Relationship Between Heart Failure Hospitalization Costs and Left Ventricular Ejection Fraction in an Advanced Aging Society

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Supplementary Appendix for Relationship Between Heart Failure Hospitalization Costs and Left Ventricular Ejection Fraction in an Advanced Aging Society

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CONTENTS

Supplementary Table 1. Baseline Characteristics and Treatments and Outcomes in the Study Patients by Age

Supplementary Table 2. Results of Univariate and Multivariable Liner Regression Analyses for Log-Transformed Hospitalization Costs in the Study Patients

Supplementary Table 3. The Standardized Regression Coefficients for the Log-Transformed Hospitalization Costs in Older Adults

Supplementary Figure 1. Distribution of hospitalization costs for heart failure

Supplementary Figure 2. The absolute values of standardized β in the best predictive model of older adults
Supplementary Table 1. Baseline Characteristics and Treatments and Outcomes in the Study Patients by Age

| Baseline Characteristics | Total population (n=346) | Age <75 years (n=94) | Age ≥75 years (n=252) | P value |
|--------------------------|--------------------------|----------------------|-----------------------|---------|
| Age, y                   | 78±13                    | 62±11                | 85±6                  | <0.001  |
| Male, n (%)              | 188 (54)                 | 67 (71)              | 121 (48)              | <0.001  |
| Body mass index, kg/m²   | 21.8±4.3                 | 23.9±4.5             | 21.1±3.8              | <0.001  |
| Ambulance use, n (%)     | 243 (70)                 | 65 (69)              | 178 (71)              | 0.788   |
| Smoking history, n (%)   | 143 (41)                 | 60 (63)              | 83 (33)               | <0.001  |
| De novo HF hospitalization, n (%) | 240 (69) | 63 (67) | 177 (70) | 0.563 |
| NYHA functional class, n (%) |                        |                      |                      | 0.251   |
| I                        | 0 (0)                    | 0 (0)                | 0 (0)                 |         |
| II                       | 5 (1)                    | 3 (3)                | 2 (1)                 |         |
| III                      | 93 (27)                  | 25 (27)              | 68 (27)               |         |
| IV                       | 248 (72)                 | 66 (70)              | 182 (72)              |         |
| Comorbidities, n (%)     |                          |                      |                      |         |
| Hypertension             | 265 (77)                 | 70 (74)              | 195 (77)              | 0.569   |
| Dyslipidemia             | 78 (23)                  | 25 (27)              | 53 (21)               | 0.272   |
| Diabetes mellitus        | 163 (47)                 | 56 (60)              | 107 (42)              | 0.004   |
| AF                       | 143 (41)                 | 30 (32)              | 113 (45)              | 0.029   |
| Stroke                   | 54 (16)                  | 10 (11)              | 44 (17)               | 0.119   |
| CKD                      | 50 (14)                  | 8 (9)                | 42 (17)               | 0.054   |
| Malignant tumor          | 44 (12)                  | 8 (9)                | 36 (14)               | 0.151   |
| Renal dialysis           | 12 (3)                   | 7 (7)                | 5 (2)                 | 0.013   |
| HF etiology              |                          |                      |                      | <0.001  |
| Ischemic heart disease, n (%) | 112 (32) | 33 (35) | 79 (31) |         |
| Valvular disease, n (%)  | 86 (25)                  | 13 (14)              | 73 (29)               |         |
| Cardiomyopathy, n (%)    | 36 (10)                  | 21 (22)              | 15 (6)                |         |
| Hypertensive heart disease, n (%) | 67 (19) | 19 (20) | 48 (19) |         |
| Unclassified, n (%)      | 45 (13)                  | 8 (9)                | 37 (15)               |         |
| Hemodynamic parameters   |                          |                      |                      |         |
| Systolic blood pressure, mmHg | 147±36   | 150±44              | 147±33                | 0.493   |
| Diastolic blood pressure, mmHg | 88±25   | 98±28               | 84±23                 | <0.001  |
| CS1, n (%)               | 192 (55)                 | 46 (49)              | 146 (58)              | 0.134   |
| Heart rate, bpm          | 98±27                    | 109±27               | 95±26                 | <0.001  |
| Laboratory data          |                          |                      |                      |         |
| BNP, pg/mL               | 595 [343-1117]           | 542 [295-1096]       | 608 [357-1127]        | 0.551   |
| Creatinine, mg/dL        | 1.51±1.29                | 1.83±1.88            | 1.39±0.98             | 0.005   |
| Measure                                | Baseline | Intervention 1 | Intervention 2 | p-value |
|----------------------------------------|----------|----------------|----------------|---------|
| **Clinical variables**                 |          |                |                |         |
| Albumin, g/dL                          | 3.43±0.53| 3.63±0.51      | 3.43±0.53      | 0.003   |
| Serum sodium, mEq/L                    | 139.0±4.9| 139.3±3.9      | 138.9±5.2      | 0.606   |
| Hemoglobin, g/dL                       | 11.7±2.4 | 13.0±2.5       | 11.3±2.3       | <0.001  |
| CRP, mg/dL                             | 0.63 [0.18-2.56] | 0.56 [0.17-2.11] | 0.68 [0.18-2.92] | 0.926   |
| **Echocardiographic variables**        |          |                |                |         |
| Septal wall thickness, mm              | 10.2±1.8 | 10.3±2.1       | 10.2±1.7       | 0.677   |
| Posterior wall thickness, mm           | 10.6±1.7 | 10.8±2.0       | 10.6±1.6       | 0.332   |
| Diastolic LV diameter, mm              | 49.1±9.1 | 53.9±9.3       | 47.3±8.4       | <0.001  |
| Systolic LV diameter, mm               | 38.4±10.5| 44.2±10.8      | 36.3±0.6       | <0.001  |
| LVEF, %                                | 44.4±14.6| 38.3±13.9      | 46.7±14.3      | <0.001  |
| Left atrium diameter, mm               | 40.2±7.5 | 41.4±7.5       | 39.7±7.5       | 0.069   |
| TRPG, mmHg                             | 36.4±14.6| 31.2±12.2      | 38.2±14.9      | <0.001  |

**Treatments and Outcomes**

| Treatment/Operation, n (%)            |          |                |                |         |
|---------------------------------------|----------|----------------|----------------|---------|
| Central venous injection              | 16 (5)   | 1 (4)          | 12 (5)         | 0.841   |
| Transfusion                           | 22 (6)   | 5 (5)          | 17 (6)         | 0.628   |
| Temporary pacing                      | 4 (1)    | 1 (1)          | 3 (1)          | 0.921   |
| Pacemaker implantation                | 6 (2)    | 2 (2)          | 4 (2)          | 0.732   |
| Ventilator                            | 100 (29) | 35 (37)        | 65 (26)        | 0.036   |
| CRRT                                  | 7 (2)    | 4 (4)          | 3 (1)          | 0.071   |
| CAG                                   | 106 (31) | 45 (48)        | 61 (24)        | <0.001  |
| PCI                                   | 18 (5)   | 6 (6)          | 12 (4)         | 0.545   |
| IABP                                  | 1 (0)    | 1 (1)          | 0 (0)          | 0.101   |
| ECMO                                  | 1 (0)    | 1 (1)          | 0 (0)          | 0.101   |
| Other operation                       | 4 (1)    | 0 (0)          | 4 (2)          | 0.219   |
| Myocardial perfusion scintigraphy     | 10 (3)   | 5 (5)          | 5 (2)          | 0.099   |
| Cardiac rehabilitation                | 187 (54)| 39 (41)        | 148 (59)       | 0.004   |
| Discharge destination (%)             |          |                |                | 0.016   |
| Home                                  | 245 (71) | 77 (82)        | 168 (67)       |         |
| Hospital                              | 67 (19)  | 11 (12)        | 56 (22)        |         |
| Nursing facility                      | 11 (3)   | 0 (0)          | 11 (4)         |         |
| In-hospital death                     | 23 (7)   | 6 (6)          | 17 (7)         |         |

| Length of stay (LOS), median          |          |                |                |         |
| LOS, overall days                     | 17 [11-23]| 15.5 [9-20]    | 17 [11-24]     | 0.458   |
| LOS, HCU or ICU days                 | 3 [2-5]  | 2.5 [2-3.3]    | 3 [2-5]        | 0.843   |
| Patients with any ICU, HCU stays, n (%)| 175 (51) | 46 (49)        | 129 (51)       | 0.709   |
| The costs ($) of the bundled paymentA | 5549 [4013-7423] | 5495 [3859-7230] | 5571 [4040-7587] | 0.756   |
| The costs ($) of the service feeA     | 1057 [652-1545] | 1221 [727-1723] | 983 [648-1488] | 0.150   |
| Total Costs ($) of HF hospital stayA  | 6780 [5016-8970] | 6909 [4913-8789] | 6743 [5110-9038] | 0.311   |
Data given as the mean ± SD, median [IQR, interquartile range] or n (%). AF, atrial fibrillation; BNP, brain natriuretic peptide; CKD, chronic kidney disease; CRP, c-reactive protein; CS1, clinical scenario; ECMO, extracorporeal membrane oxygenation; HF, heart failure; LVEF, left ventricular ejection fraction; NYHA, new york heart association; TRPG, tricuspid regurgitation pressure gradient; CAG, coronary angiography; CRRT, continuous renal replacement therapy; DPC, diagnosis procedure combination; HCU, high care unit; IABP, intra-aortic balloon pumping; ICU, intensive care unit; PCI, percutaneous coronary intervention. ^Costs presented in US$ 2017. P values for costs presents are for comparisons of log-transformed costs.
Supplementary Table 2. Results of Univariate and Multivariable Linear Regression Analyses for Log-Transformed Hospitalization Costs in the Study Patients

| Variable                                      | Total population (N=346) | Univariate Analysis | Model 1 A | Best predictive model B |
|-----------------------------------------------|--------------------------|---------------------|-----------|------------------------|
|                                               |                          | un-standardized β   | 95% CI    | P value                | un-standardized β | 95% CI    | P value    | un-standardized β | 95% CI    | P value |
| Age, per 1 y increment                        | -0.0003                  | -0.0024, 0.0019     | 0.783     | -0.0022                | -0.0047, 0.0006  | 0.125     |
| Male                                          | -0.0363                  | -0.0913, 0.0188     | 0.196     | -0.0195                | -0.0791, 0.0400  | 0.518     |
| Body mass index, per 1 kg/m² increment        | -0.0063                  | -0.0127, 0.0002     | 0.056     | -0.0016                | -0.0091, 0.0058  | 0.665     |
| Systolic blood pressure, per 1 mmHg increment | -0.0006                  | -0.0013, 0.0002     | 0.118     | -0.0012                | -0.0021, -0.0003 | 0.009     |
| Heart rate, per 1 bpm increment               | -0.0001                  | -0.0011, 0.0009     | 0.823     | -0.0005                | -0.0016, 0.0006  | 0.358     |
| NYHA class IV                                 | 0.0833                   | 0.0229, 0.1436      | 0.007     | 0.0824                 | 0.0193, 0.1455  | 0.010     |
| De-novo HF hospitalization                    | 0.0557                   | -0.0036, 0.1151     | 0.065     | 0.0648                 | 0.0016, 0.1280  | 0.044     |
| Ischemic etiology                             | 0.0534                   | -0.0051, 0.1118     | 0.073     | 0.0178                 | -0.0447, 0.0803 | 0.576     |
| Ambulance use                                 | 0.0637                   | 0.0040, 0.1234      | 0.037     | 0.0681                 | 0.0027, 0.1334  | 0.041     |
| Comorbidities                                 |                          |                     |           |                        |                     |           |
| Hypertension                                  | -0.0174                  | -0.0823, 0.0474     | 0.598     | 0.0031                 | -0.0645, 0.0707  | 0.928     |
| Dyslipidemia                                  | 0.0687                   | 0.0033, 0.1340      | 0.040     | 0.0627                 | -0.0029, 0.1284  | 0.061     |
| Diabetes mellitus                             | 0.0370                   | -0.0179, 0.0919     | 0.186     | 0.0085                 | -0.0470, 0.0640  | 0.763     |
| AF                                            | -0.0370                  | -0.0927, 0.0186     | 0.192     | 0.0104                 | -0.0502, 0.0709  | 0.736     |
| Renal dialysis                                | 0.0403                   | -0.1098, 0.1904     | 0.598     | 0.0415                 | -0.1631, 0.2461  | 0.690     |
| Laboratory data                               |                          |                     |           |                        |                     |           |
| Creatinine, per 1 mg/dL increment             | -0.0030                  | -0.0241, 0.0181     | 0.780     | -0.0139                | -0.0442, 0.0165  | 0.368     |
| Serum sodium, per 1 mEq/L increment           | -0.0036                  | -0.0090, 0.0019     | 0.198     | -0.0038                | -0.0095, 0.0019  | 0.187     |
| Hemoglobin, per 1 g/dL increment | -0.0073 | -0.0181, 0.0034 | 0.181 | -0.0146 | -0.0270, -0.0023 | 0.020 |
|--------------------------------|---------|-----------------|------|---------|-----------------|------|
| **Echocardiographic variables** |         |                 |      |         |                 |      |
| Posterior wall thickness, per 1 mm increment | -0.0173 | -0.0330, -0.0014 | 0.033 | -0.0030 | -0.0197, 0.0137 | 0.726 |
| LVEF, per 10 % increment | -0.0186 | -0.0372, 0.0001 | 0.051 | -0.0164 | -0.0374, 0.0045 | 0.123 |
| Left atrium diameter, per 1 mm increment | -0.0042 | -0.0077, -0.0006 | 0.024 | -0.0033 | -0.0073, 0.0008 | 0.111 |

AF, atrial fibrillation; CI, confidence interval; HF, heart failure; LVEF, left ventricular ejection fraction; NYHA, new york heart association.

A Multivariable linear regression model included variables by simultaneous forced entry method, which was based on significant results of the univariate analysis and relevant factors for HF hospitalization costs (age, sex, systolic blood pressure, heart rate, de novo HF hospitalization, ischemic heart disease as HF etiology, hypertension, diabetes mellitus, atrial fibrillation, chronic obstructive pulmonary disease, renal dialysis, creatinine level, serum sodium level, hemoglobin level, and LVEF). Septal wall thickness was not used due to high collinearity.

B Best predictive model, adjusted for significant predictors selected by stepwise linear regression using factors based on Model 1.

C The percent change of the hospitalization costs due to each variable can be calculated from the un-standardized β value by the following equation; The percent change of the hospitalization costs = (exp (un-standardized β) − 1) × 100.
## Supplementary Table 3. The Standardized Regression Coefficients for the Log-Transformed Hospitalization Costs in Older Adults

| Variable                              | Older adult subgroup (N=252) |                   |                |                |                   |                |                |                   |                |
|---------------------------------------|-----------------------------|-------------------|----------------|----------------|-------------------|----------------|----------------|-------------------|-----------------|
|                                       | Univariate Analysis Model 1 |                       |                | Best predictive model B |                   |                |                   |                |                |
|                                       | standard 95% CI            | 5% CI              | P value        | standardized 95% CI | P value           | standardized 95% CI | P value     |                   |                |                |
| Age, per 1 SD increment               | -0.0350                    | -0.1260, 0.0700    | 0.581          | -0.0795         | -0.2120, 0.0574  | 0.244          |                |                   |                |
| Male                                  | -0.0460                    | -0.1705, 0.0785    | 0.468          | -0.0097         | -0.1471, 0.1275  | 0.903          |                |                   |                |
| Body mass index, per 1 SD increment   | -0.1511                    | -0.2757, -0.0249   | 0.019          | -0.0786         | -0.2201, 0.0613  | 0.274          |                |                   |                |
| Systolic blood pressure, per 1 SD increment | -0.1147                   | -0.2356, 0.0130    | 0.069          | -0.1347         | -0.2993, 0.0149  | 0.072          | -0.1551        | -0.2961, -0.0282 | 0.016           |
| Heart rate, per 1 SD increment        | -0.0764                    | -0.2002, 0.0421    | 0.232          | -0.1262         | -0.2638, 0.0114  | 0.071          |                |                   |                |
| NYHA class IV                         | 0.1373                     | 0.0140, 0.2605     | 0.029          | 0.1600          | 0.0221, 0.2980   | 0.024          | 0.1720         | 0.0093, 0.0589  | 0.007           |
| De-novo HF hospitalization            | 0.0188                     | -0.1061, 0.1439    | 0.766          | 0.0433          | -0.0937, 0.1803  | 0.562          |                |                   |                |
| Ischemic etiology                     | 0.1394                     | 0.0160, 0.2627     | 0.027          | 0.0580          | -0.0860, 0.2020  | 0.418          |                |                   |                |
| Ambulance use                         | 0.0870                     | -0.0371, 0.2109    | 0.168          | 0.0840          | -0.0543, 0.2225  | 0.238          |                |                   |                |
| Comorbidities                         |                            |                   |                |                   |                   |                |                |                   |                |
| Hypertension                          | -0.0191                    | -0.1432, 0.1050    | 0.762          | 0.0303          | -0.1028, 0.1637  | 0.634          |                |                   |                |
| Dyslipidemia                          | 0.1014                     | -0.0225, 0.2252    | 0.108          | 0.0844          | -0.0435, 0.2125  | 0.185          |                |                   |                |
| Diabetes mellitus                     | 0.0905                     | -0.0335, 0.2145    | 0.152          | 0.0734          | -0.0563, 0.2031  | 0.271          |                |                   |                |
| AF                                    | -0.0399                    | -0.1641, 0.0843    | 0.528          | 0.0723          | -0.0665, 0.2113  | 0.302          |                |                   |                |
| Renal dialysis | 0.0712 | -0.0529, 0.1954 | 0.260 | 0.0553 | -0.1143, 0.2254 | 0.517 |
| Laboratory data |
| Creatinine, per 1 SD increment | 0.0834 | -0.0409, 0.2077 | 0.123 | -0.0011 | -0.2321, 0.2293 | 0.998 |
| Serum sodium, per 1 SD increment | -0.0594 | -0.1852, 0.0660 | 0.348 | -0.0427 | -0.1729, 0.0854 | 0.547 |
| Hemoglobin, per 1 SD increment | -0.1279 | -0.2521, -0.0046 | 0.062 | -0.1512 | -0.2846, -0.0168 | 0.031 |
| Echocardiographic variables |
| Posterior wall thickness, per 1 SD increment | -0.1683 | -0.2912, -0.0457 | 0.007 | -0.0751 | -0.2104, 0.0588 | 0.288 |
| LVEF, per 1 SD increment | -0.1760 | -0.3040, -0.0543 | 0.005 | -0.1604 | -0.2989, -0.0212 | 0.025 |
| Left atrium diameter, per 1 SD increment | -0.0750 | -0.2002, 0.0484 | 0.235 | -0.0401 | -0.1789, 0.0956 | 0.605 |

AF, atrial fibrillation; CI, confidence interval; HF, heart failure; LVEF, left ventricular ejection fraction; NYHA, new york heart association; SD, standard deviation.

A Multivariable linear regression model included variables by simultaneous forced entry method, which was based on significant results of the univariate analysis and relevant factors for HF hospitalization costs (age, sex, systolic blood pressure, heart rate, *de novo* HF hospitalization, ischemic heart disease as HF etiology, hypertension, diabetes mellitus, atrial fibrillation, chronic obstructive pulmonary disease, renal dialysis, creatinine level, serum sodium level, hemoglobin level, and LVEF). Septal wall thickness was not used due to high collinearity.

B Best predictive model, adjusted for significant predictors selected by stepwise linear regression using factors based on Model 1.
Supplementary Figure 1. Distribution of hospitalization costs for heart failure

| Percentile | Hospitalization Costs ($) |
|------------|---------------------------|
| 25%        | $5,016                    |
| 50%        | $6,780                    |
| 75%        | $8,970                    |
Supplementary Figure 2. The absolute values of standardized $\beta$ in the best predictive model of older adults