Advance Publication

Circulation Journal
doi:10.1253/circj.CJ-23-0350

ORIGINAL ARTICLE

Management and Outcomes of Acute Heart Failure Hospitalizations in Japan

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Background: Heart failure (HF) is a global burden on healthcare systems, but the literature regarding nationwide trends in the care and outcomes of HF hospitalization in Japan is limited. Therefore, we aimed to investigate the trends in patient characteristics, treatment patterns, and outcomes of patients hospitalized with acute HF.

Methods and Results: We used data from the Japanese Registry of All Cardiac and Vascular Diseases and the Diagnosis Procedure Combination database between April 2012 and March 2021 to analyze 840,357 patients aged ≥18 years who were hospitalized with an acute HF diagnosis. Over the study period (2012–2020), the mean (±standard deviation) age increased from 78.9 (±11.9) years to 80.9 (±11.8) years (P for trend <0.001), the proportion of female patients decreased from 48.7% to 47.5% (P for trend=0.02), crude in-hospital mortality rate decreased from 11.5% to 10.9%, and 30-day HF readmissions decreased from 7.4% to 7.0% (both P for trend <0.001). The reduction in outcomes was more apparent in the older age groups. The standardized outcomes demonstrated the same trends as the crude outcomes.

Conclusions: Our nationwide hospital admission analysis clarified that patients hospitalized with acute HF were getting older, but mortality and readmission rates also decreased, especially in older patients during the 2010s.

Key Words: Heart failure; In-hospital mortality rate; Japanese Registry of All Cardiac and Vascular Diseases and the Diagnosis Procedure Combination; Readmission

Despite advances in treatment strategies, heart failure (HF) is a leading cause of cardiovascular hospitalizations worldwide.[1,2] An estimated 64.3 million people have HF; its prevalence is 2.5% in the USA and 1–2% in European countries.[3–5] The burden of HF in aging societies, including developed nations, has increased. In Japan, older individuals (age ≥65 years) accounted for 28.7% of the total population in 2020, and the number of HF hospitalizations has increased over the years.[6]

In previous large-scale analyses of HF in the USA, the in-hospital mortality rate for HF in 2018 was 2.6%, with a modest decline seen in the all-cause death trend for patients with HF.[7,8] Other studies in European countries have also reported nationwide trends for readmissions and deaths in patients with HF.[9,10] However, the literature describing nationwide trends of care and outcomes of HF hospitalization in Japan is lacking, so the present study was designed to investigate the trends in patient characteristics, treatment patterns, and outcomes of patients with acute HF in Japan using a large real-world administrative database from 2012 to 2020.

Methods

Data Source

We used the Japanese Registry of All Cardiac and Vascular Diseases and the Diagnosis Procedure Combination (JROAD-DPC) database to study the trends in acute HF in Japan. JROAD-DPC is the claims database derived from the Japanese DPC/Per Diem Payment System, which is provided by the Japanese Circulation Society (JCS). This database contains claims data for hospitalizations related to cardiovascular diseases such as HF, coronary artery disease, and aortic diseases.[11,12] JROAD-DPC covered more than 1,000 JCS-certified (associated) training hospitals during the study period. It included patient information such as age, sex, body mass index, Charlson Comorbidity Index, New York Heart Association class, and diagnostic codes based on the 10th revision of the International Statistical Classification of Diseases (ICD-10) codes and outcome categories. This is an anonymized database that is not linked to other medical records and does not include detailed patient characteristics, such as

Received May 21, 2023; revised manuscript received August 28, 2023; accepted September 11, 2023; J-STAGE Advance Publication released online October 27, 2023 Time for primary review: 24 days

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ISSN-1346-9843

vital signs and test results. The JROAD-DPC database was merged with a hospital-level database (JROAD), which included hospital characteristics, such as the number of board-certified cardiologists and cardiology beds in each hospital.[13]

Study Design and Patient Selection

We conducted a retrospective analysis using JROAD-DPC to identify patients aged ≥18 years who were hospitalized with acute HF between April 2012 and March 2021. HF, defined by ICD-10 code I50, was used as the main diagnosis, admission-precipitating diagnosis, or most resource-consuming diagnosis. Among patients with HF, acute HF was defined as an emergency admission and additional disease codes of 30101 (acute HF) or 30102 (acute exacerbation of chronic HF). In a previous validation study, the positive predictive value of the diagnosis was 0.83.[14] Patients hospitalized with acute HF during the study period were included if they had multiple readmissions for acute HF. The number and characteristics of participating facilities are shown in **Supplementary Table 1**.

Study Outcomes

We examined the changes in patient characteristics, treatment patterns, and outcomes over the fiscal year. The study outcomes were in-hospital death, 30-day readmission, hospitalization costs, and length of hospital stay. In the 30-day readmission analysis, patients who were discharged alive were included, and those discharged in March (the last month of the fiscal year in Japan) were

Table. Trends in the Characteristics of Patients With Acute HF

Year	2012–2014	2015–2017	2018–2020
N	227,300	292,895	320,162
Age, years			
<65	26,220 (11.5)	29,625 (10.1)	30,355 (9.5)
65–74	36,645 (16.1)	46,343 (15.8)	46,517 (14.5)
75–84	77,967 (34.3)	95,684 (32.7)	101,073 (31.6)
≥85	86,468 (38.0)	121,243 (41.4)	142,217 (44.4)
Female	110,600 (48.7)	141,692 (48.4)	153,917 (48.1)
Body mass index, kg/m^2*	21.9 (19.4–24.8)	22.0 (19.4–24.9)	22.1 (19.5–25.0)
Charlson Comorbidity Index			
≤1	83,875 (36.9)	100,885 (34.4)	103,103 (32.2)
2	65,897 (29.0)	82,961 (28.3)	85,804 (26.8)
≥3	77,528 (34.1)	109,049 (37.2)	131,255 (41.0)
Barthel index at admission			
<90	77,015 (33.9)	101,784 (34.8)	111,967 (35.0)
≥90	56,906 (25.0)	73,701 (25.2)	83,487 (26.1)
Missing	93,379 (41.1)	117,410 (40.1)	124,708 (39.0)
Japan coma scale at admission			
Alert	185,323 (81.5)	233,979 (79.9)	250,612 (78.3)
Dizziness	29,938 (13.2)	44,175 (15.1)	53,643 (16.8)
Somnolence	5,677 (2.5)	7,485 (2.6)	7,910 (2.5)
Coma	6,362 (2.8)	7,256 (2.5)	7,997 (2.5)
NYHA class at admission			
I or II	65,646 (28.9)	37,985 (13.0)	13,236 (4.1)
III or IV	149,012 (65.6)	97,664 (33.3)	51,760 (16.2)
Missing	12,642 (5.6)	157,246 (53.7)	255,166 (79.7)
Comorbidities associated with HF			
Coronary artery disease	68,851 (30.3)	87,499 (29.9)	90,605 (28.3)
Valvular disease	31,317 (13.8)	41,962 (14.3)	45,747 (14.3)
Atrial fibrillation	65,670 (28.9)	99,712 (34.0)	114,555 (35.8)
Cardiomyopathy	10,920 (4.8)	13,166 (4.5)	12,897 (4.0)
Pulmonary hypertension	2,495 (1.1)	3,442 (1.2)	3,733 (1.2)
Congenital heart disease	1,449 (0.6)	1,845 (0.6)	1,740 (0.5)
Other comorbidities			
Hypertension	118,479 (52.1)	161,316 (55.1)	177,936 (55.6)
Diabetes	59,647 (26.2)	82,448 (28.1)	91,780 (28.7)
Dyslipidemia	39,220 (17.3)	62,755 (21.4)	77,820 (24.3)
COPD	9,075 (4.0)	13,129 (4.5)	14,528 (4.5)
Malignancy	11,554 (5.1)	16,863 (5.8)	20,097 (6.3)
Dementia	11,112 (4.9)	22,902 (7.8)	30,026 (9.4)

(**Table 1** continued the next page.)

Medications during hospitalization			
ACE inhibitors	52,990 (23.3)	73,005 (24.9)	81,239 (25.4)
ARBs	75,476 (33.2)	91,965 (31.4)	103,048 (32.2)
ARNIs	–	–	2,202 (0.7)
β-blockers	119,995 (52.8)	174,273 (59.5)	203,365 (63.5)
MRAs	101,143 (44.5)	133,483 (45.6)	153,763 (48.0)
SGLT2is	60 (0.03)	4,697 (1.6)	26,309 (8.2)
Ivabradine	–	–	753 (0.2)
Calcium-channel blockers	75,907 (33.4)	105,261 (35.9)	122,730 (38.3)
Thiazide	20,895 (9.2)	24,232 (8.3)	26,743 (8.4)
Loop diuretics	194,429 (85.5)	250,363 (85.5)	274,149 (85.6)
Tolvaptan	32,563 (14.3)	89,238 (30.5)	136,585 (42.7)
Oral antidiabetics	39,320 (17.3)	59,510 (20.3)	73,723 (23.0)
Insulin	36,062 (15.9)	45,735 (15.6)	50,690 (15.8)
Statin	59,397 (26.1)	84,936 (29.0)	105,087 (32.8)
Digoxin	23,227 (10.2)	18,863 (6.4)	15,940 (5.0)
Intravenous furosemide	169,111 (74.4)	220,995 (75.5)	247,366 (77.3)
Carperitide	94,968 (41.8)	98,789 (33.7)	79,299 (24.8)
Dobutamine	27,773 (12.2)	37,527 (12.8)	45,492 (14.2)
In-hospital treatments			
Oxygenation	176,786 (77.8)	223,278 (76.2)	236,818 (74.0)
Respirator or NPPV	46,776 (20.6)	65,276 (22.3)	68,319 (21.3)
Mechanical circulatory support	1,733 (0.8)	2,049 (0.7)	2,512 (0.8)
ICU or HCU	29,452 (13.0)	54,397 (18.6)	59,925 (18.7)
PCI	8,250 (3.6)	9,428 (3.2)	10,498 (3.3)
Cardiac rehabilitation	63,624 (28.0)	133,503 (45.6)	178,514 (55.8)
No. of board-certified cardiologists			
≤3	76,636 (33.7)	97,920 (33.5)	96,264 (30.1)
4–6	90,158 (39.7)	106,527 (36.4)	103,084 (32.3)
≥7	60,348 (26.6)	88,245 (30.1)	120,107 (37.6)
No. of cardiology beds			
≤30	69,009 (30.6)	88,222 (30.4)	96,742 (30.5)
31–60	134,006 (59.4)	174,100 (60.0)	186,581 (58.9)
≥61	22,715 (10.1)	27,866 (9.6)	33,377 (10.5)
Discharge destination			
Home	168,525 (74.1)	206,029 (70.3)	220,359 (68.8)
Hospital	20,756 (9.1)	30,107 (10.3)	36,512 (11.4)
Nursing facility	11,228 (4.9)	22,445 (7.7)	25,278 (7.9)
In-hospital death	25,248 (11.1)	31,704 (10.8)	34,830 (10.9)
Others	1,543 (0.7)	2,610 (0.9)	3,183 (1.0)

Data are presented as number (%) or median (interquartile range). *79,912 patients had a missing value for body mass index. ACE, angiotensin-converting-enzyme; ARB, angiotensin II receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; COPD, chronic obstructive pulmonary disease; CR, cardiac rehabilitation; HCU, high-care unit; HF, heart failure; ICU, intensive care unit; MRA, mineralocorticoid receptor antagonist; NPPV, non-invasive positive pressure ventilation; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

excluded. Because the JROAD-DPC database is updated annually, patient follow-up information may not be updated in the next fiscal year if hospitals do not provide the data. Hospital readmission was defined as admission to the same hospital as the index hospitalization because the JROAD-DPC database did not include follow-up data when patients were transferred to another hospital.

Statistical Analysis

Patient clinical characteristics are described as numbers and percentages for categorical variables or median and interquartile ranges for continuous variables. The study period was divided into 2012–2014, 2015–2017, and 2018–2020. Trends in patient age, sex, hospital-based HF medication use, and outcomes were described and analyzed using Cochran–Armitage trend test or Jonckheere–Terpstra test. Crude outcomes were analyzed by age and sex groups. The age- and sex-standardized in-hospital mortality and 30-day readmission rates were analyzed by the direct method using the standard population from the 2015 Japanese population census (age groups were categorized as ≤65, 65–74, 75–84, and ≥85 years). Two-sided $P<0.05$ was considered statistically significant. Data analysis was performed using Stata 17 (Stata Corp., College Station, TX, USA).

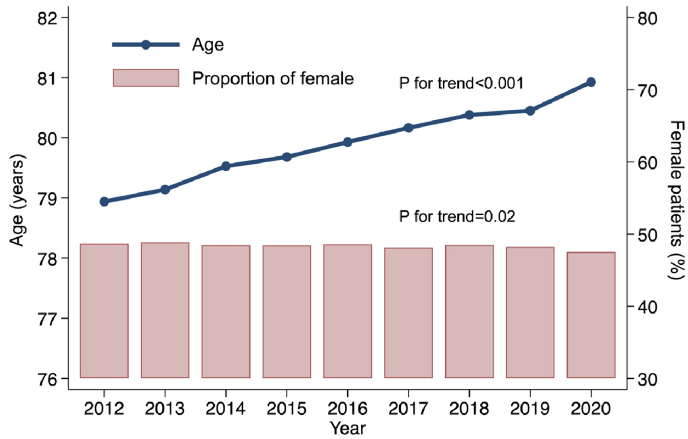

Figure 1. Trends for age and sex in patients with acute heart failure. Mean age of patients with acute heart failure increased during the study period (P for trend <0.001). The proportion of female patients decreased slightly during the study period (P for trend=0.02).

Ethics Approval

Ethics committees of the National Cerebral and Cardiovascular Center (registration no. R22021) approved the study protocol and this study was conducted in accordance with the Declaration of Helsinki.

Results

Trends in Patient Characteristics

During the study period, 840,357 patients hospitalized with acute HF were included in this study (**Table**, **Supplementary Table 2**). The mean (±standard deviation) age increased from 78.9 (±11.9) years in 2012 to 80.9 (±11.8) years in 2020 (P for trend <0.001, **Figure 1**). The proportion of female patients decreased slightly from 48.7% to 47.5% (P for trend=0.02). The proportion of patients with Charlson Comorbidity Index ≥3 increased from 34.1% in 2012–2014 to 41.0% in 2018–2020. The proportion of patients with atrial fibrillation, dyslipidemia, and dementia also increased during the study period. Regarding medical treatment, the use of *β*-blockers, sodium-glucose cotransporter 2 inhibitors (SGLT2i), tolvaptan, oral antidiabetics, and statins increased. The use of carperitide decreased during the study period. Furthermore, participation in in-hospital cardiac rehabilitation increased during the study period.

In the hospital-level analysis, the proportion of the use of HF medications (*β*-blocker, angiotensin-converting enzyme [ACE] inhibitor, angiotensin II receptor blocker [ARB], angiotensin receptor-neprilysin inhibitor, mineralocorticoid receptor antagonist [MRA], and SGLT2i) increased (P for trend <0.05) (**Figure 2**).

Supplementary Table 3 and **Supplementary Table 4** present the patient characteristics according to age and sex categories. Older patients had a lower Barthel index, higher proportion of valvular disease and atrial fibrillation, and a lower proportion of use of ACE inhibitors, ARBs, *β*-blockers, and MRAs.

Clinical Outcomes

During the study period, the length of hospital stay decreased (median: 18 days in 2012 and 17 days in 2020; P for trend <0.001), and median hospitalization costs increased from 0.78×10^6 yen in 2012 to 0.87×10^6 yen in 2020 for patients discharged alive (**Figure 3**). Length of hospital stay and hospitalization cost according to age and sex are shown in **Supplementary Table 5**.

The crude outcomes according to age and sex categories are shown in **Figure 4**. In-hospital mortality rate and 30-day all-cause emergency readmission were significantly reduced among older patients (aged ≥75 years, all P for trend <0.05). However, these proportions did not decrease among patients aged <65 years (all P for trend >0.05). In-hospital mortality and 30-day readmission rates were similar between the sex categories.

Figure 5 shows the trends in crude and standardized in-hospital mortality, 30-day emergency readmission, and 30-day HF readmission rates. The crude in-hospital mortality rate decreased from 11.5% in 2012 to 10.9% in 2020 (P for trend <0.001). Age- and sex-standardized in-hospital mortality rates also decreased, from 6.2% in 2012 to 5.7% in 2020 (P<0.001). Among patients who were discharged alive, the proportion of patients discharged home decreased while the proportion of patients transferred to a nursing facility increased (**Table**). The crude 30-day all-cause emergency and HF 30-day readmission rates decreased from 11.7% in 2012 to 11.2% in 2020, and from 7.4% in 2012 to 7.0% in 2020, respectively (P for trend <0.001). The standardized 30-day all-cause emergency readmission and HF readmission rates demonstrated the same trend (both P for trend <0.001).

Discussion

This large-scale observational study showed the temporal trends in the characteristics, treatment patterns, and outcomes of patients with acute HF. We found that (1) the age of patients hospitalized with acute HF increased and they had more comorbidities; (2) the length of hospital stay decreased slightly but hospitalization costs increased; and (3) in-hospital mortality and 30-day readmission rates decreased. This large-scale comprehensive presentation of the trends in HF care provides fundamental information for future research and resource planning.

The results of this study revealed that in-hospital mortality and 30-day readmission rates improved slightly during the study period. The decline in in-hospital deaths from acute HF was consistent with the results of prior studies completed in the USA and Germany.[15,16] Although the in-

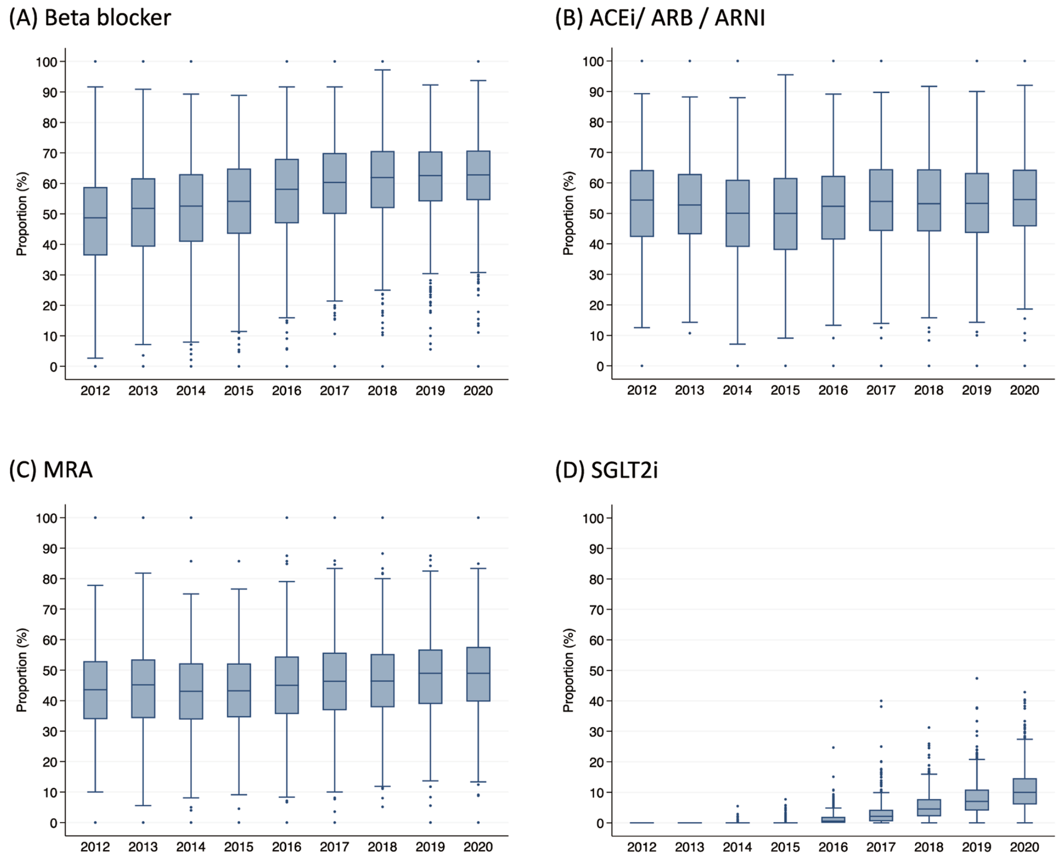

Figure 2. Distribution trends in hospital-level prescription for heart failure medications (**A**) β-blockers, (**B**) ACEis/ARBs/ARNIs, (**C**) MRAs, and (**D**) SGLT2is. The proportion of medication use increased during the study period (all P for trend <0.001). ACEi, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

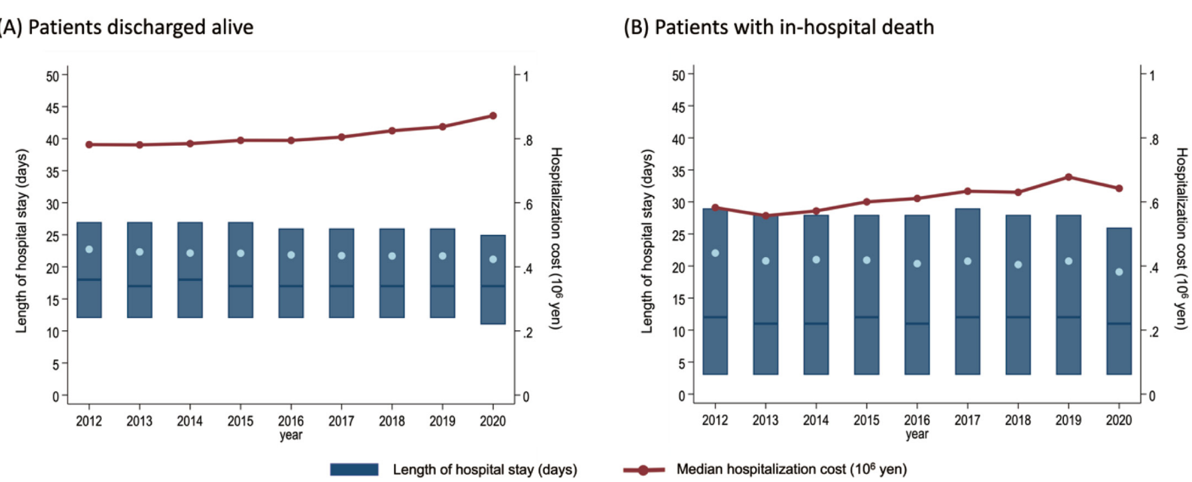

Figure 3. Trends in hospital stay and hospitalization costs for acute heart failure by prognosis at discharge. The box plot presents the median (interquartile range), with the right blue marker indicating the mean length of hospital stay. The median hospitalization cost is depicted by the red line. (**A**) Length of hospital stay slightly decreased, and hospitalization cost slightly increased during the study period for patients who were discharged alive (both P for trend <0.001). (**B**) Hospitalization costs slightly increased (P for trend <0.001), but the length of hospital stay was unchanged (P for trend=0.43) for patients who died during hospitalization.

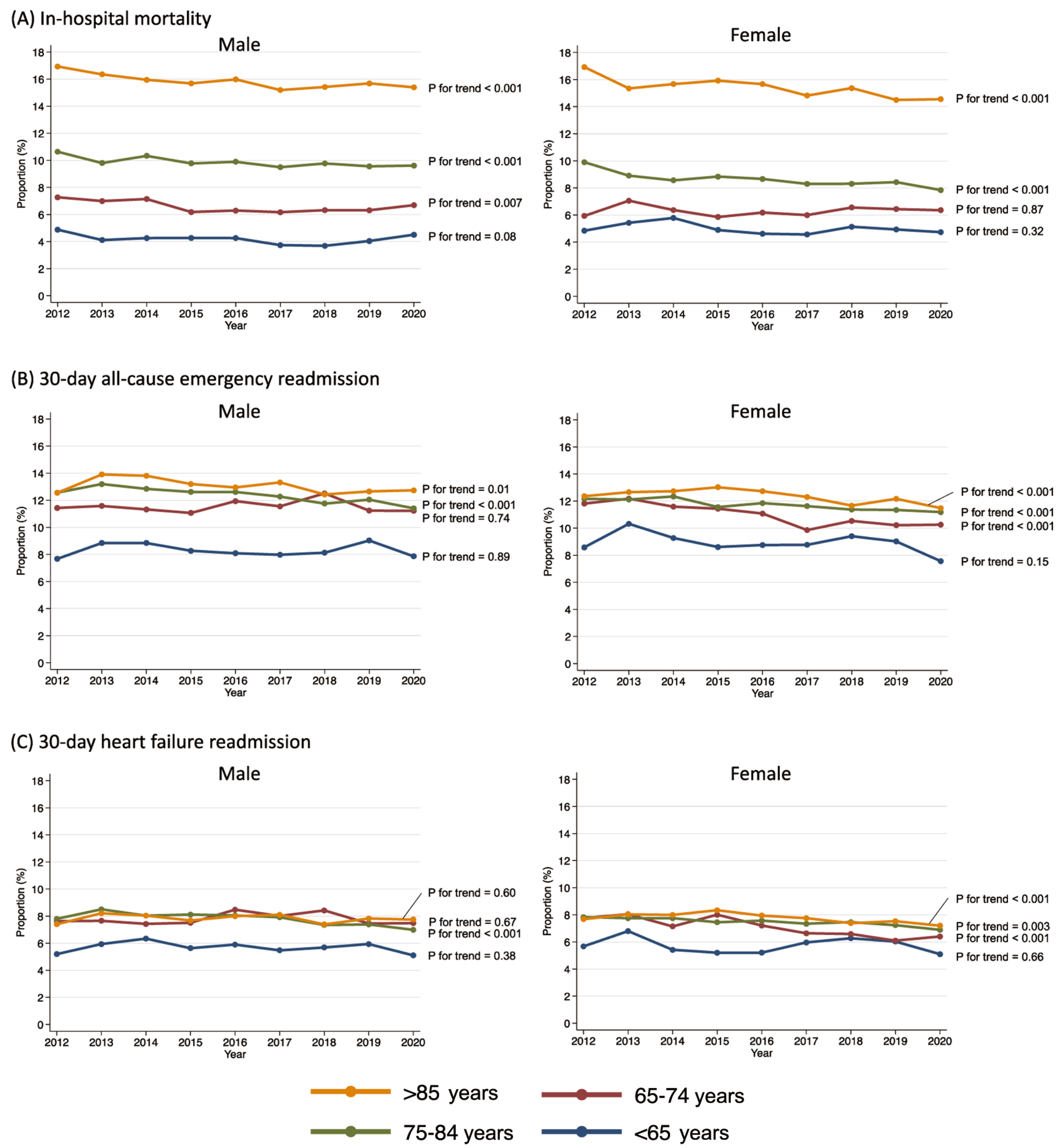

Figure 4. Trends in the in-hospital mortality and readmission rates for acute hear failure by age and sex. (**A**) Crude in-hospital mortality, (**B**) crude 30-day heart failure readmission and (**C**) crude 30-day emergency readmission. In-hospital mortality and 30-day all-cause emergency readmission rates reduced in older patients.

hospital mortality rate showed a decreasing trend, deaths had not substantially changed in the 2010s, with crude mortality at ≥10% during the study period in Japan. The prior hospital-based trends in HF in Japan demonstrated that the proportion of acute HF accounted for 51.2% among all patients with HF and in-hospital deaths among all HF patients did not change significantly during the study period.[6] Although prior studies showed that HF-related deaths significantly decreased until approximately 2010, current changes in this decline were modest,[17,18] comparable to our results. Additionally, although 30-day all-cause and HF-specific readmissions increased in the USA,[19] our study revealed a decreasing trend of readmission in Japan with a higher proportion of older patients. The longer average hospital stay in Japanese patients compared with other countries might be attributable to the reduction in readmissions, with increasing numbers of prescriptions for HF medications during hospitalization.[20,21]

Although the number of older patients with HF increased, the standardized in-hospital mortality and all-cause mor-

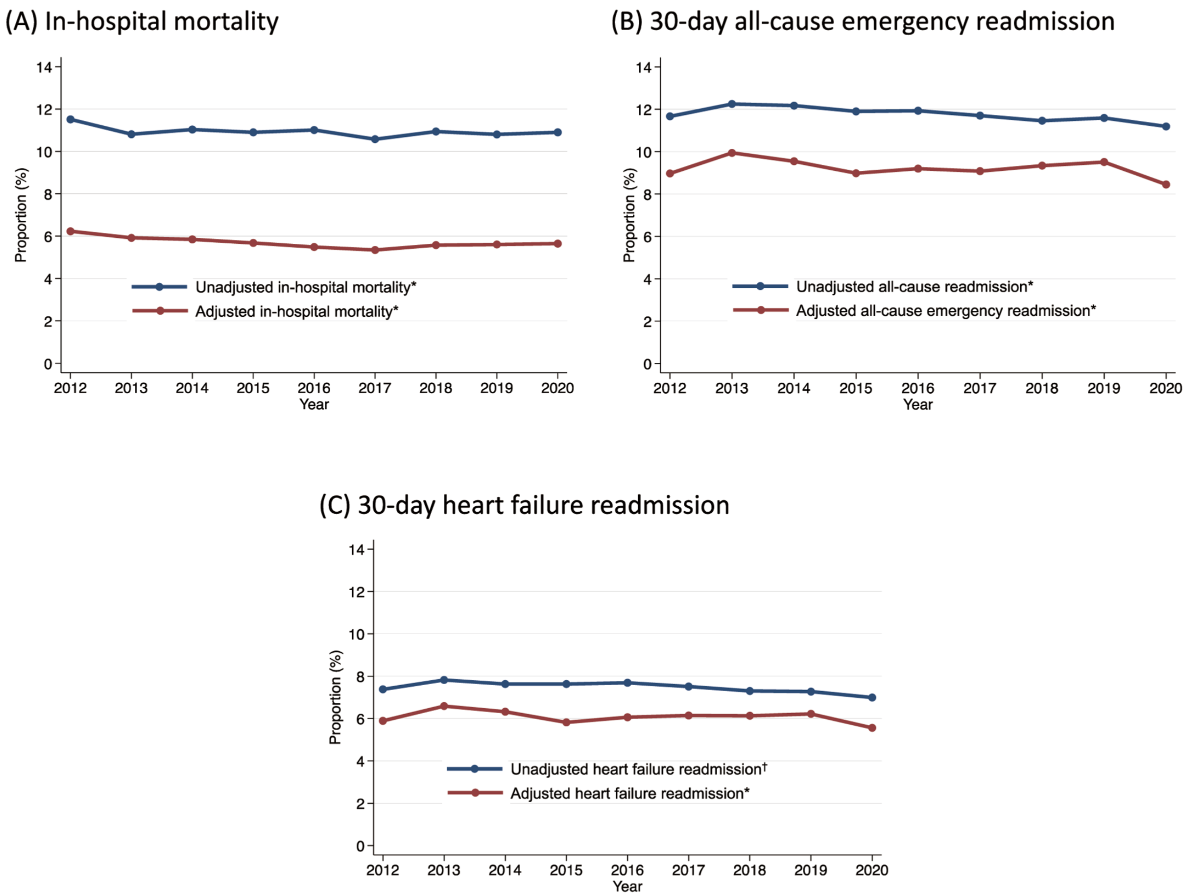

Figure 5. Trends in the unadjusted and adjusted in-hospital mortality and readmission rates for acute heart failure. (**A**) Crude and standardized in-hospital mortality rates decreased slightly during the study period. (**B**) Crude and standardized 30-day all-cause emergency readmission rates decreased slightly during the study period. (**C**) Crude and standardized 30-day heart failure readmission rates decreased slightly during the study period. *P for trend <0.001; †P for trend=0.001.

tality rates decreased. A study carried out in the USA showed this to be a consistent trend among older patients.[22] Related to new HF medications and changes in guideline recommendations approved in 2017, the trends in HF medication prescriptions changed during the study period,[23] and these changes may have contributed to the decreased mortality rate in patients with HF. However, in younger patients, there was no decreasing trend in these outcomes. Therefore, in the future, we need to assess the quality of care and follow the trends in outcomes.

Our study demonstrated that hospitalization costs increased during the study period. Although the medical payment system related to the DPC contributed, the increasing proportion of older patients with complex needs may have contributed to the increasing hospitalization costs. The increasing use of intensive care and high-care units may have resulted in a shorter length of hospital stay. A hospital-based survey for cardiovascular care in Japan showed that the number of patients hospitalized with HF per cardiologist increased in the 2010s; thus, the burden on cardiologists may also be increasing over time.[6] In a rapidly aging Japanese society, these results indicate that the cardiovascular care system may have adapted to the increasing number of older patients with HF.

To date, there are few descriptive studies investigating the current trends regarding patients hospitalized with HF in Japan. A previous study of 3 cohort analyses showed results that are consistent with ours, including increasing age and shortened length of hospital stay in patients hospitalized with HF.[24] There are many in-hospital mortality and 30-day readmission rates that were lower in this previous study when compared with our study, which might be attributable to differences in the study populations. Notably, our study included most JCS-certified hospitals; thus, a generalizable description of HF care in Japan was possible.

Study Limitations

Although our study used a large real-world database, there were some limitations. First, our results were based on ICD-10 with additional codes and some facilities did not provide the DPC dataset in every consecutive year, which might have led to incomplete data acquisition for patients hospitalized with HF. There is a lack of studies that have reported the sensitivity of the algorithm used in this study, using acute HF as the gold standard. In the JROAD hospital-based database of 2020, it was noted that around

132,000 patients were hospitalized due to acute HF across 1,355 facilities. The total number of patients included in this study in 2020 was 107,000. Therefore, the outcomes of this study hold the potential to offer generalizable evidence within cardiovascular training facilities across Japan. Our findings were consistent with those of previous studies. However, it is important to note that the JROAD-DPC database exclusively comprises DPC hospitals, primarily collecting data from JCS training and associated hospitals. Thus, for more widely applicable results, future research should encompass non-DPC and non-cardiovascular hospitals. Finally, the JROAD-DPC database does not encompass patient outcomes if the patient was subsequently admitted to a different hospital, potentially leading to an underestimation of 30-day readmission rates. Additionally, the DPC database lacks certain test results such as B-type natriuretic peptide levels and left ventricular ejection fraction. Moreover, the requirement for NYHA classification ceased after the middle of the study period, posing challenges in accurately assessing the severity of HF within this study.

Conclusions

This nationwide study of the trends in the characteristics, treatment and outcomes of patients hospitalized with HF revealed that patients tended to be older with more comorbidities, although the in-hospital mortality and 30-day readmission rates decreased slightly during the study period. Overall, these results should provide feedback on the care of patients with HF and essential information for policy makers and medical staff to develop and assess new strategies for HF management.

Acknowledgments

We thank the Meiji Yasuda Life Insurance Company and Meiji Yasuda Research Institute, Inc. for assistance with data preparation.

Sources of Funding

This work was supported by an Intramural Research Fund (22-6-5) for Cardiovascular diseases of the National Cerebral and Cardiovascular Center.

Disclosures / Conflict of Interest

None.

IRB Information

Ethics committees of the National Cerebral and Cardiovascular Center, Registration number: R22021.

Author Contributions

K.K. and Y.I. conceived the study. K.K., Y.S., and M.N. managed the data. Y.M. provided statistical advice on study design and analysis. K.K. drafted the manuscript. All authors contributed substantially to revision of the manuscript and agreed on its content.

Data Availability

The deidentified participant data will not be shared.

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Supplementary Files

Please find supplementary file(s);
https://doi.org/10.1253/circj.CJ-23-0350