 26–65). These findings suggest that the increasing incidence rate of hospitalization for HF in Japan can be attributed to aging. Moreover, the findings suggest that policies and medical developments in Japan over the past decade have not been sufficiently effective in reducing hospitalization for HF. However, differences in geology (e.g., temperature) and lifestyle between the 2 study regions may influence the incidence rate of hospitalization for HF. Therefore, it is difficult to discuss the longitudinal trends of hospitalization for HF in Japan based on these 2 studies alone. It is necessary to accumulate data from other regions.

Furthermore, our results show that HF was treated in many hospitals that did not have a board-certified cardiologist. This emphasizes the importance of a regional population-based study that includes all hospitals and clinics for the assessment of the epidemiological features of HF.

In the elderly group, although the incidence rate of hospitalization for HF was lower in females than in males (**Figure 1**), the incidence rate ratio compared with the non-elderly group was higher in females than in males (**Figure 2**), implying that the incidence rate of hospitalization for HF in non-elderly females was much lower than in non-elderly males. This could be reflected by a higher proportion of HF with a preserved ejection fraction in women[29] and the difference in the etiology of HF according sex: for example, HF in females has a lower correlation with ischemic etiology.[30] One of the major mechanisms underlying the low incidence rate of hospitalization for HF in non-elderly females may be cardioprotection elicited by sex hormones.[31] Specifically, estrogen promotes angiogenesis and vasodilation and reduces reactive oxygen species, oxidative stress, and fibrosis.[32]

Study Limitations

This study has some limitations. First, our study population (120,000) was smaller than that of previous studies conducted in Western countries.[8–11] However, the study was conducted in a region isolated from other areas and included approximately twice the size of the population in a previous Japanese study.[12] Second, the incidence rate of hospitalization for HF observed in this study may reflect genetic and/or environmental factors. The Japanese population is quite homogeneous and has the longest life expectancy.[33] However, the availability of comprehensive information

from Japan with its rapidly aging population may be a crucial factor in the development of future perspectives in other countries.

Conclusions

This population-based study explored the current incidence rate of hospitalization for HF in a region of Japan, which was higher than that in a previous study conducted in another region in early 2000.[12] By presenting detailed age-related data, the research findings will contribute to estimating the number of hospitalizations for HF in other areas of Japan.

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Disclosures

Y.M. is a member of *Circulation Reports*' Editorial Team. The remaining authors have no conflicts of interest to declare.

IRB Information

This study was approved by the Miyazaki Prefectural Nobeoka Hospital (No. 20210628-4) and the National Cerebral and Cardiovascular Center (No. M30-007-6).

Data Availability

The deidentified participant data will not be shared.

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Appendix

The Nobeoka Heart Study Investigators contributing to the present study are listed below:

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