# Sequential organ failure assessment score on admission predicts long-term mortality in acute heart failure patients

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# Abstract

**Aims** The sequential organ failure assessment (SOFA) score has been a widely used predictor of outcomes in the intensive care unit, whereas short-term and long-term survivals of heart failure (HF) patients are predicted by the American Heart Association Get With the Guidelines–Heart Failure (GWTG-HF) risk score. The purpose of present study was to examine whether the SOFA score on admission is more useful for predicting long-term mortality in acute HF patients than the GWTG-HF risk score.

**Methods and results** A total of 269 patients (mean age,  $78.5 \pm 10.9$  years; all-cause mortality, 53.9%) seen in a single facility from January 2007 to December 2016 were enrolled retrospectively. They were followed up for a mean of  $32.1 \pm 22.3$  months. All-cause death was associated with higher SOFA and GWTG-HF risk scores. However, no significant difference was observed in the area under the curve value between the scores. Kaplan–Meier survival analysis indicated that higher SOFA scores (P < 0.001) and GWTG-HF risk scores (P < 0.001) were related to increased probabilities of all-cause death. On multivariate Cox proportional hazard model analysis, the SOFA score (P < 0.001) and GWTG-HF (P < 0.001) score were independent predictors of all-cause death. Incorporating the SOFA score into the GWTG-HF risk score yielded a significant net reclassification improvement and integrated discrimination improvement. On decision curve analysis, the net benefit of the SOFA score model when compared with the reference model was greater across the range of threshold probabilities.

**Conclusions** In acute HF patients, long-term all-cause mortality can be predicted by the SOFA score. Discriminative performance metrics, such as net reclassification improvement, integrated discrimination improvement, and decision curve analysis, for predicting mortality were improved when the SOFA score was incorporated.

**Keywords** Heart failure; SOFA score; GWTG-HF risk score; Long-term mortality

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# Introduction

The sequential organ failure assessment (SOFA) score was developed in order to provide an objective and quantitative assessment of organ dysfunction of patients in septic intensive care unit (ICU). $@^{1-3}$  In recent years, the SOFA score has been a widely used predictor of outcomes in the ICU, $@^4$  and it predicted higher long-term mortality in unselected cardiac ICU patients. A published study involving 9961 unselected patients admitted to a cardiac ICU showed that the SOFA score

obtained on Day 1 was a good discriminator of short-term and long-term mortality, similar to the Acute Physiology and Chronic Health Evaluation (APACHE)-III and APACHE-IV scores.@<sup>5</sup> The prior study showed that disease-specific risk scores [e.g. The American Heart Association Get With the Guidelines–Heart Failure (GWTG-HF) risk score, APACHE-III, and APACHE-IV] can predict short-term outcomes in HF patients.@<sup>6,7</sup> The GWTG-HF risk score allows for 30-day risk stratification for patients hospitalized with HF with reduced (HFrEF) and preserved ejection fraction (HFpEF),@<sup>6</sup> and it is

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associated with intermediate and long-term mortality outcomes, along with median survival.@<sup>8,9</sup>

In this study, the objective was to determine whether the admission SOFA score is useful for predicting long-term mortality in acute HF patients and to assess its discriminative performance compared with the GWTG-HF risk score.

## **Methods**

#### **Patient selection**

In this single-centre, retrospective, cohort analysis, the institutional database of patients admitted to the University of Fukui Hospital was used to identify patients  $\geq$ 18 years old with HF admitted between 1 January 2007 and 31 December 2016. HF was diagnosed based on the Framingham criteria.  $@^{10}$  Patients whose SOFA and GWTG-HF risk scores were calculated were included. Event-free survival patients who were followed up for less than 1 year were excluded. The follow-up period was truncated at 5 years since a prior study about GWTG-HF risk score demonstrated 5-year survival of HF patients. $@^{8}$ 

#### **Risk score**

The SOFA score was developed as a measure of the severity of organ failure in septic patients by focusing on six organ systems (central nervous, respiratory, cardiovascular, hepatic, renal, and coagulation) that were identified by a literature review. The level of function of each organ is scored from 0 (normal function) to 4 (most abnormal), so that the range of scores is from 0 to 24.@<sup>5</sup> On the other hand, the GWTG-HF risk score was developed using a multivariable model that identified seven predictor variables. Using the sum of the points assigned for each predictor, the estimated probability of in-hospital mortality for a particular patient can be determined, with the total point score ranging from 0 to 100. @<sup>8,9</sup> In post hoc analysis, we performed postmortem analysis for acute HF patients with or without sepsis. Sepsis was diagnosed based on the current clinical criteria and more than 2  $\geq$ SOFA score.@<sup>11</sup>

#### Heart failure management

Optimal tolerated medical therapy, including beta blockers, diuretics, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and digoxin, was given as appropriate to all HF patients.

# Definition of HF with preserved, mid-range, and reduced ejection fraction

HF comprises a wide range of patients, from those with a normal left ventricular (LV) ejection fraction (EF) [typically considered  $\geq$ 50%; HF with preserved EF (HFpEF)] to those with a reduced LVEF [typically considered 40%; HF with reduced EF (HFrEF)]. HF with an LVEF in the range of 40–49% was defined as HFmrEF.@<sup>12</sup> LVEF in all patients was measured using transthoracic echocardiography by the Simpson method of disks or M-mode.

#### Follow-up and endpoint

This was a single-centre, retrospective, observational study. The primary endpoint of the study was all-cause mortality, based on an electronic review of medical records used for patient death notification and the most recent follow-up date.

#### **Statistical analysis**

The categorical variables are reported as numbers (percentages), and groups were compared using the  $\chi^2$  test. Continuous variables are reported as mean ± standard deviation, and the groups were compared using Student's t-test. When continuous and categorical variables were compared among more than two groups, ANOVA and the  $\chi^2$  test, respectively, were used. Significance was defined as P < 0.05. A Cox proportional hazard model was used for univariate and multivariate analyses to identify risk factors for all-cause death. Multivariate analyses were adjusted for age, sex, EF, SOFA score, GWTG-HF risk score, history of cerebral infarction, and administration of aldosterone blockers. Kaplan-Meier survival analysis was used to evaluate long-term survival in HF patients as a function of the admission SOFA score tertile, with the log-rank test used to compare groups. A previous study showed that a low Day 1 SOFA score (<2), which is associated with a low short-term mortality risk, may suggest that a cardiac ICU may not be needed for the safe management of a subset of these patients. Hospital survivors who had higher tertiles of the Day 1 SOFA score, grouped as <2, 2 to 3, and  $\geq$ 4, appeared to have poorer long-term survival.  $@^5$  The group with SOFA scores  $\geq 4$  was separated into two groups. A prior study demonstrated that the GWTG-HF risk score grouped into  $\leq$ 33, 34 to 50, 51 to 57, and  $\geq$ 58 groups demonstrated good discrimination for hospital mortality. @<sup>8,9</sup> Additive information of the SOFA score was evaluated by integrated discrimination improvement (IDI), net reclassification improvement (NRI), and the area under the curve (AUC), as well as decision curve analysis (DCA).@13

Statistical analyses were performed using JMP version 12.0 and R version 3.5.1.

#### Ethics approval and consent to participate

This trial was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The institutional review board or independent ethics committee of this participating facility approved the protocol. The need for informed consent was waived by the Research Ethics Committee, because the data were collected retrospectively from electronic medical records. The trial was conducted under the guidance of a steering committee.

Clinical Trial Registration: UMIN000023840

## Results

#### **Baseline characteristics**

A total of 661 eligible consecutive acute HF patients with acute HF who were seen at our tertiary care hospital from January 2007 to December 2016 were screened. The SOFA score on admission could be calculated retrospectively for 294 patients. A total of 269 patients (136 men) who could complete follow-up evaluation for more than 1 year were enrolled (Figure @1). Their mean age was 78.5 ± 10.9 years, and LVEF was 49.8 ± 16.6%. Mean follow-up was 32.1 ± 22.3 months, with all-cause death occurring in 146 patients (53.9%) (Figure @1). Patients with all-cause death had higher SOFA (4.2  $\pm$  2.3 vs. 2.8  $\pm$  1.8, P < 0.001) and GWTG-HF risk scores (44.0 ± 7.6 vs. 38.1 ± 7.9, P < 0.001) (Table @1). In contrast, no significant difference was observed in the AUC value between the SOFA score (AUC, 0.689) and the GWTG-HF risk score (AUC, 0.692). Receiver operating characteristic curve analysis indicated that the optimal cut-off values for the SOFA and GWTG-HF risk scores were 3 (sensitivity 78.8%, specificity 50.4%) and 44 (sensitivity 50.7%, specificity 61.3%), respectively. SOFA score  $\geq$ 3 and GWTG-HF risk score  $\geq$ 44 were predictors of all-cause death [hazard ratio (HR), 2.825, 95% confidence interval (CI), 1.922 to 4.279, P < 0.001; and HR, 2.62; 95% CI, 1.885 to 3.634, P < 0.001].





Sepsis was diagnosed based on the current clinical criteria and more than  $2 \ge$  SOFA score. HF study population into two subgroups: one group with acute HF+ sepsis and the second group with acute HF+ any other cause. There were 40 patients of acute HF+ sepsis. This result showed that there were no significant differences of death [21 (52.5%) vs. 102 (44.5%), P = 0.35] and SOFA score (4.2 ± 2.0 vs. 3.5 ± 2.2, P= 0.056) between two subgroups except for the aetiology of HF and history of chronic obstructive pulmonary disease (*Table @3*).

#### Kaplan–Meier analysis

We divided the patients into four groups in proportion to the SOFA score (SOFA score < 2, 2 to 3, 4 to 5, and  $\geq$ 6) or the GWTG-HF risk score (GWTG risk score  $\leq$  33, 34 to 50, 51 to 57, and  $\geq$ 58). Kaplan–Meier survival analysis demonstrated that higher SOFA scores (P < 0.001) and GWTG-HF risk scores (P < 0.001) were associated with higher probabilities of all-cause death (*Figure @2A*,B). The clinical course was significantly worse in patients with higher SOFA and GWTG-HF risk scores significant associations with death in patients with preserved and reduced EF on Kaplan–Meier survival analysis (*Figure @2C*,D).

#### Multivariate Cox proportional hazard model

A multivariate Cox proportional hazard model was developed with adjustment for age, sex, EF, SOFA score, GWTG-HF risk score, history of cerebral infarction, and aldosterone blocker therapy. The SOFA score (HR 1.227, 95% CI 1.130 to 1.326, P < 0.001), GWTG-HF risk score (HR 1.054, 95% CI 1.029 to 1.078, P < 0.001), and age (HR, 1.069, 95% CI 1.048 to 1.092, P < 0.001) were found to be independent predictors of all-cause death, and the HR of the SOFA score was the highest of these parameters (*Table @2*).

#### Analysis of improvement in predicted probability

Incorporating the SOFA score into the GWTG-HF risk score yielded a significant NRI (0.528, 95% CI 0.291 to 0.765) and IDI (0.046, 95% CI 0.020 to 0.072). On the DCA, the SOFA score model showed a net benefit compared with the reference model across the entire range of threshold probabilities (*Figure @3*).

## Discussion

Several important findings came out of this study. First, higher SOFA scores and GWTG-HF risk scores on admission

 Table 1 Characteristics of the study population

	No. with available data	Overall ( $N = 269$ )	Nonsurvivors ( $n = 146$ )	Survivors ( $n = 123$ )	P value
Age (years)	269	78.5 ± 10.9	82.7 ± 8.7	73.6 ± 11.1	< 0.001
Male, n (%)	269	136 (50.6%)	70 (48.9%)	65 (52.8%)	0.49
Height (cm)	269	154.2 ± 9.5	152.7 ± 9.4	155.6 ± 9.4	0.016
Weight (kg)	269	52.0 ± 12.5	$66.9 \pm 29.8$	$68.2 \pm 9.6$	0.005
BMI (kg/m <sup>2</sup> )	269	$22.0 \pm 4.7$	$21.2 \pm 5.1$	$22.8 \pm 4.2$	0.006
HF aetiology, n (%)	269				0.069
IHD		79 (29.3%)	37 (25.3%)	42 (34.1%)	
Arrhythmia		27 (10.0%)	15 (10.3%)	11 (8.9%)	
VHD		40 (14.9%)	29 (19.9%)	11 (8.9%)	
Cardiomyopathy		23 (8.6%)	12 (8.2%)	11 (8.9%)	
HHD		73 (27.1%)	35 (24.0%)	38 (30.9%)	
PH		5 (1.9%)	2 (1.4%)	3 (2.4%)	
Others		23 (8.6%)	16 (11.0%)	7 (5.7%)	
Clinical history, n (%)	269				
Diabetes mellitus		87 (32.3%)	49 (33.6%)	38 (30.9%)	0.64
COPD		16 (5.9%)	11 (7.5%)	5 (4.1%)	0.22
AMI		72 (26.8%)	33 (22.6%)	39 (31.7%)	0.093
Stroke		33 (12.3%)	27 (18.5%)	6 (4.9%)	< 0.001
Cancer		33 (12.3%)	18 (12.3%)	15 (12.2%)	0.97
Medication, n (%)	269				
ACE inhibitor or ARB		92 (34.2%)	52 (35.6%)	40 (32.5%)	0.59
Beta blocker		53 (19.7%)	31 (21.2%)	22 (17.9%)	0.49
Aldosterone antagonist		46 (17.1%)	32 (21.9%)	14 (11.4%)	0.020
Diuretics		113 (42.0%)	63 (43.2%)	50 (40.7%)	0.68
Digoxin		13 (4.8%)	10 (6.8%)	3 (2.4%)	0.083
Systolic BP (mmHg)	269	146.7 ± 36.3	139.9 ± 33.8	154.6 ± 37.6	< 0.001
Diastolic BP (mmHg)	269	83.0 ± 25.4	76.6 ± 22.4	90.6 ± 26.7	< 0.001
Heart rate (bpm)	269	94.1 ± 27.9	90.1 ± 25.3	98.9 ± 30.2	< 0.001
GCS	269	14.7 ± 1.7	$14.4 \pm 2.0$	14.9 ± 1.1	0.028
Platelets ( $\times 10^3/\mu$ L)	269	196.4 ± 135.7	198.6 ± 176.2	193.9 ± 59.4	0.77
Total bilirubin (mg/dL)	269	$0.9 \pm 0.6$	$0.8 \pm 0.6$	$0.9 \pm 0.5$	0.74
Creatinine (mg/dL)	269	$1.8 \pm 5.7$	2.3 ± 7.7	$1.2 \pm 0.8$	0.12
BUN (mg/dL)	269	27.8 ± 15.6	32.3 ± 15.6	22.3 ± 13.8	< 0.001
Na (mEq/L)	269	139.3 ± 4.3	$138.9 \pm 4.9$	139.7 ± 3.5	0.15
PaO <sub>2</sub> (mmHg)	269	101.3 ± 57.8	96.1 ± 51.4	107.5 ± 64.2	0.11
PaO <sub>2</sub> /FiO <sub>2</sub> ratio	269	257.9 ± 126.4	242.6 ± 113.3	276.0 ± 138.7	0.030
$HCO_{3}$ (mEq/L)	269	$23.0 \pm 5.0$	$22.5 \pm 5.4$	$23.5 \pm 4.4$	0.081
LVEF (%)	263	49.8 ± 16.6	50.6 ± 17.0	48.8 ± 16.2	0.39
SOFA score (points)	269	$3.6 \pm 2.2$	$4.2 \pm 2.3$	$2.8 \pm 1.8$	< 0.001
GWTG-HR risk score (points)	269	41.3 ± 8.3	$44.0 \pm 7.6$	38.1 ± 7.9	< 0.001

ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; FiO<sub>2</sub>, fraction of inspiratory oxygen; GCS, Glasgow coma scale; GWTG-HF, the American Heart Association Get With the Guidelines-Heart Failure; HF, heart failure; HHD, hypertensive heart disease; IHD, ischaemic heart disease; LVEF, left ventricular ejection fraction; PaO<sub>2</sub>, partial pressure of arterial oxygen; PH, pulmonary hypertension; SOFA, sequential organ failure assessment; VHD, valvular heart disease.

Values are reported as means ± standard deviation or numbers of patients (%) unless otherwise noted.

appeared to be related to increased probabilities of all-cause death. Second, the SOFA score and the GWTG-HF risk score predicted long-term mortality in HF patients whose EF was reduced or preserved. Lastly, the SOFA score on admission was a stronger predictor of long-term all-cause mortality than the GWTG-HF risk score.

The present study evaluated the value of the SOFA score describing organ failure severity for predicting long-term mortality in HF patients. Previous studies addressed the prediction of long-term mortality by parameters of compensated HF patients, although the calculations of these studies were complicated.@<sup>14-17</sup> To the best of our knowledge, there have been few studies demonstrating a long survival advantage associated with care at centres with better short-term mortality rates for HF patients. The GWTG-HF risk score was the only

one to be related to short-term and long-term mortality.  $@^{8,9}$  In the present results, the SOFA risk score on admission was useful for long-term mortality prediction in HF patients, even without taking into account other potentially relevant variables, such as age, aetiology of HF, and LVEF. The SOFA score provides an objective and quantitative measure of organ dysfunction over time and of morbidity in ICU patients with sepsis. $@^{1-3}$  Furthermore, in recent years, the SOFA score was found to predict higher long-term mortality in unselected cardiac ICU patients even without taking into account other potentially relevant variables, such as patients' diagnosis and age. $@^5$  In past study, renal and hepatic dysfunction in acute HF is associated with various adverse outcomes: longer hospital stay, higher rehospitalization rate, and higher mortality. $@^{18,19}$  Additionally, it is well known that

**Figure 2** A. Kaplan–Meier survival curves for all-cause death, according to admission sequential organ failure assessment (SOFA) score tertile, P < 0.001 between groups by the log–rank test. B. Kaplan–Meier survival curves for all-cause death, according to the admission American Heart Association Get With the Guidelines-Heart Failure (GWTG-HF) risk score tertile, P < 0.001 between groups by the log–rank test. C. Kaplan–Meier survival curves for all-cause death, according to admission sequential organ failure assessment (SOFA) score tertile. (A) Long-term survival of patients with heart failure with reduced (HFrEF) and mid-range ejection fraction (HFmrEF). (B) Long-term survival of patients with heart failure with reduced (HFrEF) and mid-range ejection fraction gratients with heart failure to the admission American Get With the Guidelines-Heart Failure (GWTG-HF) risk score tertile. (A) Long-term survival of patients with heart failure with reduced (HFrEF) and mid-range ejection fraction (HFmrEF). (B) Long-term survival of patients with heart failure with reduced (HFrEF) risk score tertile. (A) Long-term survival of patients with heart failure with reduced (HFrEF) and mid-range ejection fraction (HFmrEF). (B) Long-term survival of patients with heart failure with reduced (HFrEF) and mid-range ejection fraction (HFmrEF). (B) Long-term survival of patients with heart failure with reduced (HFrEF) and mid-range ejection fraction (HFmrEF). (B) Long-term survival of patients with heart failure with reduced (HFrEF) and mid-range ejection fraction (HFmrEF). (B) Long-term survival of patients with heart failure with reduced (HFrEF).



HF is a complex syndrome that, in analogy with a neoplasm, starts from heart with an involvement of systemic organs malfunction as lung, kidney, liver, and coagulation. It was uncovered that other scores which take into account this natural history of HF in this literature.@<sup>20</sup> The SOFA score was developed as a measure of the severity of organ failure by





focusing on six organ systems (central nervous, respiratory, cardiovascular, hepatic, renal, and coagulation). Moreover,

Table	2	Comparisons	between	survivors	and	patients	with	all-
cause death on multivariate analysis								

	Hazard ratio (95% confidence interval)	P value
Age (year)	1.054 (1.031-1.078)	< 0.0001
Male	1.160 (0.783–1.721)	0.46
Weight (kg)	0.971 (0.952-0.990)	0.0030
Stroke	1.712 (1.067–2.638)	0.027
Aldosterone antagonist	1.153 (0.740–1.751)	0.52
LVEF (%)	1.005 (0.993–1.016)	0.37
SOFA score (points)	1.238 (1.136–1.350)	< 0.0001
GWTG-HF risk score (points)	1.047 (1.023–1.071)	0.00011
anna minisk score (points)	1.017 (1.025 1.071)	0.00011

Comparisons between survivors and patients with all-cause death on multivariate analysis using baseline data, left ventricular ejection faction (LVEF), sequential organ failure assessment (SOFA) score, and the American Heart Association Get With the Guidelines-Heart Failure (GWTG-HF) risk score on admission. The SOFA score evaluated systemic organs malfunction (central nervous, respiratory, hepatic, and coagulation) that could not be evaluated by the GWTG-HF risk score. The SOFA score provides a satisfactory way to risk-stratify complex or undifferentiated patients, whereas disease-specific risk scores remain useful for patients who have clearly defined disease processes.@<sup>5,21</sup>

In the recent study, the GWTG-HF risk score indicated similar results to the SOFA score, predicting long-term mortality in patients with HFrEF or HFpEF. Previous data showed that the GWTG-HF risk score evaluates short-term and long-term mortality in patients with HFrEF or HFpEF.@<sup>6,8,9</sup> There are some differences in terms of pathophysiology and clinical characteristics between HFpEF and HFrEF.@<sup>22</sup> Various parameters have been previously established for risk stratification.@<sup>6,7</sup> However, each of these parameters alone is insufficient for predicting prognosis, because each parameter represents only a certain aspect of the complicated

	No. with available data	Overall ( $N = 269$ )	With sepsis $(n = 40)$	Without sepsis ( $n = 229$ )	P value
Age (years)	269	78.5 ± 10.9	78.9 ± 12.5	78.5 ± 10.6	0.80
Male, n (%)	269	136 (50.6%)	21 (52.5%)	115 (50.2%)	0.79
Height (cm)	269	$154.2 \pm 9.5$	$154.2 \pm 11.2$	$154.2 \pm 9.2$	0.98
Weight (kg)	269	52.0 ± 12.5	53.7 ± 11.9	51.7 ± 12.6	0.37
BMI (kg/m <sup>2</sup> )	269	$22.0 \pm 4.7$	$22.7 \pm 4.4$	$21.9 \pm 4.8$	0.32
Death, n (%)	269	146 (54.3%)	21 (52.5%)	102 (44.5%)	0.35
HF aetiology, n (%)	269	· · ·		. ,	0.029
IHD		79 (29.3%)	10 (25.0%)	69 (30,1%)	
Arrhythmia		27 (10.0%)	3 (7.5%)	23 (10.0%)	
VHD		40 (14.9%)	8 (20.0%)	32 (14.0%)	
Cardiomyopathy		23 (8.6%)	4 (10.0%)	19 (8.3%)	
HHD		73 (27.1%)	5 (12.5%)	68 (29.7%)	
PH		5 (1.9%)	1 (2.5%)	4 (1.7%)	
Others		23 (8.6%)	9 (22.5%)	14 (6,1%)	
Clinical history, n (%)	269	20 (0.070)	5 (221070)		
Diabetes mellitus	200	87 (32.3%)	11 (27,5%)	76 (33,2%)	0.47
COPD		16 (5.9%)	6 (15.0%)	10 (4.4%)	0.021
AMI		72 (26.8%)	8 (20.0%)	64 (27.9%)	0.28
Stroke		33 (12.3%)	2 (5.0%)	31 (13.5%)	0.095
Cancer		33 (12.3%)	3 (7.5%)	30 (13.1%)	0.29
Medication, n (%)	269	00 (121070)	0 (11070)		0.25
ACE inhibitor or ARB	200	92 (34,2%)	14 (35.0%)	78 (34,1%)	0.91
Beta blocker		53 (19.7%)	5 (12.5%)	48 (21.0%)	0.19
Aldosterone antagonist		46 (17.1%)	8 (20.0%)	38 (16.6%)	0.60
Systolic BP (mmHa)	269	146.7 + 36.3	140.0 + 31.7	147.8 + 37.0	0.21
Diastolic BP (mmHg)	269	$83.0 \pm 25.4$	$76.4 \pm 20.9$	$84.2 \pm 27.5$	0.074
Heart rate (bpm)	269	$94.1 \pm 27.9$	$86.7 \pm 22.9$	$95.4 \pm 28.6$	0.068
GCS	269	$14.7 \pm 1.7$	$14.8 \pm 0.8$	$14.6 \pm 1.8$	0.52
Platelets ( $\times 10^3/\mu L$ )	269	$196.4 \pm 135.7$	$181.5 \pm 84.9$	$199.1 \pm 142.7$	0.45
Total bilirubin (mg/dL)	269	$0.9 \pm 0.6$	$0.9 \pm 0.6$	$0.8 \pm 0.5$	0.55
Creatinine (mg/dL)	269	$1.8 \pm 5.7$	$1.4 \pm 0.9$	$1.8 \pm 6.2$	0.72
BUN (mg/dL)	269	$27.8 \pm 15.6$	$26.3 \pm 12.6$	$28.0 \pm 16.1$	0.62
Na (mEg/L)	269	$139.3 \pm 4.3$	$139.0 \pm 4.6$	$139.3 \pm 4.3$	0.61
$PaO_{2}$ (mmHg)	269	$101.3 \pm 57.8$	$87.7 \pm 45.7$	$103.7 \pm 59.4$	0.11
PaO <sub>2</sub> /FiO <sub>2</sub> ratio	269	$257.9 \pm 126.4$	$223.2 \pm 107.8$	$263.9 \pm 128.6$	0.060
$HCO_{2}$ (mEq/L)	269	$23.0 \pm 5.0$	$22.9 \pm 4.0$	$23.0 \pm 5.1$	0.87
LVEF (%)	263	$49.8 \pm 16.6$	$53.5 \pm 15.0$	$49.1 \pm 16.8$	0.13
SOFA score (points)	269	$3.6 \pm 2.2$	$4.2 \pm 2.0$	$3.5 \pm 2.2$	0.056
GWTG-HR risk score (points)	269	41.3 ± 8.3	$42.0 \pm 8.6$	41.2 ± 8.2	0.60

ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; FiO<sub>2</sub>, fraction of inspiratory oxygen; GCS, Glasgow coma scale; GWTG-HF, the American Heart Association Get With the Guidelines-Heart Failure; HF, heart failure; HHD, hypertensive heart disease; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; PaO<sub>2</sub>, partial pressure of arterial oxygen; PH, pulmonary hypertension; SOFA, Sequential Organ Failure Assessment; VHD, valvular heart disease.

Values are reported as means±standard deviation or numbers of patients (%) unless otherwise noted.

pathophysiological mechanisms of HFpEF or HFrEF. Taken together, a novel risk stratification model created from various parameters such as the GWTG-HF risk score would reflect the systemic condition more precisely in patients with HF.

The simplicity and ease of use of the SOFA score are its most important advantages, since it can be calculated at the bedside and can provide mortality discrimination at least as well as more complex scores.@<sup>1,4</sup> Though diagnosis-related and procedure-related data and age are not included in the SOFA score, the admission diagnosis can provide a substantial contribution to the accuracy of mortality prediction with other models. In the multivariate Cox proportional hazard model, the HR of the SOFA score was the highest of these parameters. Patients with an increasing SOFA score on admission are at increased risk of long-term all-cause death. NRI and IDI are valuable tools when evaluating the ability of a modified model to discriminate, which was assessed by examining changes in the AUC. Finally, a DCA, a method of calculating the net benefit in which the true positive value is subtracted from the false positive value, of the SOFA score and GWTG-HF risk score was performed. The GWTG-HF risk score is an established evaluation for predicting long-term prognosis of patients with HF.  $@^{8,9}$  New models combining the SOFA and GWTG-HF risk score alone when assessed by NRI, IDI, and DCA.

#### Limitations

There are some limitations of this study. First, it was a single facility, retrospective study of a selected cohort of HF patients. Second, not all patients' records included values for Figure 3 Decision curve analysis for heart failure prediction in total participants, with and without the sequential organ failure assessment (SOFA) score. The grey line is the net benefit of treating all participants similarly, assuming that all would die; the net benefit of treating participants without the SOFA score is shown by the dotted black line, and that with the SOFA score is shown by the dotted red line.



variables needed to calculate the SOFA score, because of absence of arterial blood gas measurements. Additionally, most patients were not evaluated by Day 2, Day 3, or Day 4 SOFA score. There are several SOFA score derived measures are proposed in critically ill patients, such as delta SOFA score, total maximum SOFA score, and average SOFA score. However, we could not calculate delta SOFA score of patients in this study. Further study is required to examine the prognostic value of these SOFA-derived score in heart failure settings.  $@^{23-25}$  Third, we evaluated LVEF of patients by 2-D echocardiography since all patients were not evaluated by m-Simpson echocardiography. Finally, information about medication changes, clinical events following hospital discharge, and cause of death was not available.

# Conclusions

Using an electronic algorithm, it is easy to calculate the SOFA score for HF patients. The SOFA score is a simple and

# validated mortality risk score for the short term. In acute HF patients, long-term all-cause mortality can also be predicted by the SOFA score. Discriminative performance metrics such as NRI, IDI, and DCA were improved on incorporation of the SOFA score for prediction of mortality.

# **Conflict of interest**

None declared.

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