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Heart Failure

Treatment Performance Measures Affect Clinical Outcomes in Patients With Acute Systolic Heart Failure

– Report From the Korean Heart Failure Registry –

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Background: There is a paucity of data on the effects of adherence to treatment on outcomes for patients with acute heart failure (HF) in Korea. We used HF performance measures to evaluate overall adherence and whether this affects clinical outcomes.

Methods and Results: Among 3,466 patients in the Korean Heart Failure Registry, 1,527 patients with left ventricular systolic dysfunction (LVSD) who survived hospitalization were evaluated. Modified validated performance measures were defined as follows: use at discharge of angiotensin-converting enzyme inhibitor (ACEI), angiotensin-receptor II blocker (ARB), β-blocker or aldosterone receptor antagonist. Adherence to performance measures were as follows: ACEI or ARB at discharge, 68.0%; β-blocker at discharge, 40.9%; aldosterone receptor antagonist at discharge, 37.5%. On multivariate analysis, adherence to the measure of ACEI or ARB use at discharge was significantly associated with mortality (odds ratio (OR), 0.344; 95% confidence interval (CI), 0.123–0.964), readmission (OR, 0.180; 95%CI, 0.062–0.522) and mortality/readmission (OR, 0.297; 95%CI, 0.125–0.707) at 60 days and that for β-blocker with mortality (OR, 0.337; 95%CI, 0.147–0.774) at 1 year.

Conclusions: For patients with LVSD in Korea, adherence to treatment performance measures, including prescription of an ACEI/ARB and β-blocker use at discharge, is associated with improved clinical outcomes. (*Circ J* 2012; **76:** 1151–1158)

Key Words: Left ventricular systolic dysfunction; Mortality; Performance measures

The American College of Cardiology (ACC)/American Heart Association (AHA) and the European Society of Cardiology (ESC) have developed evidence-based guidelines for the treatment of heart failure (HF) to help practitioners ensure appropriate and consistent treatment for patients.[1,2] Despite extensive evidence and recommendations from clinical trials, HF remains a substantial cause of morbidity and mortality. In addition, guidelines have been slowly and inconsistently applied in clinical practice, and certain evidence-based, guideline-driven HF therapies are significantly underused.[3–5]

To promote adherence to clinical guidelines, some investigators have created performance measures, which have been adapted to create core performance measures for patients hospitalized with HF.[3,4,6–8] Selection of appropriate performance measures for use in evaluating appropriative management is

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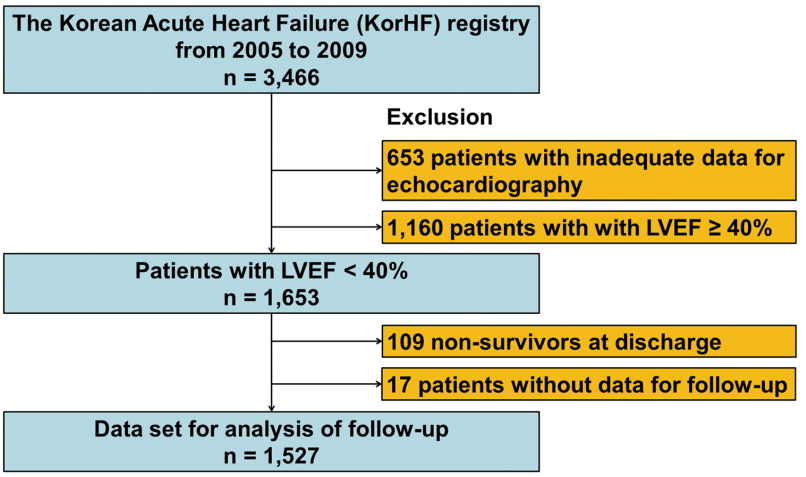

Figure 1. Dataset for the study population. LVEF, left ventricular ejection fraction.

critically important because of the potential implications for the health system and patients' outcomes. Whether the selected performance measures are associated with patient outcome is important. In addition, ethnic and racial differences in etiology, outcome, and response to therapy in HF have been demonstrated, so performance measures for different circumstances must be validated.[9,10]

Little is known about adherence to performance measures and the effect on the clinical outcomes of patients with acute systolic HF in Korea and other Asian countries. In the present study, we evaluated overall adherence to HF performance measures identified or modified by either an organization[6] or investigator,[3,4] and investigated if adherence to these performance measures affected patients outcomes.

Methods

Ethical Approval of the Study Protocol

The study protocol was approved by the Research Committee of the Korean Society of Heart Failure. It was also approved by the ethical committees of each participating hospital. Informed consent was obtained from each patient and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institutions' human research committees. Data were collected and managed by the Control of Data Committee of the Korean Heart Failure (KorHF) Registry.

Study Design and Study Population

The KorHF Registry enrolled patients with acute decompensated HF from June 2004 to April 2009. This was a nationwide, observational, prospective, and multicenter study by the Korean Society of Heart Failure, and used to investigate the clinical characteristics and prognostic factors of Korean HF patients. Eligible patients were those who presented with HF symptoms as the primary reason for admission and with signs of congestion such as pulmonary congestion or systemic edema. Diagnosis of left ventricular (LV) dysfunction was decided by the attending physician using the medical record or echocardiographic findings. There were no exclusion criteria except in case of an inconclusive diagnosis of HF and patients who did not give informed consent. Data on the demographic features, medical history, clinical characteristics, initial evaluations, therapeutic management, and in-hospital outcomes were collected and clinical follow-up undertaken using the data on vital status, readmission to hospital, and major cardiovascular events.

From this population, we selected patients with LV systolic dysfunction (LVSD) and who had survived hospitalization with 1 year of follow-up data. Acute decompensated HF was defined as new-onset HF or decompensation of chronic, established HF with symptoms or signs sufficient to warrant hospitalization. LVSD was defined as LV ejection fraction (LVEF) <40% by echocardiography.

Performance Measures

Performance measures were modified using the definitions defined by the ACC/AHA clinical performance measures for adults with chronic HF, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) study, and the Medical Management of Chronic Heart Failure in Europe and Its Related Costs (MAHLER) survey.[3,4,6] Of these previously validated parameters, we excluded discharge instructions, anticoagulant at discharge for HF patients with atrial fibrillation (AF), and smoking cession counseling because these measures were either not performed or our protocol did not include them. We added a performance measure for aldosterone receptor antagonists because they have proven benefit in patients with acute HF.[11]

The modified validated performance measures were defined as follows.

1. Angiotensin-converting enzyme inhibitor (ACEI) or angiotensin-receptor II blocker (ARB) for LVSD at discharge: "HF patients with LVSD and without contraindications for both ACEI and ARB who were prescribed an ACEI or ARB at hospital discharge."
2. Beta-blocker for LVSD at discharge: "HF patients with LVSD and without β-blocker contraindications who were prescribed a β-blocker at hospital discharge."
3. Aldosterone receptor antagonist at discharge; "HF patients with LVSD and without aldosterone receptor antagonist contraindications (males with serum creatinine >2.5 mg/dl or females with serum creatinine >2.0 mg/dl at any time during hospitalization, and excluding patients with potassium >5.0 mmol/L) who were prescribed an aldosterone receptor antagonist at hospital discharge."

Outcomes

The 60-day and 1-year mortality rates, readmission rate and combined mortality/readmission rates were collected. Mortality was defined as death from any cause. Readmission was defined as admission because of aggravated HF, serious ventricular arrhythmia or myocardial infarction (MI) after discharge.

Statistical Analysis

Statistical analyses were undertaken using SPSS version 15 (SPSS, Chicago, IL, USA). Continuous variables are expressed as the mean±standard deviation. Categorical variables are expressed as absolute numbers and percentages. To adjust for significant covariates, multivariable models were developed for post-discharge all-cause mortality and morbidity. We used binary logistic regression models to estimate the unadjusted and adjusted relationships between each performance measure and patient outcome. The unadjusted models included only each component of the performance measures as a predictor. The adjusted models were controlled for baseline demographic characteristics and clinical characteristics, which included age, sex, history of previous HF, acute MI, hypertension (HT), diabetes mellitus, peripheral vascular disease, prior cerebral infarction and chronic pulmonary disease, atrial arrhythmia, systolic and diastolic blood pressures, serum creatinine and hemoglobin levels, body weight and New York Heart Association (NYHA) functional classification. Kaplan-Meier analyses were used to compare endpoints such as mortality, readmission and mortality/admission, and each component of the performance measures. The log-rank test was used to test for differences in unadjusted survival curves. A 2-sided P value <0.05 was considered significant.

Results

Baseline Characteristics of Patients

The KorHF Registry enrolled 3,466 patients, among whom 653 with inadequate data for LVEF by echocardiography and 1,160 with LVEF ≥40% were excluded. Of the remaining 1,653 patients with LVSD, 1,527 who survived hospitalization and had follow-up data were evaluated (Figure 1).

The median age of the study population was 69.1 years (interquartile range (IQR) 58.9–76.5) and the percentage of males was 55.9%. The percentage of patients graded as NYHA classification Ⅲ or Ⅳ was 59.6%. A total of 40.1% of patients had ischemic heart disease. The median EF by echocardiography was 28.7% (IQR, 23.0–34.0%). A total of 20.8% of patients showed AF or atrial flutter at hospital admission. The most common comorbid condition was HT (42.0%). A total of 30.8% of patients had a history of HF. Baseline clinical and laboratory characteristics of the study population are presented in Table 1.

Performance Measures and Clinical Outcomes

Of the entire cohort, assessment of LV function by echocardiography (79.8%) or measurement of the level of natriuretic peptide (76.6%) was done in 3,621 (89.1%) patients. All the patients with systolic HF underwent echocardiographic evaluation, and 83.4% of patients had their levels of natriuretic peptide measured. We did not evaluate anticoagulant use at discharge for AF, smoking session counseling, or discharge instructions even though they are currently an ACC/AHA standardized performance measure.[6]

According to the performance measures, the highest prevalence of adherence was for use of ACEI or ARB at discharge (68.0%), followed by β-blocker at discharge (40.9%) and aldo-

Table 1. Baseline Characteristics of the Study Population

	Patients (n=1,527)
Male sex, n (%)	853 (55.9)
Age, median (IQR), year	69.1 (58.9–76.5)
Anthropometric data, mean±SD	
Height, cm	161.1±9.8
Weight, kg	60.1±13.5
BMI, kg/m^2	23.2±3.6
Vital signs at admission, mean±SD	
SBP, mmHg	129.3±29.5
DBP, mmHg	79.0±18.5
Heart rate, beats/min	93.9±24.4
Comorbid conditions, n (%)	
Hypertension	641 (42.0)
Diabetes mellitus	479 (31.4)
Previous heart failure	471 (30.8)
Myocardial infarction	235 (15.4)
PCI or CABG	172 (11.3)
PAOD	20 (1.3)
Valvular heart disease	200 (13.1)
Chronic pulmonary disease	48 (3.1)
Chronic renal insufficiency	112 (7.3)
Cerebral infarction	124 (8.1)
Smoking in the past	244 (15.9)
Laboratory findings at admission (mean±SD)	
Hb, g/dl	12.7±2.3
Cr, mg/dl	1.4±1.0
TC, mg/dl	163.9±46.1
LDL-C, mg/dl	101.6±38.4
Na, mmol/L	138.2±5.0
K, mmol/L	4.3±0.8
hs-CRP, mg/dl	2.54±4.58
CK-MB, ng/ml	14.46±56.67
Troponin I, ng/ml	3.18±12.41
BNP, pg/ml (n=399)	1,976.4±3,552.2
NT-proBNP, pg/ml (n=994)	9,251.4±9,806.6
NYHA classification III–IV, n (%)	910 (59.6)
HF characteristics, n (%)	
Ischemic heart disease	612 (40.1)
Idiopathic dilated cardiomyopathy	335 (21.9)
Valvular heart disease	163 (10.7)
ECG finding at admission, n (%)	
Atrial flutter or fibrillation	318 (20.8)
LBBB	114 (7.5)
LV systolic function by echocardiography	
LVEF, median (IQR), %	28.7 (23.0–34.0)

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor II blocker; BMI, body mass index; BNP, B-type natriuretic peptide; BT, body temperature; CABG, coronary artery bypass graft; Cr, creatinine; hs-CRP, high-sensitivity C-reactive protein; DBP, diastolic blood pressure; Hb, hemoglobin; HF, heart failure; IQR, interquartile range; LBBB, left bundle branch block; LDL-C, low-density lipoprotein cholesterol; LV, left ventricular; LVEF, left ventricular ejection fraction; PAOD, peripheral artery obstructive disease; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol.

Table 2. Adherence of Performance Measures Modified by the ACC/AHA

Measure	Adherence, n (%)
ACEI or ARB at discharge	1.039 (68.0)
Ramipril	280 (26.9)
Captopril	174 (16.7)
Losartan	155 (14.9)
Candesartan	75 (7.2)
Valsartan	63 (6.1)
Perindopril	62 (6.0)
Other	230 (22.1)
β-blocker at discharge	624 (40.9)
Carvedilol	507 (81.3)
Bisoprolol	54 (8.7)
Atenolol	26 (4.2)
Other	37 (5.9)
Aldosterone antagonist at discharge	572 (37.5)

Abbreviations see in Table 1.

sterone antagonist at discharge (37.5%). Adherence to performance measures is presented in Table 2.

The in-hospital mortality was 6.6%. Survivors (n=1,527) at discharge were followed for a median of 365 days (IQR, 198–365). Among these survivors, mortality was 3.8% at 60 days and 9.2% at 1 year. The prevalence of readmission was 3.1% at 60 days and 9.8% at 1 year. The prevalence of combined mortality/readmission was 4.6% at 60 days and 14.1% at 1 year.

Figure 2 shows the Kaplan-Meier curves for mortality, readmission and mortality/readmission according to each component of the performance measures. Use of ACEI or ARB at discharge was associated with a reduction in mortality (log-rank P=0.003), readmission (log-rank P=0.030) and combined mortality/readmission (log-rank P=0.013) for 1 year of follow-up. Use of a β-blocker at discharge was associated with a reduction in mortality only (log-rank P=0.016).

Table 3 shows the relationships between the performance measures and outcomes at 60 days and 1 year. Before adjustment, use of ACEI or ARB at discharge was significantly associated with mortality (odds ratio (OR), 0.561; 95% confidence interval (CI), 0.330–0.952), readmission (OR, 0.475;

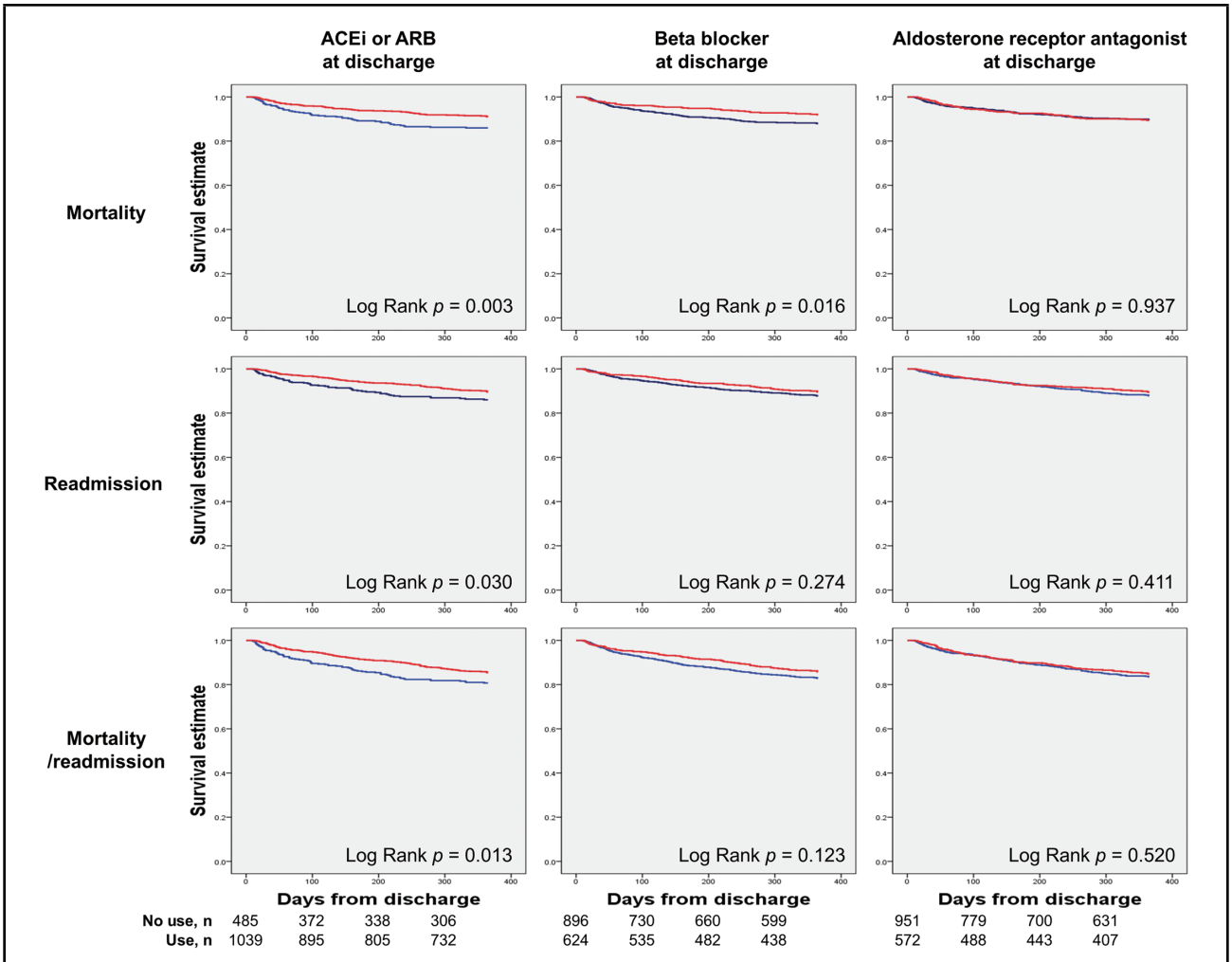

Figure 2. Unadjusted event-free curves for mortality, readmission and mortality/readmission between patients with each component of the performance measures including use of ACEI or ARB at discharge, β-blockers at discharge and aldosterone antagonist at discharge (red line) and the patients without (blue line). ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers.

Table 3. Relationships Between Performance Measures and Patient Outcomes

	Unadjusted		Adjusted*	
	HR (95%CI)	P value	HR (95%CI)	P value
Mortality at 60 days, n=58 (3.8%)				
ACEI or ARB at discharge	0.561 (0.330–0.952)	0.032	0.344 (0.123–0.964)	0.042
β-blocker at discharge	0.748 (0.431–1.298)	0.301	0.291 (0.079–1.077)	0.064
Aldosterone receptor antagonist at discharge	0.871 (0.501–1.511)	0.622	0.839 (0.286–2.458)	0.749
Readmission at 60 days, n=47 (3.1%)				
ACEI or ARB at discharge	0.475 (0.265–0.850)	0.012	0.180 (0.062–0.522)	0.002
β-blocker at discharge	0.734 (0.398–1.354)	0.323	0.680 (0.229–2.020)	0.488
Aldosterone receptor antagonist at discharge	0.773 (0.415–1.441)	0.418	0.732 (0.243–2.202)	0.578
Mortality or readmission at 60 days, n=71 (4.6%)				
ACEI or ARB at discharge	0.520 (0.322–0.840)	0.008	0.297 (0.125–0.707)	0.006
β-blocker at discharge	0.822 (0.502–1.348)	0.437	0.546 (0.213–1.399)	0.207
Aldosterone receptor antagonist at discharge	0.788 (0.474–1.310)	0.359	0.850 (0.343–2.107)	0.726
Mortality at 1 year, n=141 (9.2%)				
ACEI or ARB at discharge	0.631 (0.442–0.900)	0.011	0.575 (0.280–1.182)	0.575
β-blocker at discharge	0.647 (0.445–0.940)	0.022	0.337 (0.147–0.774)	0.010
Aldosterone receptor antagonist at discharge	1.062 (0.742–1.519)	0.742	1.050 (0.516–2.137)	0.893
Readmission at 1 year, n=150 (9.8%)				
ACEI or ARB at discharge	0.738 (0.521–1.046)	0.088	0.635 (0.342–1.177)	0.149
β-blocker at discharge	0.851 (0.601–1.206)	0.365	0.815 (0.443–1.498)	0.510
Aldosterone receptor antagonist at discharge	0.899 (0.632–1.279)	0.899	1.053 (0.572–1.938)	0.869
Mortality or readmission at 1 year, n=216 (14.1%)				
ACEI or ARB at discharge	0.739 (0.547–0.997)	0.047	0.616 (0.354–1.073)	0.087
β-blocker at discharge	0.812 (0.602–1.097)	0.175	0.659 (0.379–1.144)	0.138
Aldosterone receptor antagonist at discharge	0.946 (0.701–1.277)	0.718	0.972 (0.562–1.682)	0.920

*Adjusted for age, sex, history of HF, acute myocardial infarction, hypertension, diabetes mellitus, peripheral vascular disease, prior cerebral infarction and chronic pulmonary disease, atrial arrhythmia, SBP and DBP, serum creatinine and Hb levels, weight and NYHA functional classification.
HR, hazard ratio; CI, confidence interval. Other abbreviations see in Table 1.

95%CI, 0.265–0.850) and combined mortality/readmission (OR, 0.520; 95%CI, 0.322–0.840) at 60 days and to mortality (OR, 0.631; 95%CI, 0.442–0.900) at 1 year. However, use of a β-blocker at discharge was significantly associated with mortality only (OR, 0.647; 95%CI, 0.445–0.940) at 1 year. After adjustment for risk factors (age, sex, history of previous HF, acute MI, HT, diabetes mellitus, peripheral vascular disease, prior cerebral infarction and chronic pulmonary disease, atrial arrhythmia, systolic and diastolic blood pressures, serum creatinine and hemoglobin levels, body weight and NYHA functional classification), ACEI or ARB at discharge was the only performance measure was significantly associated with mortality (OR, 0.344; 95%CI, 0.123–0.964), readmission (OR, 0.180; 95%CI, 0.062–0.522) and mortality/readmission (OR, 0.297; 95%CI, 0.125–0.707) at 60 days, and at 1 year β-blocker was the only measure significantly associated with mortality (OR, 0.337; 95%CI, 0.147–0.774).

Discussion

We evaluated the overall adherence to modified and identified HF performance measures as well as the relationship between these measures and early and long-term outcomes of hospitalized systolic HF patients in Korea. We found that adherence to performance measures in "real-world practice" was relatively low and variable. We also found that the use of ACEI or ARB at discharge and use of β-blocker at discharge were associated with early outcome and with long-term mortality, respectively. These findings are in accordance with data from Western studies and provide important implications for improvements in patients' quality of life.

Recent large-scale registry databases have been conducted mainly in the USA and Europe. Very limited information is available on the characteristics and outcomes of hospitalized HF patients in Korea.[3,4,12–16] When comparing the KorHF Registry with the Acute Decompensated Heart Failure National Registry (ADHERE),[12] Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF),[15] EuroHeart Failure Survey (EHFS)[14] or the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD),[17] many similarities are observed in the patients' clinical characteristics (**Table 4**). However, there are several important differences among them. In particular, compared with Western cohorts, the patients in the present study were more often female and less frequently had a history of coronary artery disease and HT. With respect to medication at hospital discharge, adherence to using an ACEI or ARB and β-blocker in the present study was lower, but adherence to using an aldosterone antagonist was higher when compared with other Western studies. In comparison with JCARE-CARD conducted in Japan, the demographic characteristics were similar to our results except that there were more females in the KorHF Registry. Also, discharge medications were similar but adherence to using ACEI or ARB was higher in the Japanese study. With respect to prognosis, mortality after survivor discharge was similar among the different studies but the KorHF population had a relatively lower rate of readmission after discharge. From recent large-scale registry data-

Table 4. Comparison of Characteristics Among Recent Large-Scale HF Registries in Patients With Systolic HF

	OPTIMIZE-HF[15] (n=20,118)	ADHERE[12] (n=25,865)	EHFS[14] (n=3,658)	JCARE-CARD[17] (n=947)	KorHF (n=1,527)
Baseline characteristics					
Age, years	70.4	69.8	67	66.6	69.1
Male sex, %	62	60	71	72.2	55.9
BMI, kg/m^2	NA	NA	NA	22.7	23.2
Mean LVEF, %	24.3	NA	33	27.0	28.7
Comorbid conditions					
Coronary artery disease, %	54	59	69	39.8	40.1
Hypertension, %	66	69	50	50.4	42.0
Diabetes, %	39	40	28	33.3	31.4
Chronic renal failure, %	NA	26	6	10.4	7.3
Atrial fibrillation, %	28	17	23	24.5	20.8
Medication at discharge					
ACEI or ARB, %	NA	71.3	82	83.5	68.0
ACEI, %	62	61.5	78	44.2	45.6
ARB, %	11	11.0	6	45.9	24.5
β-blocker, %	73	62.6	46	65.9	40.9
Aldosterone antagonist, %	18	24.7	29	45.9	37.5
Outcomes after survivor discharge					
Follow-up duration	60–90 days	NA	12 weeks	1 year	1 year
All-cause mortality, %	9.8	NA	12	8.9	9.2
Rehospitalization, %	29.9	NA	21	23.7	9.8

NA, not available. Other abbreviations see in Table 1.

bases, the risk of mortality and readmission across studies was variable because of the heterogeneity of the demographic factors of the population and the status of healthcare frameworks.[18] In the ADHERE Registry, there was significant individual variability in conformity to quality-of-care indicators and outcomes between academic and non-academic hospitals.[19] In Korea, the National Health Insurance Program as an insured employee or self-employed individual covers all Korean people who are residing in the territory of the Republic of Korea and family support for the elderly is relatively strong because of the Confucian culture. In addition, all participating centers in this study were university hospitals across the country. It is possible that the rate of readmission was relatively low in this study because patients had easy accessibility to medical service and most of them had been treated before they were admitted to a tertiary medical center. Therefore, it is possible that there would be under detection of the actual rate of readmission. However, it is not clear if this difference is true or a survey bias among large-scale registries (although there is are differences in the demographic factors, adherence and outcomes from recent large-scale HF registries). A precise and coordinated study using an identical protocol and the same clinical criteria worldwide (including Western and oriental populations) is required.

The current version of the ACC/AHA Clinical Performance Measures for Adults with Chronic Heart Failure includes the following HF inpatient performance measures: (1) discharge instructions including activity level, diet, discharge medications, follow-up appointment, weight monitoring, and what to do if symptoms worsen, (2) evaluation of LV systolic function, (3) ACEI or ARB for LVSD, (4) adult smoking cessation advice/counseling, and (5) anticoagulant at discharge for HF patients with AF.[6] Although it is expected that application of these measures would result in substantial improvement in outcomes for HF patients, guideline recommendations for these measures are based on expert opinion. In the present study, we did not evaluate smoking cessation counseling, discharge instructions and anticoagulant use at discharge for AF.

Based on quality assessment of healthcare, the role of behavioral measures, including patient counseling and education, is important.[18] However, the role of smoking cessation and discharge instructions is unclear. Two studies found no difference in mortality, or combined mortality/readmission rates for the smoking cessation counseling performance measure alone.[3,20] Although 2 studies of discharge instructions were intensive or systematized and showed a reduction in readmission or combined mortality/readmission,[21,22] there was no difference in post-discharge mortality rates for the discharge instructions measure.[3,21,22]

Although anticoagulant use at discharge for AF is a performance measure that would be expected to reduce mortality by preventing cerebral infarction, this measure also showed conflicting results in three studies.[3,23]

Randomized controlled trials showed that ACEI can reduce the risk of death and the combined risk of death or hospitalization.[24–26] Although experience with ARB in controlled clinical trials of patients with HF is considerable less than that with ACEI, ARB also has demonstrated benefit by reducing hospitalization and mortality for patients unable to tolerate ACEI because of cough and angioedema.[27,28] In our prospective registry, ACEI or ARB use at discharge showed a significant reduction in mortality, readmission and mortality/readmission at 60 days, and a trend for reducing mortality/readmission at 1 year. The results of the present study are similar to those of the OPTIME-HF study, in which ACEI or ARB use at discharge was associated with a lower combined risk of rehospitalization and mortality post-discharge in the 60–90-day follow-up period (OR 0.51, 95%CI 0.34–0.78, P=0.002).[3]

Although β-blocker use at discharge is not currently an ACC/AHA standardized HF performance measure, it is strongly associated with a reduced risk of mortality and combined mortality/readmission rate.[3] The abundant accumulated evidence of β-blocker use at discharge in improving outcomes from effectiveness studies makes this a strong candidate for consideration as an additional HF performance indicator.[3,29] In placebo-controlled clinical trials, 3 β-blockers have been shown to be effective in reducing the risk of death in patients with chronic HF: bisoprolol, sustained-release metoprolol (succinate), and carvedilol.[30–33] Similar to an ACEI or ARB, β-blocker can reduce the risk of death and the combined risk of death or hospitalization.[30,32,34–36] In our prospective registry, β-blocker use at discharge showed a significant reduction in mortality at 1 year, similar to JCARE-CARD.[37] Although doses of 50–100 mg of carvedilol are recommended in the USA based on the results of large clinical trials, even a small dose of carvedilol (2.5 mg/day) exhibited a beneficial effect on long-term outcomes in Japanese patients with mild-to-moderate HF and reduced LV systolic function in the Multicenter Carvedilol Heart Failure Dose Assessment (MUCHA) trial.[38] Japanese subjects are believed to be more sensitive to β-blockers and tend to use lower doses. In addition, investigators in the Japanese Chronic Heart Failure (J-CHF) study recommended that higher doses of carvedilol are not associated with additional clinical benefit but do cause side effects.[39] The sensitivity of the β-adrenergic receptor may be different in different races.[40]

Evidence of a relationship between evidence-based performance measures and outcomes is unclear because of the heterogeneity of study designs, study populations and the performance measures. Also, ethnic or racial differences are a concern because ethnic and racial differences in etiology, outcome, and response to therapy in HF have been demonstrated. Although we did not present the dose-response relationship of β-blockers, we demonstrated that the use of β-blockers before hospital discharge was important in reducing mortality in Korean patients with systolic HF, just as in the JCARE and OPTIMIZE-HF trials.[3,17] We believed that the genetic and environmental backgrounds were similar to the Japanese population but further study is needed to confirm the effective and safe dose of drugs for HF patients in Korean or Oriental populations.

The Randomized Aldactone Evaluation Study (RALES) demonstrated that spironolactone reduces the risk of mortality and morbidity in patients with systolic HF.[11] Current guidelines recommend the use of an aldosterone receptor antagonist in HF patients with LVSD who are symptomatic under the use of ACEI or ARB and diuretics.[1,2] However, the patients in the RALES trial were clearly different from those in the current study, and the relationship between an aldosterone antagonist and outcome would be different. Despite the heterogeneity of the study population and clinical severity, this evidence has been strengthened in the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) trial, which demonstrated that eplerenone, as compared with placebo, reduced the risk of death and the risk of hospitalization among patients with systolic HF after acute MI and mild symptoms.[41] However, an aldosterone antagonist is not currently an ACC/AHA standardized HF performance measure, and has not shown a statistical reduction in mortality or readmission in several recent large-scale registry databases. Therefore, this discrepancy between the randomized controlled trials and cohort registries should be evaluated.

Study Limitations

First, this was a hospital-based observational study and therefore might not be entirely representative of national care patterns and outcomes. Second, we undertook a multivariate analysis but other unmeasured variables might have influenced the outcomes in the post-discharge period. Third, the outcomes assessed to date were restricted to hospital readmissions and mortality. Other important outcomes such as health-related quality of life, patient satisfaction, and functional capacity should also be considered as supplemental metrics because it is relatively unknown if HF performance measures have any impact on these important outcomes, and the literature in this area is emerging. Fourth, we did not assess exposure to medications after hospital discharge. Patients discharged without medication may have started treatment and those discharged with medication may have discontinued or not fully adhered to therapy after discharge. Finally, we did not assess non-pharmacological management. Fluid and alcohol intake, immunization, pregnancy, sleep disorders, and depression should be considered because these factors are associated with the prognosis. Because of the aforementioned limitations, the association found between the HF performance measures and outcomes and its causality should be interpreted with caution.

Conclusions

Adherence to modified performance measures was variable in the KorHF Registry. ACEI/ARB and β-blocker use at discharge was associated with improving the outcomes of patients with LVSD in Korea.

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Disclosure

No conflicts of interest.

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Appendix

The KorHF Registry was conducted from 24 medical centers: Catholic University Seoul St. Mary's Hospital, Chungnam National University Hospital, Chungbuk National University Hospital, Chonnam National University Hospital, Ewha Womans University Hospital, Eulji University Daejeon Hospital, Gacheon University Gil Hospital, Hallym University Sacred Heart Hosptial, Hanyang University Guri Hospital, Jeju National University Hospital, Konkuk University Medical Center, Keimyung University Hosptial, Korea University Guro Hospital, Kyungpook National University Hospital, Sungkyunkwan University Samsung Medical Center, Seoul National University Bundang Hospital, Seoul National University Hosptial, Ulsan University Asan Medical Center, Wonkwang University Hosptial, Yonsei University Wonju Christian Hospital, Yeungnam University Hospital, Yonsei University Severance Hospital, Dongguk University Ilsan Hosptial, Soonchunhyang University Cheonan Hospital, Inje University Busan Paik Hospital.