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Characteristics, Outcomes and Predictors of Long-Term Mortality for Patients Hospitalized for Acute Heart Failure: A Report From the Korean Heart Failure Registry

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ABSTRACT

Background and Objectives: Acute heart failure (AHF) is associated with a poor prognosis and it requires repeated hospitalizations. However, there are few studies on the characteristics, treatment and prognostic factors of AHF. The aims of this study were to describe the clinical characteristics, management and outcomes of the patients hospitalized for AHF in Korea. **Subjects and Methods:** We analyzed the clinical data of 3,200 hospitalization episodes that were recorded between June 2004 and April 2009 from the Korean Heart Failure (KorHF) Registry database. The mean age was 67.6 ± 14.3 years and 50% of the patients were female. **Results:** Twenty-nine point six percent (29.6%) of the patients had a history of previous HF and 52.3% of the patients had ischemic heart disease. Left ventricular ejection fraction (LVEF) was reported for 89% of the patients. The mean LVEF was $38.5 \pm 15.7\%$ and 26.1% of the patients had preserved systolic function (LVEF $\geq 50\%$), which was more prevalent in the females (34.0% vs. 18.4%, respectively, $p < 0.001$). At discharge, 58.6% of the patients received beta-blockers (BB), 53.7% received either angiotensin converting enzyme-inhibitors or angiotensin receptor blockers (ACEi/ARB), and 58.4% received both BB and ACEi/ARB. The 1-, 2-, 3- and 4-year mortality rates were 15%, 21%, 26% and 30%, respectively. Multivariate analysis revealed that advanced age {hazard ratio: 1.023 (95% confidence interval: 1.004-1.042); $p = 0.020$ }, a previous history of heart failure {1.735 (1.150-2.618); $p = 0.009$ }, anemia {1.973 (1.271-3.063); $p = 0.002$ }, hyponatremia {1.861 (1.184-2.926); $p = 0.007$ }, a high level of serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) {3.152 (1.450-6.849); $p = 0.004$ } and the use of BB at discharge {0.599 (0.360-0.997); $p = 0.490$ } were significantly associated with total death. **Conclusion:** We present here the characteristics and prognosis of an unselected population of AHF patients in Korea. The long-term mortality rate was comparable to that reported in other countries. The independent clinical risk factors included age, a previous history of heart failure, anemia, hyponatremia, a high NT-proBNP level and taking BB at discharge. (**Korean Circ J 2011;41:363-371**)

KEY WORDS: Heart failure; Registries; Outcome.

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Introduction

Acute Heart failure (AHF) is one of the most common conditions encountered in emergency care and AHF is associated with hospitalization and a poor prognosis.¹⁾ Even though the prevalence of AHF is increasing and its clinical outcome is fatal at its worst, there is limited data on its epidemiology, treatment and prognosis.²⁾ Many hospital-based and community-based registries have elucidated the clinical characteristics, therapeutic modalities and outcomes of patients with heart failure.³⁾⁴⁾ However, there have been no large-scale observational studies to evaluate the clinical features of Korean patients with AHF.

Several markers of a poor prognosis have been described for patients with heart failure. The widely recognized risk factors include age, ischemic heart disease, a reduced left ventricular ejection fraction (LVEF) and renal dysfunction.⁵⁾ In addition, anemia, hyponatremia, male gender and diabetes have been associated with a poor prognosis.⁶⁾⁷⁾ The values of these prognostic factors in AHF patients are less well documented. The Korean Heart Failure (KorHF) Registry is a nationwide observational, prospective, multi-centre study on AHF. It is the first multi-center registry of consecutive AHF patients according to the Korean AHF criteria. Our objectives were to investigate the etiology, clinical characteristics, treatment modalities, morbidity, mortality and prognostic markers of AHF.

Subjects and Methods

Criteria and enrolment

Between June 2004 and April 2009, the data on the clinical status and in-hospital outcomes of patients was obtained following a review of the registry data from 24 hospitals in Korea. The participating centers were evenly located nationwide in proportion to the population they serve. Heart failure was diagnosed on admission according to the Framingham criteria.⁷⁾ The institutional review board or ethics committee at each participating hospital approved the study protocol, and the patients gave their written informed consent prior to study entry.

Data collection

The patient demographic and baseline characteristics, the underlying diseases, the clinical presentation, treatments and outcomes from the initial presentation through hospitalization and at discharge were recorded. The data was entered into the KorHF Registry database via a Web-based electronic data capture system that included an electronic case report form. The diagnosis of heart failure was required to be confirmed at the time of a patient's discharge. Morbidity and the in-hospital and long-term mortality were also documented. Data collection and audit were performed by the KorHF

Registry Steering Committee at The Korean Society of Heart Failure.

Etiology of heart failure

We attempted to determine the etiology of heart failure and identify the demographic characteristics, clinical variables and biochemical markers that had prognostic impact. We compared the long-term mortality in relation to age, gender, the body mass index (BMI) and the previous medical history. A history of hypertension, dyslipidemia and/or diabetes mellitus was recorded if documented by the physician in the admitting notes, and if the clinical diagnoses and criteria conformed to the Framingham's criteria. The use of beta-blockers (BB), angiotensin converting enzyme-inhibitors (ACEi) and/or angiotensin receptor blockers (ARB) at discharge was assessed for their impact on the prognosis. We further evaluated the effect of the left ventricular systolic function on survival, the clinical presentation and the cause of heart failure. The biochemical variables included in the analysis were anemia (blood hemoglobin <12.0 g/dL), hyponatremia (sodium <135 mmol/L), azotemia (serum creatinine \geq 2.0 mg/dL), hypocholesterolemia (cholesterol <160 mg/dL) and the N-terminal pro-B-type natriuretic peptide (NT-proBNP) level at admission (over 1,000 pg/mL).

Follow-up information

Research coordinators guided by documented definitions used standardized report forms to collect the follow-up events until October 2009. The medical records were reviewed whenever possible when patients required repeat hospitalization. In addition to patient telephone interviews, the referring physicians and institutions were contacted when necessary for additional information. We obtained information on patient survival and hospital readmission for heart failure. Events related to heart failure were defined as admission for heart failure deterioration, transplantation or all-cause death.

Statistical analysis

The continuous variables are expressed as means \pm standard deviation (SD). Group comparisons were based on the Student's t-test or the χ^2 test as appropriate. Survival function estimates were derived using the Kaplan-Meier method, and differences were tested using the log-rank test. Predictors of survival were identified using univariate and multivariate Cox proportional hazard regression analyses.

The candidate independent variables included age, gender, a previous diagnosis of heart failure, the systolic blood pressure, the heart rate, the BMI, anemia, the ejection fraction and the systolic heart failure medications at discharge. The entry criterion for the multivariate analysis was a $p < 0.05$, which was considered statistically significant. The results are presented as means, SD, percentages {95% confidence interval

(CI) and hazard ratios (95% CI) where appropriate. All the analyses were conducted using the Statistical Package for the Social Sciences (SPSS) 15.0 statistical software (SPSS Inc.).

Results

The KorHF Registry database included 3,200 admission episodes for heart failure at 24 centers. The mean observational period was 1.7 years (from 0.1 to 4.9 years) from June of 2004 to April of 2009, and the follow-up rate was 81%.

Demographic and clinical characteristics

The patient demographics and the characteristics of the past medical history for the patient episodes of heart failure are summarized in Table 1. Among the 3,200 patients, 1,612 (50.4%) were over 70 years old. The average age was 67.6 ± 14.3 years old and the women were significantly older than the men (mean age: 70.7 ± 13.5 vs. 64.5 ± 14.5 years, $p < 0.0001$) and the women had a lower BMI. Twenty-nine point six percent (29.6%) of the patients had a prior history of heart failure. In addition, 46.5% of the patients had a history of hypertension, and a history of diabetes, stroke and chronic renal disease was present in 30.5%, 18.9% and 9.2%, respectively. The underlying causes of heart failure were as follows: ischemic heart disease (52.3%), myocardial infarction or coronary heart disease in 1,194 patients (77.3%), valvular heart disease (12.7%) and cardiomyopathy (26.5%). Idiopathic dilated cardiomyopathy was present in 747 patients (87.9%). However, the other clinical features were similar between the two groups, except for a higher prevalence of ischemic heart disease and valvular heart disease as the underlying disease in the female

patients.

The clinical characteristics of the patients at presentation are shown in Table 2. Acute episodes of heart failure were generally associated with dyspnea. Upon admission, 22.9% of the patients experienced dyspnea at rest (NYHA functional class IV criteria), whereas 10.5% of patients experienced other symptoms of heart failure (NYHA class I). However, 15.5% and 51.1% of the patients had symptoms of NYHA class II and III, respectively. The dyspneic symptoms and blood pressure levels were similar in both gender groups. Hypotension (systolic BP < 90 mmHg) was identified in 4.3% of the admissions and the rate was similar for females and males.

The laboratory findings of the patients at presentation are summarized in Table 2 and 3. The abnormal blood chemistry and the markers presented with AHF on admission were as follows: hyponatremia (18.0%, a level of creatinine < 135 mM), anemia (41.4%, a level of hemoglobin < 12 mg/dL), azotemia (14.9%, a level of creatinine ≥ 2.0 mg/dL) and hypocholesterolemia (51.5%, a level of total cholesterol < 160 mg/dL).

We identified LVEF in 2,843 (88.8%) patients in the present study: the mean LVEF was $38.5 \pm 15.7\%$, and preserved systolic function, which was defined as a LVEF $> 50\%$, was evident in 743 patients (26.1%). The female patients presented with a higher LVEF (female vs. male: $41.6 \pm 16.1\%$ vs. $35.4 \pm 14.7\%$, respectively, $p < 0.001$) and a higher prevalence of heart failure with preserved systolic function (34.0% vs. 18.3%, respectively, $p < 0.001$).

Intravenous diuretic infusions/boluses were given to 68.6% of the patients, and 35.8% received intravenous nitrates. Inotropic treatment was used in 21.7% of the patients, and 22.4%

Table 1. Demographic and clinical features

Characteristics	Total, n=3,200	Female, n=1,600 (50%)	Male, n=1,600 (50%)	P*
Age (year, mean \pm SD)	67.6 \pm 14.3	70.7 \pm 13.5	64.5 \pm 14.5	<0.001
BMI (kg/m ²)	23.2 \pm 4.0	23.0 \pm 4.2	23.4 \pm 3.8	0.009
Previous medical history (%)				
Heart failure	871 (29.6)	453 (30.4)	418 (28.7)	0.313
Hypertension	1,486 (46.5)	787 (49.2)	699 (43.7)	0.002
Diabetes	975 (30.5)	489 (30.6)	486 (30.4)	0.927
Stroke	299 (18.9)	137 (18.0)	162 (19.8)	0.361
Chronic renal disease	295 (9.2)	134 (8.4)	161 (10.1)	0.970
Chronic pulmonary disease	104 (3.5)	43 (2.9)	61 (4.2)	0.055
Underlying disease (%)				
Ischemic heart disease	1,544 (52.3)	828 (53.6)	716 (46.4)	<0.001
Hypertension	1,143 (36.7)	596 (38.1)	547 (35.3)	0.103
Cardiomyopathy	760 (26.5)	351 (24.3)	409 (28.8)	0.007
Valvular heart disease	407 (12.7)	255 (16.4)	152 (9.7)	<0.001
Myocarditis	22 (0.7)	8 (0.6)	14 (1.0)	0.187
Infiltrative disease	12 (0.4)	5 (0.3)	7 (0.5)	0.545

*Comparison between the female and male groups. BMI: body mass index

Table 2. Clinical presentation and the hospital course

Characteristics	Total	Female, n=1,600 (50%)	Male, n=1,600 (50%)	p*
Clinical findings				
SBP (mmHg)	130.5±30.2	131.7±30.5	129.3±29.8	0.240
DBP (mmHg)	77.9±18.0	77.7±17.4	78.1±18.7	0.517
Hypotension (SBP <90 mmHg) (%)	135 (4.3)	65 (4.2)	70 (4.5)	0.622
PR (bpm)	91.2±25.4	91.5±25.8	91.0±25.0	0.615
NYHA functional class at admission (%)				
I	283 (10.5)	123 (9.1)	160 (12.0)	NS
II	419 (15.5)	196 (14.5)	223 (16.7)	NS
III	1,376 (51.1)	685 (50.5)	691 (51.6)	NS
IV	616 (22.9)	352 (26.0)	264 (19.7)	NS
Echo results				
LVEF (% mean)	38.5±15.7	41.6±16.1	35.4±14.7	<0.001
LVEF ≥50% (%)	743 (26.1)	481 (34.0)	262 (18.3)	<0.001
Lab. Findings				
Sodium (mM)	138.1±26.4	138.1±5.4	138.1±4.9	0.892
Hemoglobin (mg/dL)	12.4±5.5	11.7±2.1	13.2±2.4	<0.001
Creatinine (mg/dL)	1.5±1.2	1.4±1.2	1.6±1.4	<0.001
Total-cholesterol (mg/dL)	164.1±47.1	167.6±48.7	158.7±43.9	<0.001
NT-proBNP (ng/L)	8,461±96,002	9,456.0±10,358.6	7,680.1±9,341.5	<0.001
Hospital management (%)				
Diuretics IV	1,982 (68.1)	1,009 (68.6)	973 (67.5)	0.518
Nitrate IV	1,042 (35.8)	520 (35.4)	522 (36.2)	0.632
Inotropic agents	711 (21.7)	285 (59.3)	346 (62.4)	0.001
Dobutamine	502 (17.2)	225 (15.3)	277 (19.2)	0.005
Dopamine	276 (9.5)	118 (8.0)	158 (11.0)	0.007
Hemodynamic monitoring	171 (5.9)	84 (5.7)	87 (6.0)	0.707
IABP	96 (3.3)	41 (2.8)	55 (3.8)	0.121
Medication at discharge (%)				
Beta-blocker	1,109 (58.6)	567 (58.7)	542 (58.4)	0.926
ACEi/ARB	648 (53.7)	321 (52.5)	327 (54.9)	0.417
Aldosterone antagonist	913 (53.1)	456 (52.4)	457 (53.8)	0.562

*Comparison between the female and male group. SBP: systolic blood pressure, DBP: diastolic blood pressure, PR: pulse rate, NYHA: New York Heart Association, LVEF: left ventricular ejection fraction, NT-proBNP: N-terminal pro-B-type natriuretic peptide, IABP: intraaortic balloon pump, ACEi: angiotensin converting enzyme-inhibitors, ARB: angiotensin receptor blocker

of these patients received two or more inotropes. Dobutamine (17.2%) and dopamine (9.5%) were the most commonly administered inotropes. Few patients received noradrenaline (0.9%) or mirlinone (0.2%). Inotropic agents were used more frequently in the males than in the females (59.3% vs. 62.4%, respectively, $p=0.001$). For critical care, 1,330 patients (37.7%) stayed at intensive care units during hospitalization, and 247 patients (7.1%) received mechanical ventilator assistance. Hemodialysis was performed in 4.1% of the patients. Hemodynamic monitoring was performed in 5.9% of the patients and intraaortic balloon pump was used in 3.3% of the patients.

Either ACEi or angiotensin-II receptor blockers (ARB)

were prescribed at discharge for 53.7% of the patients. BBs and spironolactone were administered to 58.6% and 53.1% of the patients, respectively. One of both, BBs or ACEi/ARB, was prescribed to 58.4% of the patients. There was no difference in discharge medication between the two gender groups (Table 2).

Clinical outcomes and predictors

Of the 3,200 consecutive admitted patients with heart failure, 2,973 (92.9%) of them were discharged alive. During the follow-up period (mean±SD: 1.7±1.2 years), 625 patients (19.5%) died. The mortality rate during hospitalization was 6.4%. The cumulative survival rates for the study patients af-

ter discharge at 1, 2, 3 and 4 years were 85%, 79%, 74% and 70%, respectively, which were similar between both gender groups (Fig. 1). The event-free survival rates at 1, 2, 3 and 4

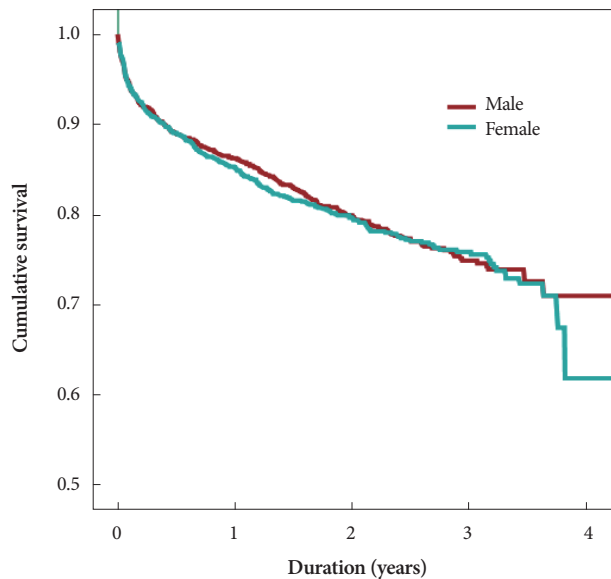


Fig. 1. The five-year follow-up results according to different gender. The five-year survival rate was 61% and 69% for the male (red line) and female (blue line), respectively.

years were 67%, 56%, 47% and 41%, respectively. Heart transplantation was performed in 0.9% (31 patients) of the patients and 24.6% (866 patients) were re-hospitalized. The demographic and clinical variables associated with all cause mortality are summarized in Table 3.

Univariate analysis for the current risk variables showed that an advanced age, a low BMI ($<23 \text{ kg/m}^2$, median value), a prior history of heart failure, a non-ischemic origin of heart failure, low blood pressure, dyspnea at rest on admission (NYHA functional class IV), hyponatremia ($<135 \text{ mM}$), anemia (hemoglobin $<12 \text{ g/dL}$), azotemia (creatinine $>2.0 \text{ mg/dL}$), low cholesterol (total cholesterol $<160 \text{ mg/dL}$) and a high plasma NT-proBNP level ($\geq 1,000 \text{ ng/dL}$) tended to be associated with an increase in subsequent all-cause mortality, while a prescription of BB and/or ACEi/ARB was related with better clinical outcomes (Table 4).

On the basis of data gathered from all the patient episodes with AHF, multivariate analysis identified an advanced age, previous heart failure, anemia, hyponatremia and a high NT-proBNP level showed a tendency of increased subsequent all-cause mortality, but a prescription of BB at discharge was associated with improved clinical outcomes. The multivariate odds ratios (ORs) and corresponding 95% CIs for all-

Table 3. Clinical factors and predictors for the long-term clinical outcomes on univariate analysis

Characteristics	Total	Expired, n=652 (19.6%)	Alive, n=2,571 (80.4%)	HR	95% CI	p*
Age (mean)	67.6 \pm 14.3	71.6 \pm 13.1	66.6 \pm 14.5	1.027	1.021-1.034	<0.001
Women (%)	1,600 (50.0)	312 (50.1)	1,285 (50.0)	1.026	0.874-1.205	0.752
BMI ($<23 \text{ kg/m}^2$) (%)	1,412 (50.4)	317 (61.9)	1,095 (47.9)	1.781	1.490-2.129	<0.001
Previous heart failure (%)	870 (29.6)	239 (40.9)	631 (26.8)	1.690	1.428-2.001	<0.001
Non-ischemic heart failure (%)	1,410 (47.7)	321 (54.2)	1,089 (46.2)	1.352	1.146-1.596	<0.001
Clinical findings						
SBP (mmHg)	130.5 \pm 30.2	124.7 \pm 30.4	131.9 \pm 29.9	0.991	0.988-0.994	<0.001
HR (bpm)	91.2 \pm 25.4	91.4 \pm 25.1	91.2 \pm 25.5	1.000	0.997-1.004	0.780
Dyspnea at rest (%)	616 (22.9)	155 (25.2)	461 (21.5)	1.499	1.238-1.815	<0.001
Echo results						
LVEF (%)	38.5 \pm 15.7	38.0 \pm 16.2	38.6 \pm 15.6	0.995	0.990-1.001	0.113
LVEF $\geq 50\%$ (%)	742 (26.1)	137 (26.4)	605 (26.0)	0.948	0.774-1.160	0.601
Lab. Findings						
Hyponatremia (Na $<135 \text{ mM}$)	572 (18.0)	180 (31.4)	392 (17.0)	2.226	1.860-2.665	<0.001
Anemia (Hb $<12 \text{ g/dL}$)	1,316 (41.4)	346 (55.5)	970 (38.0)	2.021	1.719-2.377	<0.001
Azotemia (Cr $\geq 2.0 \text{ mg/dL}$)	478 (14.9)	150 (24.3)	328 (13.0)	2.291	1.901-2.761	<0.001
Total-cholesterol ($<160 \text{ mg/dL}$)	1,431 (51.1)	318 (58.3)	1,112 (49.3)	1.393	1.169-1.659	<0.001
NT-proBNP $\geq 1,000 \text{ ng/L}$	1,844 (85.1)	374 (92.6)	1,470 (83.4)	2.425	1.661-3.541	<0.001
Medication at discharge (%)						
Beta-blocker	1,109 (58.6)	137 (40.7)	927 (62.5)	0.441	0.352-0.551	<0.001
ACEi/ARB	648 (53.7)	103 (39.3)	545 (57.7)	0.504	0.391-0.650	<0.001
Aldosterone antagonist	913 (53.1)	159 (46.2)	754 (54.8)	0.700	0.563-0.869	0.001

*Comparison between the expired and alive groups. HR: hazard ratio, CI: confidence interval, BMI: body mass index, SBP: systolic blood pressure, LVEF: left ventricular ejection fraction, NT-proBNP: N-terminal pro-B-type natriuretic peptide, ACEi: angiotensin converting enzyme-inhibitors, ARB: angiotensin receptor blocker

Table 4. Clinical predictors of the clinical outcome on multivariate analysis

Characteristics of the patients	HR	95% CI	p*
Age (mean)	1.023	1.004-1.042	0.020
Previous heart failure	1.735	1.150-2.618	0.009
Anemia (Hb <12 mg/dL)	1.973	1.271-3.063	0.002
Hyponatremia (Na <135 mM)	1.861	1.184-2.926	0.007
NT-proBNP \geq 1,000 ng/L	3.152	1.450-6.849	0.004
Beta-blocker at discharge	0.599	0.360-0.997	0.049

*Comparison between the expired and alive groups. HR: hazard ratio, CI: confidence interval, NT-proBNP: N-terminal pro-B-type natriuretic peptide

cause death are reported for each mortality risk factor identified by the Cox Regression model (Table 4). An older age, a lower BMI, lower systolic BP, low hemoglobin, low sodium, elevated creatinine, the presence of dyspnea at rest and the absence of chronic BB use may be considered as the risk factors of mortality.

The KorHF Registry is a national observational, prospective, multi-centre study and it yields new important information on the actualities of AHF patients in Korea. It is the first population study of the consecutive AHF patients, as characterized according to the Framingham criteria, in 24 medical centers in Korea.

Discussion

The age of the patients in our study was high (older than 65 year-old) and the women were older than the men, which is consistent with the findings of previous studies.¹⁻⁸⁾ The patients with a prior heart failure history constituted 29.6% of all the patients, which was comparable to that of the Japanese data from the Heart Institute of Japan-Department of Cardiology (HIJC) registry (33.5%),⁹⁾ but this was much lower than that 75.6% from the American the Acute Decompensated Heart Failure National Registry (ADHERE) registry.¹⁰⁾ This discrepancy may result from ethnic differences or the methods of registration. The patients of the KorHFR were consecutively enrolled if they were admitted with a diagnosis of heart failure, while the patients of ADHERE were retrospectively enrolled.¹¹⁾

The predominant cause of heart failure was ischemic heart disease. In this study population 52.3% of the patients experienced heart failure secondary to ischemic heart disease, which is considerably lower than the 60-75% reported in the clinical trials of Western patients.⁸⁾ Race and ethnic variations may account for the differences in the causes of heart failure because the prevalence of ischemic heart disease was also low in the studies held in Japan.¹²⁾ Thus, applying the guidelines derived from the study populations containing a higher proportion of patients with ischemic heart disease than the Ko-

rean population should be carefully considered.

A preserved LVEF is a common finding in patients with AHF and in elderly heart failure patients.²⁾¹³⁾ Among the patients with information on their LVEF, 26.1% had preserved systolic function, which was defined as an LVEF over 50%. However, transient systolic heart failure cannot be excluded. Echocardiography was not performed in 19.8% of the patients. The prevalence of heart failure with preserved systolic function is comparable to that of other studies based on registry data.

Although numerous randomized controlled trials have shown that ACEis, ARBs and BBs improved the survival of patients with heart failure, the proportions of our patients actually receiving these drugs in the present study were 58.6%, 53.7% and 58.4%, respectively. These basic agents for the treatment of heart failure are highly prescribed in Korea, and this is comparable to other countries.⁹⁾¹⁴⁾ During the hospital stay, BB, ACEi/ARB, furosemide, digoxin, spironolactone, aspirin and oral anticoagulants were frequently initiated to the AHF patients. Surprisingly, only the use of BBs at discharge affected the long-term prognosis, while ACEi/ARBs and aldosterone antagonist did not. This appears to suggest that AHF and chronic heart failure are two distinct conditions. BB and ACEi/ARB therapy were more commonly prescribed to our patients than that to the patients included in other studies, and these drugs were more often taken by the patients than that in a recent survey.¹⁵⁾ The use of ARBs was considerably higher than that in a recent survey (Table 5). Diuretics were used by 68.1% of the patients in our study. Many patients received treatment for their precipitating factor and they obviously did not have significant fluid overload. Spironolactone was frequently used since 53.1% of patients with heart failure were discharged with this medication. Inotropes are needed by AHF patients to support and stabilize the hemodynamics if the basic treatment modalities are inadequate. The use of inotropes in our study was comparable to that of other studies.¹⁶⁾ Interestingly, dopamine was used in our study twice as often as dobutamine.

Previous studies have demonstrated that advanced age, low blood pressure, NYHA associated LV dysfunction and diabetes were associated with a poor prognosis for patients with heart failure. In addition, several factors such as BNP, C-reactive protein (CRP), impaired renal function and anemia have emerged as new predictors associated with a poor prognosis in heart failure patients.¹⁷⁾ The present study evaluated both new (anemia, renal insufficiency, hyponatremia, BNP and CRP) and known prognostic factors for heart failure and we revealed that anemia, hyponatremia and natriuretic peptide were related to the long-term mortality rate. We identified several demographic and clinical variables as significant predictors of poor survival on the univariate analysis. Patients with older age, a lower BMI less than 23 kg/m², previous he-

Table 5. Comparisons of the acute heart failure trials and the KorHF

Characteristics	KorHF	ADHERE	OPTIME
Age (year, mean)	67.6	72.4	66.5
Gender (women) (%)	50	52	47
Previous medical history (%)			
Ischemic heart disease	52.3	57	NA
Myocardial infarction	14.2	31	48
Hypertension	46.5	73	68
Diabetes	30.5	44	44
Stroke	18.9	17	NA
Chronic renal disease	9.2	31	NA
Blood pressure			
SBP (mmHg)	130.5±30.2	144±32.6	120±18
Hypotension (SBP <90 mmHg) (%)	4.3	2	NA
NYHA functional class at admission (%)			
II	16	20	7
III	51	44	46
IV	23	32	47
Echo results			
LVEF (% mean)	38.5±15.7	34.4±16.1	24±8
LVEF >40% (%)	57.5	46	NA
Renal function			
Creatinine (mg/dL)	1.5±1.2	1.8±1.6	1.5±0.5
Creatinine (mg/dL) >2.0 mg/dL (%)	15.2	20	NA
Management (%)			
Diuretics	68.1	70	90
Nitrate	35.8	26	NA
Beta-blocker	58.6	48	22
ACEi	17.9	41	70
ARB	39.4	12	13

*Comparison between the expired and alive groups. KorHF: Korean Heart Failure, ADHERE: the Acute Decompensated Heart Failure National Registry, OPTIME: the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure study, SBP: systolic blood pressure, DBP: diastolic blood pressure, NYHA: New York Heart Association, LVEF: left ventricular ejection fraction, ACEi: angiotensin converting enzyme-inhibitors, ARB: angiotensin receptor blocker

art failure, lower BP and dyspnea at rest showed poorer clinical outcomes, while heart rate, gender and preserved LV function did not affect this. However, only age and previous heart failure were risk factors of a poor prognosis of AHF. Since the women were significantly older than men, male gender emerged as a prognostic risk factor only after correcting for age. The reported association between a previous history of heart failure and a worse prognosis appears meaningful, although it is contrary to a previous study.¹⁸⁾ Among the biochemical variables, we found hyponatremia, anemia, renal dysfunction and a high NT-proBNP level in AHF patients were associated with a poor prognosis. Mortality did not change with a declining LVEF in our study, and a LVEF <50% was not independently associated with any outcome.¹⁹⁾ We also found a relationship between higher systolic blood pressure at ad-

mission and better survival on the univariate analysis, but not on the multivariate analysis (Table 3 and 4). In contrast to the recently reported association between blood pressure and the clinical outcome,²⁰⁾ low blood pressure was not a predictor of mortality in our patients. The same as in previous reports, chronic heart failure, anemia, hyponatremia, and azotemia emerged as predictors of mortality in our population.²¹⁾ The admission NT-proBNP level was also predictive of the long-term outcome on multivariable analysis. Indeed, a previous study that evaluated the serial or pre-discharge natriuretic peptide measurements in AHF patients revealed that the pre-discharge natriuretic peptide measurement had better prognostic significance than the admission natriuretic peptide levels.²²⁾ However, our findings are representative of the value of a point measurement of NT-proBNP in an unselected pop-

ulation hospitalized for AHF.

This report describes the first population date of all the consecutive AHF patients who were characterized according to the Framingham criteria and who were from a wide range of hospitals in Korea. In contrast to our registry, the patients in the randomized clinical trials were younger, the proportion of women was smaller than that in real-life and moderate-to-severe renal dysfunction and significant anemia were the common exclusion criteria.⁹⁾⁽¹²⁾⁽²²⁾ The all-cause mortality at 12 months and over the long-term in our study were better than that described in the previously published reports.²⁾ Owing to the lack of results of long-term follow-up in the ADHERE and OPTIME-HF, no comparison can be drawn on the long-term prognosis. However, the in-hospital and 1-year mortality data are similar.¹⁰⁾⁽²³⁾ Also, the long-term prognosis was similar to the Japanese heart failure registries, that is, the HIJC-HF and JCARD-CARE.⁹⁾⁽²⁴⁾ This large-scale, prospective cohort study of the KorHF registry with long-term follow-up indicated that patients with heart failure in Korea have clinical features that are compatible with those in other countries

Conclusion

The KorHF Registry is a large multi-centre study that included a broad spectrum of patients with AHF. This study determined the actual nationwide status of heart failure in Korea. The registry contains multiple demographic and clinical variables of a large consecutive group of patients admitted to university hospitals. As a whole, the long-term mortality was high and the independent clinical predictors included age, a previous history of heart failure, anemia, hyponatremia, a high NT-proBNP level and pre-discharge use of BB. This data is vital for evaluating the impact of the advances in diagnostics and therapy on the natural history of heart failure in Korea so as to develop improved therapeutic strategies. Further studies are surely warranted to improve heart doctors' adherence to the diagnostic and therapeutic strategies described in the recently published guidelines.

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