ORIGINAL RESEARCH

Clinical Significance of Get With the Guidelines–Heart Failure Risk Score in Patients With Chronic Heart Failure After Hospitalization

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***Background*—**The Get With the Guidelines–Heart Failure (GWTG-HF) risk score was developed using American Heart Association GWTG-HF program data and predicts in-hospital mortality in patients with acute heart failure (HF). We aimed to clarify the prognostic impacts of the GWTG-HF risk score in patients with HF after discharge.

***Methods and Results*—**We examined the GWTG-HF score in 1452 patients with HF, who were admitted to our hospital and discharged after treatment, by calculating 7 predetermined variables. We divided all subjects into 3 groups according to the GWTG-HF risk score (low, moderate, and high score groups). The plasma B-type natriuretic peptide level significantly increased with increasing GWTG-HF risk score severity (median values of B-type natriuretic peptide: 167.0 in low, 260.7 in moderate, and 418.2 pg/mL in high score groups). We followed up all subjects after discharge, and there were 347 (23.9%) all-cause deaths and 407 (28.0%) cardiac events in follow-up periods. A Kaplan-Meier survival curve demonstrated that event rates of all-cause death and cardiovascular events, including worsening HF and cardiac death, significantly increased with increasing GWTG-HF risk score severity in all subjects, and also in 749 patients with HF with preserved ejection fraction (ejection fraction ≥50%) and 703 patients with HF with reduced ejection fraction (ejection fraction <50%) patients. The multivariable Cox proportional hazard regression analysis demonstrated that the GWTG-HF risk score was one of the significant predictors of all-cause mortality and cardiac events (all-cause mortality: hazard ratio, 1.537, 95% confidence interval, 1.172–2.023; cardiac events: hazard ratio, 1.584, 95% confidence interval, 1.344–1.860, per 10-point increase of GWTG-HF score).

***Conclusions*—**The GWTG-HF risk score is a useful multivariable score model for several years after hospitalization in patients with HF in a Japanese population. **(*J Am Heart Assoc*. 2018;7:e008316. DOI: 10.1161/JAHA.117.008316.)**

Key Words: GWTG-HF risk score • heart failure • heart failure with preserved ejection fraction • long-term follow-up • prognosis

Heart failure (HF) is a common disease with high morbidity and mortality, and an increasing prevalence and burden on healthcare systems.[1,2] The number of patients with HF is predicted to increase gradually along with the increasingly aging population.[3] In order to manage patients with HF properly, including frequency of outpatient examination, doses of optimal medications, and indications for cardiac resynchronization therapy or ventricular assist device, risk classification is a high priority. Previously, several parameters for differentiating high- and low-risk patients with HF have been reported, including age, blood pressure, heart rate, renal function, plasma B-type natriuretic peptide (BNP) level, inflammatory markers, cytokines, echocardiographic parameters, respiratory function, and anemia or presence of sleep-disordered breathing.[4–8] Because each parameter represents only a certain aspect of HF, a comprehensive risk evaluation might be important.

Recently, several risk stratification scores using various parameters have been reported for the prediction of all-cause mortality, sudden cardiac death, and cardiovascular events in patients with HF.[9–16] For example, the AHEAD (atrial fibrillation, hemoglobin, elderly, abnormal renal parameters, diabetes mellitus) score was established for long-term risk prediction in acute HF.[15] In 2010, Peterson et al established the GWTG-HF (Get With the Guidelines–Heart Failure) risk score to predict in-hospital mortality based on a cohort of 39 783 patients in 198 hospitals.[17] Multivariable logistic

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Clinical Perspective

What Is New?

- The Get With the Guidelines–Heart Failure risk score is a useful multivariable score model for several years after hospitalization in Japanese patients with heart failure, including heart failure with reduced ejection fraction and heart failure with preserved ejection fraction.

What Are the Clinical Implications?

- Although the Get With the Guidelines–Heart Failure risk score is created from the cohort for risk classification of in-hospital mortality, this score provides prognostic prediction in not only the acute phase during hospitalization but also the chronic phase after discharge.

regression identified the following 7 predictors from the derivation samples; age, systolic blood pressure, blood urea nitrogen, heart rate, sodium, chronic obstructive pulmonary disease, and race.[17] The GWTG-HF score predicted the risk of in-hospital mortality in patients with acute HF with preserved and reduced left ventricular ejection fraction (LVEF).[17,18] However, the clinical impact of this GWTG-HF risk score on prognosis in patients with chronic HF has not been evaluated. Moreover, it is recognized that there are 2 types of HF based on LVEF, HF with preserved EF (HFpEF) and HF with reduced EF (HFrEF), and these 2 types of HF have a similarly poor prognosis.[19,20] Chen et al reported that the AHEAD score was useful in predicting long-term mortality in an Asian cohort with HFpEF and HFrEF.[16]

Therefore, the purpose of this study was to evaluate the GWTG-HF risk scoring system for prognostic prediction in patients with HF after discharge, taking into consideration the differences between HFpEF and HFrEF. Moreover, we hypothesized that new modified GWTG-HF risk score model, derived from the results in the present study, provides helpful information. We compared the GWTG-HF risk score with the AHEAD score for prognostic prediction.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Subjects and Protocol

This was a prospective observational study. A total of 1680 consecutive patients with symptomatic HF, hospitalized with decompensated HF and discharged from Fukushima Medical University Hospital between March 2010 and April 2015, were enrolled. Symptomatic HF diagnosis was determined by well-trained cardiologists using the American College of Cardiology Foundation and American Heart Association Guidelines.[2] All patients with HF were diagnosed on first admission by attending cardiologists. We investigated the patients' backgrounds, including age, sex, vital signs, New York Heart Association (NYHA) functional class, comorbidities, laboratory data, and echocardiographic data at hospital discharge. The patient flowchart is shown in Figure 1. Of all 1680 patients, those patients who were lacking any components of GWTG-HF (n=182), received dialysis (n=17), had acute coronary syndrome (n=19), and/or had advanced cancer (n=10) were excluded, leading to a total of 1452 patients who were finally enrolled (mean age 64.5 years, and 880 men). We were able to follow up all patients for cardiac events and/or all-cause mortality until December 2016 (9–2611, mean 965.8 days). A cardiac event was adjudicated as cardiac death and/or worsening HF, which was defined as hospitalization because of decompensated HF. Cardiac death was adjudicated by independent experienced cardiologists and included death caused by worsened HF attributable to ventricular fibrillation documented by ECG or implantable devices, and acute coronary syndrome. Survival time was calculated from the date of discharge until the date of death or last follow-up. Actual event time of worsening HF was the hospitalization date for treatment of HF. The status and/or dates of death were obtained from the patients' medical records or attending physicians at the patient's referring hospital. If these data were unavailable, the patients were contacted by telephone and interviewed by trained researchers the same as in our previous report.[21] We could follow up all the patients. Written informed consent was obtained from all study subjects. The study protocol was approved by the Ethics Committee of Fukushima Medical University and was carried out in accordance with the principles outlined in the Declaration of Helsinki. Reporting of the study conforms to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) along with references to STROBE and the broader EQUATOR (Enhancing the Quality and Transparency of Health Research) guidelines.[22]

Plasma BNP concentrations were measured using a commercially available radioimmunoassay specific to human BNP (Shionoria BNP kit; Shionogi, Osaka, Japan). Echocardiography was blindly performed by experienced echocardiographers using standard techniques. Two-dimensional echocardiographic images were acquired from the parasternal long and short axes, apical long axis, and apical 4-chamber views. The following echocardiographic parameters were investigated: interventricular septum thickness; left ventricular end-diastolic diameter (LVEDD); left ventricular end-diastolic volume (LVEDV); LVEF; tricuspid valve regurgitation pressure gradient; inferior vena cava diameter; and right ventricular fractional area change.[2] LVEF was calculated using

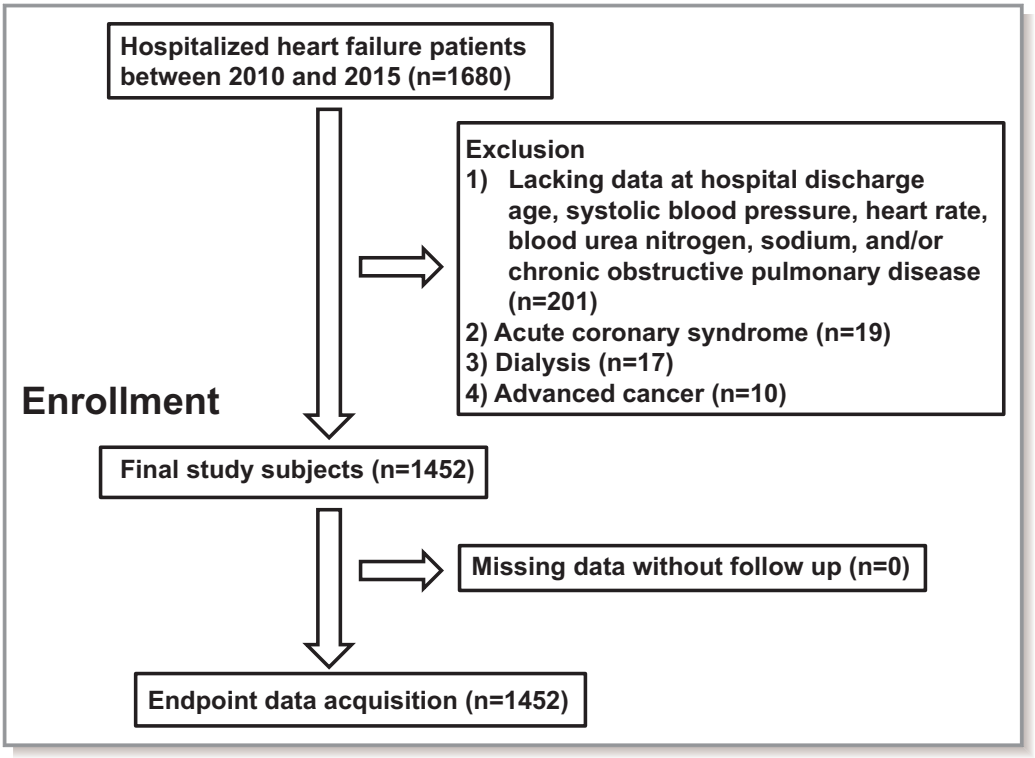

Figure 1. Patient flowchart of this study.

a modified Simpson's method, and we defined HFpEF as heart failure with LVEF of 50% or higher.

Estimation of GWTG-HF Risk Score

The GWTG-HF risk score was calculated using the 7 variables as previously reported.[17,18] A risk score was established using the following 7 predictor variables: age, systolic blood pressure, heart rate, blood urea nitrogen, sodium, chronic obstructive pulmonary disease, and race.[17] A patient's score is obtained by summing points assigned to the value of each predictor. The values of the score are between 0 and 100. We divided the subjects into 3 groups (low, moderate, high) based on the GWTG-HF risk score. Each group included 484 patients.

Statistical Analysis

Results are expressed as mean±standard deviation in normally distributed data, and skewed variables are presented as median (interquartile range). Categorical variables are expressed as numbers and percentages, and *P* values of <0.05 were considered statistically significant. If data were not distributed normally, the Mann-Whitney *U* test was used for comparisons. To compare the 3 groups, we used 1-way ANOVA followed by Tukey's post hoc test. Kaplan-Meier survival curves determined the time-dependent cumulative cardiac event-free rates in patients stratified among 3 groups and were analyzed by a log-rank test. The Cox proportional hazard regression analysis was used to determine which variables were related significantly to all-cause mortality and cardiac event rate. Parameters with statistical significance in the univariable analysis ($P<0.05$) were included in the multivariable analysis. From this Cox-proportional hazard regression analysis, we established the new model, which is adding NYHA functional class, the presence of anemia, LVEF, and the plasma level of BNP to the GWTG-HF risk score in the present study (modified model). Discrimination power was quantified using comparison of concordance statistics (C-statistics) designed by the area under the receiver operating characteristics curve for each model with all-cause deaths and cardiac events. Statistical analyses were performed using a standard statistical program package (SPSS ver. 24.0; IBM, Armonk, NY, USA). We used Schonlau's cross-validation program by Stata (StataCorp LP, Lakeway, TX, USA) and compared R^2.[23]

Results

Basic Clinical Characteristics of HF Patients on the Basis of GWTG-HF Risk Score

We divided all HF patients into 3 groups on the basis of the GWTG-HF risk score: low (16–35, n=484), moderate (36–41,

Table 1. Comparisons of Clinical Characteristics Among 3 GWTG-HF Score Groups at Hospital Discharge

	Low (N=484)	Moderate (N=484)	High (N=484)	*P* Value
GWTG-HF risk score	16–35	36–41	42–67	
Age, y	58.6±15.8	68.0±12.3†	74.0±9.9†§	<0.001
Sex (male/female)	318/166	285/199	277/207	0.017
NYHA III and IV, n (%)	177 (36.6)	163 (33.7)	206 (42.6)	<0.001
Systolic BP, mm Hg	149.9±33.2	126.4±23.4†	108.5±21.0†§	<0.001
Diastolic BP, mm Hg	84.2±23.8	71.8±17.1†	63.6±14.6†§	<0.001
Heart rate, beats/min	78.6±23.8	79.3±23.0	85.0±27.0†§	<0.001
Hypertension, n (%)	371 (76.7)	354 (73.1)	350 (72.3)	0.263
Diabetes mellitus, n (%)	177 (36.5)	192 (39.7)	213 (44.0)	0.060
Dyslipidemia, n (%)	381 (78.7)	378 (78.1)	368 (76.0)	0.576
Anemia, n (%)	191 (39.5)	262 (54.1)	327 (67.6)	<0.001
Atrial fibrillation, n (%)	130 (26.9)	190 (39.3)	218 (45.0)	<0.001
CKD, n (%)	195 (40.3)	258 (53.3)	349 (72.1)	<0.001
IHD, n (%)	134 (27.7)	134 (27.7)	130 (26.9)	0.946
HFpEF/HFrEF	281/203	255/229	213/271	<0.001
Blood sample data				
WBC, cells/μL	7420±3115	7150±3241	7110±3121	0.244
Hemoglobin, g/dL	13.4±2.3	12.5±2.2†	11.7±2.3†§	<0.001
Creatinine, mg/dL	1.08±1.06	1.29±1.31*	1.61±1.57†§	<0.001
Albumin, g/dL	3.86±0.60	3.76±0.57*	3.51±0.65†§	<0.001
HbA_{1c}, %	5.87±1.05	5.89±0.88	5.96±0.96	0.513
LDL cholesterol, mg/dL	110.2±37.1	101.7±34.4†	98.5±32.9†	<0.001
Triglyceride, mg/dL	135.8±100.2	116.3±67.5†	105.0±64.3†	<0.001
Troponin I, mg/dL	0.040 (0.132)	0.040 (0.175)	0.047 (0.204)	0.631
BNP, pg/mL¶	167.0 (370.5)	260.7 (483.7)	418.2 (672.5)†§	<0.001
hs-CRP, mg/dL¶	0.13 (0.43)	0.20 (0.70)	0.33 (1.76)†	<0.001
Echocardiographic data				
IVST, mm	11.3±3.1	10.9±2.8	10.8±2.8	0.054
LVEDD, mm	51.3±11.1	51.9±10.9	51.5±11.1	0.784
LVEDV, mL	110.7±56.3	111.8±62.3	105.9±56.9	0.318
LVEF, %	52.2±15.8	51.1±15.2	48.1±16.7†‡	0.001
TR-PG, mm Hg	30.3±17.1	31.1±18.3	28.9±12.8	0.234
IVC, mm	14.8±4.5	15.1±5.1	14.7±4.8	0.352
RV-FAC, %	40.7±11.6	40.3±13.4	41.1±11.4	0.775
Mean follow-up days	1113.49±743.4	953.2±663.0†	830.8±680.0†§	<0.001

BNP indicates B-type natriuretic peptide; BP, blood pressure; CKD, chronic kidney disease; GWTG-HF, Get With the Guidelines–Heart Failure; HbA_{1c}, hemoglobin A_{1c}; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; hs-CRP, high-sensitivity C-reactive protein; IHD, ischemic heart disease; IVC, inferior vena cava; IVST, interventricular septum thickness; LDL, low-density lipoprotein; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association classification; RV-FAC, right ventricular fractional area change; TR-PG, tricuspid regurgitation pressure gradient; WBC, white blood cells.
*$P<.05$, †$P<0.01$ vs low group.
‡$P<0.05$, §$P<0.01$ vs moderate group.
¶Skewed data are reported as median (interquartile range).

n=484), and high (42–67, n=484) groups. The comparison of baseline clinical characteristics among the 3 groups is shown in Table 1. Age, heart rate, prevalence of NYHA functional class III and IV, anemia, atrial fibrillation, and chronic kidney disease increased with increasing GWTG-HF score; systolic and diastolic blood pressures decreased with increasing

GWTG-HF score (P<0.001). The proportion of female sex was proportional to GWTG-HF risk score severity (P=0.017). Blood sample data demonstrated that hemoglobin, serum albumin, low-density lipoprotein cholesterol, and triglyceride levels were lower, and that creatinine, plasma BNP, and high-sensitivity C-reactive protein levels were higher with increasing GWTG-HF risk score (P<0.001). In echocardiographic data, there were no significant differences in left ventricular end-diastolic diameter and left ventricular end-diastolic volume among the 3 groups. Moreover, LVEF was decreasing (P<0.001); therefore, the ratio of HFrEF patients was higher with increasing GWTG-HF risk score.

Prognostic Analysis of Chronic HF Patients Based on the GWTG-HF Risk Score

There were 347 all-cause deaths and 407 cardiac events, including worsening HF and cardiac death, during the follow-up period. Cumulative event-free survival curves were illustrated with the Kaplan-Meier method and compared by a log-rank test (Figure 2). The event rates of all-cause deaths (60 in the low group, 112 in the moderate group, and 175 in the severe group; Figure 2A) and cardiac events, including worsening HF and cardiac deaths (85 in the low group, 137 in the moderate group, and 185 in the severe group; Figure 2B), significantly increased with increasing GWTG-HF risk score severity in all subjects (log-rank, P<0.001, respectively).

The univariable and multivariable Cox proportional hazard regression analyses for predicting all-cause mortality are shown in Table 2. We selected the variables that are well-known adverse prognostic factors for HF but were not included in the GWTG-HF risk score measurement. NYHA functional class, the presence of anemia and atrial fibrillation, LVEF, plasma levels of BNP, creatinine, high-sensitivity C-reactive protein, and GWTG-HF risk score (GWTG-HF score per 10-point increase: hazard ratio [HR], 1.916; 95% confidence interval [CI], 1.676–2.179; P<0.001) were significantly associated with all-cause mortality. Those significant variables were entered into the multivariable Cox proportional hazard regression analysis (Table 2). According to this analysis, the GWTG-HF risk score was one of the independent predictors of all-cause mortality, similar to NYHA functional class, the presence of anemia, LVEF, and plasma BNP level, as shown in Table 2 (GWTG-HF score per 10-point increase: HR, 1.537; 95% CI, 1.172–2.032; P=0.002). Similarly, Table 3 demonstrates that the GWTG-HF risk score was one of the independent predictors for cardiac events (GWTG-HF score per 10-point increase: HR, 1.584; 95% CI, 1.344–1.860; P<0.001).

Next, we evaluated this GWTG-HF risk score with adding NYHA functional class, the presence of anemia, LVEF, and plasma BNP level (modified model). The C-statistics of the existing GWTG-HF risk score for all-cause death and cardiac event were 0.687 (95% CI, 0.649–0.725) and 0.663 (95% CI, 0.626–0.700). The C-statistics of the modified model for all-cause death and cardiac event were significantly improved to 0.772 (95% CI, 0.739–0.805; P<0.001) and 0.750 (95% CI, 0.718–0.781; P<0.001), respectively (Figure 3). Of note, we performed a 5-fold cross validation within our data set and confirmed that R^2 of our modified model was higher than for the original GWTG-HF scoring, indicating that the improvement of the modified model was not merely due to the fact that the modified score was derived and validated in the same

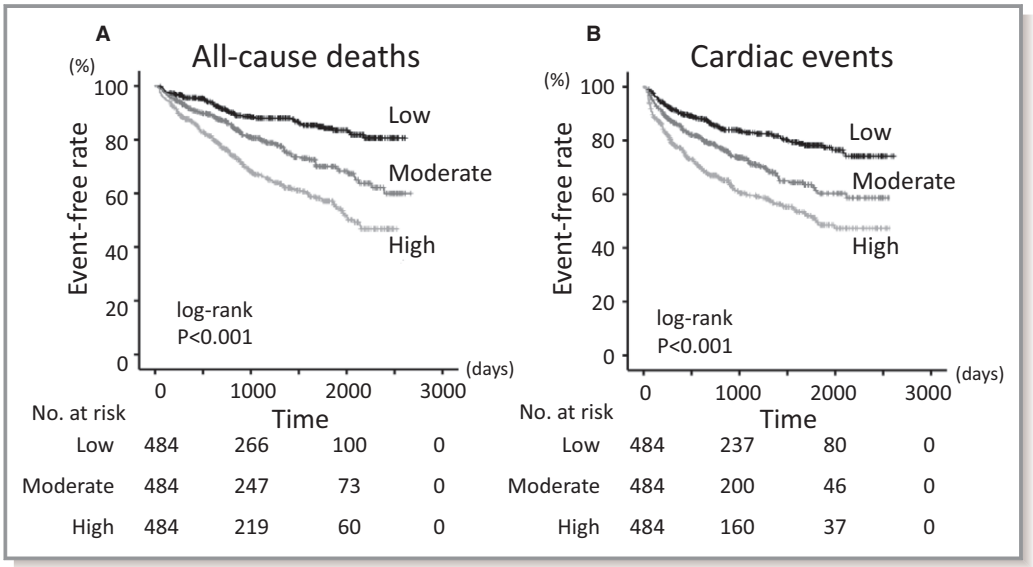

Figure 2. Kaplan-Meier analyses for all-cause deaths (A) and cardiovascular events, including worsening heart failure and cardiac deaths (B), among the 3 GWTG-HF risk score groups. Numbers at risk of respective groups were described at the bottom of figures.

Table 2. Results of Univariable and Multivariable Cox Proportional Hazard Analyses for All-Cause Mortality

	Univariable Analysis			Multivariable Analysis		
Variables	HR	95% CI	*P* Value	HR	95% CI	*P* Value
NYHA, per I grade increase	4.363	3.157–6.029	<0.001	2.906	1.830–4.615	<0.001
Presence of						
Anemia	0.335	0.261–0.430	<0.001	0.486	0.305–0.773	0.002
Atrial fibrillation	0.767	0.621–0.949	0.014	1.216	0.806–1.835	0.352
Echocardiography						
LVEF, per 1 SD (15.9%) increase	0.813	0.714–0.909	0.001	0.705	0.577–0.852	0.001
BNP, per 1 SD (851.4 pg/mL) increase	1.332	1.261–1.409	<0.001	1.163	1.028–1.315	0.017
Creatinine, per 1 SD (1.43 mg/dL) increase	1.194	1.115–1.278	<0.001	1.111	0.973–1.270	0.120
hs-CRP, per 1 SD (3.36 mg/dL) increase	1.110	1.017–1.212	0.019	0.898	0.702–1.148	0.393
GWTG-HF score, per 10-point increase	1.916	1.676–2.179	<0.001	1.537	1.172–2.023	0.002

BNP indicates B-type natriuretic peptide; CI, confidence interval; GWTG-HF, Get With the Guidelines–Heart Failure; HR, hazard ratio; hs-CRP, high-sensitivity C-reactive protein; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association classification; SD, standard deviation.

data set. Also, another multiple score model, the existing AHEAD score, was calculated in this study. Univariable Cox proportional hazard regression analyses of the AHEAD score were statistically significant (all-cause mortality: HR, 1.594; 95% CI, 1.465–1.735, $P<0.001$; cardiac events: HR, 1.484; 95% CI, 1.374–1.604; $P<0.001$). The C-statistics of the AHEAD score for all-cause death and cardiac event were 0.669 (95% CI, 0.665–0.728) and 0.658 (95% CI, 0.627–0.689). The predictive values of the AHEAD score for both events did not significantly differ compared to GWTG-HF score.

We then analyzed the HFpEF (n=749) and HFrEF (n=703) patients separately. All-cause deaths and cardiac events occurred in 141 and 206 patients with HFpEF, and 168 and 239 patients with HFrEF, respectively. Kaplan-Meier survival curves demonstrated that event rates were significantly higher with increasing GWTG-HF risk score severity in both the patients with HFpEF and the patients with HFrEF (log-rank, $P<0.001$; Figures 4 and 5, respectively). We did similar Cox proportional hazard regression analysis as above. GWTG-HF risk score was one of the independent predictors of all-cause mortality and cardiac events in both HFpEF (GWTG-HF score per 10-point increase for all-cause mortality: HR, 1.568; 95% CI, 1.207–2.023; $P=0.001$; cardiac events: HR, 1.859; 95% CI, 1.466–2.346; $P<0.001$) and HFrEF groups (GWTG-HF score per 10-point increase for all-cause mortality: HR, 1.600; 95% CI, 1.305–1.949; $P<0.001$; cardiac events: HR, 1.297; 95% CI, 1.072–1.553; $P=0.008$), respectively. C-statistics for all-cause mortality and cardiac events were 0.643 and 0.646 in patients with HFpEF, and 0.675 and 0.603 in patients with HFrEF, respectively.

Table 3. Results of Univariable and Multivariable Cox Proportional Hazard Analyses for Cardiac Events

	Univariable Analysis			Multivariable Analysis		
Variables	HR	95% CI	*P* Value	HR	95% CI	*P* Value
NYHA, per I grade increase	3.221	2.602–3.988	<0.001	2.221	1.680–2.934	<0.001
Presence of						
Anemia	0.418	0.337–0.518	<0.001	0.475	0.362–0.623	<0.001
Atrial fibrillation	0.697	0.573–0.848	<0.001	0.840	0.662–1.067	0.153
Echocardiography						
LVEF, per 1 SD (15.9%) increase	0.787	0.702–0.866	<0.001	0.800	0.714–0.909	<0.001
BNP, per 1 SD (851.4 pg/mL) increase	1.240	1.165–1.320	<0.001	1.106	1.004–1.217	0.040
Creatinine, per 1 SD (1.43 mg/dL) increase	1.129	1.053–1.212	0.001	0.982	0.886–1.088	0.729
hs-CRP, per 1 SD (3.36 mg/dL) increase	1.007	0.912–1.115	0.870		. . .	. . .
GWTG-HF score, per 10-point increase	1.733	1.523–1.949	<0.001	1.584	1.344–1.860	<0.001

BNP indicates B-type natriuretic peptide; CI, confidence interval; GWTG-HF, Get With the Guidelines–Heart Failure; HR, hazard ratio; hs-CRP, high-sensitivity C-reactive protein; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association classification; SD, standard deviation.

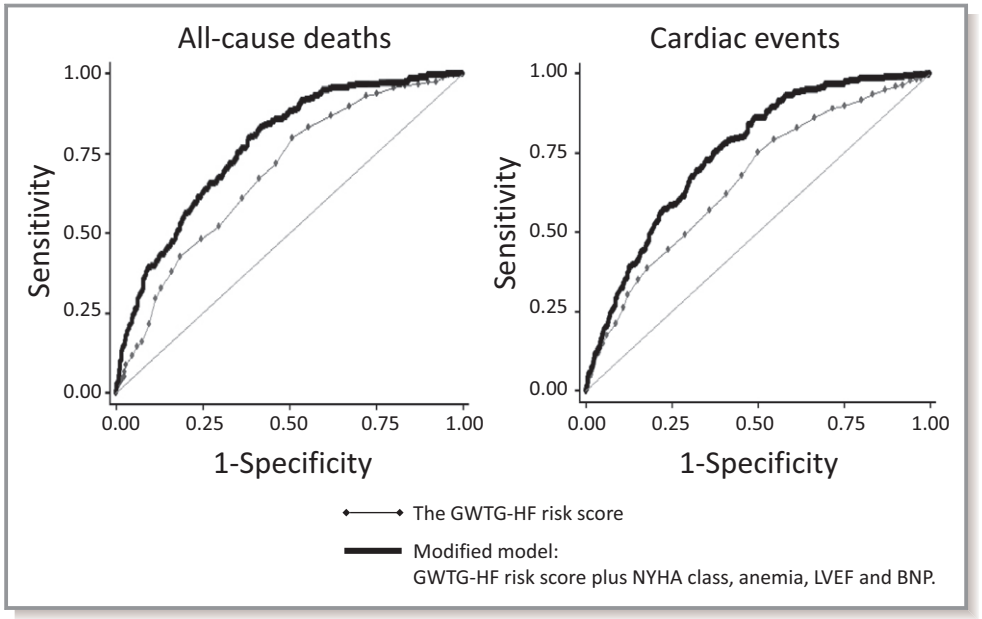

Figure 3. Area under the curves of receiver operating characteristics in the GWTG-HF risk score and modified model (the GWTG-HF risk score adding NYHA functional class, the presence of anemia, left ventricular ejection fraction, and plasma BNP level) for all-cause deaths and cardiac events. BNP indicates B-type natriuretic peptide; GWTG-HF, Get With the Guidelines–Heart Failure; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association classification.

Discussion

In the present study, we demonstrated that the GWTG-HF risk score is a potential predictor for prognosis in both patients with HFpEF and patients with HFrEF.

The GWTG-HF program was designed by the American Heart Association. The GWTG-HF risk score consists of 7 commonly available clinical variables, and it can be used to establish the probability of in-hospital mortality.[15,17] From the GWTG-HF registry cohort, several studies have reported the

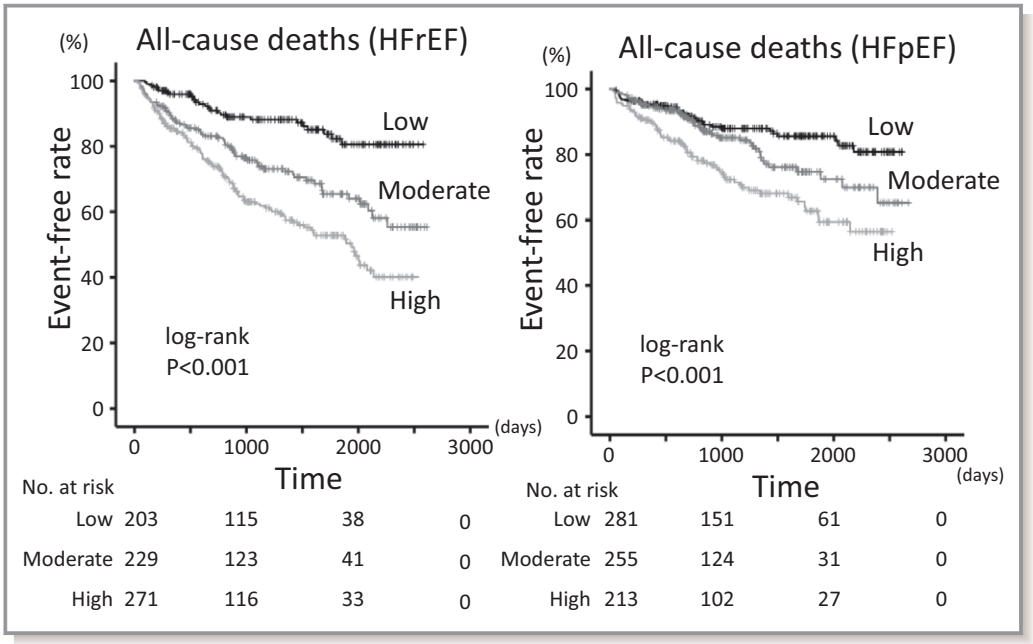

Figure 4. Kaplan-Meier analyses for all-cause deaths in patients with HFrEF and HFpEF among the 3 GWTG-HF risk score groups. Numbers at risk of respective groups were described at the bottom of figures. GWTG-HF indicates Get With the Guidelines–Heart Failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

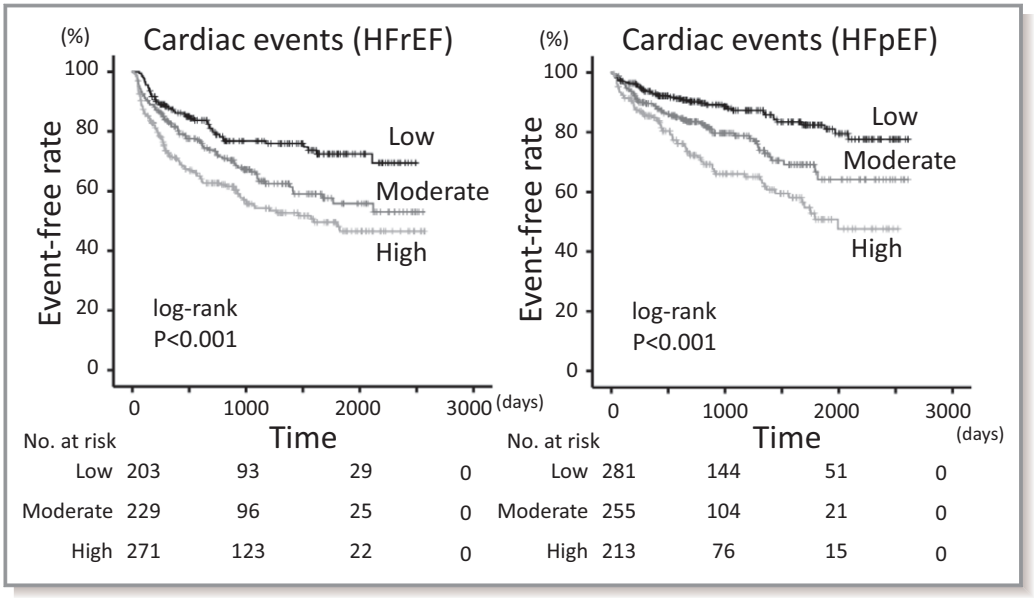

Figure 5. Kaplan-Meier analyses for cardiac events, including worsening heart failure and cardiac deaths, in patients with HFrEF and HFpEF among the 3 GWTG-HF risk score groups. Numbers at risk of respective groups were described at the bottom of figures. GWTG-HF, Get With the Guidelines–Heart Failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

risk of mortality and rehospitalization after discharge.[24–26] There were no reports that revealed the significance of risk prediction beyond 1 year, and our present study demonstrated that the GWTG-HF risk score could be a useful predictor for risk stratification for several years after discharge in patients with HF, both HFpEF or HFrEF.

There are some differences in terms of pathophysiology and clinical characteristics between HFpEF and HFrEF.[27] Various parameters have been previously established for risk stratification[4–8,28]; however, each of these parameters alone is insufficient for prognostic prediction because each parameter represents only a certain aspect of the complicated pathophysiological mechanisms of HFpEF or HFrEF. From these points of view, a novel risk stratification model created from various parameters such as the GWTG-HF risk score would indicate systemic condition more precisely in patients with HF. We showed that the GWTG-HF risk score would be useful for prognostic prediction after hospitalization in both patients with HFpEF and patients with HFrEF. Although Chen et al reported that the AHEAD score was useful in predicting long-term mortality in an Asian cohort with HFrEF or HFpEF,[16] we could not indicate the preference of the GWTG-HF risk score compared to the AHEAD score in this study. Moreover, we derived the modified GWTG-HF model on the basis of the multivariable Cox proportional hazard regression analysis, and this model demonstrated significantly higher C-statistics in both all-cause deaths and cardiac events. This modified model improves prognostic prediction, although the larger number of variables is a disadvantage for multiple scoring models.

It seems that one of the novel aspects of this study is the application of the GWTG-HF risk score in a Japanese population that has somewhat different characteristics from the original GWTG-HF cohort. Coronary artery disease, as the etiology of HF, is relatively lower in Japan than in Western countries.[29,30] Use of angiotensin-converting enzyme inhibitors and β-blockers was comparably lower. Angiotensin receptor blockers were more commonly used in Japan, while angiotensin-converting enzyme inhibitors were more frequently used than angiotensin receptor blockers in Western countries.[30] Although the mean length of hospital stay was considerably longer than in Western countries,[29,30] in-hospital mortality was comparable, and mortality rate after discharge was lower in Japan than in Western countries.[29]

One of the essential uses of a risk score is the identification of patients with severe heart failure who would have major cardiac events. More intensive observation and treatment for these patients could help to decrease mortality and repeated hospitalizations attributable to worsening heart failure. Our results suggest that the GWTG-HF risk score is a useful multivariable score model not only in the acute phase but also for several years after hospitalization in patients with HF, including HFpEF and HFrEF.

Study Limitations

The current study has several limitations. First, the sample size was small and the study was conducted in a single center. Second, the cutoff line between HFpEF and HFrEF is controversial: 40% or 50%. The latest European Society of

Cardiology guideline for HF categorizes EF into 3 groups: HFrEF (EF <40%); mid-range EF (EF=40–50%); and HFpEF (EF >50%).[31] We could not analyze our study subjects according to this classification because of the small sample size. Third, all subjects were Japanese in the present study; therefore, racial factors could not be considered. Hence, large-population and multicenter studies including various races are needed.

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