ORIGINAL RESEARCH

Prognostic Implications of Early and Midrange Readmissions After Acute Heart Failure Hospitalizations: A Report From a Japanese Multicenter Registry

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BACKGROUND: Although 30-day readmission is thought to be an important quality indicator in patients with hospitalized heart failure, its prognostic impact and comparison of patients who were readmitted beyond 30 days has not been investigated. We assessed early (0–30 days) versus midrange (31–90 days) readmission in terms of incidence and distribution, and elucidated whether the timing of readmission could have a different prognostic significance.

METHODS AND RESULTS: We examined patients with hospitalized heart failure registered in the WET-HF (West Tokyo Heart Failure) registry. The primary outcomes analyzed were all-cause death and HF readmission. Data of 3592 consecutive patients with hospitalized heart failure (median follow-up, 2.0 years [interquartile range, 0.8–3.1 years]; 39.6% women, mean age 73.9±13.3 years) were analyzed. Within 90 days after discharge, HF readmissions occurred in 11.1% patients. Of them, patients readmitted within 30 and 31 to 90 days after discharge accounted for 43.1% and 56.9%, respectively. Independent predictors of 30- and 90-day readmission were almost identical, and after adjustment, readmission for HF within 90 days (including both early and midrange readmission) was an independent predictor of subsequent all-cause death (hazard ratio, 2.36; P<0.001). Among 90-day readmitted patients, the time interval from discharge to readmission was not significantly associated with subsequent all-cause death.

CONCLUSIONS: Among patients readmitted within 90 days after index hospitalization discharge, ≈60% of readmission events occurred beyond 30 days. Patients readmitted within 90 days had a higher risk of long-term mortality, regardless of the temporal proximity of readmission to the index hospitalization.

Key Words: early readmission heart failure Hospital Readmission Reduction Program outcome

Readmission within 30 days after a heart failure (HF) hospitalization is both a recognized indicator for disease progression and a source of considerable financial burden to the healthcare system. Consequently, the identification of patients at risk for 30-day readmission is recognized as a key step in improving disease management and patient outcome although controversy remains in its implementation. First, few studies investigated the impact of early readmission among patients with HF outside of Western countries, despite the regional differences in HF management and healthcare system organization. Second, the clinical impact of HF readmission on a 30-day postdischarge period and beyond has been scarcely investigated; the vulnerable period after discharge is considered to continue for 2 to 3 months after discharge, and “30-day” could be an arbitrary cutoff that is not supported by the pathophysiologic rationale related to HF. This is an important hypothesis to investigate given a recent increase in postdischarge...
mortality in patients with HF.11 Indeed, a recent post hoc analysis of a large-scale clinical trial revealed that HF readmission for worsening of symptoms and/or signs resulting in augmentation or new administration of HF therapies continued beyond 30 days after patient discharge.12 Given the continued risk of readmissions beyond the 30-day period, more recent episode payment models have shifted the focus from 30- to 90-day readmission for the management of patients with acute myocardial infarction.13 Accordingly, we investigated: (1) the incidence, distribution, predictors, and prognostic impact of readmission 0 to 30 and 31 to 90 days after index hospitalization discharge in Japan, and (2) whether the timing of readmission (early [0–30 days] versus mid-range [31–90 days]) could have prognostic significance among the patients with hospitalized HF (HHF).

**METHODS**

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

**Study Design and Participants**

Details of the WET-HF (West Tokyo Heart Failure) registry have been previously described.14,15 Briefly, this database is a prospective, multicenter cohort registry designed to collect data pertaining to the clinical backgrounds and outcomes of patients hospitalized with acute HF who met the Framingham criteria for HF16 as the primary cause of admission. Before the launch of this registry, information on the objective of the present study, its social significance, and an abstract were provided for clinical trial registration to the University Hospital Medical Information Network of Japan (UMIN000001171). The present study was conducted at 3 university hospitals and 3 tertiary referral hospitals within the metropolitan Tokyo area. To obtain a robust assessment of the care and patient outcomes, baseline data and outcomes were collected by dedicated clinical research coordinators from medical records and interviews with treating physicians. Data were entered into an electronic data-capturing system with a robust data query engine and system validations for data quality; outliers in the continuous variables or unexpected values in the categorical variables were selected by established criteria, and the originating institution was notified to verify the value. Moreover, the quality of the reporting was also verified by principal investigators (Y.S. and S.K.) at least once a year, and periodic queries were conducted to ensure its quality. Patients who refused to participate in the study or presented with concurrent HF and acute coronary syndrome were excluded from the registration. The study protocol was approved by the institutional review boards at each site, and research was conducted in accordance with the Declaration of Helsinki. Written or

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**Nonstandard Abbreviations and Acronyms**

| Abbreviation | Description |
|--------------|-------------|
| ATTEND       | Acute Decompensated Heart Failure Syndromes |
| EVEREST      | Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan |
| GWTG-HF      | Get With The Guidelines-Heart Failure |
| HF           | heart failure |
| HHF          | hospitalized heart failure |
| HR           | hazard ratio |
| LVEF         | left ventricular ejection fraction |
| OPTIMIZE-HF  | Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure |
| RAS          | renin-angiotensin system |
| REALITY-AHF  | Registry Focused on Very Early Presentation and Treatment in Emergency Department of Acute Heart Failure |
| SBP          | systolic blood pressure |
| SHFM         | Seattle Heart Failure Model |
| WET-HF       | West Tokyo Heart Failure
oral informed consent was obtained from each patient before the study.

Data of 4000 consecutive patients with HHF registered in the WET-HF registry between 2006 and 2017 were analyzed. Figure 1A shows a flowchart describing the study design. Of the 4000 patients included in this cohort, 164 patients with in-hospital death and 244 patients without recorded follow-up information were excluded. After exclusion, data of 3592 patients who were stably discharged after index hospitalization were analyzed.

**Definitions of Outcomes and Variables**

Following discharge, a survey was performed using chart or telephone review. The following information regarding specific outcomes was obtained from participating cardiologists and investigators: (1) all-cause

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**Figure 1.** The study design and time distribution of 90-day readmission.

A. Flowchart describing the study design from the WET-HF (West Tokyo Heart Failure) registry. Patients were divided into 2 groups according to the presence of 90-day readmission. Ninety-day readmission groups were subdivided into 2 groups according to the timing of readmission (early [0–30 days] vs midrange [31–90 days]).

B. Time distribution of 90-day readmission after discharge of index hospitalization.
death, and (2) HF readmission. Our registry obtained HF-specific readmission information in order to elucidate the clinical significance exclusively focusing on HF readmission. Regarding HF readmission, treating physicians at each participating hospital made decisions according to the usual standard of care. Since non-HF readmissions can involve noncardiac factors (eg, psychological, social, and environmental factors), they were not considered to be the primary end point of the present analysis. Follow-up survey using a chart or telephone review was performed, and the date of index hospitalization discharge, HF rehospitalization, and mortality were properly collected and confirmed by site investigators and dedicated clinical research coordinators. The data acquisition rate for follow-up clinical events (eg, HF-related readmission and mortality) was 93.9%. Patients lost to follow-up were censored at the date of last contact.17

For the present analysis, the patients were further divided into 2 groups according to the presence or absence of HF readmission within 90 days after discharge from index HF hospitalization (90-day readmission and non–90-day readmission groups; Figure 1A). Then, the patients readmitted within 90 days were subdivided into 2 groups according to the readmitted time interval (early [0–30 days] and midrange [31–90 days] groups). The primary end point of this study was all-cause death. Prognostic impact of 90-day readmission (versus no 90-day readmission) as well as 0–30 days readmission (versus 31–90 days) during 2 years of follow-up was investigated. Time to all-cause mortality was defined as the time elapsed between the day of hospital discharge of the index hospitalization and the date of death. Patients who died before 30 days (or 90, 120, 180, 360 days) after discharge following index hospitalization were included in this study, not censored.

The Seattle Heart Failure Model (SHFM) score to predict annual all-cause mortality was calculated in accordance to the statistical model described in the original and our previous articles.18,19 All laboratory data were evaluated at discharge, except for the percentage of lymphocytes, which was evaluated during the course of hospitalization. As Table S1 demonstrates, overall missing data were ≤5%, with the exception of SHFM score (20.8%) mainly because of lack of laboratory values such as total cholesterol and lymphocytes. These missing values were imputed as follows: (1) for variables pertaining to medication and device therapy, missing data were imputed to “no”; (2) for New York Heart Association class, missing data were imputed to “II” based on the frequency (class II; 63.1%) in the entire cohort; (3) for body weight, missing values were imputed to the sex-specific median; and (4) for systolic blood pressure (SBP), left ventricular ejection fraction (LVEF), total cholesterol, and percentage of lymphocytes, missing values were imputed to the median values of the entire cohort. These imputation rules have been previously shown to yield results similar to those obtained with multiple imputation methods.4,20

### Statistical Analysis

Continuous variables were expressed as mean±SD for normally distributed variables as well as median with interquartile range for non-normally distributed variables (length of stay, SHFM score, and laboratory data that included uric acid, serum urea nitrogen, brain natriuretic peptide, lymphocyte, and total cholesterol). Categorical variables were expressed as percentages. Student t test or Mann–Whitney U test were used to compare normally or non-normally distributed variables, and Pearson chi-square test was used to compare categorical variables. The Cox proportional hazard model was used to analyze the determinants of 30- and 90-day readmission. Kaplan–Meier method was used to evaluate the impact of the readmission or its timing on subsequent all-cause death, and the calculation of the follow-up period began from the date of discharge of index hospitalization for both readmission and non-readmission groups; time-to-readmission interval and length of stay during readmission were included in the follow-up periods in the readmission groups. To evaluate the impact of readmission within 90 days on long-term death beyond 90 days, we conducted the landmark analysis at 90 days. Furthermore, to verify the timing of readmission that has no effect on survival rate, we analyzed the prognostic impact of readmission based on further timeline (ie, 120, 180, and 360 days) from initial discharge. In multivariate Cox proportional hazards models for predicting 30- or 90-day readmission, the models were adjusted for age, sex, previous HF admission, SBP, estimated glomerular filtration rate, sodium level, hemoglobin level, LVEF, and β-blocker, renin-angiotensin system (RAS) inhibitor, and mineralocorticoid receptor antagonist use. For readmission outcomes, death was assumed to be a competing risk; thus, we additionally performed Fine and Gray analysis. Further, for predicting all-cause death, variables of “90-day readmission” were added. For all statistical analyses, statistical significance was accepted at P<0.05. Data analysis was performed using SPSS 24.0 for Windows (IBM) except for Fine and Gray analysis, which was performed using R 3.4.2 (The R Foundation).

### RESULTS

Of 3592 patients with HHF (39.6% women; mean age, 73.9±13.3 years), 397 patients (11.1%) were readmitted within 90 days after discharge (90-day readmission group). The median follow-up period
of the survivors was 2.0 years (interquartile range, 0.8–3.1 years), and the median time of HF readmission was 34 days (interquartile range, 16–58 days) after the discharge from index HF hospitalization. Overall, 171 patients (43.1% of readmitted patients within 90 days) had been readmitted within 30 days after discharge, and 226 patients (56.9% of readmitted patients within 90 days) had been readmitted 31 to 90 days after discharge (Figure 1B).

The characteristics of patients with and without 90-day readmission in the overall cohort are summarized in Table 1. Patients who were readmitted within 90 days were more frequently women of older age with lower body mass index, hemoglobin level, and estimated glomerular filtration rate, and had a higher prevalence of ischemic cardiomyopathy and previous HF admission than non–90-day readmitted patients. In addition, 90-day readmitted patients had higher SHFM scores. Multivariate analysis showed that previous HF admission (hazard ratio [HR], 1.73; 95% CI, 1.40–2.13), older age (HR, 1.02; 95% CI, 1.01–1.03), lower SBP (HR, 0.99; 95% CI, 0.98–1.00), lower hemoglobin level (HR, 0.88; 95% CI, 0.83–0.93), lower LVEF (HR, 0.99; 95% CI, 0.98–0.99), and nonuse of RAS inhibitors (HR, 0.68; 95% CI, 0.56–0.84) were independent determinants of 90-day readmission (Table 2). The results persisted in the additional analysis for predicting 90-day readmission after accounting for competing risk of death for readmission outcome (Table S2). Independent determinants of 30-day readmission were similar to those of 90-day readmission including previous HF admission (HR, 1.98; 95% CI, 1.44–2.73), older age (HR, 1.02; 95% CI, 1.00–1.03), lower LVEF (HR, 0.98; 95% CI, 0.97–0.99), and nonuse of RAS inhibitors (HR, 0.53; 95% CI, 0.39–0.72) but also included nonuse of mineralocorticoid receptor antagonists (HR, 0.69; 95% CI, 0.49–0.98) (Table S3).

During a median follow-up of 2.0 years (interquartile range, 0.8–3.1 years), 122 (30.7%) and 461 (14.4%) patients died in the 90-day readmission and non–90-day readmission groups, respectively. Kaplan–Meier estimates demonstrated higher crude rates of all-cause mortality among patients with 90-day readmission in the overall cohort (Figure 2A). After adjustment, 90-day readmission remained an independent risk factor for all-cause death (HR, 2.36; 95% CI, 1.92–2.91) along with older age, male sex, lower SBP, estimated glomerular filtration rate, sodium level, hemoglobin level, LVEF, and nonuse of β-blockers and RAS inhibitors (Table 3). By a landmark analysis performed at 90 days after index hospitalization, 90-day readmission was associated with increased subsequent mortality both within and beyond 90 days of follow-up (Figure 2A). Furthermore, landmark analysis performed at 120, 180, and 360 days after index hospitalization revealed that each of the readmission timeframes was associated with an increased subsequent mortality, although the difference narrowed as the time interval from index hospitalization increased (Figure S1A through S1C).

We then subdivided the 90-day readmitted patients into 2 categories according to the timing of readmission: early (0–30 days) and midrange (31–90 days) readmission groups. No significant differences in patient characteristics were detected between these groups, except for the percentage of lymphocytes and prescription of loop diuretics and RAS inhibitors (Table 1). Further, the incidence of all-cause mortality did not differ between early and midrange readmission groups (Figure 2B). Among 90-day readmitted patients, multivariate analysis showed that older age, lower SBP, estimated glomerular filtration rate, sodium level, LVEF, and nonuse of β-blockers and RAS inhibitors were independently associated with all-cause death (Table 4).

DISCUSSION

The present study demonstrated the following key points: (1) among 90-day readmitted HF patients, 57% of patients were readmitted beyond 30 days after discharge; (2) independent predictors of 30- and 90-day readmissions were almost identical; (3) readmission within 90 days after discharge was associated with a higher risk for subsequent all-cause death but its timing (0–30 days versus 31–90 days) was not.

To date, several studies that investigated the impact of short-term (eg, 30-day) readmission on subsequent mortality have been reported. In the Alabama Heart Failure Outcome Study With Tolvaptan, a US registry created during an earlier era of HF management (1998–2002), all-cause mortality occurred more frequently in patients with compared with patients without 30-day all-cause readmission.21 A Spanish study using linked administrative data also demonstrated that readmission at 30 days after HF hospitalization was associated with higher in-hospital mortality.8 More recently, the continued incidence of HF readmissions beyond 30 days after discharge of index hospitalization has also been reported.22,23 In the EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan) trial,12 24% of readmissions occurred within the first 30 days after discharge, whereas 20% of them were within 31 to 60 days after discharge and 56% of them were beyond 60 days after discharge. Additionally, cumulative data from 3 trials with newly discharged patients with HHF also demonstrated that a high number of HF readmissions occurred beyond 30 days after discharge.24,25 These findings, together with ours, support the perspective that present readmission monitoring programs (eg, Hospital Readmission Reduction Program, in which 30-day readmission has been used...
| Variables                                      | Overall Cohort | 90-d Readmission (n=397) | 90-d Readmitted Patients | P Value |
|-----------------------------------------------|----------------|--------------------------|--------------------------|---------|
| Demographics and medical history              |                |                          |                          |         |
| Age, y                                        | 73.5±13.5      | 76.7±11.7                | <0.001                   | 0.417   |
| Men, %                                        | 61.1           | 54.4                     | 0.010                    | 0.536   |
| Body mass index, kg/m²                        | 21.8±4.1       | 20.9±3.6                 | <0.001                   | 0.465   |
| Hypertension, %                               | 65.7           | 67.5                     | 0.478                    | 0.579   |
| Diabetes mellitus, %                          | 33.6           | 37.3                     | 0.146                    | 0.875   |
| Dyslipidemia, %                               | 39.0           | 36.4                     | 0.306                    | 0.811   |
| Atrial fibrillation, %                        | 47.0           | 56.2                     | 0.001                    | 0.105   |
| Chronic obstructive pulmonary disease, %      | 4.9            | 3.5                      | 0.217                    | 0.100   |
| Chronic kidney disease, %                     | 67.2           | 77.3                     | <0.001                   | 0.205   |
| Stroke, %                                     | 13.2           | 12.7                     | 0.757                    | 0.089   |
| Cause of HF, %                                |                |                          |                          |         |
| Ischemic                                      | 28.2           | 33.0                     | 0.045                    | 0.460   |
| Dilated                                       | 14.6           | 10.6                     | 0.032                    | 0.976   |
| Valvular                                      | 25.4           | 31.2                     | 0.013                    | 0.928   |
| Previous HF admission, %                      | 27.8           | 46.8                     | <0.001                   | 0.628   |
| New York Heart Association class at discharge, %|                |                          | <0.001                   | 0.665   |
| I                                            | 16.2           | 11.3                     | 11.1                     | 11.6    |
| II                                           | 64.6           | 58.2                     | 60.6                     | 55.8    |
| III                                          | 18.0           | 27.5                     | 24.7                     | 29.9    |
| IV                                           | 1.2            | 3.0                      | 3.6                      | 2.7     |
| Vital signs at discharge                      |                |                          |                          |         |
| Heart rate, beats per min                     | 71.0±12.7      | 72.8±12.3                | 0.008                    | 0.400   |
| SBP, mm Hg                                    | 112.8±17.8     | 109.7±18.3               | 0.003                    | 0.053   |
| Echocardiographic parameters                  |                |                          |                          |         |
| LVEF, %                                       | 44.8±15.2      | 43.0±15.8                | 0.026                    | 0.776   |
| Left atrial dimension, mm                     | 44.7±9.1       | 46.1±10.3                | 0.006                    | 0.400   |
| Laboratory data at discharge                  |                |                          |                          |         |
| Hemoglobin, g/dL                              | 12.2±2.2       | 11.5±2.0                 | <0.001                   | 0.121   |
| Sodium, mEq/L                                 | 138.6±3.5      | 138.3±4.0                | 0.120                    | 0.699   |
| Potassium, mEq/L                              | 4.3±0.5        | 4.3±0.6                  | 0.828                    | 0.139   |
| Uric acid, mg/dL                              | 6.8 (5.6–8.0)  | 6.8 (5.7–7.8)            | 0.790                    | 0.874   |
| Blood urea nitrogen, mg/dL                    | 22.2 (16.4–31.6)| 25.1 (18.2–35.5)       | <0.001                   | 0.631   |
| Estimated glomerular filtration rate, mg/dL per 1.73 m² | 51.4±23.5     | 45.9±23.7                | <0.001                   | 0.808   |
| Brain natriuretic peptide, pg/mL             | 237 (121–465)  | 450 (218–729)            | <0.001                   | 0.054   |
| N-terminal pro–brain natriuretic peptide, pg/mL| 1958 (1029–3817) | 1906 (1340–5915) | 0.720                  | 0.216   |
| Lymphocyte, %                                 | 21.0 (15.6–27.2)| 21.0 (15.0–27.0)       | 0.357                    | 0.014   |
| Total cholesterol, mg/dL                      | 157.0 (137.0–179.0)| 157.0 (136.4–176.5) | 0.196                  | 0.375   |
| Medication or device therapy                  |                |                          |                          |         |
| Loop diuretics, %                             | 75.1           | 77.8                     | 0.241                    | 0.001   |
| β-Blockers, %                                 | 78.6           | 77.1                     | 0.839                    | 0.846   |
| RAS inhibitors, %                             | 64.6           | 55.2                     | <0.001                   | 0.021   |
as a quality benchmark) could be shortsighted, as the actual time window of the vulnerable period for readmission extends beyond 30 days. Recently, evolving concepts of value-based reimbursement have shifted the focus to 90-day readmission after hospital discharge. The substantial proportion of cost within 90 days of an acute myocardial infarction is estimated to be incurred from readmission, and the Centers for Medicare & Medicaid Services announced the implementation of a voluntary 90-day episode payment model for acute myocardial infarction.

In addition, the impact of early readmission on subsequent death was manifested both within and beyond 90 days after index hospitalization based on our landmark analysis, and its impact was remarkable beyond 30 days. Further, the prognostic impact of readmission did not differ, regardless of the time from the index hospitalization, meaning that not only 30-day readmission but also the readmission within 90 days after discharge could be perceived as an alarming sign of subsequent worse prognosis in patients with HF. These findings can have significant clinical implications for several reasons, especially for early-readmitted patients with HF. Because the prognostic impact of early readmission was not manifested within 30 days, this timeframe (within 30 days) could be an opportunity to implement shared decision-making (eg, individualized decision regarding device-based therapy and advanced care planning) and multidisciplinary patient educational programs with optimal medical therapy and strict adherence to recommended lifestyle modifications.

Our study revealed that the incidence of readmission within 30 days and 90 days were 4.8% and 11.1%, respectively. The incidence of early HF readmission in Japan has been reported to be low compared with that in Western countries; around 5% (30-day) in 3 large-scale quality acute HF registries (ATTEND [Acute Decompensated Heart Failure Syndromes], REALITY-AHF [Registry Focused on Very Early Presentation and Treatment in Emergency Department of Acute Heart Failure], and WET-HF) and 3.3% (30-day) and 8.0% (90-day) in the most recently published data from a single university hospital, which were consistent with our data. The incidence of 30-day HF readmission in Western countries was around 10% to 20% in OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) and the GWTG-HF (Get With The Guidelines-Heart Failure) registry. The precise reason for the lower early readmission rates in Japan remains unclear. However, a relatively longer length of hospital stay, a well-known determinant of readmission outcomes, could contribute to the lower incidence

### Table 1. Continued

| Variables                         | Overall Cohort | 90-d Readmitted Patients |
|-----------------------------------|----------------|-------------------------|
|                                   | Non–90-d Readmission (n=3195) | 90-d Readmission (n=397) | P Value | 0 to 30 d (n=171) | 31 to 90 d (n=226) | P Value |
| Mineralocorticoid receptor antagonists, % | 34.9 | 33.3 | 0.537 | 28.1 | 37.2 | 0.062 |
| Statins, %                        | 35.1 | 34.5 | 0.801 | 36.3 | 33.2 | 0.524 |
| Allopurinol, %                    | 21.7 | 27.2 | 0.012 | 26.9 | 27.4 | 0.906 |
| Implantable cardioverter-defibrillator, % | 3.4 | 4.0 | 0.526 | 4.7 | 3.5 | 0.568 |
| Cardiac resynchronization therapy, % | 0.8 | 1.0 | 0.584 | 1.2 | 0.9 | 0.779 |
| Length of stay, d                 | 14 (10–23) | 15 (10–22) | 0.592 | 16 (9–25) | 15 (11–22) | 0.733 |
| SHFM score                        | 0.239 (−2.85 to 0.78) | 0.542 (0.07–1.05) | <0.001 | 0.462 (0.016–1.03) | 0.589 (0.078–1.10) | 0.472 |

Data are shown as mean±SD or median with interquartile range or percentage. HF indicates heart failure; LVEF, left ventricular ejection fraction; RAS, renin-angiotensin system; SBP, systolic blood pressure; and SHFM, Seattle Heart Failure Model.

### Table 2. Cox Proportional Hazard Analysis for Predicting 90-Day Readmission in the Overall Cohort

| Variables                         | HR   | 95% CI      | P Value |
|-----------------------------------|------|-------------|---------|
| Age                               | 1.02 | 1.01–1.03   | <0.001  |
| Men                               | 0.86 | 0.70–1.06   | 0.153   |
| Previous HF admission             | 1.73 | 1.40–2.13   | <0.001  |
| SBP                               | 0.99 | 0.98–1.00   | 0.002   |
| Estimated glomerular filtration rate | 1.00 | 0.99–1.00 | 0.161 |
| Sodium                            | 0.99 | 0.96–1.01   | 0.330   |
| Hemoglobin                        | 0.88 | 0.83–0.93   | <0.001  |
| LVEF                              | 0.99 | 0.98–0.99   | <0.001  |
| β-Blockers                        | 0.98 | 0.77–1.26   | 0.881   |
| RAS inhibitors                    | 0.68 | 0.56–0.84   | <0.001  |
| Mineralocorticoid receptor antagonists | 0.88 | 0.71–1.10 | 0.266 |

HF indicates heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction; RAS, renin-angiotensin system; and SBP, systolic blood pressure.
of HF readmissions in Japanese patients with HF. For instance, longer length of stay could be associated with sufficient decongestion at discharge, or more comprehensive multidisciplinary transitional care management. In fact, we previously showed a nonlinear relationship between length of hospital stay and readmission; relatively short and long length of hospital stay were associated with increased rate of early HF readmission. To further evaluate and establish these hypotheses precisely, a comprehensive assessment of congestion as well as the details of multidisciplinary intervention at discharge will likely be required.

**Study Limitations**

The present study has some limitations that should be considered when interpreting the results. First, this study was based on data from an observational registry and, despite covariate adjustment, unmeasured or unknown variables may have influenced the outcomes.
Table 3. Cox Proportional Hazard Analysis for Predicting All-Cause Death in the Overall Cohort

|                      | HR   | 95% CI       | P Value |
|----------------------|------|--------------|---------|
| Age                  | 1.04 | 1.03–1.05    | <0.001  |
| Men                  | 1.24 | 1.04–1.48    | 0.018   |
| Previous HF admission| 1.08 | 0.90–1.28    | 0.417   |
| SBP                  | 0.99 | 0.99–0.99    | <0.001  |
| Estimated glomerular filtration rate | 0.99 | 0.99–1.00    | <0.001  |
| Sodium               | 0.95 | 0.93–0.97    | <0.001  |
| Hemoglobin           | 0.82 | 0.78–0.86    | <0.001  |
| LVEF                 | 0.99 | 0.98–0.99    | <0.001  |
| β-Blockers           | 0.82 | 0.68–0.99    | 0.039   |
| RAS inhibitors       | 0.68 | 0.57–0.80    | <0.001  |
| Mineralocorticoid receptor antagonists | 1.07 | 0.89–1.29    | 0.455   |
| 90-d readmission     | 2.36 | 1.92–2.91    | <0.001  |

HF indicates heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction; RAS, renin-angiotensin system; and SBP, systolic blood pressure.

Table 4. Cox Proportional Hazard Analysis for Predicting All-Cause Death in 90-Day Readmitted Patients

|                      | HR   | 95% CI       | P Value |
|----------------------|------|--------------|---------|
| Age                  | 1.03 | 1.01–1.05    | 0.013   |
| Men                  | 0.85 | 0.58–1.25    | 0.411   |
| Previous HF admission| 1.21 | 0.83–1.78    | 0.323   |
| SBP                  | 0.99 | 0.98–1.00    | 0.043   |
| Estimated glomerular filtration rate | 0.99 | 0.98–1.00    | 0.004   |
| Sodium               | 0.95 | 0.90–0.99    | 0.027   |
| Hemoglobin           | 0.93 | 0.84–1.02    | 0.128   |
| LVEF                 | 0.98 | 0.97–0.99    | 0.004   |
| β-Blockers           | 0.43 | 0.29–0.64    | <0.001  |
| RAS inhibitors       | 0.62 | 0.42–0.90    | 0.012   |
| Mineralocorticoid receptor antagonists | 1.10 | 0.71–1.68    | 0.678   |

HF indicates heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction; RAS, renin-angiotensin system; and SBP, systolic blood pressure. Still remains elusive. One of the plausible explanations for this is that the reduced use of loop diuretics could be associated with insufficient decongestion at discharge, which may consequently lead to a higher 30-day readmission rate. Comprehensive predischarge evaluation on congestion will be needed to examine this hypothesis. Finally, our registry did not obtain data on the number of readmissions in identical patients; the prognostic impact of the number of readmissions for a particular period (eg, 6 months) could not be evaluated; however, this has been described elsewhere. Despite these limitations, this study highlights the continuous HF readmission beyond 30 days and its poor prognosis, which underlines the universal characteristics of patients readmitted with HF and challenges the current excessive focus on 30-day readmission bringing unintended consequence.

CONCLUSIONS

Among 90-day readmitted HF patients, approximately 60% of readmissions occurred beyond 30 days after discharge in a contemporary Japanese HHF registry. The readmitted patients within 90 days had higher risk of long-term mortality, regardless of the temporal proximity of readmission to the index hospitalization.

ARTICLE INFORMATION

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Disclosures

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Supplementary Materials

Tables S1–S3

Figure S1
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SUPPLEMENTAL MATERIAL
Table S1. Frequency of missing data.

| Variables                      | n  | %   |
|-------------------------------|----|-----|
| Demographics and medical history |    |     |
| Age                           | 0  | 0.00|
| Male                          | 0  | 0.00|
| BMI                           | 166| 4.62|
| Hypertension                  | 1  | 0.03|
| Diabetes mellitus             | 3  | 0.08|
| Dyslipidemia                  | 28 | 0.78|
| Atrial fibrillation           | 2  | 0.06|
| COPD                          | 18 | 0.50|
| CKD                           | 0  | 0.00|
| Stroke                        | 13 | 0.36|
| Etiology of HF                | 0  | 0.00|
| Previous HF admission         | 30 | 0.84|
| NYHA at discharge             | 26 | 0.72|
| Vital signs at discharge      |    |     |
| Heart rate                    | 24 | 0.67|
| SBP                           | 19 | 0.53|
| Echocardiographic parameters  |    |     |
| LVEF                          | 34 | 0.95|
| Laboratory data at discharge  |    |     |
| Hemoglobin                    | 15 | 0.42|
| Sodium                        | 18 | 0.50|
| eGFR                          | 25 | 0.70|
| Lymphocyte                    | 384| 10.69|
| Total-Cholesterol             | 462| 12.86|
Medication or device therapy

| Therapy              | Count | Probability |
|----------------------|-------|-------------|
| Loop diuretics       | 4     | 0.11        |
| Beta-blockers        | 3     | 0.08        |
| RAS inhibitors       | 2     | 0.06        |
| MRA                  | 142   | 3.95        |
| ICD                  | 3     | 0.08        |
| CRT                  | 4     | 0.11        |

| Length of stay       | 0     | 0.00        |
| SHFM Score           | 747   | 20.80       |

Prognostic information

| Outcome                           | Count | Probability |
|-----------------------------------|-------|-------------|
| In-hospital death                 | 0     | 0.00        |
| HF-related readmission            | 0     | 0.00        |
| Mortality                         | 0     | 0.00        |

BMI: body mass index, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, HF: heart failure, NYHA: New York heart association, SBP: systolic blood pressure, LVEF: left ventricular ejection fraction, eGFR: estimated glomerular filtration rate, RAS: renin-angiotensin system, MRA: mineralocorticoid receptor antagonists, ICD: implantable cardioverter defibrillator, CRT: cardiac resynchronization therapy, SHFM: Seattle heart failure model.
Table S2. Cox proportional hazard analysis and Fine and Gray competing analysis for predicting 90-day readmission in overall cohort.

|                                     | Cox proportional hazard analysis | Competing risk analysis |
|-------------------------------------|----------------------------------|-------------------------|
|                                     | HR (95% CI, p-value)             | HR (95% CI, p-value)    |
| Age                                 | 1.02 (1.01-1.03, <0.001)         | 1.02 (1.01-1.03, 0.002) |
| Male                                | 0.86 (0.70-1.06, 0.153)          | 0.83 (0.70-1.02, 0.074) |
| Previous HF admission               | 1.73 (1.40-2.13, <0.001)         | 1.82 (1.48-2.25, <0.001) |
| SBP                                 | 0.99 (0.98-1.00, 0.002)          | 0.99 (0.99-1.00, 0.016) |
| eGFR                                | 1.00 (0.99-1.00, 0.161)          | 1.00 (0.99-1.00, 0.380) |
| Sodium                              | 0.99 (0.96-1.01, 0.330)          | 1.00 (0.97-1.03, 0.800) |
| Hemoglobin                          | 0.88 (0.83-0.93, <0.001)         | 0.90 (0.85-0.96, <0.001) |
| LVEF                                | 0.99 (0.98-0.99, <0.001)         | 0.99 (0.98-1.00, 0.002) |
| Beta-blockers                       | 0.98 (0.77-1.26, 0.881)          | 1.04 (0.81-1.33, 0.760) |
| RAS inhibitors                      | 0.68 (0.56-0.84, <0.001)         | 0.75 (0.61-0.92, 0.005) |
| MRA                                 | 0.88 (0.71-1.10, 0.266)          | 0.91 (0.74-1.12, 0.370) |

HR: hazard ratio, CI: confidence interval, HF: heart failure, SBP: systolic blood pressure, eGFR: estimated glomerular filtration rate, LVEF: left ventricular ejection fraction, RAS: renin-angiotensin system, MRA: mineralocorticoid receptor antagonists
Table S3. Cox proportional hazard analysis for predicting 30-day readmission in overall cohort.

|                         | HR   | 95% CI      | p Value |
|-------------------------|------|-------------|---------|
| Age                     | 1.02 | 1.00 - 1.03 | 0.016   |
| Male                    | 0.76 | 0.55 - 1.05 | 0.090   |
| Previous HF admission   | 1.98 | 1.44 - 2.73 | <0.001  |
| SBP                     | 1.00 | 0.99 - 1.01 | 0.846   |
| eGFR                    | 1.00 | 0.99 - 1.01 | 0.562   |
| Sodium                  | 0.99 | 0.94 - 1.03 | 0.466   |
| Hemoglobin              | 0.94 | 0.86 - 1.03 | 0.160   |
| LVEF                    | 0.98 | 0.97 - 0.99 | 0.003   |
| Beta-blockers           | 0.97 | 0.66 - 1.41 | 0.858   |
| RAS inhibitors          | 0.53 | 0.39 - 0.72 | <0.001  |
| MRA                     | 0.69 | 0.49 - 0.98 | 0.040   |

HR: hazard ratio, CI: confidence interval, HF: heart failure, SBP: systolic blood pressure, eGFR: estimated glomerular filtration rate, LVEF: left ventricular ejection fraction, RAS: renin-angiotensin system, MRA: mineralocorticoid receptor antagonists.
Figure S1. Kaplan-Meier analysis demonstrating survival rate of readmitted patients and non-readmitted patients in 2-year-follow up with Landmark analysis at 0 day and 120 (A), 180 (B), and 360 (C) day.