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## Supplementary File

# Incidence and Clinical Significance of 30-Day and 90-Day Rehospitalization for Heart Failure Among Patients With Acute Decompensated Heart Failure in Japan

— From the NARA-HF Study —

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**Supplementary Table 1. Baseline Characteristics of the Patients Who Died Within 90 Days**

|  | <b>Without<br/>90-day re-HHF or death<br/>(n=683)</b> | <b>With<br/>90-day death<br/>(n=43)</b> | <b>P-value</b> |
|--|---|---|----------------|
| <b>Demographic</b>                               |   |   |                |
| Age (years)                                      | 72.8 ± 12.6   | 79.4 ± 9.2                              | 0.001          |
| Male (%)   | 53.7  | 67.4                                    | 0.076          |
| BMI (kg/m <sup>2</sup> )                         | 23.6 ± 4.3  | 21.3 ± 3.1                              | 0.001          |
| NYHA class III or IV on admission (%)            | 89.2  | 95.3                                    | 0.156          |
| NYHA class III or IV at discharge (%)            |   |   |                |
| Length of hospitalization (days)                 | 19 [13-29]  | 24 [16-45]                              | 0.051          |
| Discharged home (%)                              | 89.5  | 62.8                                    | <0.001         |
| <b>Causes of HF, %</b>                           |   |   |                |
| Ischemic heart disease                           | 36.5  | 34.9                                    | 0.835          |
| Dilated cardiomyopathy                           | 15.2  | 7.0                                     | 0.106          |
| Hypertensive heart disease                       | 7.9   | 2.3                                     | 0.123          |
| Valvular heart disease                           | 15.7  | 20.9                                    | 0.378          |
| <b>Medical history, %</b>                        |   |   |                |
| Diabetes mellitus                                | 45.1  | 55.8                                    | 0.172          |
| AF   | 31.2  | 41.9                                    | 0.154          |
| <b>Vital sign on admission</b>                   |   |   |                |
| Heart rate (beats/min)                           | 97.9 ± 27.7   | 98.7 ± 28.0                             | 0.862          |
| SBP (mmHg)                                       | 149.6 ± 35.9  | 135.4 ± 35.9                            | 0.013          |
| <b>Vital sign at discharge</b>                   |   |   |                |
| Heart rate (beats/min)                           | 71.5 ± 11.1   | 77.3 ± 15.8                             | 0.001          |
| SBP (mmHg)                                       | 113.4 ± 17.9  | 108.8 ± 20.3                            | 0.104          |
| <b>Echocardiographic parameters at discharge</b> |   |   |                |
| LVEF (%)   | 45.7 ± 16.5   | 45.5 ± 18.1                             | 0.931          |

|                                     |                |                 |        |
|-------------------------------------|----------------|-----------------|--------|
| LVEF≥50% (%)                        | 39.2           | 44.2            | 0.728  |
| <b>Laboratory data on admission</b> |                |                 |        |
| BNP (pg/ml)                         | 886 [451-1570] | 1305 [557-1797] | 0.309  |
| Hemoglobin (g/dl)                   | 11.6 ± 2.4     | 10.7 ± 1.8      | 0.015  |
| eGFR (ml/min/1.73m <sup>2</sup> )   | 47.1 ± 27.6    | 39.0 ± 23.5     | 0.061  |
| BUN (mg/dl)                         | 29.6 ± 21.0    | 43.4 ± 29.7     | <0.001 |
| CRP (mg/dl)                         | 0.5 [0.2-2.0]  | 1.8 [0.5-4.9]   | <0.001 |
| Sodium (mEq/L)                      | 138.7 ± 4.1    | 137.4 ± 4.7     | 0.052  |
| <b>Laboratory data at discharge</b> |                |                 |        |
| BNP (pg/ml)                         | 234 [129-464]  | 444 [273-857]   | 0.001  |
| Hemoglobin (g/dl)                   | 11.5 ± 2.1     | 10.5 ± 1.7      | 0.002  |
| eGFR (ml/min/1.73m <sup>2</sup> )   | 43.3 ± 25.4    | 43.2 ± 24.4     | 0.963  |
| BUN (mg/dl)                         | 31.1 ± 17.7    | 41.4 ± 23.6     | <0.001 |
| CRP (mg/dl)                         | 0.3 [0.1-1.0]  | 0.9 [0.3-2.0]   | <0.001 |
| Sodium (mEq/L)                      | 138.0 ± 3.7    | 137.1 ± 4.5     | 0.105  |
| <b>Medication at discharge</b>      |                |                 |        |
| β-blockers (%)                      | 58.6           | 72.1            | 0.073  |
| ACE-I/ARBs (%)                      | 88.6           | 73.8            | 0.011  |
| MRA (%)                             | 34.9           | 32.6            | 0.759  |
| Diuretics (%)                       | 78.4           | 81.4            | 0.639  |
| Loop diuretics (%)                  | 77.0           | 81.4            | 0.490  |

Data are presented as the mean ± SD for continuous normally distributed variables, the median (25th to 75th interquartile range [IQR]) for continuous non-normally distributed variables, or n (%).

re-HHF, rehospitalizations for heart failure; BMI, body mass index; NYHA, New York Heart Association; AF, atrial fibrillation; SBP, systolic blood pressure; LVEF, left ventricular ejection fraction; BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen; CRP, C-reactive protein; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; MRA, mineralocorticoid receptor antagonist.

P-values are generated from the comparison of the patients without 90-day re-HHF or death vs. the patients with 90-day death.

**Supplementary Table 2. Baseline Characteristics of Patients According to Sex (A) and Patients With Early (Within 30 Days) and Late (31–90 Days) Rehospitalization (B)**

**Supplementary Table 2A**

|                                       | <b>Male<br/>(n=432)</b> | <b>Female<br/>(n=351)</b> | <b>P-value</b> |
|---------------------------------------|-------------------------|---------------------------|----------------|
| <b>Demographic</b>                    |                         |                           |                |
| Age (years)                           | 71.9 ± 12.2             | 75.0 ± 12.3               | <0.001         |
| BMI (kg/m <sup>2</sup> )              | 23.8 ± 4.0              | 23.0 ± 4.4                | 0.019          |
| NYHA class III or IV on admission (%) | 90.3                    | 89.2                      | 0.613          |
| NYHA class III or IV at discharge (%) | 4.2                     | 4.8                       | 0.649          |
| Length of hospitalization (days)      | 20 [14-29]              | 19 [13-29]                | 0.680          |
| Days until re-HHF                     | 245 [73-728]            | 336 [122-801]             | 0.052          |
| Discharged home (%)                   | 91.0                    | 84.9                      | 0.009          |
| <b>Causes of HF, %</b>                |                         |                           |                |
| Ischemic heart disease                | 46.3                    | 25.6                      | <0.001         |
| Dilated cardiomyopathy                | 15.5                    | 13.1                      | 0.340          |
| Hypertensive heart disease            | 6.7                     | 8.8                       | 0.269          |
| Valvular heart disease                | 9.5                     | 23.7                      | <0.001         |
| <b>Medical history, %</b>             |                         |                           |                |
| Diabetes mellitus                     | 51.9                    | 39.3                      | <0.001         |
| AF                                    | 31.3                    | 33.1                      | 0.592          |
| <b>Vital sign on admission</b>        |                         |                           |                |
| Heart rate (beats/min)                | 98.3 ± 27.4             | 97.0 ± 28.0               | 0.502          |
| SBP (mmHg)                            | 149.1 ± 36.8            | 148.3 ± 34.7              | 0.749          |
| <b>Vital sign at discharge</b>        |                         |                           |                |
| Heart rate (beats/min)                | 71.4 ± 11.2             | 72.0 ± 12.0               | 0.467          |
| SBP (mmHg)                            | 113.0 ± 18.6            | 113.9 ± 17.9              | 0.481          |

| <b>Echocardiographic parameters at discharge</b> |                |                |        |
|--|----------------|----------------|--------|
| LVEF (%)   | 43.1 ± 16.3    | 49.3 ± 16.3    | <0.001 |
| LVEF≥50% (%)                                     | 32.4           | 48.2           | <0.001 |
| <b>Laboratory data on admission</b>              |                |                |        |
| BNP (pg/ml)                                      | 931 [500-1618] | 806 [417-1555] | 0.786  |
| Hemoglobin (g/dl)                                | 12.0 ± 2.6     | 10.9 ± 2.1     | <0.001 |
| eGFR (ml/min/1.73m <sup>2</sup> )                | 44.8 ± 26.3    | 47.6 ± 28.4    | 0.154  |
| BUN (mg/dl)                                      | 31.8 ± 22.4    | 29.1 ± 20.7    | 0.086  |
| CRP (mg/dl)                                      | 0.8 [0.2-2.7]  | 0.5 [0.2-1.7]  | 0.045  |
| Sodium (mEq/L)                                   | 138.7 ± 3.9    | 138.4 ± 4.5    | 0.373  |
| <b>Laboratory data at discharge</b>              |                |                |        |
| BNP (pg/ml)                                      | 279 [137-499]  | 234 [126-465]  | 0.094  |
| Hemoglobin (g/dl)                                | 11.8 ± 2.3     | 11.0 ± 1.7     | <0.001 |
| eGFR (ml/min/1.73m <sup>2</sup> )                | 42.8 ± 24.0    | 42.8 ± 26.3    | 0.993  |
| BUN (mg/dl)                                      | 32.4 ± 18.5    | 31.8 ± 18.5    | 0.692  |
| CRP (mg/dl)                                      | 0.4 [0.1-1.2]  | 0.4 [0.1-0.9]  | 0.194  |
| Sodium (mEq/L)                                   | 137.7 ± 3.6    | 138.2 ± 4.1    | 0.068  |
| <b>Medication at discharge</b>                   |                |                |        |
| β-blockers (%)                                   | 64.1           | 53.6           | 0.003  |
| ACE-I/ARBs (%)                                   | 90.0           | 84.8           | 0.029  |
| MRA (%)  | 31.9           | 37.0           | 0.136  |
| Diuretics (%)                                    | 78.4           | 79.1           | 0.807  |
| Loop diuretics (%)                               | 76.8           | 78.0           | 0.690  |

**Supplementary Table 2B**

|  | <b>With<br/>early rehospitalization<br/>(n=26)</b> | <b>With<br/>late rehospitalization<br/>(n=37)</b> | <b>P-value</b> |
|--|--|---|----------------|
| <b>Demographic</b>                               |  |   |                |
| Age (years)                                      | 73.5 ± 10.7  | 76.0 ± 7.9  | 0.285          |
| Male (%)   | 73.1   | 62.2  | 0.362          |
| BMI (kg/m <sup>2</sup> )                         | 23.8 ± 3.4   | 22.7 ± 3.5  | 0.219          |
| NYHA class III or IV (%)                         | 88.5   | 97.3  | 0.157          |
| Length of hospitalization (days)                 | 22 [13-26]   | 21 [12-37]  | 0.256          |
| <b>Causes of HF, %</b>                           |  |   |                |
| Ischemic heart disease                           | 42.3   | 46  | 0.775          |
| Dilated cardiomyopathy                           | 15.4   | 5.4   | 0.187          |
| Hypertensive heart disease                       | 0  | 13.5  | 0.018          |
| Valvular heart disease                           | 23.1   | 10.8  | 0.193          |
| <b>Medical history, %</b>                        |  |   |                |
| Diabetes mellitus                                | 57.7   | 54.1  | 0.775          |
| AF   | 42.3   | 32.4  | 0.424          |
| <b>Vital sign at discharge</b>                   |  |   |                |
| Heart rate (beats/min)                           | 70.4 ± 8.1   | 70.3 ± 14.2                                       | 0.978          |
| SBP (mmHg)                                       | 119.8 ± 15.3                                       | 114.6 ± 23.8                                      | 0.331          |
| <b>Echocardiographic parameters at discharge</b> |  |   |                |
| LVEF (%)   | 46.4 ± 15.0  | 48.5 ± 17.4                                       | 0.611          |
| LVEF≥50% (%)                                     | 42.3   | 35.1  | 0.564          |
| <b>Laboratory data at discharge</b>              |  |   |                |
| BNP (pg/ml)                                      | 281 [136-650]                                      | 331 [115-692]                                     | 0.755          |
| Hemoglobin (g/dl)                                | 11.7 ± 2.1   | 10.8 ± 1.7  | 0.061          |
| eGFR (ml/min/1.73m <sup>2</sup> )                | 40.9 ± 19.2  | 32.0 ± 20.0                                       | 0.081          |
| BUN (mg/dl)                                      | 32.3 ± 13.9  | 42.1 ± 23.2                                       | 0.062          |

|                                |               |               |       |
|--------------------------------|---------------|---------------|-------|
| CRP (mg/dl)                    | 0.5 [0.1-1.6] | 0.6 [0.1-1.1] | 0.473 |
| Sodium (mEq/L)                 | 138.6 ± 4.2   | 135.9 ± 5.0   | 0.029 |
| <b>Medication at discharge</b> |               |               |       |
| β-blockers (%)                 | 57.7          | 62.2          | 0.721 |
| ACE-I/ARBs (%)                 | 84.6          | 88.6          | 0.652 |
| MRA (%)                        | 30.8          | 27.0          | 0.747 |
| Diuretics (%)                  | 84.6          | 81.1          | 0.715 |
| Loop diuretics (%)             | 84.6          | 78.4          | 0.531 |

Data are presented as the mean ± SD for continuous normally distributed variables, the median (25th to 75th interquartile range [IQR]) for continuous non-normally distributed variables, or n (%).

re-HHF, rehospitalizations for heart failure; BMI, body mass index; NYHA, New York Heart Association; AF, atrial fibrillation; SBP, systolic blood pressure; LVEF, left ventricular ejection fraction; BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen; CRP, C-reactive protein; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; MRA, mineralocorticoid receptor antagonist.

*P*-values are generated from the comparison of male patients vs. female patients (A).

*P*-values are generated from the comparison of the patients with early rehospitalization vs. the patients with late rehospitalization (B).

**Supplementary Table 3. Predictors of the Composite Outcome Using 90-Day All-Cause Death and HF Rehospitalization**

| Covariate                                | Univariate |               |         | Multivariate |               |         |
|--|------------|---------------|---------|--------------|---------------|---------|
|  | HR         | 95% CI        | P-value | HR           | 95% CI        | P-value |
| Age (per 1 year)                         | 1.030      | (1.012-1.050) | 0.001   | 1.026        | (1.004-1.048) | 0.021   |
| Male/Female                              | 1.555      | (1.038-2.369) | 0.032   | 1.966        | (1.242-3.179) | 0.004   |
| Length of hospitalization (days)         | 1.003      | (0.994-1.009) | 0.410   |              |               |         |
| Discharged home/Transfer                 | 0.507      | (0.317-0.850) | 0.011   | 0.603        | (0.353-1.084) | 0.089   |
| Diabetes mellitus                        | 1.384      | (0.934-2.057) | 0.105   |              |               |         |
| AF                                       | 1.332      | (0.882-1.984) | 0.170   |              |               |         |
| <b>Vital sign on admission</b>           |            |               |         |              |               |         |
| Heart rate (per 1 bpm)                   | 0.998      | (0.991-1.005) | 0.574   |              |               |         |
| SBP (per 10 mmHg)                        | 0.953      | (0.900-1.007) | 0.090   |              |               |         |
| <b>Vital sign at discharge</b>           |            |               |         |              |               |         |
| Heart rate (per 1 bpm)                   | 1.012      | (0.996-1.029) | 0.149   |              |               |         |
| SBP (per 10 mmHg)                        | 0.999      | (0.896-1.111) | 0.983   |              |               |         |
| LVEF at discharge (per 1%)               | 1.001      | (0.991-1.006) | 0.775   |              |               |         |
| <b>Laboratory data on admission</b>      |            |               |         |              |               |         |
| BNP (per 100 pg/ml)                      | 1.006      | (0.987-1.022) | 0.536   |              |               |         |
| Hemoglobin (per 1 g/dl)                  | 0.906      | (0.834-0.983) | 0.017   | 0.972        | (0.848-1.115) | 0.690   |
| BUN (per 1 mg/dl)                        | 1.012      | (1.005-1.019) | 0.002   | 1.005        | (0.992-1.018) | 0.485   |
| eGFR (per 1 ml/min/1.73 m <sup>2</sup> ) | 0.990      | (0.982-0.997) | 0.008   | 1.004        | (0.993-1.016) | 0.475   |
| <b>Laboratory data at discharge</b>      |            |               |         |              |               |         |
| BNP (per 100 pg/ml)                      | 1.035      | (1.004-1.058) | 0.030   | 1.026        | (0.996-1.057) | 0.089   |
| Hemoglobin (per 1 g/dl)                  | 0.865      | (0.780-0.956) | 0.004   | 0.978        | (0.828-1.154) | 0.789   |
| BUN (per 1 mg/dl)                        | 1.017      | (1.008-1.025) | <0.001  | 1.013        | (1.001-1.025) | 0.038   |
| eGFR (per 1 ml/min/1.73 m <sup>2</sup> ) | 0.994      | (0.985-1.002) | 0.115   |              |               |         |

**Medication at discharge**

|                    |                        |       |
|--------------------|------------------------|-------|
| β-blockers (%)     | 1.283<br>(0.857-1.955) | 0.229 |
| ACE-I/ARBs (%)     | 0.598<br>(0.367-1.029) | 0.062 |
| MRA (%)            | 0.810<br>(0.521-1.230) | 0.328 |
| Loop diuretics (%) | 1.193<br>(0.746-2.000) | 0.473 |

HF, heart failure; HR, hazard ratio; CI, confidence interval, AF, atrial fibrillation; SBP, systolic blood pressure; LVEF, left ventricular ejection fraction; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; MRA, mineralocorticoid receptor antagonist.