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(Citation)
Circulation Journal,85(10):1860-1868

(Issue Date)
2021-09-24

(Resource Type)
journal article

(Version)
Version of Record

(URL)
https://hdl.handle.net/20.500.14094/90009513

Circulation Journal
Circ J 2021; 85: 1860–1868
doi:10.1253/circj.CJ-20-1154

Estimating Incidence of Acute Heart Failure Syndromes in Japan

— An Analysis From the KUNIUMI Registry —

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Background: Few registries have provided precise information concerning incidence rates for acute heart failure syndrome (AHFS) in Japan.

Methods and Results: All hospitals with acute care beds in Awaji Island participated in the Kobe University heart failure registry in Awaji Medical Center (KUNIUMI Registry), a retrospective, population-based AHFS registration study, enabling almost every patient with AHFS in Awaji Island to be registered. From 1 January 2015 to 31 December 2017, 743 patients with de novo AHFS had been registered. Mean age was 82.1±11.5 years. Using the general population of Japan as of 2015 as a standard, age- and sex-adjusted incidence rates for AHFS were 133.8 per 100,000 person-years for male and 120.0 for female. In 2015, there were an estimated 159,702 new-onset patients with AHFS, which was predicted to increase to 252,153 by 2040, and reach a plateau. The proportion of patients aged >85 years accounted for 42.6% in 2015, which was predicted to increase up to 62.5% in 2040. The proportion of patients with heart failure with preserved ejection fraction was estimated at 52.0% in 2015, which was predicted to increase gradually to 57.3% in 2055.

Conclusions: The present analysis suggested that the number of patients with de novo AHFS keeps increasing with progressive aging in Japan. Establishment of countermeasures against the expanding burden of HF is urgently required.

Key Words: Acute heart failure syndrome; Aging society; Heart failure with preserved ejection fraction

Heart failure (HF) has been recognized as a growing public health emergency because of the rapid increase in the number of patients, which is referred to as the "HF pandemic". In particular, the prevalence of HF has increased among elderly people.[1,2] According to data from World Population Prospects, the proportion of the population aged ≥65 years was 8.2% in 2015, and is predicted to rise to 11.0% by 2030.[3] In contrast, in Japan, the proportion of elderly people is predicted to increase from 26.6% in 2015 to 31.9% in 2030.[4] This rapid arrival of a super-aging society in Japan could lead to an explosive increase in patients with HF before the other industrialized countries. Determining the current and future status of HF in Japan may help to predict estimated incidence rates in other industrialized countries in the future.

In the USA and Europe, it has been reported that the annual incidence of patients hospitalized with acute HF syndromes (AHFS) was between 105 and 219 patients per

Received November 10, 2020; revised manuscript received December 23, 2020; accepted January 6, 2021; J-STAGE Advance Publication released online March 5, 2021 Time for primary review: 23 days

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ISSN-1346-9843

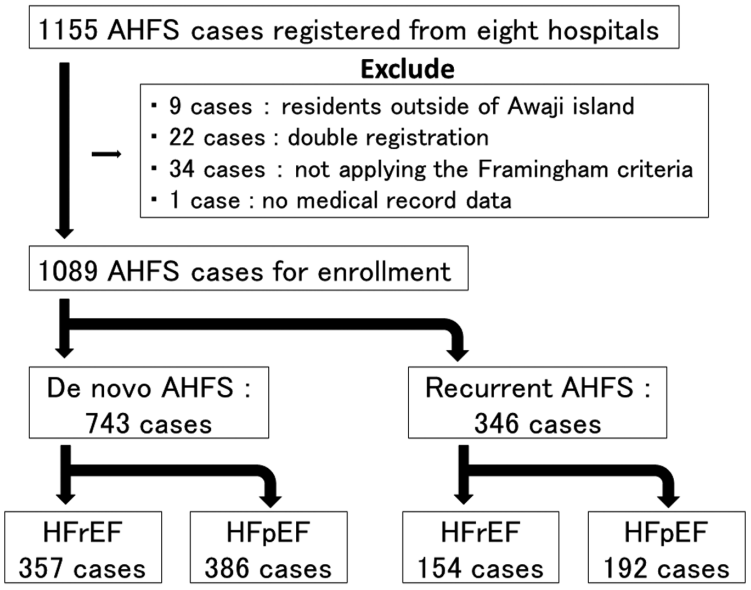


Figure 1. Flow chart of study recruitment of patients with acute heart failure syndrome is shown. Between January 2015 and December 2017, 1,155 patients were enrolled in the Kobe University heart failure registry in Awaji Medical Center (KUNIUMI).

Table 1. Comparison of Patient Characteristics for De Novo and Recurrent AHFS Cohorts

Incident cohort	All cases	De novo cohort	Recurrent cohort
Number	1,089	743	346
Mean age (year, ±SD)	81.9±11.2	82.1±11.5	81.4±10.6
Female, N (%)	545 (50.0)	376 (50.6)	169 (48.8)
Hypertension, N (%)	726 (66.7)	484 (65.1)	242 (69.9)
Diabetes mellitus, N (%)	304 (27.9)	188 (25.3)	116 (33.5)
Atrial fibrillation, N (%)	564 (51.8)	369 (49.3)	195 (56.4)
Mean LVEF±SD (%)	49.1±14.2	49.0±13.9	49.3±94.7
NYHA III or IV, N (%)	1,032 (94.8)	699 (94.1)	333 (96.2)

AHFS, acute heart failure syndrome; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD, standard deviation.

100,000, and that the incidence rate increased for those of more advanced ages.[1,2,5,6] In Japan, The Chronic Heart Failure Registry and Analysis in the Tohoku district-2 (CHART-2), the largest scale registry of HF in Japan, has demonstrated the increase in patients with chronic HF.[7] The Sado Heart Failure Study, based on data of outpatients with left ventricular dysfunction, predicted that the number of patients with HF will increase from 979,000 in 2005 to 1.3 million by 2030.[8] In contrast, Japan lacks exact data concerning the incidence of AHFS.

Awaji Island, one of the largest outlying islands in Japan, had a demographic structure that comprised 34.2% of the population aged ≥65 years in 2015, similar to the estimated proportion of the population aged ≥65 years in Japan in 2035. Moreover, Awaji Island is a semi-closed area with a low migration rate; therefore, higher-quality incidence and follow-up data can be compared with previous registry data. We undertook a multicenter, retrospective, population-based AHFS registration study on Awaji Island, referred to as the Kobe University heart failure registry in Awaji Medical Center (KUNIUMI Registry). We aimed to accurately identify the current incidence rate and characteristics of patients with AHFS on Awaji Island, including data obtained from hospitals where a board-certified physician of the Japanese Circulation Society (JCS) was absent, in order to predict what the incidence of AHFS in Japan may likely be in the future. Further, these predictions may provide helpful data to predict the future incidence of AHFS globally.

Methods

Study Population

The KUNIUMI Registry is a population-based registry of AHFS on Awaji Island in Japan. The AHFS definition followed 2017 JCS and Japanese Heart Failure Society (JHFS) guideline definitions for diagnosis and treatment of acute and chronic HF.[9]

Awaji Island is one of the largest isolated islands in Japan (**Supplementary Figure 1**), with an area of 593 km^2 and a population of 135,147 inhabitants (males, 64,245; females, 70,902), as reported in the 2015 census. Awaji

Table 2. (A) Characteristics and Outcomes for Patients With AHFS in Different Age Groups, (B) Characteristics and Outcomes for Patients With AHFS According to LVEF

(A)	≤64 years	65–84 years	≥85 years	P value*
Number	64	298	381	
Female (%)	23.4	39.6	63.8	<0.001
Comorbidities				
Hypertension (%)	64.1	61.1	68.5	0.107
Diabetes mellitus (%)	42.2	32.3	17.3	<0.001
Atrial fibrillation (%)	34.4	48.3	53.3	0.007
LVEF ≥50% (%)	36.2	44.0	65.0	<0.001
In-hospital mortality (%)	4.8	6.8	20.2	<0.001
Non-JCS (%)	6.3	15.8	35.2	<0.001
(B)		**LVEF <50**	**LVEF ≥50**	**P value****
Number		306	355	
Age (years, mean±SD)		79.1±12.0	84.1±10.4	<0.001
Female (%)		41.8	56.1	<0.001
Comorbidities				
Hypertension (%)		58.2	70.7	<0.001
Diabetes mellitus (%)		25.8	25.1	0.826
Atrial fibrillation (%)		48.7	52.1	0.381
In-hospital mortality (%)		4.9	8.8	0.049
Non-JCS (%)		15.4	29.9	<0.001

JCS, Japanese Circulation Society; Non-JCS, percentage of patients who were admitted to hospitals where a board-certified physician from the JCS was absent. Other abbreviations as in Table 1. *Cochran-Armitage trend test. **Chi-squared test, t-test.

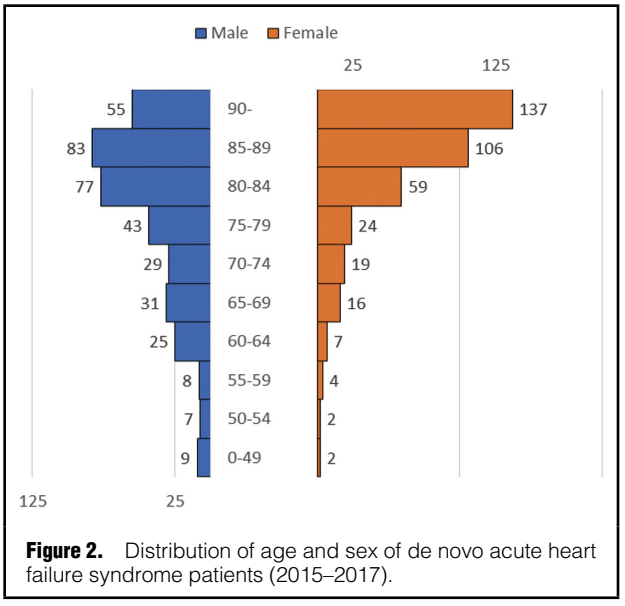


Figure 2. Distribution of age and sex of de novo acute heart failure syndrome patients (2015–2017).

Island also has one of the most aging populations in Japan and a low migration rate with a relatively stable population (in 2015, 0.53% of elderly persons moved to Awaji Island and 0.51% moved away) (Annual report).

Data Collection

The study area comprised 6 acute care hospitals (Awaji Medical Center, Seirei Awaji Hospital, Higashiura Heisei Hospital, Junshin Awaji Hospital, Sumoto Itsuki Hospital, and Nakabayashi Hospital). No other hospital in the area had an acute ward, other than one psychiatric specialist hospital. Therefore, these 6 acute care hospitals were selected for this registration study. In principle, no patients with AHFS had been transported off of the island by ambulance; therefore, almost all patients with AHFS were believed to have been hospitalized in 1 of the 5 acute care hospitals. However, as a limited number of patients with AHFS may have directly visited other medical centers located outside of the study area using their own cars or other forms of transport, the registration study was extended to include 2 hospitals located in the remote urban areas of Akashi and Naruto cities (Akashi Medical Center and Naruto Hospital) to capture such patients. All data were extracted from medical records from each of the 8 participating hospitals (**Supplementary Figure 2**). Among the participating hospitals, Awaji Medical Center, Akashi Medical Center and Naruto Hospital employ board-certified physicians of the JCS on a full-time basis.

From the 8 hospitals, patients hospitalized between January 2015 and December 2017 were screened according to whether the primary cause of admission included "heart failure". All patients were identified through medical records, and patients who did not meet the Framingham HF criteria were excluded.[10] Patients who had been transferred to another hospital were counted at the index admission only. Patients who lived outside of Awaji Island were excluded.

Ethical Considerations

This study conformed to the principles outlined in the Declaration of Helsinki. Approval was obtained from the Ethics Review Board of the Awaji Medical Center (approval no. 30-43), and each participating hospital was provided with the opportunity to opt out of the study

Table 3. Sex- and Age-Specific Incidence Rates for Patients With Acute HF Syndrome

Age (years) and sex	Awaji population	HF			HFpEF		
		n*	IR	95% CI	n*	IR	95% CI
Male							
0–49	30,606	3	9.8	3.2–30.4	1.7	5.6	1.3–25.0
50–54	3,882	2.3	60.1	16.7–216.9	0	NA	NA
55–59	4,287	2.7	62.2	18.7–206.6	1.3	31.1	5.7–169.8
60–64	5,279	8.3	157.9	80.1–311.3	3.4	64.6	22.3–186.7
65–69	6,179	10.3	167.2	90.9–307.7	2.5	40.4	11.7–139.6
70–74	4,309	9.7	224.3	119.4–421.4	2.4	56.1	15.9–197.9
75–79	3,522	14.3	407	242.5–683.0	5.5	156.5	67.9–360.7
80–84	3,134	25.7	819	556.2–1,205.8	12.1	386.1	219.8–678.3
85–89	2,008	27.7	1,377.80	949.2–2,000.0	16.8	837.9	519.6–1,351.1
≥90	835	18.3	2,195.60	1,389.2–3,470.2	11.7	1,405.2	792.9–2,490.2
Total	64,041	122.3	191	160.0–228.1	57.5	89.9	69.4–116.3
Age – adjusted rate**			133.8	109.4–158.1		59.5	43.7–75.3
Female							
0–49	30,458	0.7	2.2	0.2–24.1	0.3	1.1	0.0–32.6
50–54	4,105	0.7	16.2	1.5–179.1	0	NA	NA
55–59	4,499	1.3	29.6	5.4–161.8	0.6	12.4	0.9–171.3
60–64	5,393	2.3	43.3	12.0–156.1	0.7	12.4	1.1–136.3
65–69	6,259	5.3	85.2	36.5–199.1	1.5	24.4	5.0–119.1
70–74	4,868	6.3	13.1	59.7–283.5	3.3	68.5	23.4–200.3
75–79	4,414	8	181.2	90.6–362.4	6	135.9	61.1–302.6
80–84	4,537	19.7	433.5	278.6–674.4	10.2	224.8	121.7–415.2
85–89	3,654	35.3	967	695.4–1,344.7	23.9	655.4	439.1–978.2
≥90	2,546	45.7	1,793.70	1,342.1–2,397.2	30.2	1,185.1	829.4–1,693.2
Total	70,733	125.3	177.2	148.7–211.1	76.7	108.5	86.7–135.7
Age – adjusted rate**			120	98.7–141.4		71.9	55.6–88.3
Male and Female							
0–49	61,064	3.7	6	2.2–16.7	2	3.4	0.9–13.2
50–54	7,987	3	37.6	12.1–166.5	0	NA	NA
55–59	8,786	4	45.5	17.1–121.3	1.9	21.5	5.2–89.5
60–64	10,672	10.7	100	54.8–182.1	4.1	38.2	14.5–100.8
65–69	12,438	15.7	126	76.8–206.7	4	32.3	12.2–85.9
70–74	9,177	16	174.3	106.8–284.6	5.8	62.7	27.7–141.9
75–79	7,936	22.3	281.4	185.9–426.1	11.5	145.1	81.4–258.5
80–84	7,671	45.3	591	441.7–790.7	22.3	290.7	191.9–440.2
85–89	5,662	63	1,112.70	869.2–1,424.3	40.8	720.1	529.8–978.8
≥90	3,381	64	1,892.90	1,481.6–2,418.4	41.9	1,239.4	915.7–1,677.7
Total	134,774	247.7	183.8	162.2–208.1	134.3	99.6	84.1–118.0
Age – and sex – adjusted rate**			126.7	110.6–142.8		65.9	54.5–77.3

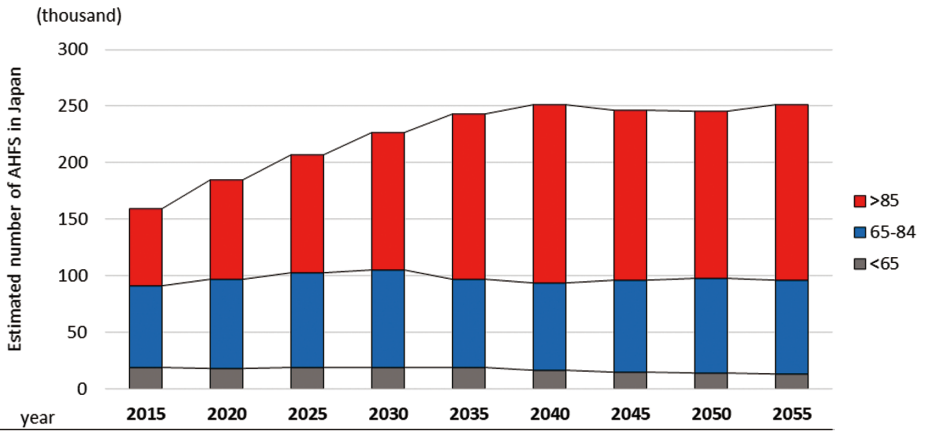
*Average number from 2015 to 2017. **Standardized for age and sex to the 2015 Japanese Population using direct method. HF, heart failure; HFpEF, heart failure with preserved ejection fraction; IR, incident rates; CI, confidence interval; NA, not available.

through a post on the hospital website. This study was registered as a retrospective study with the Protocol Registration System of the UMIN Clinical Trials Registry (UMIN000038637).

Statistical Analysis

Continuous variables were presented as mean±standard deviation (SD) and were compared using a t-test. Categorical variables were summarized as frequencies with percentages and were compared using the chi-squared test or Cochran-Armitage trend test.

The incidence rate for AHFS was estimated by the person-year approach (per 100,000 person-years) using 2015 vital statistics in Awaji Island. Incidence rate was standardized for age and sex using direct method with the 2015 Japanese general population. The 95% confidence intervals (CIs) and incidence rates were calculated using a Poisson distribution. We applied age- and gender-specific estimated de novo AHFS incidences in Japan from the KUNIUMI registry to the projected Japanese population in each age group and gender for the future until 2055, to provide a future estimate of the number of these patients. The projected numbers of Japanese patients were calculated by multiplying each ratio by the projected count of its corresponding population category, which was provided by population projections in the report of the Japanese



year	2015	2020	2025	2030	2035	2040	2045	2050	2055
Estimated number of AHFS (thousand)									
≥85	67.9	88.3	104.3	121.6	146.0	157.1	150.9	147.7	155.2
65-84	72.3	78.5	83.7	85.9	78.2	77.2	80.6	83.6	82.7
<65	19.0	18.3	19.0	19.3	18.8	16.8	15.2	14.1	13.6
Total	159.2	185.1	207.0	226.8	243.0	251.1	246.7	245.4	251.5
Population in Japan (million)									
≥85	4.9	6.1	7.2	8.3	9.4	10.2	9.7	9.7	10.2
65-84	28.7	30.0	29.9	28.8	28.0	29.0	29.6	28.7	26.7
<65	92.3	89.2	85.8	82.1	77.4	71.8	67.3	63.5	60.4
Total	125.9	125.3	122.9	119.2	114.8	111.0	106.6	101.9	97.3

Figure 3. The number of de novo acute heart failure syndrome (AHFS) patients in Japan was estimated by 5-year intervals from 2015 until 2055, using the Kobe University heart failure registry in Awaji Medical Center (KUNIUMI) data.

National Institute of Population and Social Security Research.[4] Furthermore, the number of patients with HF with preserved ejection fraction (HFpEF) in Japan was estimated using the annual number of patients with AHFS on Awaji Island through the same method. All tests were 2 tailed, and P<0.05 was considered statistically significant. SAS software version 9.4 (SAS Institute, Inc., Cary, NC, USA) was used for statistical analysis.

Results

Incidence of AHFS

A total of 1,155 patients who had been admitted for HF as the primary cause between January 2015 and December 2017 were identified (**Figure 1**). Of these, patients residing outside of Awaji Island (n=9) and double-registered patients (n=22) were excluded. We were unable to verify the medical records for 1 patient. We excluded patients for whom the Framingham HF criteria did not apply (n=34). Finally, 1,089 patients with AHFS were enrolled (**Figure 1**). Among them, 743 patients (68.2%) had been hospitalized for the first time due to AHFS (De novo cohort, **Table 1**).

Characteristics of Patients With De Novo AHFS

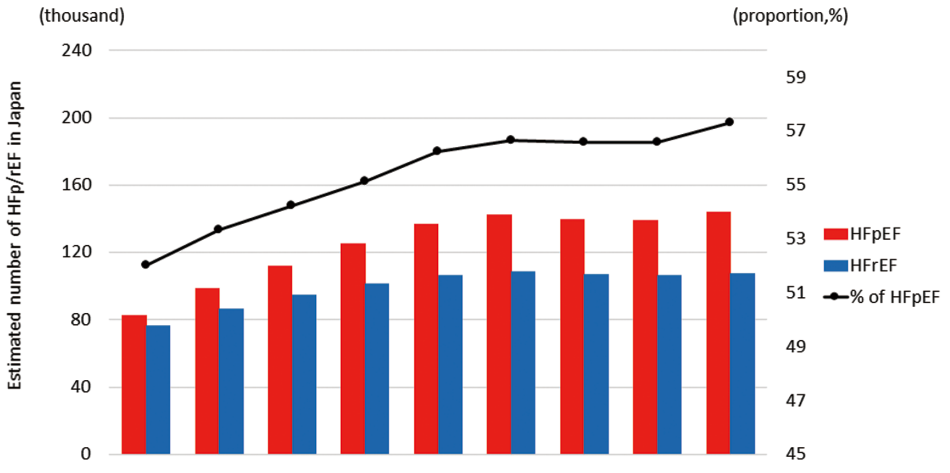
Of 743 patients with de novo AHFS, 50.6% were female. The mean age was 82.1±11.5 years (mean±SD) (**Table 1**). Clinical classifications concerning HF were found to be relatively severe, with 94.1% of patients classified with New York Heart Association stages III or IV (**Table 1**). **Table 2A** shows characteristics of patients with de novo AHFS according to age. Of 381 patients, 51.3% were ≥85 years. Of these patients, 63.8% were female and 65.0% had HFpEF, defined as left ventricular ejection fraction ≥50%; both proportions were significantly higher than that for younger patients (both P<0.001). In contrast, the prevalence rate of diabetes mellitus was significantly higher in patients aged <85 years (P<0.001). Elderly patients were admitted to hospital at a higher rate where a board-certified physician of the JCS was absent (P<0.001). In addition, in-hospital mortality was found to be associated with patients of increased age (P<0.001).

Table 2B shows characteristics of patients with de novo AHFS according to LVEF. Age, proportion of females, and prevalence of hypertension were significantly higher in patients with HFpEF (LVEF ≥50%) than those with HF reduced ejection fraction (HFrEF) (LVEF <50%) (all P<0.001). Patients with HFpEF were admitted to hospital at a higher rate where a board-certified physician of the JCS was absent and they also had high in-hospital mortality (P<0.001 and P=0.049, respectively).

Sex- and Age-Specific Incidence Rate for AHFS

Figure 2 shows the baseline age distribution for males and females with de novo AHFS. For males, the number of patients reached a peak between ages 85 and 89 years, whereas the number of patients kept increasing with age for females.

Table 3 shows the sex- and age-specific incidence rate of patients with AHFS. The incidence rate increased exponentially with advancing age in both males and females. AHFS incidence rates were 62 and 30 per 100,000 person-years for 55- to 59-year-old males and females, respectively, which



year	2015	2020	2025	2030	2035	2040	2045	2050	2055
Estimated number of HFpEF and HFrEF (thousand)									
HFpEF	82.8	98.8	112.2	125.1	136.7	142.3	139.6	138.9	144.1
HFrEF	76.4	86.4	94.7	101.8	106.4	108.9	107.1	106.5	107.4
% of HFpEF	52.0	53.3	54.2	55.1	56.3	56.7	56.6	56.6	57.3
Total population in Japan (million)									
	125.9	125.3	122.9	119.2	114.8	111.0	106.6	101.9	97.3

Figure 4. The number of heart failure preserved ejection fraction (HFpEF) or heart failure reduced ejection fraction (HFrEF) patients in Japan was estimated by 5-year intervals from 2015 until 2055, using the Kobe University heart failure registry in Awaji Medical Center (KUNIUMI) data.

increased to 2,196 and 1,794 per 100,000 person-years in patients aged ≥90 years. The incidence rates of HFpEF similarly increased with age in both sexes.

Incidence Rate and Estimated Number of Hospitalized Patients With De Novo AHFS in Japan

On Awaji Island, the 2015–2017 incidence rate of patients hospitalized due to de novo AHFS was 192 per 100,000 person-years for males and 177 for females per 100,000 person-years. The age- and sex-adjusted incidence rates for patients hospitalized due to de novo AHFS using the general population of Japan as of 2015 as a standard were 133.8 for males per 100,000 person-years and 120.0 for females per 100,000 person-years.

Figure 3 shows the estimated current and future number of patients hospitalized due to de novo AHFS in Japan from 2015 to 2055. In 2015, there were approximately 159,702 newly diagnosed patients with AHFS. The number of hospitalized patients with de novo AHFS is estimated to increase to 252,153 patients in 2040, and then reach a plateau. In this result, the proportion of patients aged >85 years accounted for 42.6% in 2015, predicted to increase up to 62.5% in 2040.

Estimated Number of Hospitalized Patients With HFpEF in Japan

Figure 4 shows the estimated number and proportion of HFpEF among hospitalized patients with de novo AHFS in Japan from 2015 to 2055. In 2015, 52% of AHFS patients (approximately 83,000 patients) were hospitalized due to HFpEF, increasing incrementally to 57.3% (144,000 patients) in 2055 (**Figure 4**). The percentage of HFrEF with AHFS is also expected to increase every year, but the increase rate tends to be lower and reaches a plateau earlier compared with that of HFpEF (**Figure 4**).

Discussion

The present analysis of retrospective, population-based data from the KUNIUMI registry revealed the features of hospitalized patients with AHFS in a super-aging society and, to our knowledge, estimated the current burden and future incidence rates of AHFS in Japan for the first time. Similar to Western countries, it has been assumed that a very large number of patients develops HF every year in Asia, including Japan.[11] Our study findings may provide helpful information for planning a strategy to manage the predicted 'HF pandemic' in the future.

Features of Patients With AHFS in the KUNIUMI Registry

Our study findings showed the actual current situation concerning patients with AHFS on Awaji Island, where the mean age of patients with de novo AHFS was 82 years, and 51.3% of patients with de novo AHFS were found to be aged ≥85 years. In contrast, in the Acute Decompensated Heart Failure Syndromes (ATTEND) registry, a multicenter cohort study of patients hospitalized for AHFS, the mean age was 73 years, and 20% of the patients were aged

≥85 years.[12] In the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD), the median age was 73 years,[13] and in the KICKOFF Registry, a community-based HF registry, the mean age was 78 years.[14] All of these registries had participant ages lower than that in the present study. Because it is thought that the proportion of the population aged ≥65 years on Awaji Island in 2015 is similar to that which is predicted for Japan in 2035, other regions in Japan are likely to follow similar trends in the future.

The proportion of females and the prevalence of HFpEF in elderly patients were significantly higher than that of younger patients in the present study. The ATTEND registry also found that elderly patients were more likely to be female and had a high HFpEF prevalence.[12] In contrast, the present study found that the prevalence of diabetes mellitus reduced significantly in elderly patients, which is also consistent with the findings of the ATTEND registry.[12]

We found that in-hospital mortality was significantly higher in patients aged ≥85 years than those in patients aged <85 years. It has been reported that greater board-certified cardiologist age/experience range is associated with a lower risk of in-hospital mortality.[15] The higher rate of admission of elderly patients to hospitals where a board-certified physician of the JCS was absent might account for the present findings.

Features of Patients With HFpEF in the KUNIUMI Registry

In this study, patients hospitalized due to HFpEF were older, more often females, and had a higher prevalence of hypertension. These findings were consistent with findings from previous studies.[16–18] In contrast, inconsistent with previous studies,[17,19] in-hospital mortality was significantly higher in patients with HFpEF than for those with HFrEF. In JCARE-CARD, in-hospital mortality of patients with HFpEF tended to be higher compared to patients with HFrEF, but this was not statistically significant.[17] In contrast, in-hospital mortality was higher in HFrEF patients than in HFpEF patients in the Kyoto Heart Congestive Failure (KCHF) Registry.[19] The discrepancy might be attributed to a difference in medical services for HF patients (e.g., the KCHF registry was mainly conducted in hospital facilities offering advanced cardiac therapies).[19] In contrast, on Awaji Island, Awaji Medical Center is the only one facility where board-certified physicians from the JCS are employed on a full-time basis. Under the relative shortage and uneven distribution of specialized medical services, patients with HFpEF in the present study were commonly admitted to hospitals where cardiovascular specialists were absent. Because patients with HFpEF were more likely to be older, the present study findings could pose challenges for health systems in an upcoming super-aging society.

Estimating Incidence of AHFS in Japan: Current and Future

We estimated the current and future incidence rate and total number for patients hospitalized with de novo AHFS in Japan. Age- and sex-standardized incidence rates of AHFS were 133.8 per 100,000 person-years for males and 120.0 per 100,000 person-years for females in 2015. The estimated number of hospitalized patients with de novo AHFS was approximately 160,000 in Japan in 2015, increasing to 250,000 patients until 2040 before reaching a plateau. The present study findings indicated that the number of patients with de novo AHFS increases with progressive aging in Japan, although the overall population is expected to shrink.[4] The total number of new-onset patients with AHFS in this study exceeded the numbers reported in the Japanese Registry of All Cardiac and Vascular Diseases (JROAD), a nationwide registry launched by the JCS.[20] In annual survey data from the JROAD, the total number of hospitalized patients with onset AHFS in Japan in 2015 was 97,526.[21] This discrepancy may be attributable to differences in data collection methods. In the JROAD, a response rate of both JCS training and associated-training hospitals was 100%, whereas that of non-JCS training hospitals was only 15.2% in 2015. In contrast, this study revealed that approximately 30% of patients with AHFS had been admitted in hospitals where a board-certified physician of the JCS is absent. Therefore, the number of patients with AHFS might be greater than those treated only in JCS training hospitals. Additionally, as Awaji Island is a semi-closed society, there was less probability of missing patients with HF. It is likely, therefore, that our study data reflect the current status in Japan.

The AHFS incidence rate in the present study increased with age for both males and females, which is consistent with findings reported in the Framingham study.[1] However, the AHFS incidence rate of patients aged ≥85 years in the present study seems to be lower compared with that of Western countries. In the Rotterdam Study, the incidence rate for HF was reported to be approximately 140 per 100,000 person-years in those aged 55–59 years, and approximately 4,740 per 100,000 person-years in those aged ≥90 years.[2] In the United States, it has been reported that an incidence rate for patients hospitalized with acute HF was 181 per 100,000 person-years in those aged 55–64 years and approximately 1,820 per 100,000 person-years in those aged ≥85 years.[6] One plausible reason is that the lower prevalence of predisposing factors for HF such as coronary artery disease might be related to the lower incidence of AHFS in Japan.[22]

Incidence of HFpEF in Japan

The proportion of HFpEF in patients with AHFS has been reported to range from 34% to 43% in Japan.[18,19,23] In Western countries, HFpEF has been reported to account for 34% of patients in the EuroHeart Failure Survey-2,[24] and 51% in the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) and the Acute Decompensated Heart Failure National Registry (ADHERE).[25,26] In the KUNIUMI registry, patients with HFpEF comprised 54.5%, and the proportion of patients with HFpEF increased with age, especially in those aged ≥85 years, where 65% of these patients had HFpEF. Based on the data from this registry, the proportion of patients with HFpEF in Japan was estimated at 52.0% in 2015, which was higher than what was reported in the previous studies.[18,19,23] Tragically, that rate will increase year-by-year up to 57.3% in 2055. This is a significant issue because effective treatment for patients with HFpEF has yet to be established.[27]

Study Limitations

This study had several limitations. We had no information about patients with minor HF who visited chronic care hospitals, as they were not subjects of this study; HF-related deaths occurring in the community may not have been recorded due to insufficient details; there may have been patients with secondary HF preceded by and recorded as

another disease. These limitations may have lead to an underestimation of the actual incidence of AHFS. We also had no information on patients being admitted to other hospitals outside of Awaji Island; however, we considered any underestimation in the incidence of AHFS due to such potential bias to be limited because no patients were transported from the island using the public ambulance service. Second, Awaji Island is an outlying island, which may not accurately represent a typical Japanese urban community. However, Awaji Island is located near large cities such as Kobe and Osaka, and the inhabitants can easily access urban areas; the island offers a reasonable model of the future Japanese population. Third, the estimation of future incidence rates concerning patients hospitalized with AHFS was undertaken on the assumption that the incidence of patients hospitalized with AHFS would remain constant in the future in Japan. It has been reported that the age-adjusted incidence of HF remained stable in men, but decreased in females in Japan.[28] Therefore, the number of patients hospitalized with AHFS in the future may differ when compared with our results.

Conclusions

The current Japanese population-based AHFS registry suggested that the number of patients with de novo AHFS increased dramatically with progressive aging in Japan. The present study findings re-emphasize the importance of public health measures needed to reduce the burden of HF in Japan and in other developing countries with rapidly aging populations.

Perspectives

Competency in Medical Knowledge: The present study findings reinforce an explosive increase in the number of patients hospitalized with AHFS in future Japan, based on accurate population-based data. The burden of patients with HFpEF or those aged >85 years will become increasingly higher.

Translational Outlook: Further evidence is needed to prevent developing HF, especially in high-aged patients. Furthermore, a new approach is required to improve the outcome of patients who are older or who have HFpEF.

Acknowledgments

The authors thank Masaru Kuroda of Akashi Medical Center, Katsuya Kuroda of Seire Awaji Hospital, Hiroyuki Kitagawa of Higashiura Heisei Hospital, Shoji Matsui of Junshin Awaji Hospital, Toshio Kasama of Sumoto Itsuki Hospital, Yoshiaki Nakabayashi of Nakabayashi Hospital, and Takashi Todoroki of Naruto Hospital for their participating in this study.

Sources of Funding

This study was carried out with no external funding.

Disclosures

K.H. is a member of *Circulation Journal*'s Editorial Team.

IRB Information

The Ethical Committee of Hyogo Prefectural Awaji Medical Center approved this study (approval number: 30-43).

Data Availability

The deidentified participant data will not be shared.

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Supplementary Files

Please find supplementary file(s);
http://dx.doi.org/10.1253/circj.CJ-20-1154