ORIGINAL RESEARCH

Predictive Value of the Sequential Organ Failure Assessment Score for Mortality in a Contemporary Cardiac Intensive Care Unit Population

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***Background*—**Optimal methods of mortality risk stratification in patients in the cardiac intensive care unit (CICU) remain uncertain. We evaluated the ability of the Sequential Organ Failure Assessment (SOFA) score to predict mortality in a large cohort of unselected patients in the CICU.

***Methods and Results*—**Adult patients admitted to the CICU from January 1, 2007, to December 31, 2015, at a single tertiary care hospital were retrospectively reviewed. SOFA scores were calculated daily, and Acute Physiology and Chronic Health Evaluation (APACHE)-III and APACHE-IV scores were calculated on CICU day 1. Discrimination of hospital mortality was assessed using area under the receiver-operator characteristic curve values. We included 9961 patients, with a mean age of 67.5±15.2 years; all-cause hospital mortality was 9.0%. Day 1 SOFA score predicted hospital mortality, with an area under the receiver-operator characteristic curve value of 0.83; area under the receiver-operator characteristic curve values were similar for the APACHE-III score, and APACHE-IV predicted mortality ($P>0.05$). Mean and maximum SOFA scores over multiple CICU days had greater discrimination for hospital mortality ($P<0.01$). Patients with an increasing SOFA score from day 1 and day 2 had higher mortality. Patients with day 1 SOFA score <2 were at low risk of mortality. Increasing tertiles of day 1 SOFA score predicted higher long-term mortality ($P<0.001$ by log-rank test).

***Conclusions*—**The day 1 SOFA score has good discrimination for short-term mortality in unselected patients in the CICU, which is comparable to APACHE-III and APACHE-IV. Advantages of the SOFA score over APACHE include simplicity, improved discrimination using serial scores, and prediction of long-term mortality. **(*J Am Heart Assoc*. 2018;7:e008169. DOI: 10.1161/JAHA.117.008169.)**

Key Words: Acute Physiology and Chronic Health Evaluation score • cardiac critical care • cardiac intensive care unit • critical care • intensive cardiac care unit • intensive care unit • mortality • risk prediction • Sequential Organ Failure Assessment score

Risk prediction models have been important in acute cardiac care since Killip and Kimball reported the first risk-stratification paradigm for patients with acute myocardial infarction 50 years ago.[1] Since then, the cardiac intensive care unit (CICU) population has evolved to include an increasingly heterogeneous and complex mix of acute and chronic multiorgan dysfunction with superimposed cardiac pathological features.[2–5] Similarities between CICU and other ICU populations are growing, with an increasing prevalence of multisystem critical illnesses in patients in the CICU.[2,5,6] Appropriate risk stratification models are, therefore, needed to optimize patient selection for CICU admission and to predict adverse outcomes to allow for effective care planning and therapeutic intervention.[3,4,7] Disease-specific risk prediction models have been derived, but many patients in the CICU have undifferentiated clinical syndromes with multiple acute and chronic cardiovascular disease processes.[2,6–8]

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Clinical Perspective

What Is New?

- This is the first study to validate the Sequential Organ Failure Assessment (SOFA) score, a simple illness severity score used to predict mortality in general critically ill patients, for prediction of mortality in a large cohort of patients in the cardiac intensive care unit (CICU).
- The SOFA score on the first CICU day had good discrimination for hospital mortality and could stratify postdischarge mortality risk among hospital survivors.
- Discrimination of hospital mortality was improved by calculating day-to-day changes in the SOFA score or using mean or maximum values of multiple daily SOFA scores.

What Are the Clinical Implications?

- Risk stratification of patients in the CICU using the SOFA score on the first and subsequent CICU days allows identification of both low- and high-risk patients, which may facilitate triage decisions and improve outcome prognostication.
- Quantifying changes in daily SOFA scores over time provides a useful method of linking the response to treatment to future clinical outcomes for critically ill patients in the CICU.
- The SOFA score allows risk stratification of patients in the CICU independent of admission diagnosis, allowing illness severity to be quantified in patients with undifferentiated or multisystemic acute illnesses.

ICU severity of illness scoring models identify high-risk patients independent of their underlying disease process or clinical presentation.[9,10] The Sequential Organ Failure Assessment (SOFA) score was introduced to describe organ failure severity in patients with sepsis, including a 4-point assessment of dysfunction in each of 6 organ systems (central nervous system, cardiovascular, respiratory, renal, liver, and coagulation; Table S1).[10–12] In patients with sepsis, a SOFA score ≥2 reflects clinically relevant organ dysfunction and an increased risk of adverse outcomes.[13] The SOFA score has been validated in critically ill patients with diseases other than sepsis, including a small CICU population.[12,14] Advantages of the SOFA score compared with other ICU risk scores include its simplicity and ease of use, allowing it to be calculated daily at bedside without complex algorithms to demonstrate clinical improvement or deterioration over time. Daily trends in the SOFA score can predict adverse outcomes, because an increase in SOFA score over time reflects progressive organ failure and higher risk of death.[10,13,15]

The purpose of this study was to evaluate the ability of the SOFA score to predict short- and long-term mortality in a large cohort of unselected patients in the CICU and to determine if the SOFA score could differentiate high- and low-risk patient populations, with the goal of improving future CICU triage protocols.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure. This study was approved by the Mayo Clinic Institutional Review Board under an exception from informed consent as posing minimal risk to patients. This was a historical cohort analysis using an institutional database of patients admitted to the CICU at the Mayo Clinic Hospital, St Mary's Campus, a tertiary-care hospital in Rochester, MN. The CICU at this facility is a single, 16-bed, closed CICU in which all admissions are triaged, accepted, and cared for by a board-certified cardiologist (J.C.J.), with comanagement by an intensivist for patients with respiratory failure. Unique adult patients ≥18 years old admitted to the CICU between January 1, 2007, and December 31, 2015, were identified by searching the archived electronic health records; data from the first CICU admission were used for patients subsequently readmitted during the same hospitalization.[16] Patients still hospitalized on December 31, 2015, were excluded. According to Minnesota state law statute 144.295, patients must give consent before being included in observational research studies; patients who did not provide Minnesota Research Authorization were excluded from the study.

Demographic and laboratory data and use of invasive and noninvasive ventilation and continuous renal replacement therapy were collected. Daily SOFA scores and individual organ subscores were automatically generated for all patients in the CICU from data in the electronic medical record system, following imputation of missing variables to normal as the default.[17] Acute Physiology and Chronic Health Evaluation (APACHE)-III scores and APACHE-IV predicted mortality were automatically generated for all patients in the CICU from data in the electronic medical record system from the first 24 hours of CICU admission.[18,19] Charlson Comorbidity Index was calculated electronically.[20] Hospital disposition, length of stay, and all-cause mortality were determined using electronic review of medical records for notification of patient death and last follow-up date. Mortality data were extracted from Mayo Clinic electronic databases, the state of Minnesota electronic death certificates, and the Rochester Epidemiology Project database, as previously described.[21]

The primary end point of the study was all-cause hospital mortality; secondary end points included CICU mortality, 30-day mortality, and postdischarge mortality. Categorical variables are reported as number (percentage), and the χ^2 test was used to compare groups. Continuous variables are

reported as mean±SD, and Student *t* test was used to compare groups. ANOVA and χ^2 tests were used to compare >2 groups for continuous and categorical variables, respectively. Trends in categorical variables were assessed using the Cochran-Armitage trend test. Univariate analysis was performed using continuous variables as predictors of mortality, and the area under the receiver-operator characteristic curve (AUROC) values were determined from this analysis; the optimal cutoff for predicting mortality was defined as that with the highest value of Youden's J index (sensitivity+specificity−1). $P<0.05$ was considered statistically significant, receiver-operating curves were calculated via 2000 bootstrap samples, and all AUROC comparisons were performed using DeLong's method. A logistic regression model was created to determine calibration of the SOFA score using the Hosmer-Lemeshow statistic. Long-term survival in patients discharged alive from the hospital as a function of day 1 SOFA score tertile was assessed using Kaplan-Meier survival analysis, with groups compared using the log-rank test. Statistical analyses were performed using JMP, version 10.0 (SAS Institute, Cary, NC), and R, version 3.2.0 (https://www.r-project.org).

Results

We screened 12 904 adult admissions to the CICU during the study period; 2900 patients were excluded (1877 readmissions, 755 patients with no Minnesota Research Authorization, and 268 patients admitted outside of the study period). The primary admission diagnoses included acute coronary syndrome (n=3101 [31%]), arrhythmia (n=2001 [20%]), heart failure (n=1801 [18%]), respiratory failure (n=1551 [16%]), acute renal failure (n=568 [5%]), cardiac arrest (n=250 [3%]), and sepsis (n=710 [7%]).

Day 1 SOFA scores were available in 9961 patients (99.6%), who composed the final study population. Baseline characteristics are shown in Table 1. The mean±SD day 1 SOFA score was 3.45±3.15, with a median of 2 (25th/75th percentile, 1.5) (Figure 1). CICU mortality occurred in 557 patients (5.6%), and hospital mortality occurred in 893 patients (9.0%); and 1127 patients (11.3%) died within 30 days after CICU admission (Figure 2). Hospital nonsurvivors were older, had more comorbidities, and had more frequent use of mechanical ventilation and continuous renal replacement therapy (Table 1).

The mean day 1 SOFA score was higher in patients who died in the hospital (7.67 versus 3.03; $P<0.001$), and these patients had a distribution of day 1 SOFA scores that was shifted towards higher values (Figure 1). Short-term mortality increased significantly with increasing day 1 SOFA score tertile (day 1 SOFA score <2 versus 2 to 3 versus ≥4; $P<0.001$ for trend), as shown in Figure 2. Short-term mortality rates increased progressively with an increasing day 1 SOFA score (Figure 3), and day 1 SOFA score was a significant univariate predictor of hospital mortality (Table 2). The 3579 patients (35.9%) without significant organ failure (day 1 SOFA score <2) had a low risk of hospital mortality (1.51%; odds ratio, 0.101; $P<0.001$). Day 1 SOFA score predicted hospital mortality, with an optimal cutoff of ≥5 by AUROC analysis, corresponding to the top quartile of day 1 SOFA score (Table 2). A day 1 SOFA score ≥5 predicted hospital mortality (24.5% versus 3.1%; odds ratio, 10.18; 95% confidence interval, 8.68–11.94; $P<0.001$). The 2736 patients (27.5%) with day 1 SOFA score ≥5 accounted for 80.8% of patients who died in the CICU and 75.0% of patients who died in the hospital.

Mean APACHE-III score and APACHE-IV predicted mortality were higher in patients who died in the hospital ($P<0.001$) (Table 1), and APACHE-III and APACHE-IV were significant univariate predictors of hospital mortality (Table 2). AUROC values for day 1 SOFA score did not differ from either APACHE-III or APACHE-IV for predicting ICU mortality or hospital mortality (all $P>0.05$). On the basis of the Hosmer-Lemeshow statistic, calibration for probabilities produced by a logistically transformed day 1 SOFA score was acceptable ($P=0.11$) for CICU mortality and suboptimal ($P<0.05$) for hospital mortality (Figure S1).

A total of 3169 patients (31.8%) left the CICU on day 1, including 239 (7.5%) who died; 6792 patients (68.2%) remained in the CICU on day 2, and 3829 patients (38.4%) remained in the CICU on day 3. Maximum and mean SOFA scores for day 1 and day 2 (substituting the day 1 SOFA score if no day 2 SOFA score was available) had significantly higher AUROC values for hospital mortality than day 1 SOFA score (Table 2). The maximum and mean daily SOFA scores during the first 3 CICU days (substituting day 1 or day 2 SOFA scores in patients who left the CICU before day 3) and the maximum daily SOFA score over the first 7 CICU days had significantly higher AUROC values for hospital mortality than mean or maximum day 1 to 2 SOFA scores (Table 2). Mean SOFA score over days 1 to 3 had the highest AUROC value for hospital mortality, followed by maximum SOFA score over the first 7 CICU days (Table 2). All significant comparisons yielded $P<0.01$ by the DeLong test.

The mean±SD change in SOFA scores between day 1 and day 2 was −0.76±2.21. Characteristics of patients with increasing (n=1334 [19.6%]), decreasing (n=3157 [46.5%]), or unchanged (n=2301 [33.9%]) SOFA score from day 1 to day 2 are shown in Table 3. Hospital mortality was significantly higher in patients with an increasing day 2 SOFA score than in patients with a declining day 2 SOFA score ($P<0.001$; Figure 4), despite similar mean day 1+day 2 SOFA score and maximum week 1 SOFA score and lower APACHE-III score and APACHE-IV predicted mortality (Table 3). Patients with unchanged SOFA score from day 1 to day 2 were at the lowest risk.

Table 1. Baseline Characteristics of Included Patients With Available Day 1 SOFA Score, Including Hospital Survivors and Inpatient Deaths

Variable	No. With Available Data	Overall (n=9961)	Hospital Survivors (n=9404)	Nonsurvivors (n=893)	*P* Value (Survivors vs Deaths)
Age, y	9961	67.5±15.2	67.0±15.3	72.1±13.8	<0.001
Female sex	9961	3732 (37.5)	3373 (37.2)	359 (40.2)	0.0767
White race	9961	9201 (92.4)	8390 (92.5)	811 (90.8)	0.0670
Admission source	9961				<0.001
Procedural laboratory		3967 (39.8)	3760 (41.5)	207 (23.2)	
Transfer		2713 (27.2)	2429 (26.8)	284 (31.8)	
Emergency department		1393 (14.0)	1219 (13.4)	174 (19.5)	
Floor		1599 (16.1)	1415 (15.6)	184 (20.6)	
Other		289 (2.9)	245 (2.7)	44 (4.9)	
Prior myocardial infarction	9935	1972 (19.8)	1778 (19.7)	194 (21.7)	0.1408
Prior heart failure	9935	1949 (19.6)	1706 (18.9)	243 (27.2)	<0.001
Prior diabetes mellitus	9935	2823 (28.4)	2525 (27.9)	298 (33.4)	<0.001
Prior lung disease	9935	1935 (19.5)	1714 (19.0)	221 (24.8)	<0.001
Prior cancer	9935	2121 (21.4)	1873 (20.7)	248 (27.8)	<0.001
Prior stroke	9935	1227 (12.4)	1074 (11.9)	153 (17.1)	<0.001
Prior moderate-severe CKD	9935	2021 (20.3)	1767 (19.5)	254 (28.4)	<0.001
CCI (with age)	9935	5.6±3.3	5.5±3.3	6.9±3.4	<0.001
CCI (excluding age)	9935	2.4±2.6	2.3±2.6	3.2±3.0	<0.001
BMI, kg/m^2	9845	29.5±7.1	29.5±7.0	29.7±8.0	0.3851
CICU LOS, d	9961	2.5±4.6	2.4±4.6	3.1±4.2	<0.001
Hospital LOS, d	9961	7.9±13.2	7.8±1.24	9.0±19.3	0.0683
Invasive ventilator use	9961	1605 (16.1)	1125 (12.4)	480 (53.8)	<0.001
Invasive ventilator use, d	9961	0.35±1.47	0.27±1.28	1.21±2.58	<0.001
Noninvasive ventilator use	9961	1489 (14.9)	1286 (14.2)	203 (22.7)	<0.001
Noninvasive ventilator use, d	9961	0.19±0.84	0.17±0.79	0.37±1.20	<0.001
Vasopressor/inotrope use CICU day 1	9957	1767 (17.8)	1286 (14.2)	481 (53.9)	<0.001
CRRT use	9961	167 (1.7)	84 (0.9)	83 (9.3)	<0.001
APACHE-III score	9961	61.2±25.6	58.0±21.7	93.8±34.2	<0.001
APACHE-IV predicted mortality	9961	0.170±0.200	0.142±0.165	0.450±0.290	<0.001
Day 1					
SOFA score	9961	3.45±3.15	3.03±2.69	7.68±4.19	<0.001
Respiratory SOFA	3119	2.53±1.05	2.43±0.97	2.91±1.05	<0.001
Coagulation SOFA	9300	0.33±0.64	0.31±0.61	0.54±0.85	<0.001
Hepatic SOFA	2651	0.36±0.74	0.60±0.97	0.32±0.68	<0.001
Cardiovascular SOFA	9942	1.25±0.89	1.15±0.76	2.22±1.35	<0.001
Central nervous system SOFA	9673	0.35±0.94	0.26±0.78	1.33±1.66	<0.001
Renal SOFA	9429	0.83±1.12	0.74±1.05	1.76±1.36	<0.001
Day 2 SOFA score	6792	2.94±2.77	2.62±2.42	6.56±3.72	<0.001
Maximum day 1–2 SOFA score	9961	3.71±3.22	3.27±2.74	8.15±4.17	<0.001
Mean day 1–2 SOFA score	9961	3.19±2.87	2.77±2.36	7.39±3.98	<0.001
Change in SOFA (day 1 to day 2)	6792	−0.76±2.21	−0.74±2.09	−0.94±3.28	0.1779

Continued

Table 1. Continued

Variable	No. With Available Data	Overall (n=9961)	Hospital Survivors (n=9404)	Nonsurvivors (n=893)	*P* Value (Survivors vs Deaths)
Day 1 SOFA <2	9961	3579 (35.9)	3525 (38.9)	54 (6.0)	<0.001
Increasing day 2 SOFA	6792	1334 (19.6)	1171 (18.8)	163 (29.5)	<0.001
Admission systolic blood pressure, mm Hg	9911	123.1±26.2	124.1±25.9	112.9±28.2	<0.001
Admission diastolic blood pressure, mm Hg	9606	69.4±17.0	69.9±16.7	64.2±19.1	<0.001
Admission mean blood pressure, mm Hg	9606	83.5±18.1	84.1±17.6	77.8±21.1	<0.001
Admission heart rate, bpm	9912	82.1±23.4	81.4±23.2	89.5±23.6	<0.001
Admission shock index, bpm/mm Hg	9911	0.70±0.27	0.68±0.26	0.83±0.29	<0.001
Admission respiratory rate	9574	18.4±5.7	18.2±5.6	20.8±6.4	<0.001
Admission oxygen saturation, %	9908	95.7±6.0	96.1±5.1	92.1±11.3	<0.001

Data are presented as mean±SD or number (percentage). APACHE indicates Acute Physiology and Chronic Health Evaluation; BMI, body mass index; bpm, beats per minute; CICU, cardiac intensive care unit; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; LOS, length of stay; and SOFA, Sequential Organ Failure Assessment.

Data were available to calculate the cardiovascular, coagulation, central nervous system, and renal SOFA subscores in >90% of patients, whereas data to calculate the respiratory and liver SOFA subscores were available in fewer than one third of patients (Table 1). Each of the individual SOFA organ subscores was higher in patients who died in the hospital (all $P<0.001$), and each SOFA organ subscore was a univariate predictor of hospital mortality (all $P<0.001$). The distribution of day 1 SOFA subscores for each organ system in the overall population is shown in Figure 5; the distribution of organ system subscores differed between hospital survivors and nonsurvivors ($P<0.001$ by χ^2 test). The cardiovascular and renal SOFA subscores had the highest odds ratio and AUROC values for hospital mortality using the original data,

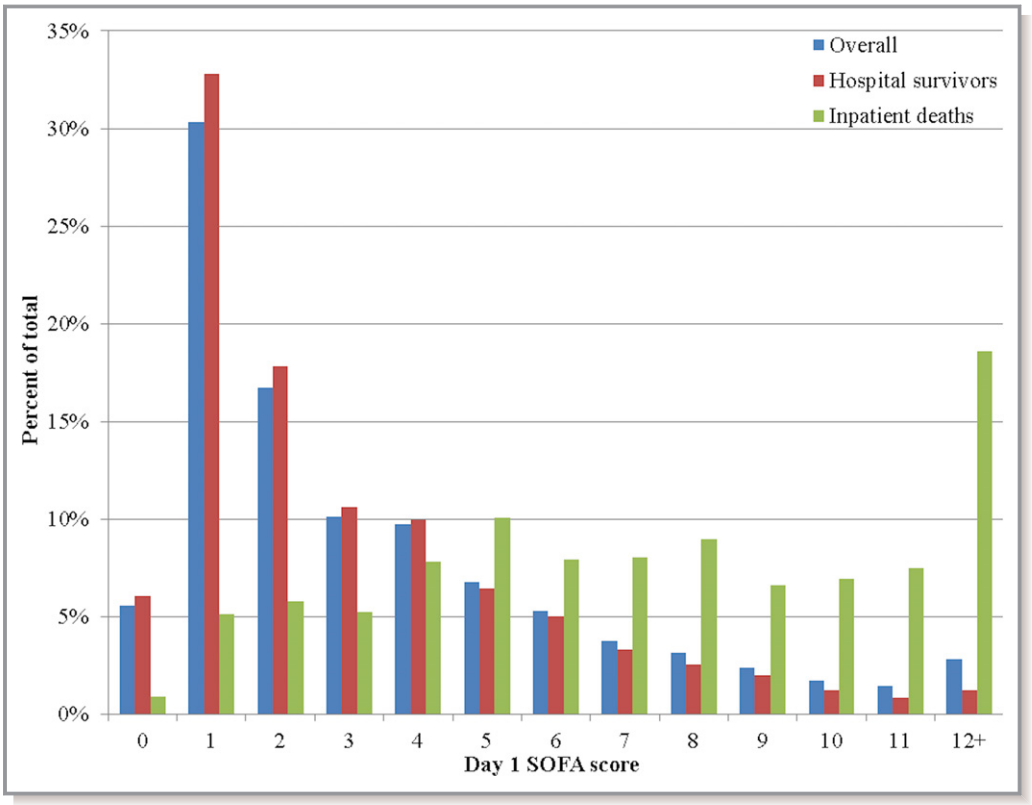

Figure 1. Distribution of day 1 Sequential Organ Failure Assessment (SOFA) scores, as a percentage of overall population, hospital survivors, and inpatient deaths. $P<0.001$ between groups.

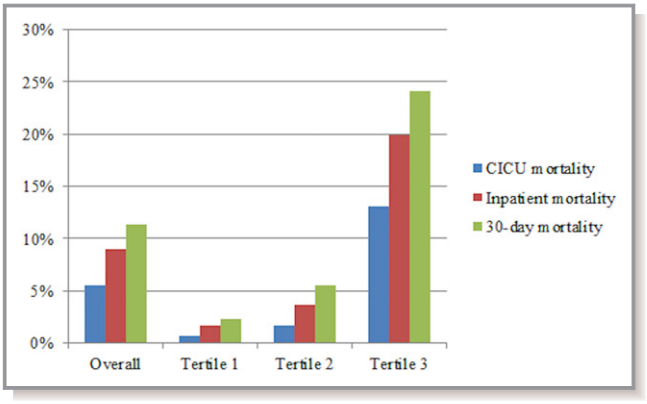

Figure 2. Short- and intermediate-term mortality as a function of day 1 Sequential Organ Failure Assessment (SOFA) score tertile. Tertile 1 includes patients with day 1 SOFA score <2, tertile 2 includes patients with day 1 SOFA score of 2 to 3, and tertile 3 includes patients with day 1 SOFA score ≥4. *P*<0.001 between groups. CICU indicates cardiac intensive care unit.

and the respiratory and cardiovascular SOFA subscores had the highest odds ratio and AUROC values when missing subscore data were imputed as normal (Table 4).

Hospital discharge disposition was available for 6328 of hospital survivors (69.7%): home in 4643 (73.4%), long-term care facility in 1375 (21.7%), rehabilitation facility in 150 (2.4%), and acute-care hospital in 93 (1.5%). A total of 2934 (32.4%) of 9068 hospital survivors died during a median follow-up of 1.64 years (25th–75th percentile, 0.25–4.17); 2326 hospital survivors (25.6%) had follow-up of <1 year. Patients with a day 1 SOFA score <2 had higher long-term postdischarge survival by Kaplan-Meier analysis (*P*<0.001 by log-rank test). Increasing tertile of day 1 SOFA score was associated with lower long-term postdischarge survival by Kaplan-Meier analysis (Figure 6; *P*<0.001 by log-rank test).

Discussion

This is the largest study examining the prognostic value of SOFA scores for short- and long-term mortality in a contemporary CICU population, demonstrating a continuous increase in mortality as a function of increasing day 1 SOFA score. Day 1 SOFA score had good discrimination for short-term mortality, and the discriminative ability was further improved by using the maximum and mean SOFA scores over the first 2 to 3 CICU days. The day 1 SOFA score had similar discrimination for short-term mortality compared with the APACHE-III and APACHE-IV scoring models. Patients with increasing SOFA scores between day 1 and day 2 had an increased risk of short-term mortality. The cardiovascular and

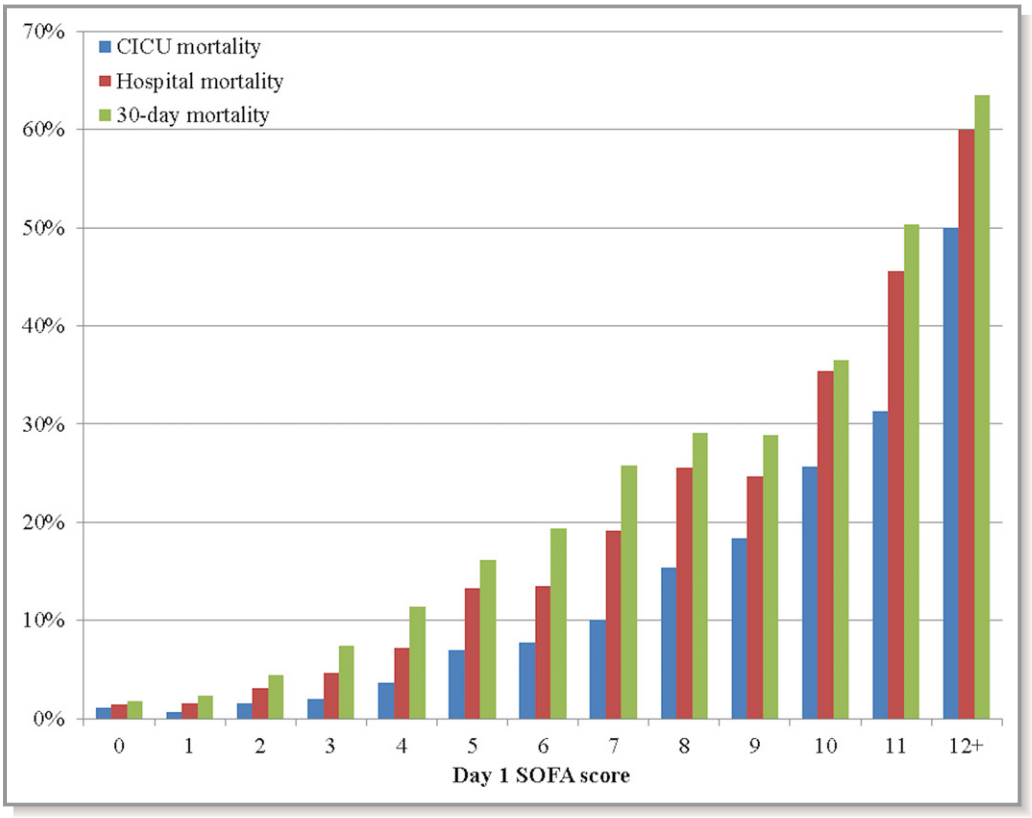

Figure 3. Short-term mortality stratified by day 1 Sequential Organ Failure Assessment (SOFA) score. CICU indicates cardiac intensive care unit.

Table 2. Univariate Analysis of SOFA and APACHE Scores for Prediction of Short-Term Mortality

	CICU Mortality				Hospital Mortality			
Variable	Unit OR	95% CI	AUROC	95% CI	Unit OR	95% CI	AUROC	95% CI
Day 1 SOFA	1.441	1.408–1.476	0.852	0.835–0.870	1.417	1.389–1.446	0.828	0.813 to 0.843
Day 2 SOFA	1.498	1.448–1.551	0.857	0.835–0.878	1.455	1.415–1.498	0.821	0.803 to 0.840
Maximum day 1–2 SOFA	1.472	1.437–1.509	0.867	0.850–0.883	1.435	1.406–1.465	0.837	0.822 to 0.851
Mean day 1–2 SOFA	1.545	1.504–1.589	0.876	0.860–0.892	1.517	1.482–1.553	0.847	0.833 to 0.861
Maximum day 1–3 SOFA score	1.489	1.453–1.527	0.875	0.859–0.891	1.444	1.415–1.475	0.842	0.828 to 0.857
Mean day 1–3 SOFA score	1.596	1.552–1.644	0.886	0.870–0.901	1.569	1.531–1.610	0.856	0.842 to 0.869
Maximum day 1–7 SOFA score	1.498	1.462–1.537	0.881	0.865–0.897	1.452	1.422–1.483	0.849	0.835 to 0.863
APACHE-III	1.049	1.046–1.052	0.847	0.829–0.865	1.047	1.044–1.050	0.823	0.808 to 0.838
APACHE-IV	179.1	130.3–247.5	0.859	0.843–0.876	141.5	107.0–188.0	0.834	0.820 to 0.849

Daily SOFA scores were only available for patients remaining in the CICU for at least part of a given day. APACHE indicates Acute Physiology and Chronic Health Evaluation; AUROC, area under the receiver-operator characteristic curve; CI, confidence interval; CICU, cardiac intensive care unit; OR, odds ratio; and SOFA, Sequential Organ Failure Assessment.

renal SOFA subscores were the strongest predictors of mortality among the SOFA organ subscores. Patients without significant organ failure (ie, SOFA score <2) on CICU day 1 were at low risk for death during hospitalization and long-term follow-up after hospital discharge. Stratification of hospital survivors by tertiles of day 1 SOFA score demonstrated significant differences in long-term survival.

These results demonstrate the utility of the SOFA score for mortality prediction in patients in the CICU, even without considering other potentially relevant prognostic variables, such as age and diagnosis.[12] The SOFA score can adequately risk stratify complex or undifferentiated patients in the CICU, even if disease-specific risk scores continue to be useful in patients with clearly defined disease processes.[7,8] Progressive organ failure (as reflected by an increase in SOFA scores between day 1 and day 2) predicted higher mortality. The maximum and mean SOFA score over the first 2 to 3 CICU days had greater discrimination when compared with the day 1 SOFA score alone; mean daily SOFA scores were superior to maximum daily SOFA scores in our population.[12] Therefore, the day 1 SOFA score provides useful early risk prediction; subsequent SOFA scores can be assessed each day to provide improved risk stratification, with the mean daily SOFA score providing the best discrimination for patients remaining in the CICU for multiple days. In addition, the change in SOFA score over time provides useful data on the progression of organ failure and clinical response to therapy. The increased risk associated with an elevated SOFA score on CICU day 1 persisted throughout follow-up, and even minimal organ failure (day 1 SOFA score ≥2) increased the risk of death at all time points.

Although it is tempting to suggest that the SOFA score can help in clinical decision making about the need for aggressive intervention or candidacy for advanced therapies by identifying patients at high risk of death, caution is warranted when applying population-based risk scores to individual patients.[9] If confirmed prospectively, the low short-term mortality risk conferred by a low day 1 SOFA score (<2) may imply that a subset of these patients could be safely cared for outside of a CICU setting. Long-term survival was lower for hospital survivors with higher tertiles of day 1 SOFA score, showing the relevance of organ dysfunction for determining long-term outcomes.

The only other published study we identified examining the SOFA score in patients in the CICU was recently reported by Argyriou et al.[14] This small study of 300 patients in the CICU from Greece during 2010 through 2012 showed excellent discrimination of the day 1 SOFA score for CICU mortality (AUROC, 0.88) and hospital mortality (AUROC, 0.90), compared with AUROC values in the present study of 0.85 and 0.83, respectively.[14] Similar to our study, Argyriou et al demonstrated equivalent discrimination for day 1 SOFA score and the older APACHE-II score.[14] The population in the study by Argyriou et al had double the prevalence of acute coronary syndromes (two thirds versus one third in our population), and a markedly higher mortality rate both in the CICU (18.3% versus 5.6%) and hospital (23.7% versus 9.1%), despite a modestly higher mean SOFA score (4.1 versus 3.5).[14] Unlike the study by Argyriou et al,[14] we examined long-term outcomes, allowing us to report a novel association between day 1 SOFA score and postdischarge survival.

A prior study by Janssens et al reported on the predictive value of the SOFA score in 303 medical patients in the ICU with predominantly cardiovascular disorders; although this was not a true CICU population, the reported AUROC value of 0.82 for day 1 SOFA as a predictor of hospital mortality is similar to the value observed in our study.[22] The AUROC values for day 1 SOFA and maximum and mean day 1 to 3

Table 3. Baseline Characteristics and Outcomes of Patients Based on Change in SOFA Score From Day 1 to Day 2

Variable	No Change in SOFA (n=2301)	Decreasing SOFA (n=3157)	Increasing SOFA (n=1334)	Left CICU on Day 1 (n=3169)	*P* Value
Age, y	66.7±15.1	68.0±15.1	68.2±14.9	67.2±15.5	0.0040
Female sex	888 (38.6)	1166 (36.9)	489 (36.7)	1189 (37.5)	0.5717
White race	2144 (93.2)	2937 (93.0)	1221 (91.5)	2899 (91.5)	0.0295
Admission source					<0.001
Procedural laboratory	925 (40.2)	1077 (34.1)	571 (42.8)	1394 (44.0)	
Transfer	653 (28.4)	977 (31.0)	380 (28.5)	703 (22.2)	
Emergency department	340 (14.8)	492 (15.6)	169 (12.7)	392 (12.4)	
Floor	332 (14.4)	509 (16.1)	175 (13.1)	583 (18.4)	
Other	51 (2.2)	102 (3.2)	39 (2.9)	97 (3.1)	
Prior myocardial infarction	467 (20.3)	643 (20.4)	289 (21.8)	573 (18.2)	0.0216
Prior heart failure	400 (17.4)	747 (23.7)	254 (19.1)	548 (17.5)	<0.001
Prior diabetes mellitus	671 (26.8)	989 (31.4)	384 (28.9)	833 (26.4)	<0.001
Prior lung disease	415 (18.1)	632 (20.1)	259 (19.5)	629 (19.9)	0.2589
Prior cancer	469 (20.4)	719 (22.8)	282 (21.2)	651 (20.6)	0.0992
Prior stroke	263 (11.4)	422 (13.4)	159 (12.0)	383 (12.1)	0.1560
Prior moderate-severe CKD	415 (18.1)	781 (24.8)	254 (19.1)	571 (18.1)	<0.001
CCI	5.4±3.2	6.0±3.4	5.7±3.2	5.5±3.4	<0.001
BMI, kg/m^2	29.4±7.1	29.7±7.1	29.4±6.7	29.4±7.2	0.2639
CICU LOS, d	3.1±5.5	3.3±4.8	3.8±6.2	0.7±0.3	<0.001
Hospital LOS, d	7.7±10.7	9.5±16.9	9.6±14.7	5.7±8.9	<0.001
Invasive ventilator use	180 (7.8)	840 (26.6)	251 (18.8)	334 (10.5)	<0.001
Invasive ventilator use, d	0.26±1.51	0.62±1.83	0.62±1.94	0.03±0.13	<0.001
Noninvasive ventilator use	304 (13.2)	712 (22.6)	246 (18.4)	227 (7.2)	<0.001
Noninvasive ventilator use, d	0.21±0.92	0.28±0.97	0.33±1.22	0.02±0.09	<0.001
Vasopressor/inotrope use on CICU day 1	930 (29.5)	192 (14.4)	439 (13.9)	209 (9.0)	<0.001
CRRT use	31 (1.4)	68 (2.2)	59 (4.4)	9 (0.3)	<0.001
APACHE-III score	55.4±19.3	69.4±26.4	60.5±22.6	57.5±26.8	<0.001
APACHE-IV predicted mortality	0.124±0.145	0.233±0.228	0.164±0.182	0.141±0.197	<0.001
Day 1 SOFA score	2.32±2.17	5.07±3.34	2.82±2.68	2.91±3.10	<0.001
Day 2 SOFA score	2.32±2.17	2.60±2.68	4.80±3.08	NA	<0.001
Maximum day 1+day 2 SOFA score	2.32±2.17	5.07±3.34	4.79±3.08	2.91±3.10	<0.001
Mean day 1+day 2 SOFA score	2.32±2.17	3.84±2.89	3.81±2.80	2.91±3.10	<0.001
Change in SOFA score (day 1 to day 2)	0.00±0.00	−2.47±1.80	1.97±1.38	NA	<0.001
Maximum week 1 SOFA score	2.65±2.52	5.19±3.42	5.13±3.34	2.91±3.10	<0.001
Day 1 SOFA score <2	1162 (50.5)	428 (13.6)	567 (42.5)	1422 (44.9)	<0.001
Admission systolic blood pressure, mm Hg	123.7±24.8	120.8±27.2	125.6±26.5	123.9±26.2	<0.001
Admission heart rate, bpm	80.6±22.3	83.6±23.8	83.3±24.7	81.0±23.0	<0.001
Admission shock index, bpm/mm Hg	0.68±0.26	0.73±0.27	0.69±0.27	0.68±0.27	<0.001
Admission oxygen saturation, %	96.2±4.8	95.3±6.2	95.8±5.7	95.7±6.7	<0.001

Patients without a day 2 SOFA score are classified as "left CICU on day 1." *P* values are for the χ^2 test (categorical variables) or ANOVA (continuous variables). APACHE indicates Acute Physiology and Chronic Health Evaluation; BMI, body mass index; bpm, beats per minute; CCI, Charlson Comorbidity Index; CICU, cardiac intensive care unit; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; LOS, length of stay; NA, not applicable; and SOFA, Sequential Organ Failure Assessment.

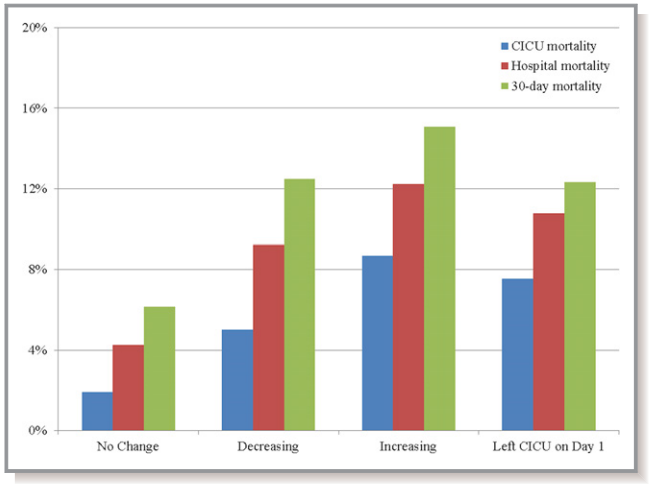

Figure 4. Short-term mortality as a function of change in Sequential Organ Failure Assessment (SOFA) score from day 1 to day 2. Patients without a day 2 SOFA score are classified as "left cardiac intensive care unit (CICU) on day 1." $P<0.001$ between groups.

SOFA scores in the present study are compatible with those reported in prior studies in other ICU populations, as reviewed by Minne et al.[12] Minne et al found superior discrimination for APACHE scores compared with SOFA score, whereas we demonstrated equivalent discrimination for day 1 SOFA score compared with both APACHE-III and APACHE-IV.[12] The good discrimination provided by the SOFA score in this CICU population likely reflects the ability of the SOFA score to differentiate the large majority of low-risk patients with single-organ dysfunction from the important minority of truly critically ill patients with multiorgan failure who account for most hospital deaths. In addition, the 2 major forms of organ failure in the CICU, cardiovascular and renal, are strongly associated with mortality and readily identified by the respective SOFA subscores.

The most important advantages of the SOFA score remain the simplicity and ease of use, allowing calculation at the bedside, with mortality discrimination similar to more complex scores.[10,12,14] The SOFA score can be calculated daily, and changes over time have important prognostic relevance.[12,15] Although the SOFA score excludes age and diagnosis- and procedure-related data, the admission diagnosis can contribute substantially to the accuracy of mortality prediction by other models.[9] Nonetheless, AUROC values for hospital mortality in this unselected CICU population compare favorably with those previously reported for the acute coronary syndrome–specific Global Registry of Acute Coronary Events risk score.[7] The organ failure variables included in the SOFA score are reflective of those commonly seen in sepsis and may be less relevant in other critical illnesses. Unlike the

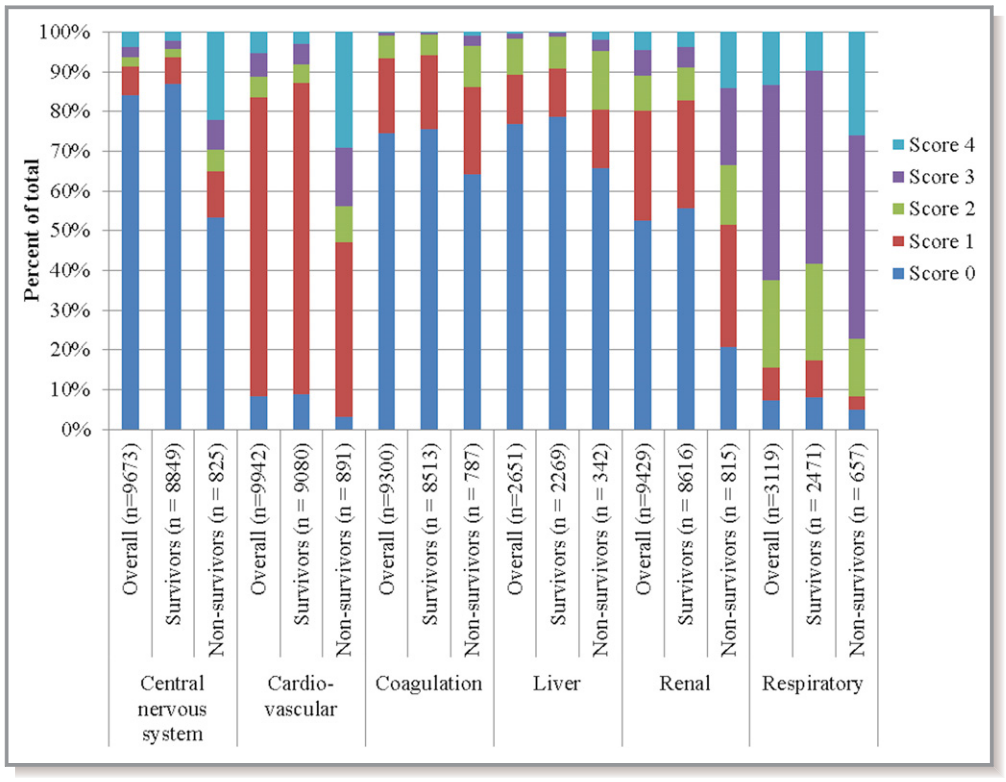

Figure 5. Distribution of day 1 Sequential Organ Failure Assessment organ system subscores in the overall population, hospital survivors, and hospital nonsurvivors ($P<0.001$ between hospital survivors and hospital nonsurvivors).

Table 4. Univariate Analysis of Individual Day 1 SOFA Organ Subscores for Prediction of Short-Term Mortality, as a Function of Whether Missing Data Were Imputed as Normal (Subscore Value of 0)

	WITHOUT Missing Data Imputed as Normal				WITH Missing Data Imputed as Normal			
	CICU Mortality		Hospital Mortality		CICU Mortality		Hospital Mortality	
SOFA Subscore	Unit OR	AUROC	Unit OR	AUROC	Unit OR	AUROC	Unit OR	AUROC
Respiratory	1.861	0.650	1.689	0.637	2.086	0.769	1.952	0.742
Coagulation	1.515	0.561	1.556	0.563	1.386	0.540	1.450	0.546
Liver	1.440	0.563	1.536	0.571	1.777	0.544	1.897	0.546
Cardiovascular	2.875	0.775	2.484	0.720	2.765	0.757	2.421	0.708
Central nervous system	2.137	0.712	1.981	0.680	2.029	0.683	1.906	0.659
Renal	1.888	0.730	1.845	0.721	1.729	0.683	1.722	0.685

AUROC indicates area under the receiver-operator characteristic curve; CICU, cardiac intensive care unit; OR, odds ratio; and SOFA, Sequential Organ Failure Assessment.

APACHE scoring system, the SOFA score was not designed to predict mortality and does not differentiate between acute and chronic organ dysfunction.[9,10] Lack of a specific mortality-prediction algorithm for the SOFA score limits assessment of calibration, which was suboptimal for hospital mortality on the basis of our analysis.[9] We chose not to perform multiple imputation for missing variables to demonstrate the real-world performance of the SOFA score in our population, representing a lower estimate of model discriminative ability.

This single-center, historical, cohort study has several limitations, including unmeasured confounding and potential bias attributable to local practice patterns and a patient population that may be distinct from other centers. CICU and hospital death rates in this study were lower than in prior CICU studies, with a lower rate of acute coronary syndromes than in most prior studies; these factors may influence mortality prediction by the SOFA score.[2,5,6,14] Holland and Moss describe a similar patient population with a significant burden of noncardiac illnesses and a lower proportion of acute coronary syndromes.[6] Serial SOFA scores were only available for patients remaining in the CICU, limiting our assessment of SOFA score changes over time. The variables needed to calculate the SOFA score were not available for all patients, so we imputed the missing variables as normal; in particular, the respiratory SOFA subscore was calculated only for patients with arterial blood gas measurements.[17] This is a significant limitation for interpreting the predictive value of the individual SOFA subscores for mortality, particularly considering the effects of imputing missing data as normal for these subscores. Prior studies have shown that missing variables in prognostic scores for critically ill patients can lead to underestimation of mortality risk.[23] Patient-level admission diagnoses were not available, preventing diagnosis-specific analysis of the predictive performance of the SOFA score. Because of inconsistent documentation, we were unable to obtain Killip classification to calculate the Global Registry of Acute Coronary Events risk score for comparison.[7] Resuscitation status was not available, although this may not substantially affect mortality prediction by APACHE models.[19] The use of electronic health record review to determine patient death may underestimate postdischarge mortality by potentially failing to capture patients dying in other health systems.

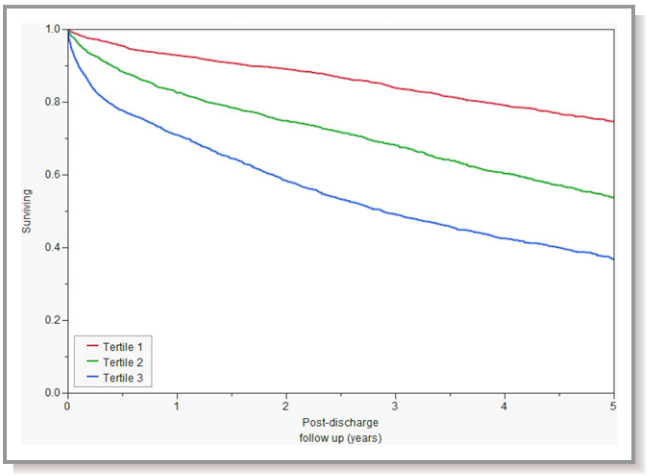

Figure 6. Kaplan-Meier survival curves for hospital survivors, by day 1 Sequential Organ Failure Assessment (SOFA) score tertile. Tertile 1 includes patients with day 1 SOFA score <2, tertile 2 includes patients with day 1 SOFA score of 2 to 3, and tertile 3 includes patients with day 1 SOFA score ≥4. $P<0.001$ between groups by log-rank test.

In conclusion, the SOFA score can be easily applied to modern patients in the CICU using an electronic algorithm. The discrimination of the day 1 SOFA score for short-term mortality was comparable to the APACHE scoring system in this large contemporary cohort of unselected patients in the CICU. Patients with a SOFA score <2 on the first CICU day had a low risk of death during follow-up. Maximum and mean SOFA scores over the first 3 CICU days strongly predicted mortality, and patients with an increasing SOFA score

between CICU day 1 and day 2 were at increased risk of death. Further research is needed to determine the optimal ways to use the prognostic information provided by this established ICU risk score in CICU populations.

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Disclosures

None.

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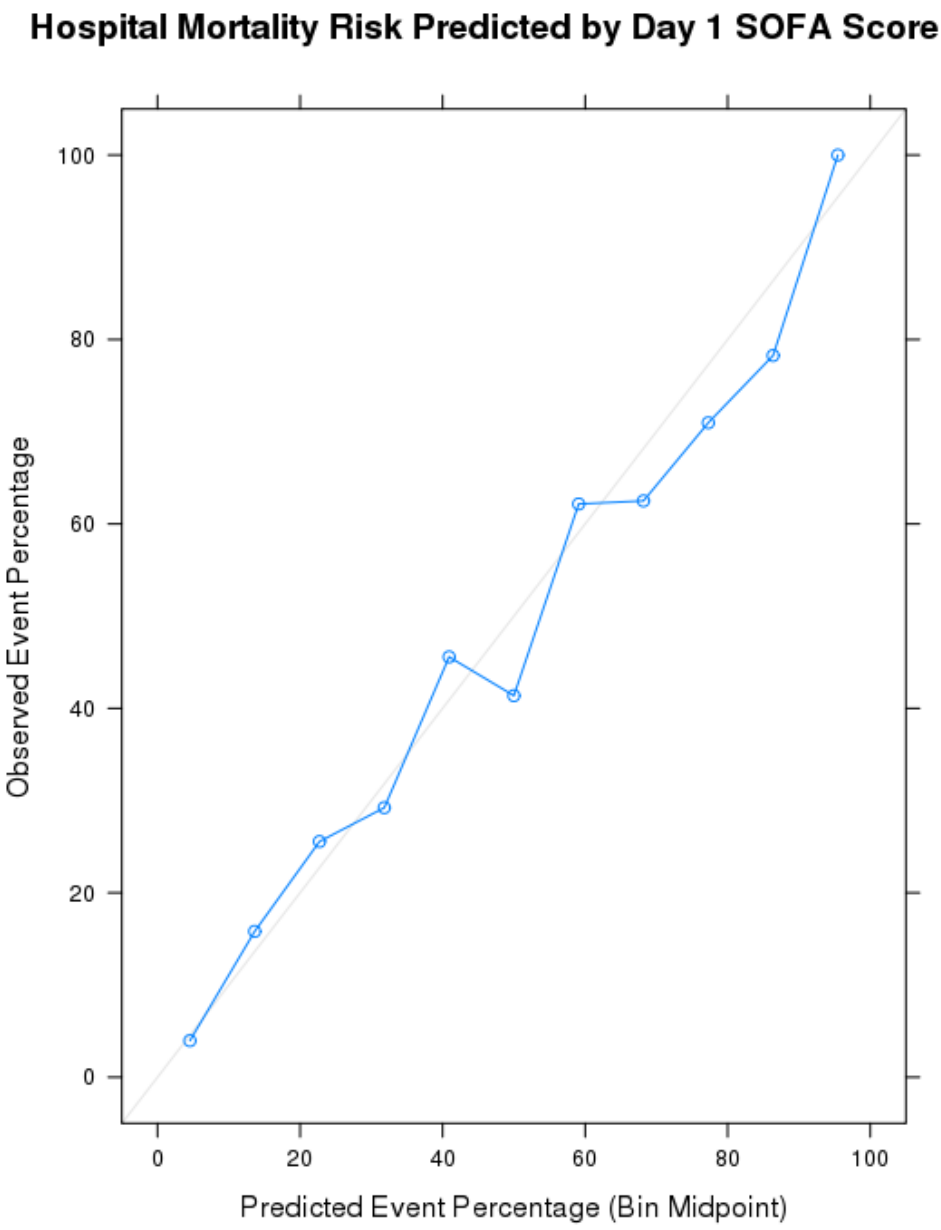
SUPPLEMENTAL MATERIAL

Table S1. Calculating the SOFA score and individual organ sub-scores.

Organ system	Score 0	Score 1	Score 2	Score 3	Score 4
Cardiovascular: Mean arterial pressure (MAP, mmHg) and vasopressors (mcg/kg/min for ≥1 hour)	MAP ≥70	MAP <70 without vasopressors	Dopamine ≤5 or any dobutamine	Dopamine >5, epinephrine ≤0.1 or norepinephrine ≤0.1	Dopamine >15, epinephrine >0.1 or norepinephrine >0.1
Central nervous system: Glasgow Coma Scale (GCS)	15	13-14	10-12	6-9	<6
Coagulation: Platelet count x $10^3/mm^3$	>150	≤150	≤100	≤50	≤20
Liver: Serum bilirubin (mg/dl)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	≥12
Renal: Serum creatinine (mg/dl) and urine output (UOP, ml/day)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or UOP <500	≥5 or UOP <200
Respiratory: Arterial PaO_2:FiO_2 (PF) ratio	>400	≤400	≤300	≤200	≤100

Worst values for each of the 6 organ sub-scores are added for a given day to calculate the total SOFA score for that day. Data derived from Vincent JL, et al. *Intensive Care Med*. 1996;22:707-10.

Figure S1. Observed versus predicted hospital mortality based on probabilities produced by a logistically transformed Day 1 SOFA score.



Based on the Hosmer-Lemeshow statistic, calibration of the Day 1 SOFA score was suboptimal ($p < 0.05$) for hospital mortality. SOFA, Sequential Organ Failure Assessment.