Shock Severity Assessment in Cardiac Intensive Care Unit Patients With Sepsis and Mixed Septic-Cardiogenic Shock

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Abstract

We sought to validate the Society for Cardiovascular Angiography and Interventions (SCAI) cardiogenic shock classification for mortality risk stratification in patients with sepsis and concomitant cardiovascular disease or mixed septic-cardiogenic shock. We conducted a single-center retropective cohort study of cardiac intensive care unit patients with an admission diagnosis of sepsis. We used clinical, vital sign, and laboratory data during the first 24 hours after admission to assign SCAI shock stage. We included 605 patients with a median age of 69.4 years (interquartile range, 57.9 to 79.8 years), 222 of whom (36.7%) were female. Acute coronary syndrome or heart failure was present in 480 patients (79.3%), and cardiogenic shock or cardiac arrest was present in 271 patients (44.8%). The median day 1 Sequential Organ Failure Assessment (SOFA) cardiovascular subscore was 1.5 (interquartile range, 1 to 4), and the admission SCAI shock stage distribution was stage B, 40.7% (246); stage C, 19.3% (117); stage D, 32.9% (199); and stage E, 7.1% (43). In-hospital mortality occurred in 177 of the 605 patients (29.3%) and increased incrementally with higher SCAI shock stage. After multivariable adjustment, admission SCAI shock stage was associated with in-hospital mortality (adjusted odds ratio per stage, 1.46; 95% CI, 1.14 to 1.88; $P=.003$). Admission SCAI shock stage had higher discrimination for in-hospital mortality than the day 1 SOFA cardiovascular subscore (area under the receiver operating characteristic curve, 0.68 vs 0.64; $P=.04$ by the DeLong test). Admission SCAI shock stage was associated with 1-year mortality (adjusted hazard ratio per stage, 1.19; 95% CI, 1.03 to 1.37; $P=.02$). The SCAI shock classification provides improved mortality risk stratification over the day 1 SOFA cardiovascular subscore in cardiac intensive care unit patients with sepsis and concomitant cardiovascular disease or mixed septic-cardiogenic shock.

hock is increasingly prevalent in the cardiac intensive care unit (CICU) and remains associated with substantial mortality.[1-3] Although cardiogenic shock (CS) predominates in the CICU, patients with concomitant sepsis or mixed cardiogenic-vasodilatory shock account for 15% to 20% of CICU patients with shock and have worse outcomes.[1,2,4] The severity of shock is an important predictor of mortality in CICU patients and in patients with sepsis, providing incremental risk stratification on top of standard severity of illness risk scores.[5,6] Shock severity can be quantified using the Sequential Organ Failure Assessment (SOFA) cardiovascular subscore[5,7,8] or the Society for Cardiovascular Angiography and Interventions (SCAI) shock

classification.[4,9-16] The SCAI shock classification was developed to grade the severity of CS, and unlike the SOFA cardiovascular subscore that was developed for sepsis, the SCAI shock classification incorporates the clinical trajectory and response to therapy.[7,16] The SCAI shock classification provides consistent mortality risk stratification in critically ill patients with underlying acute cardiac disease, including CICU patients and patients with CS.[4,9-15,17,18] Although the clinical manifestations of shock may overlap regardless of the etiology, it remains uncertain whether the SCAI shock classification framework can be used to grade the severity of other forms of shock. Accordingly, we applied the SCAI shock classification to CICU patients with sepsis and

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concomitant cardiovascular disease or mixed septic-cardiogenic shock and compared its mortality risk stratification to the day 1 SOFA cardiovascular subscore.

PATIENTS AND METHODS

The Mayo Clinic Institutional Review Board approved this retrospective cohort study (IRB #16-000722) as minimal risk. We identified consecutive unique Mayo Clinic CICU patients treated from January 1, 2007, to December 31, 2015, with an admission diagnosis of sepsis or septic shock from a previously constructed database.[4,5,9,10,12-14,17-20] Demographic characteristics, clinical data, vital signs, laboratory values, in-hospital mortality, and inpatient treatments and procedures were extracted from the medical record electronically.[3-5,9,10,14,17-19] Admission diagnoses were defined as all *International Classification of Diseases, Ninth Revision* codes documented within 1 day of CICU admission; these codes were not mutually exclusive, and the primary admission diagnosis could not be confirmed.[19] The Acute Physiology and Chronic Health Evaluation (APACHE) III score, SCAI shock stage, day 1 total SOFA score, day 1 SOFA cardiovascular subscore, and systemic inflammatory response syndrome (SIRS) criteria were assigned using previously validated algorithms incorporating data from the first 24 hours of CICU admission.[4,5,9,10,19,20] All patients with an admission diagnosis of sepsis or septic shock were assigned to SCAI shock stage B if they did not meet criteria for hypoperfusion, and the use of vasopressors was added as a criterion to define hypoperfusion (Supplemental Table 1, available online at http://www.mcpiqojournal.org); late deterioration was defined as increasing vasopressor requirements after 24 hours.[9,10]

The primary outcome was all-cause in-hospital mortality, and secondary outcomes were survival at 1 and 5 years after CICU admission. Variables were compared across SCAI shock stages by regression (linear regression for continuous variables and logistic regression for categorical variables) using SCAI shock stage as a continuous variable. Correlations between continuous variables were assessed using Spearman rank-order correlation coefficients; SCAI shock stage was treated as a continuous variable. Area under the receiver operating characteristic curve (AUC; C statistic) values were used to assess discrimination and were compared using the DeLong test. Odds ratio (OR) and 95% CI values for prediction of in-hospital mortality were generated using logistic regression after multivariable adjustment for relevant predictors of in-hospital mortality including age; comorbidities; APACHE-III score; admission Glasgow Coma Scale score; admission Braden scale score; use of invasive ventilator, dialysis, pulmonary artery catheter, Impella(R) (Abiomed, Danvers, MA) or extracorporeal membrane oxygenation device; in-hospital cardiopulmonary resuscitation; and admission diagnosis of cardiac arrest (Supplemental Table 2, available online at http://www.mcpiqojournal.org). Survival at 1 and 5 years was evaluated using Kaplan-Meier curves, with groups compared using the log-rank test. Hazard ratio and 95% CI values for prediction of 1-year mortality were generated using Cox proportional hazards analysis after similar multivariable adjustment. Survival analyses were performed initially in the overall cohort and then repeated in hospital survivors only. Statistical analyses were performed using JMP Pro, version 14.1 (SAS Institute).

RESULTS

Study Population

Among the 10,004 unique CICU patients in the database, 605 (6.0%) had an admission diagnosis of sepsis or septic shock and were included in our study. The median age was 69.4 years (interquartile range, 57.9 to 79.8 years), and 222 (36.7%) were female (Table); the median APACHE-III score was 78 (62 to 99), and the median day 1 SOFA cardiovascular subscore was 1.5 (1 to 4). Concomitant admission diagnoses included heart failure or acute coronary syndrome in 480 patients (79.3%) and CS or cardiac arrest in 271 patients (44.8%) (Table). A total of 359 patients (59.3%) required vasopressors, and SIRS criteria were present on admission in 408 (67.4%). Within the first 24 hours, blood cultures were obtained in 394 patients (65.1%; 99 of these 394 [25.1%] were positive), and intravenous antibiotics were administered in 465 (76.9%) (Table).
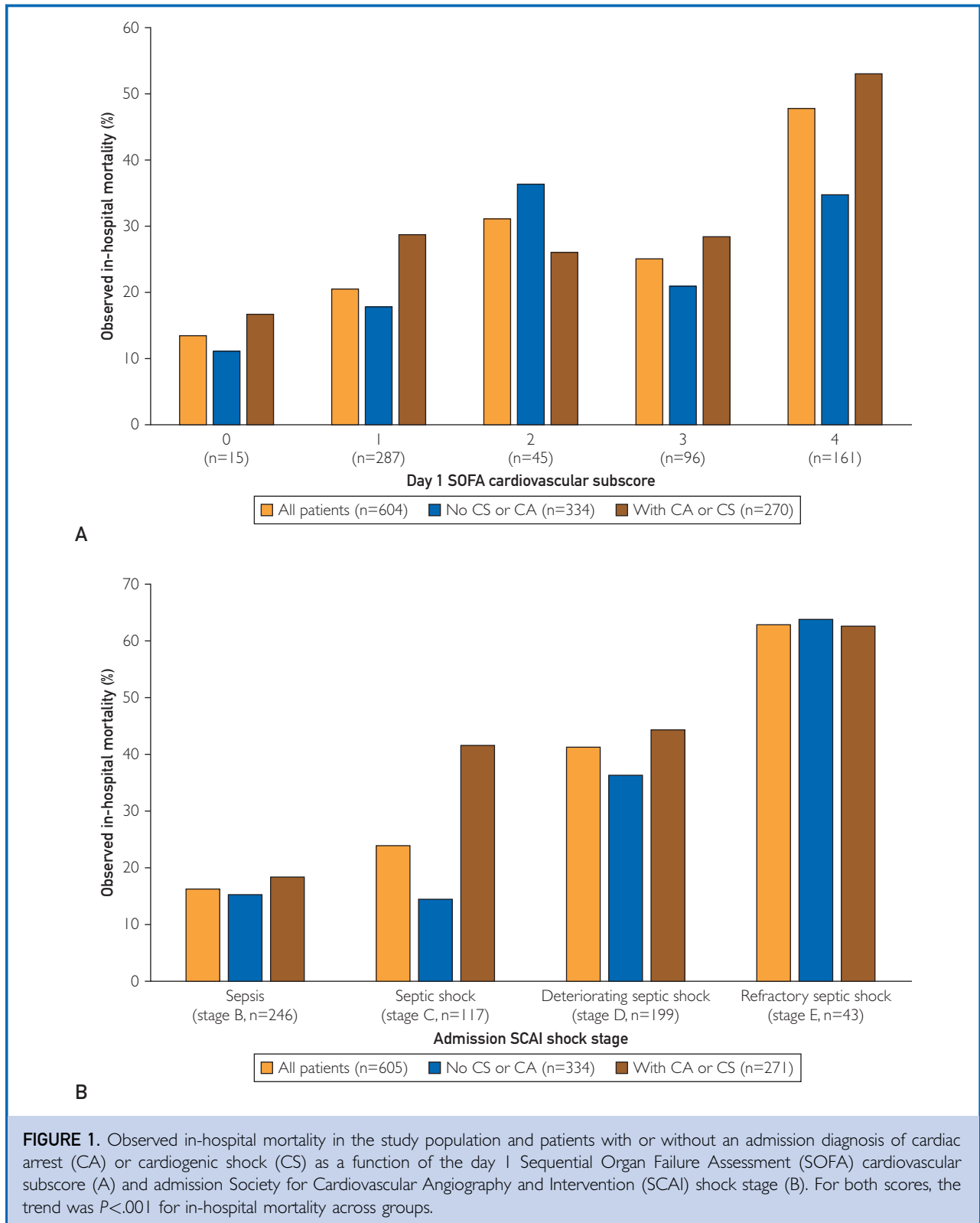
TABLE. Clinical Characteristics of the Study Population Overall and as a Function of SCAI Shock Stage[a,b]

Variable	Overall (N=605)	SCAI stage B (n=246)	SCAI stage C (n=117)	SCAI stage D (n=199)	SCAI stage E (n=43)
Age (y)	69.4 (57.9-79.8)	68.1 (57.4-77.8)	72.5 (60.9-83.6)	69.3 (57.4-79.1)	72.6 (56.2-80.9)
Female sex	222 (36.7)	77 (31.3)	49 (41.9)	83 (41.7)	13 (30.2)
White	549 (90.7)	227 (92.3)	102 (87.2)	185 (93.0)	35 (81.4)
Charlson comorbidity index	2 (1-5)	2.5 (1-5)	2 (1-5)	2 (1-4)	1 (0-4)
APACHE-III score[c]	78 (62-99)	66 (54-79)	76 (63.5-90)	97 (71-116)	108 (96-140)
Day 1 SOFA score[c]	7 (4-10)	5 (2-7)	6 (4-8)	10 (7-13)	11 (9-15)
SOFA cardiovascular subscore[c]	1.5 (1-4)	1 (1-1)	1 (1-2)	4 (3-4)	4 (3-4)
0-1	302 (49.9)	187 (76.0)	87 (74.4)	27 (13.6)	1 (2.3)
2	45 (7.4)	15 (6.1)	11 (9.4)	16 (8.0)	3 (7.0)
3	96 (15.9)	25 (10.3)	8 (6.8)	54 (27.1)	9 (20.9)
4	161 (26.6)	18 (7.3)	11 (9.4)	102 (51.3)	30 (69.8)
No. of noncardiovascular organ failures[c]	1 (0-1)	0 (0-1)	1 (0-1)	1 (1-2)	2 (1-2)
SIRS criteria on admission[c]	408 (67.4)	145 (58.9)	83 (70.9)	147 (73.9)	33 (76.7)
Admission GCS[c]	15 (8-15)	15 (14-15)	15 (11-15)	10 (5-15)	8 (3-15)
Admission Braden score[c]	15 (12-18)	16 (14-19)	15 (13-18)	13 (11-16)	12 (10-16)
Late deterioration[c]	136 (22.5)	43 (17.5)	25 (21.4)	61 (30.7)	7 (16.3)
Admission lactate (mmol/L)[c]	1.9 (1.2-3.3)	1.3 (1-1.7)	2.3 (1.5-3.5)	2.6 (1.5-3.8)	9.6 (2.5-12.5)
Estimated GFR (mL/min)[c]	46.8 (28.9-69.2)	55.7 (36.0-79.6)	43.3 (24.5-61.6)	37.6 (23.6-62.5)	36.4 (21.5-53.8)
LVEF (%)[c]	45 (28-60)	45 (30-60)	50 (33-63)	41.5 (26.2-59.8)	35.5 (21-56.8)
Mechanical ventilation[c]	287 (47.4)	75 (30.5)	35 (29.9)	141 (70.9)	36 (83.7)
Vasoactive drug infusion					
Any[c]	374 (61.8)	97 (39.4)	46 (39.3)	188 (94.5)	43 (100.0)
>1[c]	260 (43.0)	58 (23.6)	21 (18.0)	142 (71.4)	39 (90.7)
Dialysis[c]	104 (17.2)	24 (9.8)	11 (9.4)	58 (29.2)	11 (25.6)
IABP[c]	99 (16.4)	33 (13.4)	6 (5.1)	45 (22.6)	15 (34.9)
Impella/ECMO	21 (3.5)	9 (3.7)	1 (0.9)	7 (3.5)	4 (9.3)
PA catheter[c]	105 (17.4)	30 (12.2)	5 (4.3)	57 (28.6)	13 (30.2)
PCI	143 (23.6)	56 (22.8)	25 (21.4)	54 (27.1)	8 (18.6)
In-hospital CPR	28 (4.6)	9 (3.7)	5 (4.3)	7 (3.5)	7 (16.3)
Antibiotics within 24 h	465 (76.9)	174 (70.7)	86 (73.5)	168 (84.4)	37 (86.0)
Blood cultures					
Sent within 24 h[c]	394 (65.1)	147 (59.8)	78 (66.7)	136 (68.3)	33 (76.7)
Positive[c]	99 (16.4)	43 (17.5)	20 (17.1)	33 (16.6)	3 (7.0)
Endocarditis[c]	114 (18.8)	63 (25.6)	18 (15.4)	31 (15.6)	2 (4.7)
Urinary tract infection	69 (11.4)	30 (12.2)	16 (13.7)	20 (10.0)	3 (7.0)
Pneumonia/influenza	193 (31.9)	89 (36.2)	34 (29.1)	57 (28.6)	13 (30.2)
Cardiac arrest[c]	128 (21.2)	30 (12.2)	27 (23.1)	54 (27.1)	17 (39.5)
Cardiogenic shock[c]	212 (35.0)	61 (24.8)	22 (18.8)	103 (51.8)	26 (60.5)
Respiratory failure[c]	355 (58.7)	122 (49.6)	49 (41.9)	150 (75.4)	34 (79.1)
Acute coronary syndrome[c]	234 (38.7)	86 (35.0)	44 (37.6)	82 (41.2)	22 (51.2)
Heart failure[c]	401 (66.3)	155 (63.0)	70 (59.8)	148 (74.4)	28 (65.1)

[a]APACHE, Acute Physiology and Chronic Health Evaluation; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation device; GCS, Glasgow Coma Scale; GFR, glomerular filtration rate; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; PA, pulmonary artery; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Interventions; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

[b]Data are presented as No. (percentage) for categorical variables and median (interquartile range) for continuous variables. Variables were compared across SCAI shock stages by regression (linear regression for continuous variables and logistic regression for categorical variables) using SCAI shock stage as a continuous variable.

[c]$P<.05$ for regression across the SCAI shock stages.

FIGURE 1. Observed in-hospital mortality in the study population and patients with or without an admission diagnosis of cardiac arrest (CA) or cardiogenic shock (CS) as a function of the day 1 Sequential Organ Failure Assessment (SOFA) cardiovascular subscore (A) and admission Society for Cardiovascular Angiography and Intervention (SCAI) shock stage (B). For both scores, the trend was *P*<.001 for in-hospital mortality across groups.

SCAI Shock Stage

Among the 605 total patients, the admission SCAI shock stage distribution was stage B, 246 (40.7%); stage C, 117 (19.3%); stage D, 199 (32.9%); and stage E, 43 (7.1%). Late deterioration after 24 hours occurred in 136 patients (22.5%). Clinical characteristics varied by SCAI shock stage (Table), reflecting increasing illness severity in patients with higher SCAI shock stages. The admission SCAI shock stage correlated moderately with the day 1 SOFA cardiovascular subscore (Spearman correlation coefficient, 0.61; $P<.001$) and APACHE-III score (Spearman correlation coefficient, 0.51; $P<.001$). Most patients with admission SCAI shock stage B/C had a day 1 SOFA cardiovascular subscore of 0 to 1, and most patients with admission SCAI shock stage D/E had a day 1 SOFA cardiovascular subscore of 4 (Table).

In-Hospital Mortality

In-hospital mortality occurred in 177 of the 605 patients (29.3%). In-hospital mortality increased incrementally with a higher day 1 SOFA cardiovascular subscore (unadjusted OR per 1 point higher, 1.46; 95% CI, 1.28 to 1.67; $P<.001$; Figure 1 A) or higher admission SCAI shock stage (unadjusted OR per 1 stage higher, 1.99; 95% CI, 1.65 to 2.40; $P<.001$ [Figure 1 B]), with a similar association in patients with and without a diagnosis of either CS or cardiac arrest. Admission SCAI shock stage had higher discrimination for in-hospital mortality than the day 1 SOFA cardiovascular subscore (AUC, 0.68 [95% CI, 0.64 to 0.72] vs 0.64 [95% CI, 0.59 to 0.69]; $P=.04$ by DeLong test). Admission SCAI shock stage had discrimination for in-hospital mortality similar to the APACHE-III score (AUC, 0.72 [95% CI, 0.67 to 0.76]; $P=.10$ by DeLong test). Admission SCAI shock stage was incrementally associated with higher in-hospital mortality (adjusted OR per stage, 1.46; 95% CI, 1.14 to 1.88; $P=.003$), but the day 1 SOFA cardiovascular subscore was not (adjusted OR per point, 1.09; 95% CI, 0.91 to 1.31; $P=.34$). Patients with SCAI shock stage D (adjusted OR, 2.12; 95% CI, 1.21 to 3.72; $P=.008$) or E (adjusted OR, 3.05; 95% CI, 1.22 to 7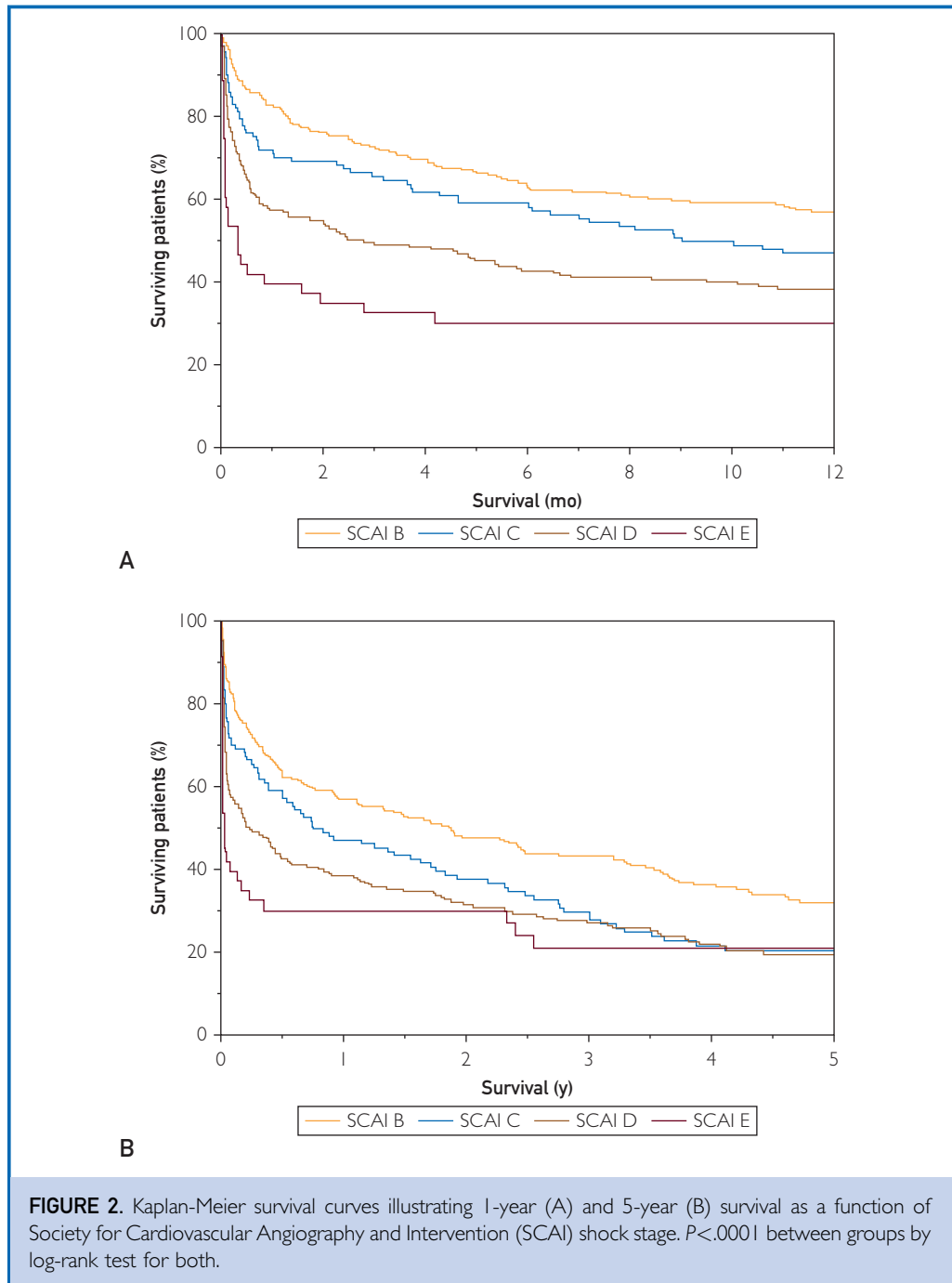.62; $P=.02$) had higher in-hospital mortality than those with SCAI shock stage B, but those with SCAI shock stage C did not (adjusted OR, 1.15; 95% CI, 0.61 to 2.15; $P=.67$). Late deterioration after 24 hours was associated with higher in-hospital mortality (adjusted OR, 1.79; 95% CI, 1.09 to 2.95; $P=.02$), but an admission diagnosis of cardiac arrest was not (adjusted OR, 1.03; 95% CI, 0.57 to 1.85; $P=.92$) (Supplemental Table 2, available online at http://www.mcpiqojournal.org).

Long-term Survival

Among the 428 hospital survivors, 32 (7.5%) had a follow-up duration of less than 1 year. Overall Kaplan-Meier survival estimates were 47.0% 293 of 605) at 1 year and 24.9% (181 of 605) at 5 years; among hospital survivors, 1-year survival was 66.7% (293 of 428) and 5-year survival was 35.3% (181 of 428). Overall, SCAI shock stage provided mortality risk stratification out to 1 year (Figure 2 A; $P<.001$ by log-rank test), although the survival curves converged by 5 years (Figure 2 B). Overall, higher SCAI shock stage was incrementally associated with an increased risk of 1-year mortality (adjusted hazard ratio, 1.19; 95% CI, 1.03 to 1.37; $P=.02$; Supplemental Table 2). Among hospital survivors, the SCAI shock stage did not provide risk stratification at 1 or 5 years by Kaplan-Meier analysis ($P>.10$ by log-rank test).

DISCUSSION

Cardiac intensive care unit patients with sepsis or septic shock have a high risk of in-hospital mortality and poor long-term survival. The SCAI shock classification provides in-hospital mortality risk stratification in CICU patients with sepsis and concomitant cardiovascular disease or mixed septic-cardiogenic shock that is superior to the day 1 SOFA cardiovascular subscore even though the latter was developed to define shock severity in patients with sepsis. These data illustrate that the SCAI shock classification is valid for mortality risk stratification among CICU patients with sepsis and concomitant cardiovascular disease or mixed septic-cardiogenic shock, as in unselected CICU patients and patients with CS.[4,9-15] Although the SCAI shock stage correlated with severity of illness measured using the APACHE-III score in our study, both of these metrics were independently associated with adjusted in-hospital

FIGURE 2. Kaplan-Meier survival curves illustrating 1-year (A) and 5-year (B) survival as a function of Society for Cardiovascular Angiography and Intervention (SCAI) shock stage. $P<.0001$ between groups by log-rank test for both.

mortality. We observed that CICU patients with sepsis who survived to hospital discharge were at substantial risk of subsequent death, but this factor was not meaningfully affected by SCAI shock stage on admission; this finding differs from the CICU population as a whole, in whom a higher SCAI shock stage predicted lower postdischarge survival.[12] Because the clinical manifestations of shock overlap between different etiologies, the SCAI shock classification may be useful to grade the severity of shock more broadly in critical care practice.[16]

The SCAI stages classification has certain advantages over the SOFA cardiovascular subscore, such as incorporating markers of perfusion and clinical trajectory (including the response to therapy) to provide a more refined assessment of shock severity.[7,16] The SOFA cardiovascular subscore has several acknowledged limitations, including lack of integration of noncatecholamine vasopressors, inability to account for the use of multiple vasopressors, use of worst values during the 24 hours, and inclusion of patients with a broad spectrum of illness severity in the highest-risk group.[5,8] Even vasopressor-based metrics such as the vasoactive-inotropic score fail to incorporate clinically relevant trends in patient condition that are integral to the SCAI shock classification.[5,16]

These results are consistent with those of prior studies revealing that a higher SCAI shock stage has been consistently associated with higher adjusted short-term mortality in this CICU cohort, illustrating incremental risk stratification on top of standard severity of illness risk scores in all relevant patient subgroups.[4,9,10,13,18] Prior studies in patients with CS have found that the SCAI shock classification provides short-term mortality risk stratification, including among patients who receive temporary mechanical circulatory support.[10,14,15,18] Notably, none of the risk scores we examined (including the SCAI shock classification and the APACHE-III score) had very good discrimination for in-hospital mortality, consistent with prior observations in patients with sepsis both within and outside the CICU; this finding emphasizes the need for development of better risk stratification tools for patients with sepsis.[6,19] The added risk of in-hospital mortality conferred by higher SCAI shock stage appeared to be present predominantly in patients with more severe (SCAI stage D/E) shock. Although the SCAI shock classification may be similarly applicable to septic and cardiogenic shock in which vasoactive drugs are typically used, it may be less relevant for hemorrhagic shock in which vasoactive drugs are not the standard therapy.

This retrospective single-center analysis should be considered hypothesis-generating due to incomplete data regarding relevant hemodynamic variables, perfusion markers, and sepsis therapies; we cannot be certain that all patients had infection or inflammation as opposed to a stress response to cardiac critical illness, and we note that only two-thirds of patients met SIRS criteria on admission.[4] Unexpectedly, we did not observe additional mortality risk stratification based on the presence of an admission diagnosis of cardiac arrest, although this factor has been an important risk modifier when added to the SCAI stages classification in prior studies.[9,13,16] The patients included in this analysis were enrolled more than 5 years ago, and changes in care patterns during the intervening time could affect the association between SCAI shock stage and outcomes in contemporary CICU patients with sepsis. While this factor is a limitation of this analysis, it allowed documentation of the poor long-term outcomes in CICU patients with sepsis; SCAI shock stage provided robust risk stratification for survival out to 1 year overall but not among hospital survivors in the current study.[12]

CONCLUSION

We propose that the SCAI shock stages classification can be used to grade the severity of shock and provide mortality risk stratification among CICU patients with sepsis and concomitant cardiovascular disease or mixed septic-cardiogenic shock, allowing a more refined assessment of circulatory failure than the SOFA cardiovascular subscore. The SCAI stages classification should be evaluated in broader populations of patients with isolated sepsis and septic shock.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

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