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Validation of SCAI Shock Staging in Critically Ill Medical Intensive Care Unit Patients With Sepsis and Septic Shock

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Abstract

Purpose: **This study evaluated the predictive value of SCAI shock staging for mortality in patients with sepsis and septic shock admitted to the medical ICU.**

Materials and methods: **This is a single-center historical cohort study. We analyzed data for adults (≥18-year-old) admitted to the medical ICU at Mayo Clinic St. Mary's campus with sepsis between June 1, 2018, and December 31, 2021. Sepsis was identified using the Sepsis-III criteria. Patients were stratified based on SCAI shock staging. Our primary outcome was all-cause 30-day mortality.**

Results: **We identified 3079 eligible adult patients with sepsis or septic shock. The distribution of SCAI shock stages A through E was 9%, 12%, 25%, 49%, and 5%, respectively. The overall 30-day mortality was 24%. There was progression in all outcomes including ICU, hospital and 30-day mortality across SCAI shock stages. However, only SCAI shock stages D and E, had statistically significant adjusted HRs of 1.6 and 3, respectively. When compared to SOFA score, SCAI shock staging performed similarly in predicting ICU mortality with no statistically significant difference in AUCs, *p*-value of 0.07.**

Conclusions: **Our results support the use of SCAI shock staging in critically ill medical patients with sepsis and septic shock for risk stratification. We propose that the SCAI shock staging may be used as a universal system for grading the severity of shock in critically ill patients regardless of etiology.**

Keywords: Critical care, Sepsis, Shock, Risk stratification, SCAI, Score, Mortality

1. Introduction

Sepsis is a life-threatening organ dysfunction that can be attributed to dysregulated host response to infection. The profound circulatory, cellular, and metabolic abnormalities that characterize septic shock may increase mortality in a subset of patients with sepsis.[1] Septic shock is a significant cause of death in critically ill patients.[2,3] The mortality rates in septic shock remain high despite advances in diagnostic and treatment strategies and are likely due to increased disease severity.[2,3] While a recent meta-analysis reported that the 30-day mortality rate in septic shock is as high as 35%, the mortality risk varies widely in any cohort of patients with sepsis depending on disease severity. Increased vasopressor requirements in the first 24 h after the onset of septic shock are associated with increased mortality.[4-6] Furthermore, sepsis is often associated with transient cardiac dysfunction, which leads to higher mortality.[7,8]

For the past 25 years, the severity of septic shock has typically been quantified using the Sequential Organ Failure Assessment (SOFA) score, which was proposed by consensus in 1996.[9] Recognition of suboptimal characterization of septic shock by

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the SOFA score has led to efforts to develop improved tools for grading septic shock severity.[10] In 2019, the Society for Cardiovascular Angiography and Intervention (SCAI) published a 5-stage classification of cardiogenic shock, which emphasized the presence of hypoperfusion and integrated multiple markers of shock severity. SCAI shock staging has been shown to predict mortality in the cardiac intensive care unit (ICU) in multiple studies.[11-15] It has been hypothesized that SCAI shock staging is not specific to cardiogenic shock, and can be used to quantify the severity of other forms of shock. Accordingly, SCAI shock staging was also validated in the cardiac ICU in patients with sepsis and concomitant cardiovascular (CV) disease or mixed septic-cardiogenic shock.[16]

This study evaluated the predictive value of SCAI shock staging for mortality in patients with sepsis and septic shock admitted to the medical ICU (*see* **Supplementary Material** (Journal of Community Hospital Internal Medicine Perspectives: EdiKit) *for the modified protocol*).

2. Material and methods

This single-center historical cohort study was reviewed and approved by the Mayo Clinic Institutional Review Board (IRB), and informed consent was waived owing to the minimal-risk nature of the study. Patients who declined authorization for observational research studies were excluded from the study based on Minnesota State laws.

2.1. Data source

Data were extracted from the Mayo Clinic ICU Data Mart, which contains real-time demographic, clinical, and administrative data for all patients admitted to the ICUs at the Mayo Clinic. The data were extracted using structured query language (SQL) queries and validated using real-time electronic medical records (EMR).

2.2. Study population

We extracted data for all adult patients (≥18-year-old) admitted to the medical ICU at Mayo Clinic St. Mary's campus with sepsis between June 1, 2018, and December 31, 2021. The medical ICU is a closed 32-bed unit serving critically ill medical patients; surgical, postoperative, oncology, transplant, cardiovascular, and extracorporeal membrane oxygenation (ECMO) patients are served in different units. Sepsis was identified using the Sepsis-III criteria (Table 1). The Quick Sequential Organ Failure Assessment (qSOFA) score was calculated for each medical ICU admission. Patients with a qSOFA score ≥2 and suspected or documented source of infection were included in the study cohort. As a surrogate for infection, we used initiation of intravenous antibiotics or a positive blood culture obtained within 6 h before or after ICU admission. For patients with multiple medical ICU encounters during the same hospitalization, only the first encounter was considered in the analysis.

Abbreviations

ALT	Alanine Transaminase
ANOVA	Analysis of Variance
APACHE	Acute Physiology and Chronic Health Evaluation
APS	Acute Physiology Score
AUC	Area Under the Curve
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CI	Confidence Interval
CV	Cardiovascular
DBP	Diastolic Blood Pressure
ECMO	Extracorporeal Membrane Oxygenation
EMR	Electronic Medical Records
Hg	Hemoglobin
HR	Hazard Ratio/Heart Rate
ICD-10-CM	International Classification of Diseases, 10th Revision, Clinical Modification
ICU	Intensive Care Unit
IRB	Institutional Review Board
LOS	Length of Stay
MAP	Mean Arterial Pressure
NEE	Norepinephrine Equivalents
OR	Odds Ratio
qSOFA	Quick Sequential Organ Failure Assessment
Ref	Reference
ROC	Receiver Operating Characteristic
RR	Respiratory Rate
RRT	Renal Replacement Therapy
SBP	Systolic Blood Pressure
SCAI	Society for Cardiovascular Angiography and Intervention
SD	Standard Deviation
SOFA	Sequential Organ Failure Assessment
SPSS®	Statistical Package for the Social Sciences
SQL	Structured Query Language
VIS	Vasoactive-Inotropic Score
WBC	White Blood Count

Table 1. Sepsis-III criteria.

Suspected or documented source of infection
AND
At least two of the following:
Systolic blood pressure ≤100 mmHg
Respiratory rate ≥22 bpm
Glasgow coma scale <15

2.3. Study variables

We extracted baseline demographic data, including age, sex, race, and body mass index (BMI). We also evaluated various clinical indicators, including ICU mortality scores (SOFA, APS - Acute Physiology Score III, and APACHE - Acute Physiology and Chronic Health Evaluation III on day 1); SOFA CV sub-score; initial shock index (the ratio of systolic blood pressure to heart rate); in-hospital cardiac arrest; the need for renal replacement therapy (RRT); and the initiation, duration, and form of ventilator support during ICU stay. Baseline vital signs and laboratory data were also reported, including the initial admission values, maximum values during the first hour, and maximum values during the first 24 h of ICU stay. Comorbidities were extracted using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes and were assessed individually, and combined using the 19-point Charlson comorbidity index. Outcome measures included hospital and ICU length of stay (LOS); and 30-day, ICU and hospital mortality. To classify patients based on SCAI shock stages, in addition to vital signs and laboratory workup, we extracted the maximum number of vasopressors, highest norepinephrine equivalent (NEE) dose, and highest Vasoactive-Inotropic Score (VIS) during the first hour and first 24 h of the ICU stay. Vasopressors analyzed to calculate NEE and VIS included norepinephrine, epinephrine, dopamine, phenylephrine, vasopressin, and angiotensin II (*see Supplementary Materials* (Journal of Community Hospital Internal Medicine Perspectives: EdiKit) *for calculations*).

2.4. Statistical analysis

Statistical Package for the Social Sciences (SPSS®) version 27.0 (SPSS Inc., Chicago, IL, U.S.A.) was used to conduct statistical analyses. Descriptive statistics were provided for all the study variables. Continuous variables were reported as mean ± standard deviation (*SD*), and categorical variables were reported as count (percentage). Inferential statistics (χ^2 test for categorical variables and one-way analysis of variance (ANOVA) for continuous variables) were used to assess between-group differences. Statistical significance was set at a two-tailed p-value <0.05. Binary logistic regression analyses were performed to calculate the odds ratios (*OR*) for ICU and hospital mortality based on SCAI shock stages and were reported as *OR* (95% confidence interval [CI]). ORs were also reported after multivariate adjustment for age, sex, comorbidities, requirement for RRT and ventilatory support. Cox regression analysis was used to generate the proportional hazard ratio (*HR*) and 95% *CI* for the 30-day mortality after adjusting for the same variables. Kaplan–Meier curves were constructed as survival functions for 30-day mortality. All cases were censored at 30 days or until death (whichever occurred earlier). Data were grouped according to SCAI shock stage, and the log-rank test was used to assess differences between the groups. Additionally, receiver operating characteristic (ROC) curves were constructed to evaluate the predictive value of SCAI shock staging, SOFA score, and APACHE III score for ICU mortality. The DeLong test was used to compare the differences in the area under the curve (AUC) between the three mortality scores.

2.5. Study primary outcomes

The primary endpoint for this study was the all-cause 30-day mortality.

3. Results

3.1. Study population

We analyzed 10,560 admissions to the medical ICU during the study period. We excluded 7481 patients who were readmitted, did not provide research authorization, or did not have sepsis. Our final study cohort included 3079 adult patients admitted to the medical ICU who met the Sepsis-III criteria. Fig. 1 shows the patient selection flowchart.

3.2. Patient characteristics

Table 2 shows the baseline characteristics of the study cohort. The mean age of the patients was 66 ± 16 years; 1687 (55%) were men and the majority (89%) were white. The average APACHE III score was 92.1 ± 31.6 points, and the predicted hospital mortality based on the APACHE IV score was 42 ± 27%. The most common comorbidity among our study cohort was chronic pulmonary disease (22%), followed by diabetes (19%) and chronic kidney disease (14%). Heart failure was observed in <10% of patients. The average Charlson comorbidity index was 4.5 ± 2.3 points. A total of 1800 (59%) patients required ventilatory support, but only 1285 (42%) received invasive ventilation. The average duration of invasive ventilation was 1.4 ± 4.0 days. In contrast, 461 patients (15%) required RRT. Vasopressors were used in 704 patients (23%) in the first hour following ICU admission and in 1400 individuals (46%) during the first 24 h. Among those

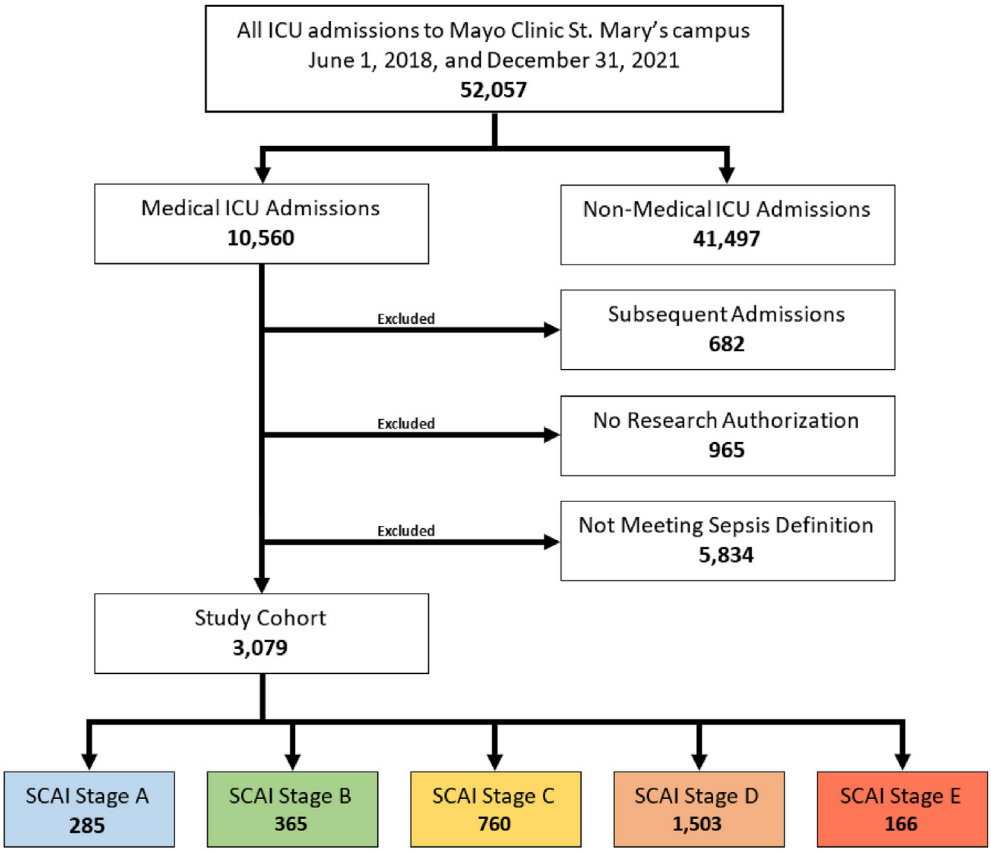

Fig. 1. Patient selection flowchart. ***ICU****, Intensive Care Unit;* ***SCAI****, Society for Cardiovascular Angiography and Intervention.*

requiring vasopressor support, the average NEE dose in the first hour and 24 h were 0.048 ± 0.158 and 0.126 ± 0.265 μg/kg/min, respectively.

3.3. SCAI shock stages

In the study cohort, the distribution of SCAI shock stages A through E was 9%, 12%, 25%, 49%, and 5%, respectively. The differences in ICU mortality scores and derangements in vital signs and baseline laboratory data reflected the progressively increasing severity of illness across SCAI shock stages (Table 2).

3.4. Mortality

Survival analyses showed progressively increasing unadjusted 30-day mortality across all SCAI shock stages A–E. The 30-day mortality rate in stage E was 48%; however, stages A and B were also associated with a mortality rate of approximately 17%. Stages C and D were associated with mortality rates of 19 and 28%, respectively. Hospital and ICU mortality rates were also the highest in stage E and increased exponentially from stages C to E (Fig. 2). The Kaplan–Meier curve (Fig. 3) demonstrated no difference in 30-day survival for SCAI shock stages A and B. However, beyond SCAI shock stage B, there was a progressive decrease in 30-day survival across SCAI shock stages C–E. The difference was statistically significant, with a log-rank p-value <0.001. The curve also revealed that the survival probability for SCAI shock stage E decreased significantly within the first 72 h compared to the other stages. The *OR*s for ICU and hospital mortality also increased across the SCAI shock stages. The *OR*s for stages D and E remained statistically significant even after adjusting for confounders for both outcome measures (**Supplemental Material** (Journal of Community Hospital Internal Medicine Perspectives: EdiKit)).

The unadjusted *HR*s for 30-day mortality in stages D and E were 1.8 and 3.9, respectively. However, when adjusted for other factors, the *HR* for 30-day mortality in stages D and E remained statistically significant at 1.6 and 3.4, respectively (Fig. 4).

3.5. ICU mortality

In the study cohort, the overall ICU mortality rate was 12%. The ICU mortality rate increased progressively across all stages of SCAI shock staging.

Table 2. Baseline characteristics of the study cohort.

Characteristics	SCAI shock stages					Total ($N = 3079$)	*p*-value
	Stage A ($n = 285$)	Stage B ($n = 365$)	Stage C ($n = 760$)	Stage D ($n = 1503$)	Stage E ($n = 166$)		
Age (years)	67 ± 17	64 ± 18	66 ± 17	67 ± 15	60 ± 16	66 ± 16	<0.001*
Sex							
Male	151 (53)	169 (46.3)	450 (59.2)	819 (54.5)	98 (59)	1687 (54.8)	0.001*
Female	134 (47)	196 (53.7)	310 (40.8)	684 (45.5)	68 (41)	1392 (45.2)	
Race							
White	253 (88.8)	331 (90.7)	678 (89.2)	1322 (88)	145 (87.3)	2729 (88.6)	0.540
Asian	5 (1.8)	8 (2.2)	17 (2.2)	35 (2.3)	3 (1.8)	68 (2.2)	
Native	3 (1.1)	1 (0.3)	6 (0.8)	12 (0.8)	1 (0.6)	23 (0.7)	
Black	10 (3.5)	8 (2.2)	21 (2.8)	32 (2.1)	9 (5.4)	80 (2.6)	
Unknown	14 (4.9)	17 (4.7)	38 (5)	102 (6.8)	8 (4.8)	179 (5.8)	
BMI (kg/m^2)	30.4 ± 9.3	29.0 ± 9.6	30.1 ± 10.3	29.8 ± 9.2	29.4 ± 8.6	29.8 ± 9.5	0.341
ICU mortality scores							
SOFA score day 1 (points)	5.0 ± 2.6	4.4 ± 2.6	6.3 ± 3.4	9.1 ± 4.1	11.3 ± 4.6	7.6 ± 4.2	<0.001*
SOFA CV sub-score (points)	0.9 ± 0.6	0.9 ± 0.6	1.5 ± 1.2	2.8 ± 1.3	3.3 ± 1.2	2.1 ± 1.4	<0.001*
APS III score day 1 (points)	61.1 ± 22.4	62.2 ± 21.5	71.3 ± 24.9	86.7 ± 31.6	108.6 ± 37.7	78.8 ± 31.2	<0.001*
APACHE III score (points)	74.5 ± 23.7	74.6 ± 23.1	84.4 ± 25.5	100.6 ± 31.6	119.7 ± 38.5	92.1 ± 31.6	<0.001*
APACHE IV predicted hospital mortality (%)	27 ± 20	27 ± 19	35 ± 23	49 ± 27	62 ± 30	42 ± 27	<0.001*
Ventilatory support	165 (57.9)	164 (44.9)	380 (50)	963 (64.1)	128 (77.1)	1800 (58.5)	<0.001*
Duration (days)	1.2 ± 4.6	0.8 ± 2.3	1.2 ± 3.5	2.2 ± 4.9	1.6 ± 2.4	1.7 ± 4.3	<0.001*
Invasive ventilation	76 (26.7)	86 (23.6)	248 (32.6)	761 (50.6)	114 (68.7)	1285 (41.7)	<0.001*
Duration (days)	0.8 ± 4.4	0.6 ± 2.1	0.9 ± 3.2	2.0 ± 4.7	1.5 ± 2.3	1.4 ± 4.0	<0.001*
Non-invasive ventilation	118 (41.4)	108 (29.6)	208 (27.4)	520 (34.6)	30 (18.1)	984 (32)	<0.001*
Duration (days)	0.4 ± 0.9	0.2 ± 0.6	0.2 ± 0.8	0.3 ± 0.7	0.2 ± 0.6	0.3 ± 0.8	<0.001*
Renal replacement therapy	19 (6.7)	26 (7.1)	99 (13)	270 (18)	47 (28.3)	461 (15)	<0.001*
Outcome measures							
Hospital LOS (days)							
All	9.0 ± 9.5	8.5 ± 7.3	9.6 ± 9.8	11.6 ± 13.0	8.3 ± 10.2	10.3 ± 11.3	<0.001*
Survivals	8.6 ± 8.9	8.3 ± 7.3	9.5 ± 9.7	12.1 ± 13.2	12.1 ± 11.5	10.5 ± 11.3	<0.001*
ICU LOS (days)							
All	3.2 ± 5.3	2.8 ± 4.0	3.3 ± 5.5	5.1 ± 8.1	3.7 ± 4.3	4.1 ± 6.8	<0.001*
Survivals	2.8 ± 3.4	2.6 ± 3.5	3.2 ± 5.5	5.0 ± 8.0	4.8 ± 4.8	4.0 ± 6.6	<0.001*
Pre-ICU LOS (days)	0.7 ± 2.0	0.6 ± 1.8	0.5 ± 2.3	0.7 ± 2.5	0.7 ± 2.3	0.6 ± 2.3	0.723
Transition to comfort care	37 (13)	47 (12.9)	112 (14.7)	355 (23.6)	65 (39.2)	616 (20)	<0.001*
Cardiac arrest	1 (0.4)	1 (0.3)	9 (1.2)	38 (2.5)	18 (10.8)	67 (2.2)	<0.001*
ICU mortality	14 (4.9)	20 (5.5)	48 (6.3)	225 (15)	65 (39.2)	372 (12.1)	<0.001*
Hospital mortality	25 (8.8)	30 (8.2)	86 (11.3)	333 (22.2)	77 (46.4)	551 (17.9)	<0.001*
30-day mortality	47 (16.5)	61 (16.7)	144 (18.9)	416 (27.7)	79 (47.6)	747 (24.3)	<0.001*
Admission vital signs							
RR (breath/min)	22 ± 5	23 ± 6	23 ± 6	23 ± 7	24 ± 6	23 ± 6	0.050
HR (beat/min)	82 ± 11	107 ± 22	99 ± 22	100 ± 23	101 ± 27	99 ± 23	<0.001*
SBP (mmHg)	124 ± 22	116 ± 26	115 ± 27	111 ± 26	103 ± 34	114 ± 27	<0.001*
DBP (mmHg)	72 ± 16	73 ± 20	70 ± 20	68 ± 22	64 ± 29	70 ± 21	<0.001*
MAP (mmHg)	89 ± 15	87 ± 21	85 ± 21	82 ± 22	77 ± 29	84 ± 22	<0.001*
Shock index	0.68 ± 0.14	0.95 ± 0.25	0.90 ± 0.28	0.94 ± 0.29	1.06 ± 0.37	0.91 ± 0.29	<0.001*
Urine output (mL/Kg/hr)	1.7 ± 1.9	1.9 ± 1.8	1.4 ± 1.6	1.3 ± 1.7	1.3 ± 1.6	1.4 ± 1.7	<0.001*
Admission laboratory data							
WBC (x 10^9/L)	12.3 ± 13.8	12.9 ± 8.7	14.0 ± 7.2	14.3 ± 9.0	15.9 ± 9.0	14.0 ± 9.2	<0.001*
Hg (g/dL)	11.0 ± 2.5	11.0 ± 2.3	11.4 ± 2.7	11.1 ± 2.6	10.7 ± 2.9	11.1 ± 2.6	0.004*
BUN (mg/dL)	29.6 ± 23.1	28.4 ± 25.4	33.4 ± 25.7	35.1 ± 26.1	38.9 ± 29.0	33.6 ± 25.9	<0.001*
Creatinine (mg/dL)	1.73 ± 2.07	1.51 ± 1.77	2.00 ± 2.26	1.92 ± 1.87	2.30 ± 2.08	1.89 ± 2.00	<0.001*
Sodium (mmol/L)	137 ± 7	138 ± 6	137 ± 7	137 ± 6	135 ± 8	137 ± 6	<0.001*
Potassium (mmol/L)	4.3 ± 0.8	4.2 ± 0.7	4.3 ± 0.9	4.4 ± 0.9	4.8 ± 1.1	4.4 ± 0.9	<0.001*
Bicarbonate (mmol/L)	26 ± 8	25 ± 7	22 ± 6	22 ± 7	16 ± 7	23 ± 7	<0.001*
Chloride (mmol/L)	100 ± 8	100 ± 7	99 ± 8	100 ± 7	97 ± 9	100 ± 8	<0.001*
Anion gap	13 ± 4	13 ± 4	16 ± 6	15 ± 5	24 ± 9	15 ± 6	<0.001*
Lactate (mmol/L)	1.3 ± 0.4	1.4 ± 0.4	3.2 ± 1.9	2.7 ± 2.0	10.2 ± 5.3	3.1 ± 2.8	<0.001*
Arterial pH	7.37 ± 0.10	7.37 ± 0.09	7.36 ± 0.11	7.33 ± 0.11	7.27 ± 0.14	7.34 ± 0.11	<0.001*
Troponin T (ng/L)	77 ± 134	61 ± 107	114 ± 236	122 ± 317	127 ± 318	111 ± 274	0.049*

(*continued on next page*)

Table 2. (continued)

Characteristics	SCAI shock stages					Total ($N = 3079$)	p-value
	Stage A ($n = 285$)	Stage B ($n = 365$)	Stage C ($n = 760$)	Stage D ($n = 1503$)	Stage E ($n = 166$)		
Serum ALT (IU/L)	45 ± 74	64 ± 194	95 ± 353	97 ± 359	274 ± 600	101 ± 355	<0.001*
Positive blood cultures	205 (71.9)	264 (72.3)	288 (37.9)	631 (42)	72 (43.4)	1460 (47.4)	<0.001*
Vasopressors use							
Initiation during first 1 h	0	0	170 (22.4)	429 (28.5)	105 (63.3)	704 (22.9)	<0.001*
Initiation during first 24 h	0	0	170 (22.4)	1093 (72.7)	137 (82.5)	1400 (45.5)	<0.001*
Max # during first 1 h	0	0	0.3 ± 0.5	0.3 ± 0.6	1.1 ± 1.1	0.3 ± 0.6	<0.001*
Max # during first 24 h	0	0	0.3 ± 0.5	1.1 ± 0.9	1.8 ± 1.2	0.7 ± 0.9	<0.001*
NEE during first 1 h (μg/kg/min)	0	0	0.032 ± 0.083	0.051 ± 0.140	0.287 ± 0.434	0.048 ± 0.158	<0.001*
NEE during first 24 h (μg/kg/min)	0	0	0.032 ± 0.083	0.189 ± 0.281	0.490 ± 0.538	0.126 ± 0.265	<0.001*
VIS during first 1 h (points)	0	0	20.2 ± 85.7	19.6 ± 81.5	124.9 ± 203.4	21.3 ± 89.1	<0.001*
VIS during first 24 h (points)	0	0	20.2 ± 85.7	138.3 ± 199.2	281.6 ± 236.0	87.6 ± 173.7	<0.001*
Comorbidities							
Charlson comorbidity index (points)	4.5 ± 2.4	4.1 ± 2.2	4.5 ± 2.4	4.7 ± 2.3	4.1 ± 2.6	4.5 ± 2.3	<0.001
Coronary artery disease	1 (0.4)	0	1 (0.1)	8 (0.5)	0	10 (0.3)	0.330
Heart failure	24 (8.4)	24 (6.6)	80 (10.5)	149 (9.9)	14 (8.4)	291 (9.5)	0.241
Hypertension	11 (3.9)	12 (3.3)	48 (6.3)	48 (3.2)	9 (5.4)	128 (4.2)	0.008*
Diabetes	62 (21.8)	49 (13.4)	158 (20.8)	280 (18.6)	25 (15.1)	574 (18.6)	0.017*
Chronic pulmonary disease	73 (25.6)	115 (31.5)	150 (19.7)	314 (20.9)	25 (15.1)	677 (22)	<0.001*
Chronic kidney disease	43 (15.1)	34 (9.3)	115 (15.1)	218 (14.5)	14 (8.4)	424 (13.8)	0.015*
Chronic liver disease	14 (4.9)	23 (6.3)	77 (10.1)	171 (11.4)	37 (22.3)	322 (10.5)	<0.001*

Data are presented as mean ± SD or count (percentage).
*p-value <0.05 is considered significant.
SCAI, Society for Cardiovascular Angiography and Intervention; **BMI**, Body Mass Index; **ICU**, Intensive Care Unit; **SOFA**, Sequential Organ Failure Assessment; **SOFA CV**, SOFA Cardiovascular; **APS**, Acute Physiology Score; **APACHE**, Acute Physiology and Chronic Health Evaluation; **LOS**, Length of Stay; **RR**: Respiratory Rate; **HR**, Heart Rate; **SBP**, Systolic Blood Pressure; **DBP**, Diastolic Blood Pressure; **MAP**, Mean Arterial Pressure; **WBC**, White Blood Count; **Hg**, Hemoglobin; **BUN**, Blood Urea Nitrogen; **ALT**, Alanine Transaminase; **NEE**, Norepinephrine Equivalents; **VIS**, Vasoactive-Inotropic Score.

The *AUC* for SCAI shock staging in predicting ICU mortality was 0.668 (95% *CI* 0.651–0.685), p-value <0.001. The *AUC* for SOFA score in predicting ICU mortality was 0.627 (95% *CI* 0.609–0.644), p-value <0.001. The difference in *AUC* between the SCAI shock stages and SOFA score was not statistically significant according to the DeLong test (p-value = 0.07). In contrast, the *AUC* for the APACHE III score was 0.792 (95% *CI* 0.778–0.807), p-value <0.001. Compared to SCAI shock staging, the

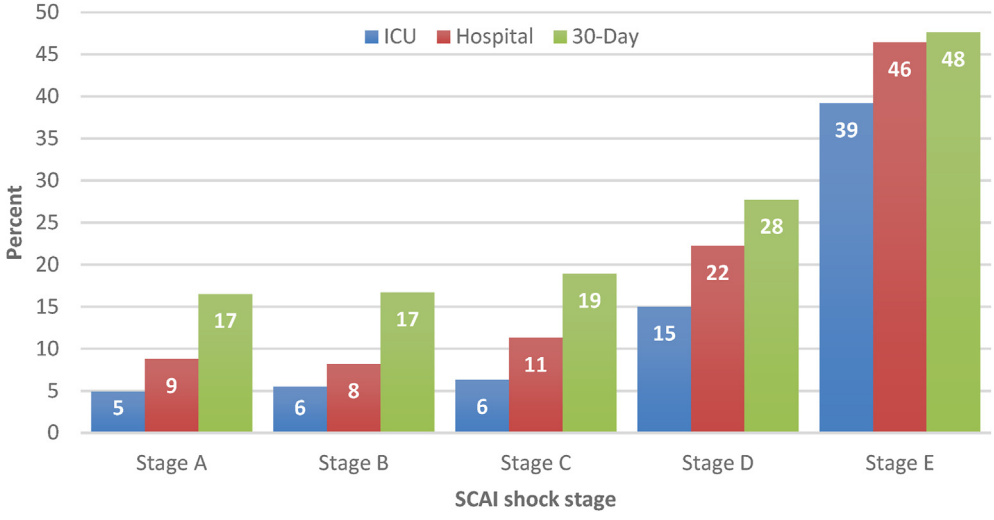

Fig. 2. Mortality by SCAI shock stages. ***ICU****, Intensive Care Unit;* ***SCAI****, Society for Cardiovascular Angiography and Intervention.*

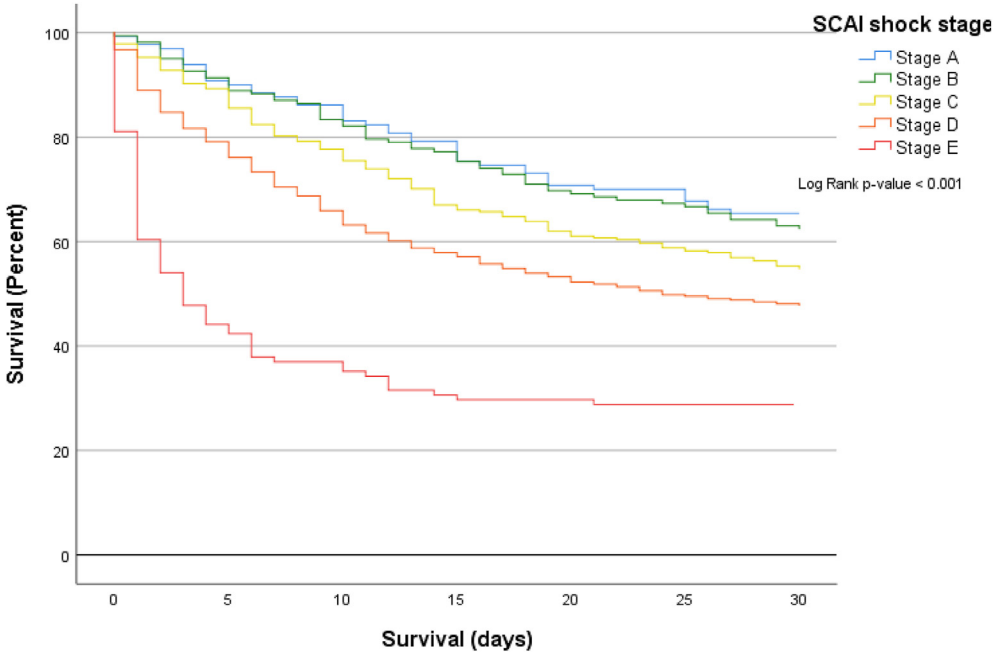

*Fig. 3. Kaplan-Meir curve demonstrating 30-day survival by SCAI shock stages. **SCAI**, Society for Cardiovascular Angiography and Intervention.*

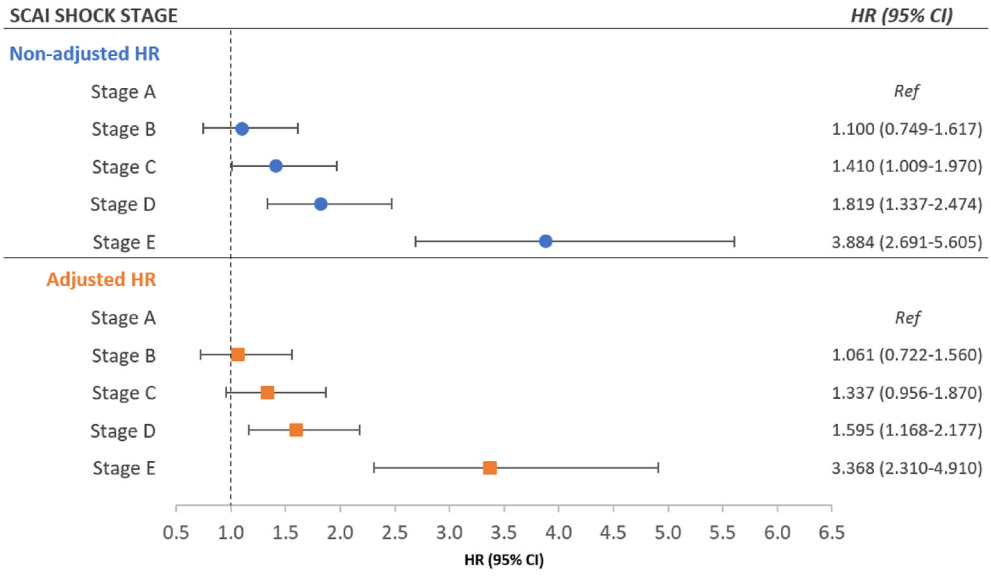

*Fig. 4. Forest tree plot for 30-day mortality based on SCAI shock stages. **SCAI**, Society for Cardiovascular Angiography and Intervention; **HR**, Hazard Ratio; **CI**, Confidence Interval; **Ref**, Reference.*

APACHE score outperformed SCAI shock staging in predicting ICU mortality using the DeLong test (p-value <0.001).

4. Discussion

Our study confirms that SCAI shock staging can effectively stratify patients with sepsis and septic shock, as exemplified by higher 30-day mortality in SCAI shock stages D (Deteriorating) and E (Extremis) than in SCAI shock stage A (At risk). Furthermore, a similar finding was observed for the secondary outcomes of hospital and ICU mortality, where SCAI stages D and E were associated with higher mortality than SCAI stage A. These data highlight the universality of shock severity assessment using SCAI shock staging and suggest that this stratification schema may be utilized across critically ill cohorts.

The 5-stage cardiogenic shock classification scheme was proposed by the Society of Cardiovascular Angiography and Intervention as a scoring scheme with the primary intent of risk stratification for cardiogenic shock. An update was released underscoring the validation of the model, with multiple studies assessing the utilization of this scoring scheme in various phenotypes of shock (cardiogenic shock with and without acute coronary syndrome, including those presenting with out-of-hospital cardiac arrest).[17] Previous studies have confirmed higher mortality in patients with systemic inflammatory response and higher SCAI shock stages in cardiac ICU patients.[12] Our results are very similar to those reported in cardiac ICU patients with sepsis, as the mortality was relatively flat across lower SCAI shock stages and increased substantially in SCAI shock stages D and E; this emphasizes that sepsis can still be associated with a high risk of adverse outcomes, even without manifest shock as we observed a 17% 30-day mortality in SCAI shock stage A. In addition, our study indicates that higher disease severity scores correlate with a higher SCAI shock stage; and yet SCAI shock staging provided additional risk stratification when adjusting for severity of illness.

SCAI shock staging has been shown to predict mortality in the cardiac ICU, even after accounting for the standard severity of illness metrics, as in this analysis.[11] In addition to providing robust risk stratification in cardiogenic shock, the SCAI shock staging also demonstrated a "dose–response relation" with higher SCAI shock stages having higher odds of mortality (Stage E having seven times higher odds of hospital mortality as compared to the reference stage A). To the best of our knowledge, no study has validated SCAI shock staging and risk stratification in the medical ICU population. Based on our findings, SCAI shock staging and outcomes (ICU, hospital, and 30-day mortality) correlate well with the outcomes observed in a different patient population in the cardiac ICU. Patients with sepsis and septic shock often have a component of left ventricular dysfunction that impairs perfusion and can worsen metabolic acidosis.[18-21] Severe metabolic acidosis is associated with a worsening shock state, vasopressor resistance and other critical illness.[22-24] This could be a mechanistic explanation for worse outcomes (ICU and hospital mortality) in higher SCAI shock stages, in addition to more prevalent organ failure. We observed a consistent trend of worsening metabolic acidosis in our cohort of patients (lower serum bicarbonate levels and lower arterial pH) with the up progression in the SCAI shock stage ladder. However, due to the retrospective nature of our study, it remains challenging to ascertain whether severe metabolic acidosis was the cause or effect of a worse shock state. There is a possibility that the patients included in our medical ICU cohort may also have a component of cardiogenic shock[18,25-28] however, no echocardiographic data were reviewed.

Our study had some limitations. First, we present retrospective data from a single academic center. The clinical profile and patient population may not represent the real-world population because of white race predominance and referral for higher disease acuity. Furthermore, approximately 9% of the medical ICU population were excluded due to lack of authorization for observational research studies. The external validity and generalization of these results need further work to be confirmed outside a single-center database. Second, we did not correlate the severity of sepsis or septic shock with echocardiographic features. We did not identify and exclude patients with significant cardiac dysfunction, as some patients may have a combination of both cardiogenic and septic shock.[29-32] Third, the retrospective nature of the study limits the inference of causality that a higher SCAI shock stage "causes" higher mortality. However, it has face validity in that a more severe shock results in worse outcomes. The effect size and adjusted OR of >3 for hospital and ICU mortality signify a stronger association than what could be explained just by chance. The long-term outcomes need to be further explored.

Despite these limitations, our study has several strengths. This is the first study to assess SCAI shock staging performance as a stratification tool in a medical ICU population with sepsis and septic shock compared to the previously available literature, predominantly from cardiac ICUs. The large sample size of our cohort and robust statistical modeling legitimized the results. Our results are relevant to the current times when resource allocation and risk stratification are crucial to balance bed utilization in medical ICUs. In addition, it can be utilized as a beneficial tool for shared decision-making with patients and their families, especially with the aging US population and the higher burden of critical illness.[33,34] Future work should focus on validating these findings in a multi-centric fashion and in multi-disciplinary ICUs to strengthen the external validity and generalizability of these results.

5. Conclusion

Our results support the use of SCAI shock staging in critically ill medical patients with sepsis and

septic shock for risk stratification and as a valuable tool for shared decision-making with patients and their families. The SCAI shock staging performed similar to the SOFA score on predicting ICU mortality. We propose that the SCAI shock staging may be used as a universal system for grading the severity of shock in critically ill patients regardless of etiology and based on our analysis is equivalent to the SOFA score for risk stratification. Future multi-center and multidisciplinary ICU studies are required to validate these findings and improve external validity.

Conflict of interest

The authors reported no potential conflicts of interest.

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