

9-Year Trend in the Management of Acute Heart Failure in Japan: A Report From the National Consortium of Acute Heart Failure Registries

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Background—Acute heart failure (AHF) is a heterogeneous condition, and its characteristics and management patterns differ by region. Furthermore, limited evidence is available on AHF outside of Western countries. A project by the National Consortium of Acute Heart Failure Registries was designed to evaluate the trends over time in patient backgrounds, in-hospital management patterns, and long-term outcomes of patients with AHF over 9 years in Japan.

Methods and Results—Between 2007 and 2015, registry data for patients with AHF were collected from 3 large-scale quality AHF registries (ATTEND/WET-HF/REALITY-AHF). Predefined end points were trends over time in age, sex, and clinical outcomes, including short- and long-term mortality and readmission for heart failure. The final data set consisted of 9075 patients with AHF. No significant differences in patient backgrounds and laboratory findings (eg, anemia or renal function) were observed, with the exception of patient age; mean age became substantially higher over 9 years (71.6–77.0 years; *P* for trend, <0.001). On the contrary, length of hospital stay became shorter (mean, 26–16 days). These changes were not associated with in-hospital mortality (4.7–7.5%) or 30-day heart failure readmission rate (4.8–5.4%), as well as 1-year mortality and heart failure readmission rate (20.1–23.3% and 23.6–26.2%, respectively).

Conclusions—Length of hospital stay in patients with AHF shortened over the 9-year period despite the increasing age of the patients. However, short- and long-term outcomes do not seem to be affected; continuous efforts to monitor clinical outcomes in patients with AHF are needed. (*J Am Heart Assoc.* 2018;7:e008687. DOI: 10.1161/JAHA.118.008687.)

Key Words: acute heart failure • Japan • mortality • readmission • time trend

Heart failure (HF) has become a public health burden globally because of the associated high morbidity and cost.^{1–3} In the United States, there are over 1 million hospital admissions annually for acute heart failure (AHF), which results in a cost-of-care of more than US\$30 billion per year.¹ Similar trends are observed in Asian and European countries.^{2,3}

Many aspects of the treatment and outcomes, as well as background information of patients with HF, have been studied extensively. For example, a study showed that aging is related to a high burden from cardiovascular diseases and is

thus a major global concern.⁴ In addition, length of hospital stay (LOHS) has implications given that it varies by region and medical system.^{5–7} Japan is known to have 1 of the highest proportions of aged persons in the world, with 27.3% of the population aged >65 years in 2016.⁸ In Japan, mean LOHS is over 20 days, which is substantially longer than that in any Western and Asian countries.⁵ A socialized medical system has allowed for a long LOHS in Japan.

Reports on the current status and trends of patient characteristics, management patterns, and outcomes of

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An accompanying Table S1 is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.008687>

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Clinical Perspective

What Is New?

- This study provides an overview of patient backgrounds, management patterns, and prognoses of Japanese patients with acute heart failure using data from modern large-scale registries.
- We demonstrated temporal changes during the past decade using individual patient data from the registries in Japan.
- We also found several important features and changes in acute heart failure practice in Japan: (1) a significant temporal increase in the number of elderly patients; (2) in-hospital mortality improved despite a significant decrease in the length of hospital stay; and (3) no changes in long-term outcomes such as 1-year mortality and heart failure readmission rate over time.

What Are the Clinical Implications?

- These data can provide up-to-date information on the current status of heart failure practice in the medical community in Japan.
- Backgrounds, treatment, and prognosis of patients with acute heart failure in Japan appear to be comparable with those reported in Western countries.
- Notably, the length of hospital stay has become shorter without impaired short-term outcomes in Japan, but is still relatively higher compared with that in other countries.
- Studies are needed to clarify the optimal length of hospital stay without impairing clinical outcomes among various countries with different practice patterns and healthcare systems.

patients with AHF within medical systems outside of Western countries are insufficient. The purpose of this study was to report the temporal trends in clinical practice of patients with AHF in Japan. With the significant increase in life expectancy globally, studies on aging patients with HF are needed.

Methods

Data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Ethical Approval

Study design involved analysis of individual patient data from 3 large-scale, prospective, hospital-based AHF registries. Representative investigators for each registry (Y.S., N.S., and Y.M.) performed preassigned analysis for the present study. Briefly, 100% of cases admitted at each participating institution that fulfilled inclusion criteria were registered.

Inclusion and exclusion criteria of each registry has been described elsewhere^{9–11}; all 3 registries did not include patients complicated with acute coronary syndrome. Data collection was patient based, but not event based, among all registries. Study protocols were approved by the institutional review boards at each site, and all research was conducted in accord with the Declaration of Helsinki. Written or verbal informed consent was obtained from each participant before the study.

Participating Registries

The following 3 cohorts are representative large-scale registries of hospitalized patients with AHF in Japan during the last decade.

ATTEND Registry

As a nation-wide, hospital-based, prospective, observational, multicenter cohort study, the ATTEND (Acute Decompensated Heart Failure Syndromes) registry accumulated data on patients with AHF admitted to 53 hospitals in all regions of Japan from 2007 to 2011.⁹ Patients were enrolled at their first admission and then followed after discharge. Patient information obtained included demographic data, medical history, baseline characteristics, initial evaluation, treatment, procedures, hospital course, and disposition.

WET-HF Registry

The WET-HF (West Tokyo Heart Failure) registry is an ongoing, prospective, multicenter cohort registry designed to collect data on clinical backgrounds and outcomes of patients hospitalized for AHF.¹⁰ From January 2006, this registry was launched as a single-center database of patients with AHF. The registry has added 2 institutions since 2011 and now consists of 6 tertiary hospitals around the metropolitan Tokyo area. Data are collected on the episode of hospitalization beginning with initial care at presentation to the emergency department (ED) and ending with a minimum follow-up of 2 years. Data on demographics, medical history, baseline characteristics (laboratory tests at several time points during hospitalization), treatment, procedures, HF-specific status (eg, Kansas City Cardiomyopathy Questionnaire), and clinical outcomes during hospitalization and after discharge are recorded.

REALITY-AHF

The registry focused on REALITY-AHF (very early presentation and Treatment in the emergency department of Acute Heart Failure syndrome) and was a prospective multicenter study (20 hospitals in all regions of Japan) that was designed to evaluate the association between time to treatment and clinical outcome in patients with AHF

presenting at the ED.¹¹ From August 2014 to December 2015, consecutive patients with AHF hospitalized through the ED at participating hospitals were included in the registry at the initial hospital admission and followed up. In REALITY-AHF, data were collected up to 48 hours from ED arrival. Drug types and doses of all intravenous treatments in this time window were recorded. Oral medication taken within 48 hours was also recorded. At the ED, baseline physical findings and blood samples were evaluated for all patients. Echocardiography was performed in the ED and steady-state phases.

Variable Definitions

Acute heart failure

In each registry, the clinical diagnosis of AHF was made by individual cardiologists at each institution based on the Framingham criteria.¹² In addition, patients with B-type natriuretic peptide level <100 pg/mL or N-terminal pro-B-type natriuretic peptide level <300 pg/mL at baseline were excluded from the REALITY-AHF registry.

Ischemic etiology

Classically, ischemic cardiomyopathy has been defined as left ventricular dysfunction (left ventricular ejection fraction $\leq 40\%$) with a history of myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, or at least 1 major epicardial coronary artery with $\geq 75\%$ stenosis.¹³ However, it is still a challenge to clinically diagnose the etiology of HF, because of its complex pathophysiology, given that many pathological processes may contribute to the development of left ventricular dysfunction. Therefore, differences in the definition of ischemic etiology exist among registries.

ATTEND. Left ventricular dysfunction with a history of myocardial infarction, at least 1 major epicardial coronary artery with $\geq 70\%$ angiographical stenosis, or diagnosis of coronary artery disease by stress test.

WET-HF. Left ventricular dysfunction with a history of myocardial infarction, history of coronary revascularization with percutaneous coronary intervention or coronary artery bypass grafting, or at least 1 major epicardial coronary artery $\geq 75\%$ angiographical stenosis.

REALITY-AHF. Presence of coronary artery disease defined as the presence of coronary stenosis documented by coronary angiography and/or computed tomography, history of myocardial infarction, or history of coronary revascularization with percutaneous coronary intervention or coronary artery bypass grafting.

Clinical Outcomes

We investigated both short- and long-term outcomes of AHF patients in the 3 registries across the study period. The 30-day and 1-year mortality events were calculated from data of hospital admission. However, 30-day and 1-year HF readmission events were calculated from the data of the first HF discharge.

Statistical Analysis

The study was planned and performed in accord with STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational studies. Results are expressed as mean \pm standard deviation or median with interquartile range for continuous variables and as percentages for categorical variables. Clinical outcomes were compared between registries using the chi-square test. If necessary, variables were transformed for further analyses. The Cochran–Armitage test was used for temporal trend analysis of the categorical variables, and linear regression with a continuous term for year was used for continuous variables.

Because there was a significant difference in age distribution between 2007 and 2015, we performed age adjustment to evaluate mortality rate (in-hospital mortality and 1-year mortality). This process was performed with indirect age adjustment method using standardized mortality ratios (SMRs) because we observed age categories in which a relatively small number of patients were categorized in certain years. To calculate SMRs, we first divided the whole cohort into 6 age groups (<50, 50–59, 60–69, 70–79, 80–89, and >90 years at the time of admission) and calculated mortality rate in each age group for the whole study cohort. Next, the expected number of deaths for each year was calculated by summing the number of expected deaths achieved by applying the age-specific expected mortality rate derived from the whole cohort to the age distribution of each year. Finally, we achieved SMRs by dividing the total number of observed deaths by the number of expected deaths for each year. We plotted the age-adjusted mortality for each year, which was obtained by multiplying SMRs by mortality in the whole population. Furthermore, we performed a risk-score adjustment to evaluate changes in the in-hospital mortality. Using the Get With The Guideline–Heart Failure (GWTG–HF) risk score, which has been validated in the Japanese AHF population,¹⁰ we calculated the predicted mortality rate of each patient. We then evaluated the ratio of the observed mean mortality rate against the predicted mean mortality rate for every year until 2015 using the Cochran–Armitage test.

All probability values were 2-tailed, and $P < 0.05$ was considered statistically significant. All statistical analyses were performed with R software (version 3.1.2; R Foundation for Statistical Computing, Vienna, Austria).

Table 1. Patient Characteristics

	ATTEND	WET-HF	REALITY-AHF
No.	4842 Patient-based	2551 Patient-based	1682 Patient-based
Time frame	2007–2011	2011–2015	2014–2015
HF definition	Framingham criteria	Framingham criteria	Framingham criteria+BNP or NT-proBNP
Age, y	73±14	75±13	78±12
Male, %	58	59	55
Body mass index, kg/m ²	23.2±4.6	23.3±4.6	23.1±4.8
Systolic BP, mm Hg	146±37	141±34	149±37
Heart rate, bpm	99±29	94±29	97±28
LVEF, %	N/A	45±15	47±16
LVEF <40%, %	53	41	37
Ischemic etiology, %	31	29	30
Medical history			
Previous admission for heart failure, %	36	30	N/A
Hypertension, %	69	71	67
Dyslipidemia, %	37	40	37
Diabetes mellitus, %	34	36	37
Atrial fibrillation, %	36	47*	39
Stroke, % [†]	14	14	11
COPD, %	10	6	9
Laboratory tests			
Hemoglobin, g/dL	12.0±2.6	11.9±2.3	11.7±2.3
Serum creatinine, mg/dL	1.4±1.6	1.5±1.6	1.4±1.1
BUN, mg/dL	27.8±26.0	27.6±17.0	29.5±17.4
Serum sodium, mEq/L	139.3±4.6	139.2±4.3	138.9±4.7
BNP, pg/mL (median)	706 (362–1284)	676 (351–1221) [‡]	744 (444–1343)

ATTEND indicates the Acute Decompensated Heart Failure Syndromes registry; BNP, B-type natriuretic peptide; BP, blood pressure; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; HF, heart failure; LVEF, left ventricular ejection fraction; N/A, not applicable; NT-proBNP, N-terminal pro-B-type natriuretic peptide; REALITY-AHF, very early presentation and Treatment in the emergency department of Acute Heart Failure syndrome; WET-HF, the West Tokyo Heart Failure registry.

*Represents atrial arrhythmias including atrial flutter.

[†]Includes transient ischemic attack.

[‡]In the 1150 patients, BNP levels were measured; in contrast, NT-proBNP levels were measured in the 1401 patients (median, 3912 pg/mL; interquartile range, 1909–8981).

Results

Patient Characteristics

Table 1 shows patient characteristics in the 3 Japanese AHF registries. Mean age of patients with AHF was higher in the most recent registry (REALITY-AHF). The trend of increasing mean age was also observed within the WET-HF registry (from 74.8 years in 2013 to 76.4 years in 2015). Figure 1 demonstrates that mean age for patients with AHF has increased significantly over time (P for trend <0.001). Overall, there was an absolute increase in mean age (71.6 years in 2007 to 77.0 years in 2015). In addition, there was a slight increase in

the percentage of female patients, but this was not statistically significant (35–44%; P for trend=0.06).

The 2 more-recent registries (WET-HF and REALITY-AHF) included a larger number of patients who had HF with an left ventricular ejection fraction of >40%, consistent with a higher proportion of elderly and female patients. The proportion of ischemic etiology was similar among the 3 registries and present in ≈30% of the patients among each registry; and there was no change in the proportion of ischemic etiology over time (P for trend=0.196). Frequency of concurrent chronic obstructive pulmonary disease remained low (6–10%). There were no differences in frequencies of other major

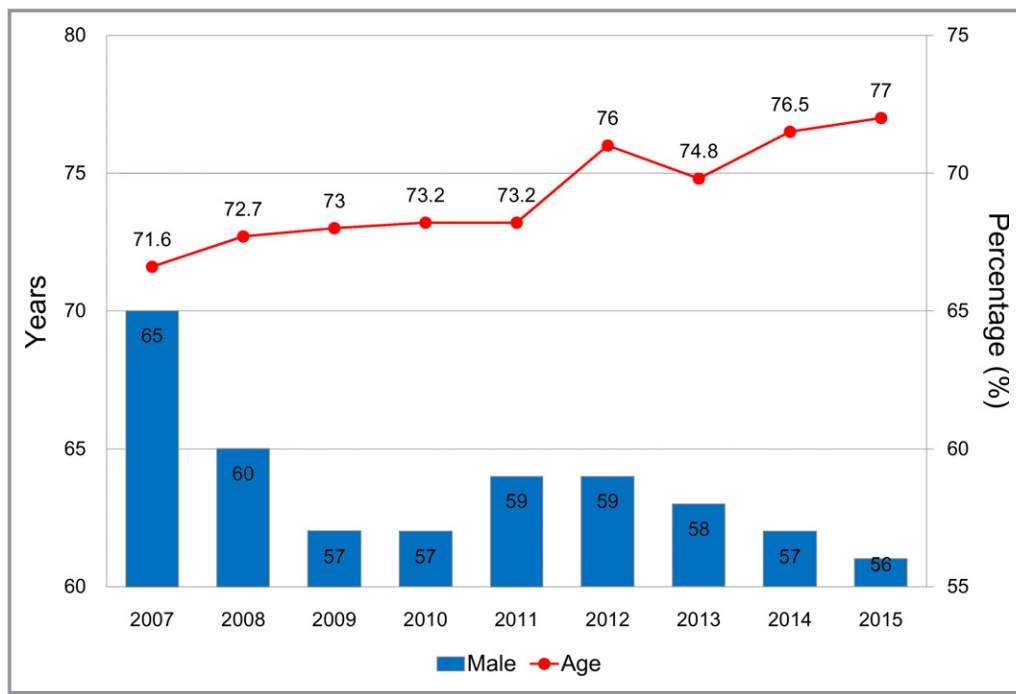


Figure 1. Temporal trends for age and sex in patients with acute heart failure (AHF). Mean age of patients with AHF increased significantly over time (P for trend, <0.001). There was a slight increase in percentage of female patients with no statistical significance (P for trend=0.06).

comorbidities such as hypertension, diabetes mellitus, dyslipidemia, and stroke.

With respect to laboratory findings, there were no significant differences in hemoglobin, creatinine, blood urea nitrogen, and sodium levels between registries, whereas B-type natriuretic peptide levels appeared to be slightly lower in the WET-HF compared to the REALITY-AHF (median [interquartile range], 676 [351–1221] versus 744 [444–1343] pg/mL, respectively).

Management Patterns

Table 2 describes treatment and procedure patterns during hospitalization. Intravenous administration of vasodilators was frequently used in acute settings among Japanese patients with AHF. In particular, carperitide was still used in $\approx 40\%$ of patients with AHF, despite a decline in carperitide use across the study period (P for trend, <0.001). Regarding nonpharmacological treatments, such as mechanical ventilation and circulatory support devices, there were no significant differences between registries.

Clinical Outcomes

Table 3 shows LOHS and clinical outcomes, including mortality and HF readmission. Compared with the ATTEND, LOHS in the WET-HF and REALITY-AHF were significantly shorter

(median, 21 days in ATTEND versus 14 days in WET-HF versus 16 days in REALITY-AHF). With respect to short-term mortality rates, there were differences between the registries (for in-hospital all-cause mortality, 4.7% in WET-HF to 6.4% in ATTEND; and for 30-day all-cause mortality, 3.3% in WET-HF to 4.5% in REALITY-AHF). In addition, rates of 1-year all-cause mortality after hospitalization ranged from 18.4% to 22.2%. Cause of death for short- and long-term mortality was similar between each registry, indicating that half of the patients died from cardiac causes.

Figure 2 shows the temporal trends for LOHS and crude mortality of patients with AHF. Despite an increasing number of elderly patients, LOHS became significantly shorter during the study period (26–16 days; P for trend, <0.001). Crude and age-adjusted in-hospital and 1-year mortality after hospitalization and further SMRs of patients are shown in Figure 3. In-hospital mortality decreased over time (8.2% in 2007 to 4.7% in 2015; P for trend for SMR=0.026), with shortening of the LOHS, whereas 1-year mortality after hospitalization remained unchanged. Furthermore, even after adjustment for the GWTG-HF risk score, in-hospital mortality decreased during the study period (Table S1). We also assessed linearity of the association between LOHS and in-hospital mortality. A longer LOHS was, in part, associated with a higher in-hospital mortality, albeit the association was less significant after adjusting for baseline patient risk (GWTG-HF risk score).

Table 2. Management Patterns During Hospitalization

	ATTEND	WET-HF	REALITY-AHF
Intravenous drugs			
Diuretics	76	67.8	82.8*
Vasodilators	78	64.7	60.7
Carperitide	58.3	52.1	45.6*
Inotropes	19	16.8	16.1*
Mechanical ventilation			
Intubation	7.5	4.9	6.7
NPPV	24.4	22.2	24.2*
IABP	2.5	2.3	1.6
PCPS	0.7	0.5	0.4
Dialysis	3.0	4.8	3.3
PCI	8.0	4.5	4.8
CABG	1.3	2.0	2.1
PMI	3.8	3.0	2.1
ICD	2.6	1.3	0.3
CRT	2.3	0.5	0.9

Values are in percentage. ATTEND indicates the Acute Decompensated Heart Failure Syndromes registry; CABG, coronary artery bypass grafting; CRT, cardiac resynchronization therapy; IABP, intra-aortic balloon pump; ICD, implantable cardiac defibrillator; NPPV, noninvasive positive pressure ventilation; PCI, percutaneous coronary intervention; PCPS, percutaneous cardiopulmonary support; PMI, pacemaker implantation; REALITY-AHF, very early presentation and Treatment in the emergency department of Acute Heart Failure syndrome; WET-HF, the West Tokyo Heart Failure registry.

*Treatment within 48 hours from arrival at emergency department.

Regarding HF readmission, notably, 30-day HF readmission is infrequent and has remained constant in Japan, with rates of $\approx 5\%$. On the contrary, rates of 1-year HF readmission appeared to be high in WET-HF and REALITY-AHF compared with those in ATTEND. Figure 4 shows the temporal trends for HF readmission of patients with AHF. During the study period, no statistical changes were observed in 30-day and 1-year HF readmission from the trend analysis.

Discussion

This study provides an overview of patient backgrounds, management patterns, and prognoses of Japanese patients with AHF using data from modern large-scale registries. We also demonstrated temporal changes during the past decade using individual patient data from the registries. We found several important features: First, there was a significant temporal increase in the number of elderly patients. Second, although LOHS decreased significantly, in-hospital mortality improved and 30-day HF readmission remained infrequent during the study period. Finally, there were no changes in long-term outcomes such as 1-year mortality and HF readmission rate over time.

Table 3. Length of Hospital Stay and Clinical Outcomes

	ATTEND	WET-HF	REALITY-AHF	P Value
Length of hospital stay, d*	21 (14–32)	14 (9–22)	16 (10–25)	<0.001
Mortality rates, % [†]				
In-hospital all-cause death	6.4	4.7	5.1	0.003
In-hospital cardiac death	4.5	3.1	3.6	0.009
30-d all-cause death	3.9	3.3	4.5	0.131
30-d cardiac death	3.0	2.2	3.3	0.072
1-y all-cause death	18.4	18.6	22.2	0.003
1-y cardiac death	11.5	10.1	13.0	0.025
Readmission rates, % [‡]				
30-d readmission for HF	4.6	5.2	5.5	0.281
1-y readmission for HF	24.4	27.1	27.1	0.057

ATTEND indicates the Acute Decompensated Heart Failure Syndromes registry; HF, Heart Failure; REALITY-AHF, very early presentation and Treatment in the emergency department of Acute Heart Failure syndrome; WET-HF, the West Tokyo Heart Failure registry.

*Values are expressed in median and interquartile range.

[†]All mortality events were calculated after admission.

[‡]All readmission events were calculated from the first HF discharge date.

Patient Characteristics

With the significant gain in life expectancy globally over the past few decades, studies on treatments and outcomes of aging patients with HF is of the utmost importance.¹⁴ In 2007, Japan became the first country worldwide to have a super-aged society, and aging of the population has continued at a rate that has not been paralleled previously.⁸ Our results showing that the age of patients with AHF has consistently increased over 9 years were in agreement with aging of the population of Japan, as well as changes in sex ratio (increases in female patients) and the proportion of HF phenotypes (eg, patients with reduced or preserved ejection fraction). Conversely, there were no remarkable changes in prevalence of most comorbidities in Japanese patients with AHF during the last decade.

Clinical Outcomes

Although LOHS decreased dramatically during the study period, it remains higher in Japan than in other countries,⁵

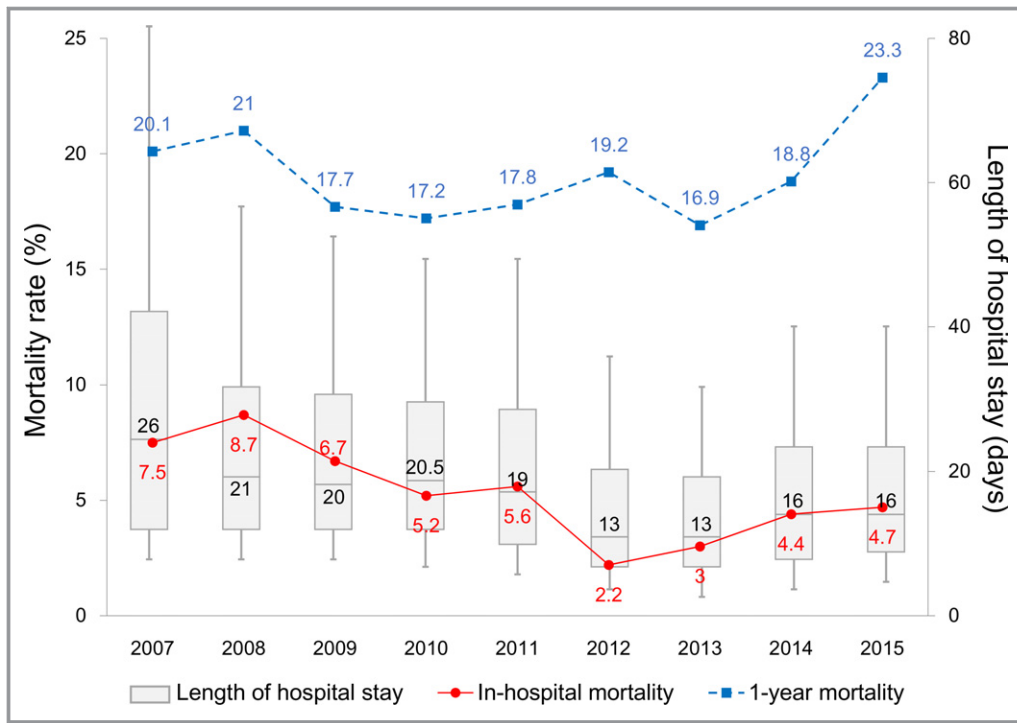


Figure 2. Temporal trends for length of hospital stay and mortality rates in patients with acute heart failure. Length of hospital stay and in-hospital mortality rate of patients have decreased over time (P for trend, <0.001 and 0.003 , respectively), whereas 1-year mortality after admission has remained unchanged (P for trend= 0.657). Changes in length of hospital stay are expressed in box-and-whisker plots.

even among other Asian countries.¹⁵ One reason for the extremely long LOHS in Japan might be the inpatient management program. In Japan, the universal health

insurance system and high-cost medical care benefit system, which compensate for excessive medical costs, allow patient financial burdens to be kept below the specified limits.

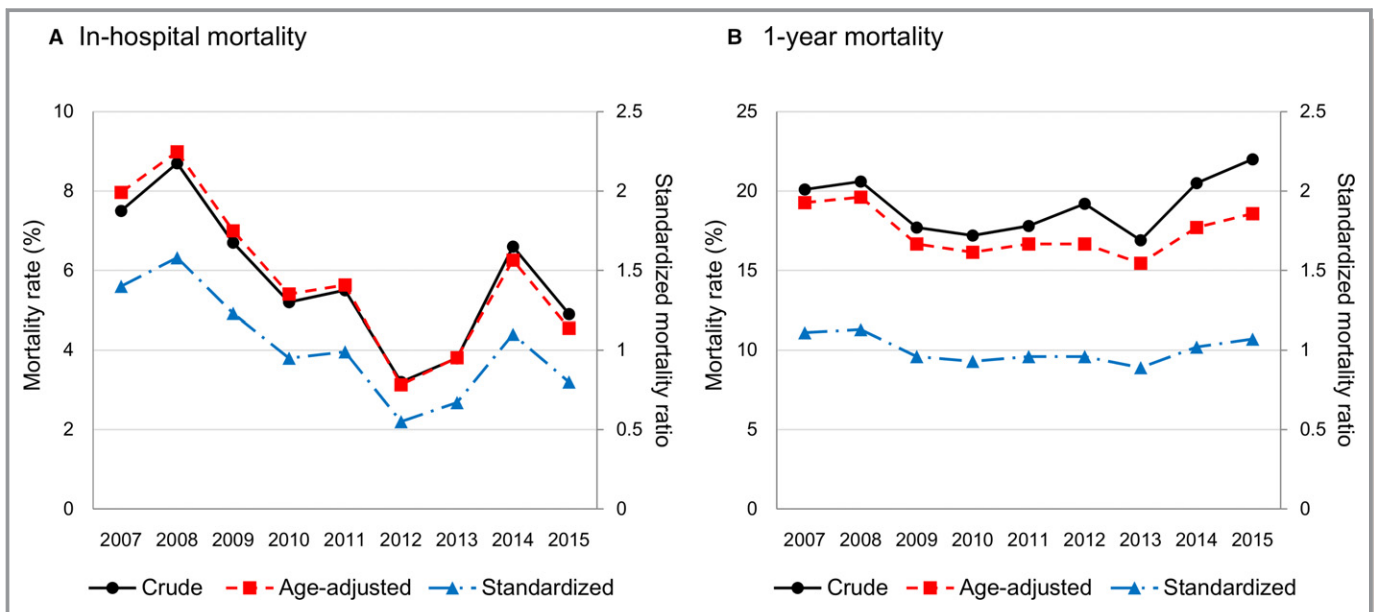


Figure 3. Temporal trends for crude and age-adjusted mortality, and standardized mortality ratios in patients with acute heart failure. The standardized mortality ratio for (A) in-hospital mortality has significantly decreased (P for trend= 0.026), but that for (B) 1-year mortality after hospitalization is unchanged (P for trend= 0.389).

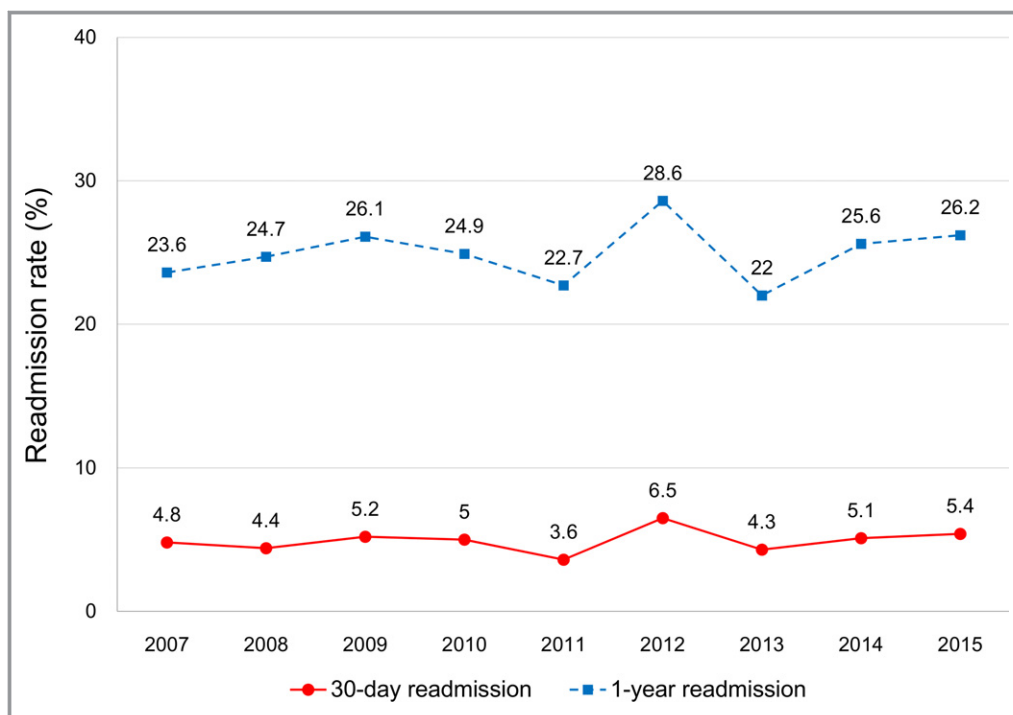


Figure 4. Temporal trends for readmission in patients with acute heart failure. Both 30-day and 1-year readmission for heart failure remained unchanged during the study period (P for trend=0.343 and 0.437, respectively).

Conversely, despite decreasing LOHS, in-hospital and 30-day mortality rate, short-term outcomes, and 1-year mortality after admission decreased or remained unchanged during the study period. Although the reason for the decline in in-hospital mortality rates can be partly related to the decrease in LOHS, as shown in a cohort study, 30-day mortality was unchanged in this study and thus such effects might be small. From the nation-wide data in the United States, the rate of in-hospital mortality among patients hospitalized with HF declined consistently between 2001 and 2014.¹⁶ More specifically, the decline was observed from 2005 onward. The improvement of in-hospital mortality might have resulted from the American College of Cardiology/American Heart Association guidelines updated in 2005, which included more-robust evidence from clinical trials. The data from a Danish nation-wide cohort study also showed that mortality rates declined consistently from 1983 to 2012, and its reduction was independent of age, sex, and comorbidity burden.¹⁷ These changes might have affected the results of our current study.

HF readmission has been recognized as an important clinical indicator in the interest of controlling medical costs. Medicare fee-for-service claims demonstrated that the 30-day readmission rate after discharge for HF was 24.8%, and one third of the reasons for readmission were heart failure in the United States. Furthermore, most readmissions occurred

within 15 days after admission.¹⁸ Compared with those in Western countries, 30-day HF readmission and 30-day mortality rates were lower in Japan; this might result from the longer LOHS that provides sufficient stabilization of patient conditions and facilitation of social support. Further studies are needed to clarify the optimal LOHS without impairing clinical outcomes among various countries with different practice patterns and healthcare systems.

Treatment

Our study found that intravenous vasodilators, particularly carperitide (alpha-human atrial natriuretic peptide), remain to be frequently used in the acute setting in patients with AHF; however, it was observed that its use was in decline during the study period. Carperitide is used almost exclusively in Japan (Class IIa recommendation in the present Japanese Society of Circulation Clinical Practice Guidelines: Diagnosis and Treatment for Acute and Chronic Heart Failure, accessed by http://www.j-circ.or.jp/guideline/pdf/JCS2017_tsutsui_h.pdf). Although a small trial demonstrated its prognostic benefit in patients with AHF,¹⁹ a retrospective cohort study using propensity-score matching showed that carperitide might even be prognostically harmful for patients with AHF.²⁰ Given its cost and high usage rate, its utility should be investigated in an adequately powered clinical study from the

clinical, prognostic, and cost-effectiveness points of view. In this context, a multicenter, randomized, open-label, controlled trial to evaluate the efficacy of carperitide in patients with AHF is currently being conducted in Japan.²¹

Limitations

There are some inherent limitations in our study. First, the present analysis was performed based on data combined from 3 registries. Each registry has a different time frame for patient inclusion and consists of different participating hospitals. Some geographical regions are over- or under-represented according to the distribution of participating hospitals. Unfortunately, no national database is available on patient characteristics, management patterns, and prognosis of HF in Japan. Temporal changes in the phenotype of HF should be interpreted with caution. Given that the clinical importance of HF with preserved ejection fraction has been recognized recently, its increase might be attributable to the increased attention it has received. In other words, HF patients with preserved ejection fraction might have been overlooked (ie, the patients were not diagnosed with HF solely because left ventricular ejection fraction was not reduced) in the past even though the HF phenotype distribution has not changed considerably. Finally, in respect with the decrease in in-hospital mortality, it is also important to consider, albeit cautiously, the effect of LOHS on mortality over time.

Conclusions

Our study clarified the temporal trends in patient characteristics, management patterns, and clinical outcomes of patients with AHF in Japan. Backgrounds, treatment, and prognosis of patients with AHF in Japan appear to be comparable with those reported in Western countries. During the last decade, patients with AHF have shown a trend to be older. Notably, LOHS has become shorter without impaired short-term outcomes in Japan, but is still relatively higher compared with that in other countries. In addition, rates of 1-year mortality and HF readmission remained unchanged during the study period. These data can provide up-to-date information on the current status of HF practice in the medical community in Japan. It is of great importance to collaborate with other countries in future studies on patients with AHF.

Author Contributions

Shiraishi, Kohsaka, and Matsue designed the study and wrote the article. Shiraishi and Matsue conducted the statistical analysis. All of the authors made comments and revisions to the final manuscript. All authors have access to the data.

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SUPPLEMENTAL MATERIAL

Table S1. Predicted vs. observed in-hospital mortality rate.

Year	Predicted mortality (%)	Observed mortality (%)	Ratio (Observed/Predicted)
2007	6.1	7.5	1.23
2008	5.6	8.7	1.55
2009	5.8	6.7	1.16
2010	5.6	5.2	0.93
2011	5.9	5.5	0.93
2012	6.2	3.2	0.52
2013	5.7	3.8	0.67
2014	5.5	6.6	1.20
2015	5.1	4.9	0.96

There was no statistical difference in the change in in-hospital mortality rates using the Cochran-Armitage test (P for trend = 0.15).