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**Supplementary File**

# Demographics, Management, and In-Hospital Outcome of Hospitalized Acute Heart Failure Syndrome Patients in Contemporary Real Clinical Practice in Japan

## — Observations From the Prospective, Multicenter Kyoto Congestive Heart Failure (KCHF) Registry —

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## Supplementary File 1

### Supplementary Methods

#### Ethics

A waiver of written informed consent from each patient was approved, because it met the following conditions in accordance with Japan's ethics guidelines for epidemiologic research[S1] and Policy for Protection of Human Research Subjects in the USA:[S2] (1) we would use clinical information obtained in routine practice on the medical record without any risk to the subjects; (2) the waiver of normal consent procedures would not adversely affect the rights and welfare of the subjects; (3) the research could not be carried out effectively without the waiver; and (4) the subjects were provided with additional pertinent information and had the right to opt out of this study whenever appropriate. Written informed consent was obtained from patients enrolled in the longitudinal cohort study.[S3]

#### Baseline Factor Definitions

The signs and symptoms of congestive heart failure (HF) included: paroxysmal nocturnal dyspnea, orthopnea, dyspnea on exertion, rales, ankle edema, neck-vein distention, pleural effusion, pulmonary edema, appetite loss, lack of sleep, general malaise, and thirst. These symptoms were assessed by attending physicians using a 4-level symptom grading (0, none; 1, seldom/mild; 2, frequent/moderate; 3, continuous/severe) at 4 time points: at hospital arrival; on admission; 24 h after hospital arrival; and at discharge. The rate of dyspnea relief at discharge was evaluated using a 7-level Likert-scale. Atrial fibrillation (AF) included paroxysmal AF, persistent AF, and permanent AF. Hypertension was defined as receiving anti-hypertensive drugs or systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg. Diabetes mellitus was defined as treatment with oral hypoglycemic agents and/or insulin, prior clinical diagnosis of diabetes, glycated hemoglobin ≥6.5%, casual blood glucose ≥200 mg/dL, or fasting blood glucose ≥126 mg/dL. Dyslipidemia was defined as receiving anti-dyslipidemic drugs or total cholesterol ≥220 mg/dL. Cerebrovascular accident was defined as ischemic stroke with neurological symptoms lasting >24 h. Transient ischemic attack was defined as temporary (i.e., <24 h) associated neurologic symptoms. Peripheral vascular disease was considered to be present if patients had been treated or were scheduled for surgical or endovascular interventions for peripheral vascular disease. Aortic disease was defined as aortic aneurysm, acute aortic syndrome including aortic dissection, intramural hematoma, penetrating atherosclerotic ulcer and inflammatory infection. The presence of chronic obstructive pulmonary disease (COPD) was determined clinically by local investigators, based on history, clinical presentation, previous examinations, and medications, and recorded as COPD in the case report form at enrolment. Poor medical adherence was judged by the attending physician. Public assistance, one of the social security systems in Japan, is explained elsewhere.[S4] Underlying heart disease was defined as the most likely cause of structural or functional cardiac disorders, of which only 1 category was chosen. The underlying heart disease was classified as (1) coronary artery disease (CAD); (2) hypertensive heart disease; (3) cardiomyopathy; (4) valvular heart disease; or (5) other heart diseases. CAD was defined as acute coronary syndrome (ACS), old myocardial infarction (MI), or prior percutaneous coronary intervention/coronary artery bypass grafting. ACS was defined as the range of myocardial ischemic states that includes ST-elevated MI, non-ST elevated MI, or unstable angina. Primary cardiomyopathy was classified as hypertrophic

cardiomyopathy, dilated cardiomyopathy, and dilated phase of hypertrophic cardiomyopathy. Valvular heart disease was classified as moderate–severe aortic stenosis, aortic regurgitation, mitral stenosis, mitral regurgitation (excluding functional mitral regurgitation), tricuspid regurgitation, and prosthetic valve dysfunction. As the valvular heart disease, we chose only 1 category that seemed to be the most closely related to acute HF. Other heart diseases included other cardiomyopathy, arrhythmia (bradycardia or tachycardia), congenital heart disease, and constrictive pericarditis. Other cardiomyopathy included arrhythmogenic right ventricular dysplasia, takotsubo cardiomyopathy, cardiac sarcoidosis, cardiac amyloidosis, left ventricular non-compaction, drug-induced cardiomyopathy, pacemaker-induced cardiomyopathy, mitochondrial cardiomyopathy, peripartum cardiomyopathy, alcoholic cardiomyopathy, beriberi heart, and others. Chronic kidney disease was defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 $m^2$ at admission.[S5–S8] eGFR was calculated using the equation for the Japanese population: $eGFR = 194 \times (\text{serum creatinine}^{-1.094}) \times (\text{age}^{-0.287}) \times 0.739$ (for women).[S9] In-hospital body weight change was defined as the absolute difference between baseline and discharge weights.

### Definitions of Cause of Death and In-Hospital Adverse Events

The causes of death were adjudicated by a clinical event committee. Every death was placed into 1 of the 2 categories in the KCHF registry: (1) cardiovascular death, which includes death related to HF, sudden death, death related to stroke, and other cardiovascular death; and (2) non-cardiovascular death, which includes pulmonary disease, sepsis, other infection, gastrointestinal disease, malignancy, renal failure, and other non-cardiovascular death. Sudden death was defined as unexplained death in a previously stable patient. Stroke was defined as ischemic or hemorrhagic stroke requiring or prolonging hospitalization with symptoms lasting >24 h. Pulmonary disease included bacterial pneumonia, interstitial pneumonia, alveolar hemorrhage, pulmonary hypertension, and other pulmonary disease. Other infection included acute cholangitis, peritonitis, purulent arthritis, and other infection except for pulmonary infection. Gastrointestinal disease included gastrointestinal hemorrhage, ileus, and others. Intracranial bleeding was defined as subarachnoid hemorrhage, hemorrhagic infarction, cerebral bleeding, and subdural hematoma. Major bleeding was defined as moderate or severe bleeding according to the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) classification. AF/atrial flutter was defined as that newly occurring during the index hospitalization in patients on sinus rhythm at presentation. Ventricular tachyarrhythmia was defined as ventricular tachycardia or ventricular fibrillation occurring during the index hospitalization.

## Supplementary Discussion

### Worsening HF (WHF)

The expert HF clinical trialists reviewed optimal clinical endpoints in HF trials, which included mortality, symptom measures, WHF, worsening renal function, adverse events, and surrogate markers.[S10,S11] The concept of WHF is becoming more common, but there are limited data on WHF in multicenter studies.[S12] We observed WHF in 20% of patients in this study. The rate of WHF was higher with decreasing LVEF and the trend was more evident with advanced age. In future studies, we should investigate the factors associated with WHF and its association with mortality and morbidity.

### Vasodilators and Tolvaptan

There is a geographic variation in the drugs used for the management of ADHF; the use of vasoactive agents is variable across countries (**Table S4**), although the use of i.v. diuretics is similar. In this registry, the frequency of vasodilator use was high due to the preference for carperitide (37%), the human atrial natriuretic peptide analogue available only in Japan. Nesiritide is approved as an i.v. vasodilator for acute HF in the USA, as is carperitide in Japan, as opposed to trinitrine or morphine in Europe.[S13] Furthermore, tolvaptan, an oral vasopressin receptor 2 antagonist, was used in a significant proportion of patients in the present registry. Tolvaptan use is limited to cases of severe euvolemic hyponatremia in Europe, while tolvaptan is available in Japan for treating subacute or chronic and even normonatremic HF as a supplement to or substitute for the loop diuretics.[S14]

### Hospital Stay

Although we did not carry out a statistical analysis, the hospital stay tended to be longer in Japan than in the USA or Europe (median, 16 days vs. 4–6 days). This may be due to the initiation of rehabilitation and patient education along with the medical insurance system. In addition, the rate of de novo HF was high in Japan; therefore, the cardiac catheterization during hospitalization was high compared to the USA and Europe. The median length of stay, however, tended to be shorter than reported in the ATTEND registry (**Table S5**).

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## Appendix S1. Kyoto Congestive Heart Failure Steering Committee Members

***Kyoto***
· Kyoto University Hospital: Hidenori Yaku, Takao Kato, Neiko Ozasa, Erika Yamamoto, Tetsuo Shioi, Koichiro Kuwahara, Takeshi Kimura
· National Hospital Organization Kyoto Medical Centre: Moritake Iguchi, Masaharu Akao
· Mitsubishi Kyoto Hospital: Masahi Kato, Shinji Miki
· Shimabara Hospital: Mamoru Takahashi
· Daini Okamoto General Hospital: Tsuneaki Kawashima, Takafumi Yagi

***Shiga***
· Japanese Red Cross Otsu Hospital: Toshikazu Jinnai, Takashi Konishi
· Shiga Medical Centre for Adults: Yasutaka Inuzuka, Shigeru Ikeguchi
· Hikone Municipal Hospital: Tomoyuki Ikeda, Yoshihiro Himura

***Osaka***
· Osaka Red Cross Hospital: Kazuya Nagao, Tsukasa Inada
· Kitano Hospital: Kenichi Sasaki, Moriaki Inoko
· Kishiwada City Hospital: Takafumi Kawai, Mitsuo Matsuda
· Kansai Electric Power Hospital: Akihiro Komasa, Katsuhisa Ishii

***Nara***
· Tenri Hospital: Yodo Tamaki, Yoshihisa Nakagawa

***Hyogo***
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· Kobe City Medical Centre General Hospital: Takeshi Kitai, Ryousuke Murai, Yutaka Furukawa

***Wakayama***
· Japanese Red Cross Wakayama Medical Centre: Yasuyo Motohashi, Takashi Tamura

***Shizuoka***
· Shizuoka General Hospital: Reiko Hozo, Ryusuke Nishikawa, Hiroki Sakamoto

***Okayama***
· Kurashiki Central Hospital: Yuichi Kawase, Keiichiro Iwasaki, Kazushige Kadota

***Fukuoka***
· Kokura Memorial Hospital: Takashi Morinaga, Kenji Ando

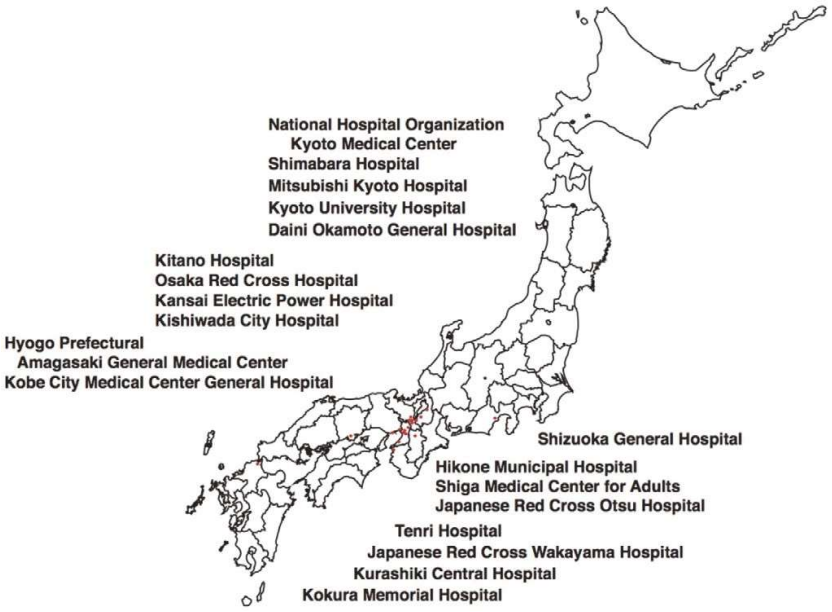
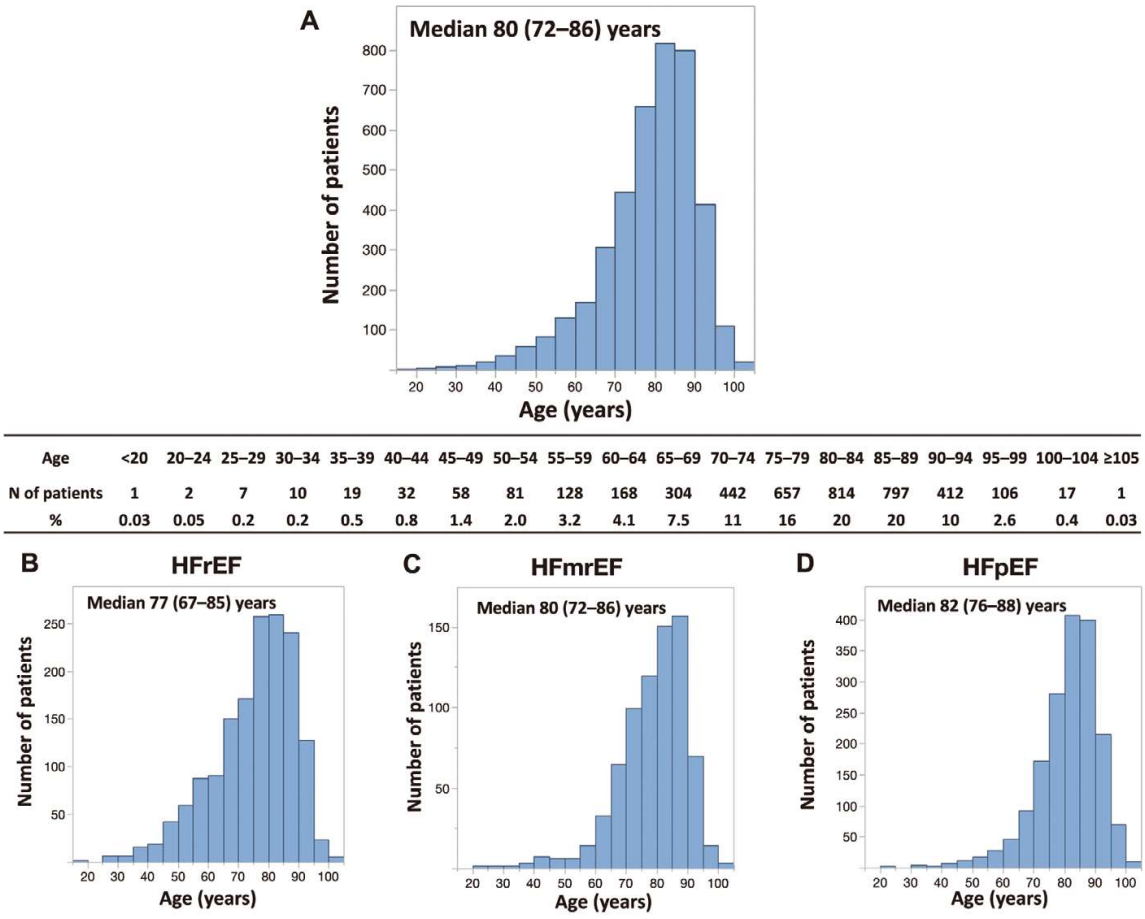



**Figure S1.** Kyoto Congestive Heart Failure Registry hospitals.




| Age | <20 | 20–24 | 25–29 | 30–34 | 35–39 | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | 65–69 | 70–74 | 75–79 | 80–84 | 85–89 | 90–94 | 95–99 | 100–104 | ≥105 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| N of patients | 1 | 2 | 7 | 10 | 19 | 32 | 58 | 81 | 128 | 168 | 304 | 442 | 657 | 814 | 797 | 412 | 106 | 17 | 1 |
| % | 0.03 | 0.05 | 0.2 | 0.2 | 0.5 | 0.8 | 1.4 | 2.0 | 3.2 | 4.1 | 7.5 | 11 | 16 | 20 | 20 | 10 | 2.6 | 0.4 | 0.03 |

**Figure S2.** Distribution of age in (**A**) the entire cohort and patients with heart failure (HF) with (**B**) reduced ejection fraction (HFrEF), (**C**) mid-range ejection fraction (HFmrEF), or (**D**) preserved ejection fraction (HFpEF). Median age was 80 years (IQR, 72–86 years) in the entire cohort. Median age in the HFrEF, HFmrEF, and HFpEF patients was 77 years (IQR, 67–85 years), 80 years (IQR, 72–86 years), and 82 years (IQR, 76–88 years), respectively.

**Table S1. Patient Characteristics vs. Age Quartile and LVEF Category**

| | Age <72 years | | | | 72 years≤Age<80 years | | | | 80 years≤Age<86 years | | | | Age≥86 years | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HFrEF (n=535) | HFmrEF (n=172) | HFpEF (n=256) | P-value | HFrEF (n=364) | HFmrEF (n=181) | HFpEF (n=394) | P-value | HFrEF (n=311) | HFmrEF (n=189) | HFpEF (n=500) | P-value | HFrEF (n=341) | HFmrEF (n=204) | HFpEF (n=594) | P-value |
| **Demographics** | | | | | | | | | | | | | | | | |
| Age (years) | 61 (53–67) | 66 (60–69) | 65 (59–69) | <0.001 | 76 (74–78) | 75 (74–78) | 76 (74–78) | 0.14 | 83 (81–84) | 83 (82–84) | 83 (81–84) | 0.17 | 89 (87–91) | 89 (87–91) | 89 (88–92) | 0.002 |
| Female | 112 (21) | 42 (24) | 114 (45) | <0.001 | 112 (31) | 63 (35) | 187 (47) | <0.001 | 118 (38) | 79 (42) | 275 (55) | <0.001 | 179 (52) | 117 (57) | 413 (70) | <0.001 |
| **Medical history** | | | | | | | | | | | | | | | | |
| Prior hospitalization due to HF | 178 (34) | 40 (24) | 75 (30) | 0.03 | 136 (38) | 60 (34) | 130 (33) | 0.34 | 153 (51) | 72 (39) | 176 (36) | <0.001 | 130 (40) | 76 (38) | 212 (36) | 0.61 |
| AF/AFL | 136 (25) | 53 (31) | 89 (35) | 0.02 | 119 (33) | 77 (43) | 201 (51) | <0.001 | 108 (35) | 88 (47) | 281 (56) | <0.001 | 124 (36) | 92 (45) | 307 (52) | <0.001 |
| Hypertension | 299 (56) | 118 (69) | 172 (67) | <0.001 | 244 (67) | 140 (77) | 288 (73) | 0.03 | 225 (72) | 152 (80) | 378 (76) | 0.13 | 249 (73) | 159 (78) | 472 (79) | 0.08 |
| DM | 240 (45) | 90 (52) | 106 (41) | 0.08 | 172 (47) | 75 (41) | 168 (43) | 0.31 | 129 (41) | 80 (42) | 176 (35) | 0.10 | 85 (25) | 55 (27) | 128 (22) | 0.22 |
| Prior MI | 133 (25) | 49 (28) | 30 (12) | <0.001 | 131 (36) | 49 (27) | 45 (11) | <0.001 | 113 (36) | 70 (37) | 64 (13) | <0.001 | 115 (34) | 55 (27) | 51 (8.6) | <0.001 |
| VT/VF | 57 (11) | 6 (3.5) | 5 (2.0) | <0.001 | 24 (6.6) | 6 (3.3) | 6 (1.5) | 0.001 | 28 (9.0) | 3 (1.6) | 6 (1.2) | <0.001 | 14 (4.1) | 3 (1.5) | 6 (1.0) | 0.004 |
| CKD | 181 (34) | 67 (39) | 89 (35) | 0.47 | 164 (45) | 70 (39) | 174 (44) | 0.34 | 165 (53) | 100 (53) | 229 (46) | 0.07 | 168 (49) | 115 (56) | 278 (47) | 0.06 |
| Dementia | 16 (3.0) | 4 (2.3) | 7 (2.7) | 0.9 | 45 (12) | 20 (11) | 47 (12) | 0.91 | 68 (22) | 41 (22) | 116 (23) | 0.87 | 133 (39) | 69 (34) | 200 (34) | 0.23 |
| **Social backgrounds** | | | | | | | | | | | | | | | | |
| Poor medical adherence | 118 (22) | 36 (21) | 46 (18) | 0.41 | 61 (17) | 21 (12) | 44 (11) | 0.06 | 59 (19) | 37 (20) | 77 (15) | 0.28 | 60 (18) | 32 (16) | 82 (14) | 0.30 |
| Employed | 230 (43) | 67 (39) | 75 (29) | 0.001 | 34 (9.3) | 15 (8.3) | 29 (7.4) | 0.61 | 9 (2.9) | 7 (3.7) | 18 (3.6) | 0.84 | 8 (2.4) | 3 (1.5) | 15 (2.5) | 0.68 |
| Public assistance | 54 (10) | 20 (12) | 22 (8.6) | 0.58 | 29 (8.0) | 10 (5.5) | 30 (7.6) | 0.57 | 13 (4.2) | 11 (5.8) | 17 (3.4) | 0.36 | 10 (2.9) | 5 (2.5) | 13 (2.2) | 0.78 |
| Lifestyle | | | | | | | | | | | | | | | | |
| Single | 154 (29) | 47 (27) | 48 (19) | 0.009 | 68 (19) | 39 (22) | 81 (21) | 0.69 | 55 (18) | 34 (18) | 108 (22) | 0.32 | 71 (21) | 41 (20) | 118 (20) | 0.94 |
| With a partner only | 245 (46) | 86 (50) | 147 (57) | 0.009 | 204 (56) | 110 (61) | 207 (53) | 0.18 | 148 (48) | 96 (51) | 196 (39) | 0.007 | 95 (28) | 52 (25) | 127 (22) | 0.07 |
| Institution for aged or hospital | 4 (0.8) | 4 (2.3) | 4 (1.6) | 0.23 | 15 (4.1) | 2 (1.1) | 14 (3.6) | 0.17 | 15 (4.8) | 7 (3.7) | 32 (6.4) | 0.33 | 68 (20) | 36 (18) | 79 (13) | 0.02 |
| **Daily life activities** | | | | | | | | | | | | | | | | |
| Ambulatory | 504 (94) | 155 (91) | 232 (92) | 0.18 | 307 (86) | 163 (91) | 337 (86) | 0.17 | 229 (75) | 148 (79) | 367 (75) | 0.44 | 206 (61) | 129 (64) | 363 (62) | 0.86 |
| **Underlying heart disease** | | | | | | | | | | | | | | | | |
| CAD | 194 (36) | 69 (40) | 51 (19) | <0.001 | 193 (53) | 76 (42) | 79 (20) | <0.001 | 164 (53) | 88 (47) | 95 (27) | <0.001 | 157 (46) | 68 (33) | 87 (15) | <0.001 |
| Hypertensive heart disease | 71 (13) | 46 (27) | 86 (34) | <0.001 | 44 (12) | 41 (23) | 139 (35) | <0.001 | 28 (9.0) | 43 (23) | 159 (32) | <0.001 | 53 (16) | 59 (29) | 213 (36) | <0.001 |
| Cardiomyopathy | 222 (42) | 23 (13) | 11 (4.3) | <0.001 | 88 (24) | 26 (14) | 29 (7.4) | <0.001 | 67 (22) | 15 (7.9) | 33 (6.6) | <0.001 | 55 (16) | 13 (6.4) | 24 (4.0) | <0.001 |
| Valvular heart disease | 32 (6.0) | 19 (11) | 62 (23) | <0.001 | 27 (7.4) | 31 (17) | 99 (25) | <0.001 | 38 (12) | 33 (17) | 146 (29) | <0.001 | 64 (19) | 63 (31) | 203 (34) | <0.001 |
| **Vital signs at presentation** | | | | | | | | | | | | | | | | |
| Heart rate (beats/min) | 104±26 | 106±29 | 101±28 | 0.16 | 101±25 | 100±27 | 90±28 | <0.001 | 98±25 | 95±29 | 88±28 | <0.001 | 98±23 | 97±26 | 88±27 | <0.001 |
| SBP (mmHg) | 140±35 | 159±38 | 154±43 | <0.001 | 143±32 | 151±38 | 150±36 | 0.009 | 142±34 | 146±35 | 150±35 | 0.007 | 142±33 | 153±33 | 149±33 | <0.001 |
| **Admission laboratory data** | | | | | | | | | | | | | | | | |
| BNP (pg/mL) | 857 (518–1,528) | 777 (419–1,434) | 439 (238–772) | <0.001 | 915 (570–1,614) | 667 (428–1,147) | 450 (243–818) | <0.001 | 1,065 (664–1,822) | 766 (409–1,281) | 499 (281–868) | <0.001 | 1,210 (655–2,000) | 887 (540–1,372) | 580 (333–951) | <0.001 |
| Creatinine (mg/dL) | 1.5±1.3 | 2.0±2.2 | 1.7±1.9 | 0.001 | 1.6±1.5 | 1.5±1.4 | 1.5±1.3 | 0.43 | 1.6±1.1 | 1.4±0.9 | 1.4±1.0 | 0.01 | 1.4±0.8 | 1.5±1.1 | 1.3±0.8 | 0.09 |
| Anemia† | 192 (36) | 96 (56) | 137 (54) | <0.001 | 206 (57) | 121 (67) | 292 (74) | <0.001 | 227 (73) | 128 (68) | 407 (81) | <0.001 | 253 (74) | 161 (79) | 477 (80) | 0.08 |

(**Table S1** continued the next page.)

| | Age <72 years | | | | 72 years≤Age<80 years | | | | 80 years≤Age<86 years | | | | Age≥86 years | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HFrEF (n=535) | HFmrEF (n=172) | HFpEF (n=256) | P-value | HFrEF (n=364) | HFmrEF (n=181) | HFpEF (n=394) | P-value | HFrEF (n=311) | HFmrEF (n=189) | HFpEF (n=500) | P-value | HFrEF (n=341) | HFmrEF (n=204) | HFpEF (n=594) | P-value |
| **In-hospital mortality** | | | | | | | | | | | | | | | | |
| Death from any cause | 24 (4.5) | 3 (1.7) | 11 (4.3) | 0.26 | 24 (6.6) | 10 (5.5) | 14 (3.6) | 0.16 | 34 (11) | 5 (2.7) | 27 (5.4) | <0.001 | 60 (18) | 18 (8.8) | 37 (6.2) | <0.001 |
| Cardiac death | 21 (3.9) | 1 (0.6) | 8 (3.1) | 0.09 | 19 (5.2) | 8 (4.4) | 9 (2.3) | 0.1 | 20 (6.4) | 5 (2.7) | 13 (2.6) | 0.01 | 47 (14) | 12 (5.9) | 24 (4.0) | <0.001 |
| **In-hospital adverse events** | | | | | | | | | | | | | | | | |
| Ventricular tachyarrhythmia | 56 (11) | 7 (4.4) | 9 (3.6) | <0.001 | 28 (8.3) | 6 (3.5) | 11 (2.9) | 0.003 | 19 (6.7) | 10 (5.7) | 15 (3.2) | 0.08 | 27 (8.4) | 4 (2.1) | 16 (2.9) | <0.001 |
| Worsening HF | 134 (25) | 45 (26) | 54 (21) | 0.38 | 93 (26) | 34 (19) | 62 (16) | 0.003 | 75 (24) | 32 (17) | 67 (13) | <0.001 | 88 (26) | 31 (15) | 72 (12) | <0.001 |
| Worsening renal function | 122 (24) | 62 (37) | 79 (33) | 0.002 | 105 (32) | 59 (35) | 134 (36) | 0.6 | 93 (34) | 80 (44) | 182 (39) | 0.1 | 97 (35) | 90 (49) | 202 (37) | 0.007 |
| **Medications at discharge** | | | | | | | | | | | | | | | | |
| RAAS inhibitors | 448 (88) | 130 (77) | 176 (72) | <0.001 | 255 (75) | 135 (79) | 282 (74) | 0.48 | 218 (79) | 139 (76) | 330 (70) | 0.02 | 195 (69) | 125 (67) | 368 (66) | 0.63 |
| $\beta$-blockers | 459 (90) | 139 (82) | 158 (64) | <0.001 | 247 (73) | 129 (75) | 232 (61) | <0.001 | 219 (79) | 131 (71) | 265 (56) | <0.001 | 168 (60) | 108 (58) | 243 (44) | <0.001 |
| Calcium channel blockers | 105 (21) | 67 (40) | 104 (42) | <0.001 | 73 (21) | 58 (34) | 171 (45) | <0.001 | 67 (24) | 71 (39) | 195 (41) | <0.001 | 66 (23) | 71 (38) | 244 (44) | <0.001 |
| Tolvaptan | 65 (13) | 8 (4.7) | 20 (8.2) | 0.006 | 43 (13) | 14 (8.2) | 39 (10) | 0.28 | 41 (15) | 18 (9.8) | 53 (11) | 0.20 | 24 (8.5) | 18 (9.7) | 57 (10) | 0.74 |
| Amiodarone | 80 (16) | 9 (5.3) | 12 (4.9) | <0.001 | 37 (11) | 12 (7.0) | 15 (4.0) | 0.002 | 23 (8.3) | 13 (7.1) | 15 (3.2) | 0.007 | 14 (5.0) | 9 (4.8) | 8 (1.4) | 0.005 |
| **Living situation after discharge** | | | | | | | | | | | | | | | | |
| Home | 486 (96) | 159 (94) | 223 (92) | 0.07 | 292 (87) | 151 (88) | 329 (87) | 0.91 | 236 (85) | 135 (74) | 364 (78) | 0.006 | 187 (68) | 126 (68) | 388 (70) | 0.81 |
| **Daily life activities at discharge** | | | | | | | | | | | | | | | | |
| Ambulatory | 472 (94) | 152 (90) | 229 (94) | 0.22 | 276 (84) | 146 (85) | 310 (83) | 0.83 | 199 (73) | 121 (66) | 320 (69) | 0.34 | 130 (48) | 97 (53) | 278 (51) | 0.63 |
| **Use of long-term care insurance at discharge** | | | | | | | | | | | | | | | | |
| Care required | 20 (7.8) | 8 (9.0) | 14 (11) | 0.59 | 51 (24) | 25 (21) | 62 (25) | 0.70 | 61 (29) | 48 (36) | 134 (39) | 0.06 | 120 (51) | 85 (53) | 249 (55) | 0.56 |

Data given as n (%), mean±SD or median (IQR). †Defined by the World Health Organization criteria (hemoglobin <12 g/dL for women and <13 g/dL for men). AF/AFL, atrial fibrillation/flutter; BNP, brain-type natriuretic peptide; CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; HF, heart failure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MI, myocardial infarction; RAAS, renin-angiotensin-aldosterone system; SBP, systolic blood pressure; VT/VF, ventricular tachycardia/fibrillation.

**Table S2. Post-Hoc Analysis of Patient Characteristics vs. LVEF Category and Age Quartile**

| | P-value | | |
|---|---|---|---|
| | HFmrEF vs. HFrEF | HFpEF vs. HFrEF | HFpEF vs. HFmrEF |
| **Age <72 years** | | | |
| Demographics | | | |
| Female | 1.00 | <0.001 | <0.001 |
| Medical history | | | |
| AF/AFL | 0.49 | 0.02 | 1.00 |
| Underlying heart disease | | | |
| CAD | 1.00 | <0.001 | <0.001 |
| Hypertensive heart disease | <0.001 | <0.001 | 0.39 |
| Cardiomyopathy | <0.001 | <0.001 | 0.002 |
| Valvular heart disease | 0.08 | <0.001 | 0.002 |
| Vital signs at presentation | | | |
| SBP (mmHg) | <0.001 | <0.001 | 0.73 |
| Admission laboratory data | | | |
| BNP (pg/mL) | 0.61 | <0.001 | <0.001 |
| Hemoglobin (g/dL) | <0.001 | <0.001 | 1.00 |
| Anemia† | <0.001 | <0.001 | 1.00 |
| **72 years≤Age<80 years** | | | |
| Demographics | | | |
| Female | 1.00 | <0.001 | 0.01 |
| Medical history | | | |
| AF/AFL | 0.07 | <0.001 | 0.18 |
| Underlying heart disease | | | |
| CAD | 0.007 | <0.001 | <0.001 |
| Hypertensive heart disease | 0.004 | <0.001 | 0.007 |
| Cardiomyopathy | 0.02 | <0.001 | 0.02 |
| Valvular heart disease | 0.002 | <0.001 | 0.10 |
| Vital signs at presentation | | | |
| Heart rate (beats/min) | 1.00 | <0.001 | <0.001 |
| SBP (mmHg) | 0.03 | 0.03 | 1.00 |
| Admission laboratory data | | | |
| BNP (pg/mL) | <0.001 | <0.001 | <0.001 |
| Hemoglobin (g/dL) | 0.06 | <0.001 | 0.07 |
| Anemia† | 0.08 | <0.001 | 0.21 |

(**Table S2** continued the next page.)

| | P-value | | |
|---|---|---|---|
| | HFmrEF vs. HFrEF | HFpEF vs. HFrEF | HFpEF vs. HFmrEF |
| **80 years≤Age<86 years** | | | |
| Demographics | | | |
| Female | 1.00 | <0.001 | 0.006 |
| Medical history | | | |
| AF/AFL | 0.03 | <0.001 | 0.07 |
| Underlying heart disease | | | |
| CAD | 0.46 | <0.001 | <0.001 |
| Hypertensive heart disease | <0.001 | <0.001 | 0.06 |
| Cardiomyopathy | <0.001 | <0.001 | 1.00 |
| Valvular heart disease | 0.31 | <0.001 | 0.005 |
| Vital signs at presentation | | | |
| Heart rate (beats/min) | 0.99 | <0.001 | 0.01 |
| SBP (mmHg) | 0.61 | 0.01 | 0.60 |
| Admission laboratory data | | | |
| BNP (pg/mL) | <0.001 | <0.001 | <0.001 |
| Hemoglobin (g/dL) | 1.00 | <0.001 | <0.001 |
| Anemia† | 0.61 | 0.01 | <0.001 |
| **Age ≥86 years** | | | |
| Demographics | | | |
| Female | 0.81 | <0.001 | 0.005 |
| Medical history | | | |
| AF/AFL | 0.13 | <0.001 | 0.31 |
| Underlying heart disease | | | |
| CAD | 0.008 | <0.001 | <0.001 |
| Hypertensive heart disease | <0.001 | <0.001 | 0.12 |
| Cardiomyopathy | 0.003 | <0.001 | 0.51 |
| Valvular heart disease | 0.004 | <0.001 | 0.39 |
| Vital signs at presentation | | | |
| Heart rate (beats/min) | 1.00 | <0.001 | <0.001 |
| SBP (mmHg) | <0.001 | 0.005 | 0.26 |
| Admission laboratory data | | | |
| BNP (pg/mL) | <0.001 | <0.001 | <0.001 |
| Hemoglobin (g/dL) | 0.12 | <0.001 | 0.06 |
| Anemia† | 0.63 | 0.08 | 0.64 |

Values are presented as number (%), mean±SD, or median (interquartile range). †Defined by the World Health Organization criteria (hemoglobin <12 g/dL for women and <13 g/dL for men). LVEF, left ventricular ejection fraction. Other abbreviations as in Table S1.

**Table S3. Patient Characteristics, Clinical Presentation, and In-Hospital Management**

| | Entire cohort (n=4,056) | HFrEF (n=1,551) | HFmrEF (n=746) | HFpEF (n=1,744) | P-value | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | HFmrEF vs. HFrEF | HFpEF vs. HFrEF | HFmrEF vs. HFpEF |
| **Medical history** | | | | | | | | |
| Dyslipidemia | 1,549 (38) | 629 (41) | 305 (41) | 611 (35) | 0.001 | 1.00 | 0.003 | 0.02 |
| Prior PCI | 863 (21) | 407 (26) | 189 (25) | 263 (15) | <0.001 | 1.00 | <0.001 | <0.001 |
| Prior CABG | 288 (7.1) | 130 (8.4) | 72 (9.7) | 85 (4.9) | <0.001 | 0.94 | <0.001 | <0.001 |
| Malignancy | 585 (14) | 203 (13) | 112 (15) | 268 (15) | 0.16 | | | |
| COPD | 333 (8.2) | 126 (8.1) | 48 (6.4) | 159 (9.1) | 0.08 | | | |
| Asthma | 240 (5.9) | 90 (5.8) | 36 (4.8) | 111 (6.4) | 0.32 | | | |
| Prior pacemaker implantation | 257 (6.3) | 69 (4.5) | 50 (6.7) | 136 (7.8) | <0.001 | 0.07 | <0.001 | 1.00 |
| Prior ICD implantation | 62 (1.6) | 51 (3.3) | 4 (0.5) | 7 (0.4) | <0.001 | <0.001 | <0.001 | 1.00 |
| Prior CRT implantation | 82 (2.0) | 65 (4.2) | 10 (1.3) | 6 (0.3) | <0.001 | <0.001 | <0.001 | 0.01 |
| **Initial evaluation** | | | | | | | | |
| Paroxysmal nocturnal dyspnea | 2,766 (71) | 1,110 (75) | 495 (70) | 1,148 (68) | <0.001 | 0.03 | <0.001 | 1.00 |
| Orthopnea | 3,151 (80) | 1,241 (83) | 572 (80) | 1,326 (78) | <0.001 | 0.16 | <0.001 | 0.85 |
| Dyspnea on exertion | 3,683 (95) | 1,397 (95) | 670 (95) | 1,601 (95) | 0.69 | | | |
| Rales | 3,101 (79) | 1,189 (80) | 581 (81) | 1,318 (78) | 0.15 | | | |
| Peripheral edema | 3,023 (77) | 1,117 (74) | 533 (74) | 1,360 (80) | <0.001 | 1.00 | <0.001 | 0.005 |
| Jugular venous distention | 2,983 (78) | 1,119 (77) | 542 (78) | 1,310 (79) | 0.37 | | | |
| **Hemodynamic profile** | | | | | | | | |
| Warm and dry | 240 (6.0) | 81 (5.3) | 53 (7.2) | 106 (6.1) | 0.19 | | | |
| Warm and wet | 3,016 (75) | 1,017 (67) | 580 (79) | 1,409 (82) | <0.001 | <0.001 | <0.001 | 0.35 |
| Cold and dry | 137 (3.4) | 69 (4.5) | 15 (2.0) | 53 (3.1) | 0.005 | 0.01 | 0.09 | 0.46 |
| Cold and wet | 613 (15) | 360 (24) | 88 (12) | 160 (9.3) | <0.001 | <0.001 | <0.001 | 0.12 |
| **NYHA functional class** | | | | | | | | |
| Class II | 499 (12) | 169 (11) | 97 (13) | 231 (13) | 0.10 | | | |
| Class III | 1,589 (39) | 581 (38) | 279 (38) | 725 (42) | 0.03 | 1.00 | 0.053 | 0.15 |
| Class IV | 1,948 (48) | 792 (51) | 367 (49) | 781 (45) | 0.001 | 1.00 | 0.001 | 0.13 |
| **Medication prior to admission** | | | | | | | | |
| RAAS inhibitors | 2,206 (54) | 832 (54) | 387 (52) | 980 (56) | 0.10 | | | |
| ACEI/ARB | 1,850 (46) | 688 (44) | 329 (44) | 827 (47) | 0.14 | | | |
| ACEI | 487 (12) | 234 (15) | 86 (12) | 166 (9.5) | <0.001 | 0.06 | <0.001 | 0.38 |
| ARB | 1,410 (35) | 471 (30) | 250 (34) | 684 (39) | <0.001 | 0.38 | <0.001 | 0.02 |
| MRA | 733 (18) | 323 (21) | 115 (15) | 293 (17) | 0.001 | 0.006 | 0.009 | 1.00 |
| β-blockers | 1,560 (38) | 613 (40) | 294 (39) | 650 (37) | 0.36 | | | |
| Calcium channel blockers | 1,500 (37) | 396 (26) | 275 (37) | 821 (47) | <0.001 | <0.001 | <0.001 | <0.001 |
| Loop diuretics | 1,976 (49) | 755 (49) | 320 (43) | 893 (51) | <0.001 | 0.03 | 0.44 | <0.001 |
| Thiazide | 262 (6.5) | 92 (5.9) | 42 (5.6) | 127 (7.3) | 0.17 | | | |
| Tolvaptan | 170 (4.2) | 85 (5.5) | 18 (2.4) | 64 (3.7) | 0.001 | 0.003 | 0.04 | 0.32 |
| Warfarin | 872 (21) | 304 (20) | 136 (18) | 428 (25) | <0.001 | 1.00 | 0.002 | 0.002 |

(**Table S3** continued the next page.)

| | Entire cohort (n=4,056) | HFrEF (n=1,551) | HFmrEF (n=746) | HFpEF (n=1,744) | P-value | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | HFmrEF vs. HFrEF | HFpEF vs. HFrEF | HFmrEF vs. HFpEF |
| DOAC | 409 (10) | 99 (6.4) | 73 (9.8) | 237 (14) | <0.001 | 0.01 | <0.001 | 0.03 |
| Aspirin | 1,322 (33) | 541 (35) | 274 (37) | 501 (29) | <0.001 | 1.00 | <0.001 | <0.001 |
| Thienopyridines | 512 (13) | 238 (15) | 114 (15) | 158 (9.1) | <0.001 | 1.00 | <0.001 | <0.001 |
| Nitrates | 534 (13) | 221 (14) | 104 (14) | 206 (12) | 0.09 | | | |
| Digoxin | 265 (6.5) | 87 (5.6) | 32 (4.3) | 146 (8.4) | <0.001 | 0.54 | 0.006 | <0.001 |
| Amiodarone | 171 (4.2) | 112 (7.2) | 23 (3.1) | 33 (1.9) | <0.001 | <0.001 | <0.001 | 0.20 |
| Pimobendan | 119 (2.9) | 89 (5.7) | 9 (1.2) | 20 (1.2) | <0.001 | <0.001 | <0.001 | 1.00 |
| NSAID | 213 (5.2) | 67 (4.3) | 39 (5.2) | 107 (6.1) | 0.07 | | | |
| **Vital signs at presentation** | | | | | | | | |
| DBP (mmHg) | 85±26 | 87±24 | 87±24 | 81±24 | <0.001 | 1.00 | <0.001 | <0.001 |
| Body temperature (°C) | 36.5±0.6 | 36.5±0.6 | 36.5±0.7 | 36.6±0.6 | <0.001 | 0.29 | <0.001 | 0.23 |
| **I.v. drugs ≤24 h after hospital presentation** | | | | | | | | |
| Inotropes | | | | | | | | |
| Dobutamine | 501 (12) | 345 (22) | 62 (8.3) | 90 (5.2) | <0.001 | <0.001 | <0.001 | 0.008 |
| Dopamine | 82 (2.0) | 40 (2.6) | 12 (1.6) | 29 (1.7) | 0.12 | | | |
| Norepinephrine | 134 (3.3) | 56 (3.6) | 25 (3.4) | 53 (3.0) | 0.66 | | | |
| PDE-III inhibitor | 38 (0.9) | 25 (1.6) | 6 (0.8) | 7 (0.4) | 0.001 | 0.35 | 0.001 | 0.60 |
| Digoxin | 87 (2.1) | 38 (2.5) | 15 (2.0) | 34 (2.0) | 0.59 | | | |
| Morphine | 69 (1.7) | 24 (1.6) | 16 (2.1) | 26 (1.5) | 0.47 | | | |
| **Procedural interventions** | | | | | | | | |
| NPPV | 920 (23) | 386 (25) | 179 (24) | 351 (20) | 0.003 | 1.00 | 0.003 | 0.09 |
| Intubation | 175 (4.3) | 81 (5.2) | 34 (4.6) | 59 (3.4) | 0.03 | 1.00 | 0.03 | 0.47 |
| Pacemaker implantation | 67 (1.7) | 4 (0.3) | 7 (0.9) | 55 (3.2) | <0.001 | 0.08 | <0.001 | 0.004 |
| ICD implantation | 12 (0.3) | 9 (0.6) | 1 (0.1) | 2 (0.1) | 0.03 | 0.38 | 0.06 | 1.00 |
| CRT implantation | 21 (0.5) | 21 (1.4) | 0 | 0 | <0.001 | 0.004 | <0.001 | |
| Hemodialysis | 206 (5.1) | 86 (5.5) | 51 (6.8) | 69 (4.0) | 0.007 | 0.66 | 0.10 | 0.006 |
| Intra-aortic balloon pumping | 105 (2.6) | 65 (4.2) | 18 (2.4) | 22 (1.3) | <0.001 | 0.10 | <0.001 | 0.11 |
| Percutaneous cardiopulmonary support | 20 (0.5) | 15 (1.0) | 2 (0.3) | 3 (0.2) | 0.003 | 0.20 | 0.006 | 1.00 |
| Valve replacement or plasty | 55 (1.4) | 15 (1.0) | 10 (1.3) | 30 (1.7) | 0.18 | 1.00 | 0.19 | 1.00 |

Data given as n (%) or mean±SD. ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronization therapy; DBP, diastolic blood pressure; DOAC, direct oral anticoagulants; ICD, implantable cardioverter defibrillator; MRA, mineralocorticoid receptor antagonists; NPPV, non-invasive positive pressure ventilation; NSAID, non steroidal anti-inflammatory drugs; PCI, percutaneous coronary intervention; PDE-III, phosphodiesterase III; RAAS, renin-angiotensin-aldosterone system; TIA, transient ischemic attack. Other abbreviations as in Table S1.

**Table S4. Clinical Outcomes, Clinical Status, and Medication at Hospital Discharge**

| | Entire cohort (n=4,056) | HFrEF (n=1,551) | HFmrEF (n=746) | HFpEF (n=1,744) | P-value | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | HFmrEF vs. HFrEF | HFpEF vs. HFrEF | HFmrEF vs. HFpEF |
| **In-hospital adverse events** | | | | | | | | |
| Acute coronary syndrome | 48 (1.2) | 21 (1.4) | 9 (1.2) | 18 (1.0) | 0.70 | | | |
| Cerebral infarction | 69 (1.7) | 23 (1.5) | 14 (1.9) | 32 (1.8) | 0.68 | | | |
| Intracranial bleeding | 15 (0.4) | 4 (0.3) | 6 (0.8) | 5 (0.3) | 0.10 | | | |
| Major bleeding† | 92 (2.3) | 33 (2.1) | 18 (2.4) | 41 (2.4) | 0.88 | | | |
| AF/AFL | 381 (10) | 125 (8.6) | 77 (11) | 177 (11) | 0.09 | | | |
| **Signs and symptoms at discharge** | | | | | | | | |
| Paroxysmal nocturnal dyspnea | 177 (4.9) | 66 (4.9) | 27 (4.0) | 83 (5.2) | 0.46 | | | |
| Dyspnea on exertion | 983 (27) | 359 (27) | 162 (24) | 458 (29) | 0.06 | | | |
| Orthopnea | 136 (3.7) | 45 (3.4) | 26 (3.8) | 64 (4.0) | 0.65 | | | |
| Rales | 186 (5.1) | 65 (4.9) | 32 (4.7) | 88 (5.5) | 0.62 | | | |
| Peripheral edema | 457 (13) | 139 (10) | 76 (11) | 239 (15) | <0.001 | 1.00 | <0.001 | 0.049 |
| Jugular venous distention | 235 (6.5) | 95 (7.1) | 31 (4.6) | 109 (6.9) | 0.07 | | | |
| Loss of appetite | 413 (12) | 145 (11) | 73 (11) | 194 (12) | 0.46 | | | |
| Sleep disturbance | 334 (9.6) | 121 (9.5) | 59 (9.1) | 153 (10) | 0.79 | | | |
| General malaise | 581 (17) | 217 (17) | 106 (16) | 257 (17) | 0.89 | | | |
| **Vital signs at discharge** | | | | | | | | |
| Heart rate (beats/min) | 71±13 | 72±13 | 71±12 | 70±13 | <0.001 | 0.42 | <0.001 | 0.20 |
| SBP (mmHg) | 116±18 | 112±17 | 119±18 | 118±18 | <0.001 | <0.001 | <0.001 | 0.16 |
| DBP (mmHg) | 64±12 | 64±13 | 65±12 | 64±12 | 0.003 | 0.16 | 0.30 | 0.003 |
| **Discharge laboratory data** | | | | | | | | |
| BNP (pg/mL) | 270 (136–522) | 371 (194–668) | 294 (151–574) | 199 (97–382) | <0.001 | <0.001 | <0.001 | <0.001 |
| NT-proBNP (pg/mL) | 1,970 (808–4,346) | 2,395 (1,119–6,227) | 2,261 (800–3,959) | 1,666 (716–3,896) | 0.008 | 0.42 | 0.005 | 1.00 |
| Creatinine (mg/dL) | 1.1 (0.9–1.6) | 1.1 (0.9–1.6) | 1.2 (0.9–1.7) | 1.1 (0.8–1.5) | 0.01 | 0.57 | 0.14 | 0.01 |
| BUN (mg/dL) | 25 (19–36) | 25 (18–34) | 26 (19–39) | 26 (19–37) | 0.10 | | | |
| Sodium (mEq/L) | 139±3.7 | 138±3.7 | 139±3.6 | 139±3.8 | 0.003 | 0.75 | 0.008 | 0.65 |
| Hemoglobin (g/dL) | 11.5±2.2 | 12.0±2.3 | 11.4±2.2 | 11.0±1.9 | <0.001 | <0.001 | <0.001 | <0.001 |
| **Medications at discharge** | | | | | | | | |
| Digoxin | 215 (5.7) | 90 (6.4) | 30 (4.2) | 95 (5.7) | 0.13 | | | |
| Nitrates | 478 (13) | 179 (13) | 112 (16) | 186 (11) | 0.01 | 0.16 | 0.64 | 0.007 |
| Pimobendan | 202 (5.3) | 151 (11) | 18 (2.5) | 32 (1.9) | <0.001 | <0.001 | <0.001 | 1.00 |
| NSAIDs | 86 (2.3) | 21 (1.5) | 14 (2.0) | 51 (3.1) | 0.01 | 1.00 | 0.01 | 0.39 |

Data given as n (%), mean±SD, or median (IQR). †Defined as moderate or severe bleeding by Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) classification. BUN, blood urea nitrogen; NT-proBNP, N-terminal pro brain-type natriuretic peptide. Other abbreviations as in Tables S1,S3.

**Table S5. Previous Representative ADHF Registries and KCHF Registry**

| | ADHERE[S15] | OPTIMIZE-HF[S16] | GWTG-HF[S17] | EHFS II[S18] | ADHERE-AP[S19] | KorAHF[S20] | ATTEND[S21] | KCHF |
|---|---|---|---|---|---|---|---|---|
| n | 105,388 | 48,612 | 158,922 | 3,580 | 10,171 | 2,066 | 4,842 | 4,056 |
| Region | USA | USA | USA | Europe | Asia-Pacific | Korea | Japan | Japan |
| Timeframe | 2001–2004 | 2003–2004 | 2008–2013 | 2004–2005 | 2006–2008 | 2011–2012 | 2007–2012 | Oct 2014–Mar 2016 |
| Settings | Prospective, 274 hospitals | Prospective, 259 hospitals | Prospective, 271 hospitals | Prospective, 133 hospitals | Prospective, 43 hospitals | Prospective, 10 hospitals | Prospective, 52 hospitals | Prospective, 19 hospitals |
| Background and baseline characteristics | | | | | | | | |
| Age (years) | 72±14 | 73±14 | 75 (63–84) | 70±13 | 67† | 69±14 | 73±14 | 80 (72–86) |
| Male | 48 | 48 | 53 | 61 | 57 | 55 | 58 | 55 |
| Etiology | | | | | | | | |
| CAD | – | 46 | – | 54 | – | 38 | 31 | 33 |
| Hypertensive | – | 23 | – | – | – | 6 | 18 | 24 |
| Comorbidities | | | | | | | | |
| AF/AFL | 31 | 31 | 35‡ | 39 | 24 | 27 | 40 | 41 |
| Hypertension | 73 | 71 | 79 | 63 | 64 | 59 | 69 | 72 |
| DM | 44 | 42 | 44 | 33 | 45 | 36 | 34 | 37 |
| Prior MI | 31 | – | – | – | – | – | – | 22 |
| CKD | 30 | – | – | 17 | 22 | – | – | 45 |
| Creatinine (mg/dL) | 1.8±1.6 | 1.8±1.8 | – | – | – | 1.5±1.6 | 1.4±1.6 | 1.5±1.3 |
| Sodium (mEq/L) | – | 137±11 | – | 135 (110–160) | – | – | 139±4 | 139±4 |
| De novo HF | – | 12 | – | 37 | 36 | 50 | 64 | 64 |
| HR (beats/min) | – | 87±22 | 82 (70–97) | 95 (77–114) | – | 91±26 | 99±29 | 96±28 |
| SBP (mmHg) | 144±33 | 143±33 | 140 (121–161) | 135 (110–160) | – | 136±31 | 146±37 | 147±35 |
| HFrEF (LVEF<40%) | 63 | 49 | 43 | 66 | 53 | 56 | 54 | 38 |
| Social backgrounds | | | | | | | | |
| With Occupation | – | – | – | – | – | – | – | 13 |
| Public income assistance | – | – | – | – | – | – | – | 5.8 |
| Living status | – | – | – | – | – | – | – | Data available |
| Daily life activities | – | – | – | – | – | – | – | Data available |
| I.v. therapy | | | | | | | | |
| Diuretics | 92 | – | – | 84 | – | 72 | 76 | 83 |
| Vasodilators | 9 | – | – | 38 | – | 40 | 78 | 71 |
| Inotropes | 15 | – | – | 30 | – | 32 | 19 | 19 |
| Outcome measures | | | | | | | | |
| In-hospital mortality | 4 | 3.8 | – | 6.7 | 48 | 6.1 | 6.4 | 6.7 |
| WHF | – | – | – | – | – | – | – | 19 |
| WRF | – | – | – | – | – | – | – | 35 |
| Length of stay (days)† | 4.3 | 4 | 4 | 9 | 6 | 8 | 21 | 16 |
| Patient-reported outcomes | – | – | – | – | – | – | – | Data available |
| Additional care or nursing required | – | – | – | – | – | – | – | Data available |

(**Table S5** continued the next page.)

| | ADHERE[S15] | OPTIMIZE-HF[S16] | GWTG-HF[S17] | EHFS II[S18] | ADHERE-AP[S19] | KorAHF[S20] | ATTEND[S21] | KCHF |
|---|---|---|---|---|---|---|---|---|
| Medication at discharge | | | | | | | | |
| ACEI/ARB | – | 83[§] | 94 | 80 | 63 | 65 | 75 | 57 |
| ACEI | 41 | – | – | – | – | – | 31 | 25 |
| ARB | 12 | – | – | – | – | – | 46 | 33 |
| MRA | – | – | 96 | 48 | 31 | 40 | – | 45 |
| *β*-blockers | 48 | 83 | 35 | 61 | 41 | 44 | 67 | 66 |

Data given as %, mean ± SD or median (IQR) or [†]median. [‡]Chronic atrial fibrillation, [§]For heart failure with reduced ejection fraction. ADHERE, Acute Decompensated Heart Failure National Registry; ADHERE-AP, Acute Decompensated Heart Failure National Registry International-Asia Pacific; ADHF, acute decompensated heart failure; ATTEND, Acute Decompensated Heart Failure Syndromes; EHFS II, European Heart Failure Survey II; GWTG-HF, Get With The Guidelines-Heart Failure; HR, heart rate; KCHF, Kyoto Congestive Heart Failure; KorAHF, Korean Acute Heart Failure Registry; MRA, mineralocorticoid receptor antagonists; OPTIMIZE-HF, Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure; WHF, worsening heart failure; WRF, worsening renal function. Other abbreviations as in Tables S1–S3.

**Table S6. KCHF Registry: Comparison With Other Studies According to LVEF Category**

| | OPTIMIZE-HF[S22] | | | GWTG-HF (in the Medicare population)[S23] | | | GWTG-HF[S24] | | | ALARM-HF[S25] | | | PROTECT trial[S26] | | | CHART-2 Study[S27] | | | KCHF | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HFrEF (n=20,118) | HFmrEF (n=7,321) | HFpEF (n=10,072) | HFrEF (n=15,716) | HFmrEF (n=5,626) | HFpEF (n=18,897) | HFrEF (n=48,950) | HFmrEF (n=12,819) | HFpEF (n=38,056) | HFrEF (n=1,698) | HFmrEF (n=811) | HFpEF (n=748) | HFrEF (n=607) | HFmrEF (n=128) | HFpEF (n=108) | HFrEF (n=730) | HFmrEF (n=596) | HFpEF (n=2,154) | HFrEF (n=1,551) | HFmrEF (n=746) | HFpEF (n=1,744) |
| Timeframe | 2003–2004 | | | 2005–2011 | | | 2005–2013 | | | 2006–2007 | | | 2007–2009 | | | October 2006–May 2010 | | | October 2014–March 2016 | | |
| Settings | Prospective, 259 hospitals | | | Prospective observational study, 220 hospitals | | | Prospective observational study, 305 hospitals | | | Prospective observational study, 666 hospitals | | | RCT, 173 hospitals | | | Prospective observational study, 23 hospitals | | | Prospective observational study, 19 hospitals | | |
| HF status | Acute HF | | | Acute HF | | | Acute HF | | | Acute HF | | | Acute HF | | | Chronic HF | | | Acute HF | | |
| Age (years) | 70.4± 14.3 | 74.3± 13.0 | 75.6± 13.1 | 79 (74–86) | 81 (74–86) | 82 (75–87) | 72 (60–81) | 77 (66–84) | 78 (68–86) | – | – | – | 74±10 | 71±11 | 68±12 | 67±13 | 69±12 | 72±11 | 77 (67–85) | 80 (72–86) | 82 (76–88) |
| Age >75 years | – | – | – | – | – | – | – | – | – | 26 | 29 | 33 | – | – | – | – | – | – | 59 | 69 | 79 |
| Male | 62 | 48 | 32 | 60 | 50 | 33 | 63 | 51 | 13 | 70 | 65 | 48 | 77 | 41 | 47 | 77 | 72 | 61 | 66 | 60 | 43 |
| Etiology | | | | | | | | | | | | | | | | | | | | | |
| Ischemic etiology | 54 | 49 | 32 | – | – | – | 68 | 69 | 56 | 38 | 39 | 24 | – | – | – | 50 | 53 | 44 | 46 | 40 | 18 |
| Hypertensive etiology | 17 | 22 | 31 | – | – | – | – | – | – | – | – | – | – | – | – | 9 | 14 | 25 | 13 | 25 | 34 |
| Comorbidities | | | | | | | | | | | | | | | | | | | | | |
| AF/AFL | 28 | 33 | 32 | 36 | 40 | 41 | 37 | 45 | 45 | 24 | 25 | 26 | 51 | 54 | 66 | 38 | 44 | 52 | 31 | 42 | 50 |
| Hypertension | 66 | 74 | 77 | 73 | 78 | 81 | 78 | 82 | 84 | 66 | 77 | 72 | 70 | 88 | 88 | 85 | 90 | 91 | 66 | 76 | 75 |
| DM | 39 | 44 | 41 | 39 | 42 | 41 | 44 | 50 | 49 | 44 | 46 | 42 | 45 | 49 | 39 | 38 | 36 | 34 | 40 | 40 | 33 |
| Dyslipidemia | 34 | 35 | 31 | 48 | 48 | 45 | 53 | 54 | 51 | 45 | 48 | 40 | – | – | – | 82 | 80 | 79 | 41 | 41 | 35 |
| Prior MI | – | – | – | 25 | 20 | 13 | 31 | 25 | 17 | 31 | 23 | 14 | 58 | 45 | 23 | 39 | 41 | 27 | 32 | 30 | 11 |
| CKD | – | – | – | 21 | 21 | 20 | – | – | – | 23 | 18 | 18 | – | – | – | – | – | – | 44 | 47 | 44 |
| Dementia | | | | | | | – | – | – | 3.3 | 4.5 | 4.2 | – | – | – | – | – | – | 17 | 18 | 21 |
| Laboratory data at admission | | | | | | | | | | | | | | | | | | | | | |
| Creatinine (mg/dL) | 1.4 (1.1–1.9) | 1.3 (1.0–1.9) | 1.2 (1.0–1.8) | 1.4 (1.0–1.8) | 1.3 (1.0–1.8) | 1.3 (1.0–1.7) | – | – | – | 1.6±1.6 | 1.5±1.5 | 1.5±1.6 | – | – | – | 1.2± 1.0 | 1.1± 0.8 | 1.0± 0.7 | 1.5± 1.2 | 1.6± 1.5 | 1.4± 1.2 |
| Sodium (mEq/L) | 138± 4.6 | 138± 4.7 | 138± 4.8 | 138 (135–141) | 138 (135–141) | 138 (135–141) | – | – | – | 136± 6.4 | 137± 7.0 | 137± 7.6 | – | – | – | – | – | – | 139± 4.4 | 139± 4.5 | 139± 4.2 |
| Hemoglobin (g/dL) | 12.5± 2.0 | 11.9± 2.0 | 11.8± 2.0 | 12.2 (10.9–13.6) | 11.7 (10.1–13.1) | 11.5 (10.2–12.8) | – | – | – | – | – | – | – | – | – | 13.4± 2.0 | 13.0± 2.0 | 12.8± 1.9 | 12.2± 2.4 | 11.5± 2.2 | 10.9± 2.2 |
| Albumin (g/dL) | – | – | – | 3.4 (3.1–3.7) | 3.4 (3.1–3.7) | 3.4 (3.0–3.7) | – | – | – | – | – | – | – | – | – | 4.0± 0.4 | 3.9± 0.4 | 4.0± 0.4 | 3.5± 0.5 | 3.5± 0.5 | 3.4± 0.5 |
| Weight (kg) | 78.5 (65.8–94.0) | 79.4 (65.0–97.5) | 78.0 (63.5–97.1) | 75.7 (64.0–89.3) | 77.1 (64.0–92.0) | 76.6 (63.0–93.0) | – | – | – | 80.0± 15.7 | 79.2± 16.7 | 76.4± 17.5 | – | – | – | – | – | – | 58.0± 15.9 | 56.3± 14.1 | 54.4± 13.5 |
| BMI (kg/m$^2$) | – | – | – | 25.7 (22.3–29.7) | 26.5 (22.8–31.5) | 27.4 (23.3–33.0) | – | – | – | – | – | – | – | – | – | 22.7± 4.8 | 22.8± 5.3 | 23.2± 4.7 | 22.8± 4.6 | 22.7± 4.3 | 22.9± 4.4 |

(**Table S6** continued the next page.)

| | OPTIMIZE-HF[S22] | | | GWTG-HF (in the Medicare population)[S23] | | | GWTG-HF[S24] | | | ALARM-HF[S25] | | | PROTECT trial[S26] | | | CHART-2 Study[S27] | | | KCHF | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HFrEF (n=20,118) | HFmrEF (n=7,321) | HFpEF (n=10,072) | HFrEF (n=15,716) | HFmrEF (n=5,626) | HFpEF (n=18,897) | HFrEF (n=48,950) | HFmrEF (n=12,819) | HFpEF (n=38,056) | HFrEF (n=1,698) | HFmrEF (n=811) | HFpEF (n=748) | HFrEF (n=607) | HFmrEF (n=128) | HFpEF (n=108) | HFrEF (n=730) | HFmrEF (n=596) | HFpEF (n=2,154) | HFrEF (n=1,551) | HFmrEF (n=746) | HFpEF (n=1,744) |
| SBP (mmHg) | 119±21 | 128±22 | 130±23 | 132 (115–151) | 142 (124–161) | 144 (125–164) | – | – | – | – | – | – | 119±17 | 127±16 | 134±17 | 118±20 | 125±19 | 128±19 | 141±34 | 152±36 | 150±36 |
| HR (beats/min) | 77±14 | 75±14 | 75±14 | 82 (71–98) | 81 (70–96) | 79 (68–92) | | | | – | – | – | 80±15 | 79±16 | 79±17 | 74±5.7 | 73±15 | 72±12 | 101±25 | 99±28 | 90±28 |
| Medication at discharge | | | | | | | | | | | | | | | | | | | | | |
| ACEI | 62 | 52 | 44 | 75 | 62 | 51 | – | – | – | 68 | 69 | 56 | – | – | – | 58 | 51 | 42 | 35 | 23 | 17 |
| ARB | 11 | 12 | 14 | 21 | 22 | 23 | – | – | – | 14 | 12 | 17 | – | – | – | 27 | 29 | 34 | 30 | 35 | 36 |
| Aldosterone antagonists | 18 | 10 | 7.0 | 25 | 13 | 9.4 | – | – | – | 37 | 27 | 23 | – | – | – | 44 | 29 | 19 | 52 | 44 | 40 |
| β-blockers | 73 | 66 | 57 | 92 | 87 | 79 | – | – | – | 53 | 52 | 41 | – | – | – | 70 | 64 | 46 | 78 | 71 | 54 |
| Length of stay (days) | – | – | – | – | – | – | 4 (3–7) | 4 (3–7) | 4 (3–7) | – | – | – | – | – | – | – | – | – | 16 (11–25) | 16 (11–24) | 16 (11–25) |
| In-hospital mortality (%) | 3.9 (3.6–4.2) | 3.0 (2.6–3.4) | 2.9 (2.5–3.2) | – | – | – | 3.2 | 2.6 | 3.0 | – | – | – | – | – | – | – | – | – | 9.2 | 4.8 | 5.1 |

Data given as mean±SD, (%), or median (IQR). †For heart failure with reduced ejection fraction, ‡chronic atrial fibrillation. BMI, body mass index; RCT, randomized controlled trial. Other abbreviations as in Tables S1–S3,S5.