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Prospective Comparison of Four Noninvasive Bedside Predictors of Mortality in Sepsis and Septic Shock

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Abstract

Sepsis stands as a critical bodily dysfunction triggered by infection and remains a primary threat to public health worldwide. Detecting it early is frequently hampered by its vague initial presentation. While simple bedside metrics—including the shock index, diastolic shock index, capillary refill time (CRT), and mottling score (MS)—allow clinicians to monitor blood flow stability and estimate survival odds, their relative accuracy has not been directly compared. This paper analyzes how effectively these four instruments forecast patient mortality at three distinct intervals: 24 hours, 7 days, and 28 days. A prospective, single-center tracking study was executed between January and September 2024. The trial enrolled adult subjects (aged ≥18 years) who displayed signs of infection and a National Early Warning Score-2 of ≥5. Researchers recorded baseline characteristics, physiological signs, and initial CRT and MS values at admission, and subsequently monitored survival status at 24 hours, 7 days, and 28 days. The final analysis tracked 135 subjects (median age: 85 years; interquartile range: 79–90 years; 44.4% female). Fatality rates reached 15.6% within the first day, 25.2% by the first week, and 35.6% at four weeks. For immediate 24-hour survival tracking, CRT yielded the strongest predictive accuracy (area under the curve [AUC], 0.829; 95% confidence interval [CI], 0.755–0.889). Meanwhile, MS proved most accurate for intermediate outcomes at 7 days (AUC = 0.732; 95% CI = 0.646–0.806) and 28 days (AUC = 0.749; 95% CI = 0.662–0.823). Direct statistical comparisons between pairs showed no major differences in performance. Even though no single metric proved significantly superior to the rest, all four noninvasive examinations offer valuable insight for estimating survival probabilities during sepsis. CRT appears best suited for rapid, immediate risk tiering, whereas MS tracks more closely with mid-term clinical trajectories, supporting the routine use of both metrics during initial medical workups.

Keywords: Capillary refill time, Diastolic shock index, Mottling score, Sepsis, Septic shock

Introduction

Sepsis describes a perilous state of organ failure brought on by a corrupted internal response to an infectious agent [1]. According to the Sepsis-3 international guidelines, this condition is identified when an active infection triggers a sudden increase in the Sequential Organ Failure Assessment (SOFA) score, indicating acute organ dysfunction [1]. Septic shock represents an advanced stage of this illness, marked by dangerously low blood pressure that persists even after aggressive fluid replenishment, dramatically driving up the likelihood of dying in the hospital [1, 2].

The global burden of this condition is massive; data indicate it strikes over 30 million individuals annually, causing roughly 6 million deaths across the globe. In wealthier nations, the overall fatality rate hovers between 15% and 30%, but it climbs to over 50% in resource-limited regions [3, 4]. These statistics highlight the urgent need for reliable methods to swiftly identify and early manage [5].

Spotting sepsis early and predicting its course remain major hurdles for frontline medical staff. The illness often starts quietly, presenting with ambiguous warning signs that mimic mild ailments. This frequently leads to

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dangerous treatment delays, making it vital to establish structured pathways for prompt identification to save lives. Modern care protocols emphasize rapid action, instructing emergency staff to screen vulnerable individuals for physiological indicators of sepsis within the opening hours of their arrival [2]. Yet, despite improved diagnostic definitions and the rollout of standardized triage protocols like the National Early Warning Score-2 (NEWS-2), delayed recognition remains a persistent issue in high-volume emergency rooms. Consequently, a large percentage of patients still arrive with advanced tissue damage, keeping overall illness and death rates stubbornly elevated [2, 5].

To address these diagnostic delays, noninvasive monitoring tools have become essential assets for tracking septic individuals at the bedside. These practical options—the shock index (SI), diastolic SI (DSI), capillary refill time (CRT), and mottling score (MS)—permit medical teams to rapidly gauge a patient's circulatory function and tissue perfusion [6–9]. The SI, calculated by dividing the heart rate by the systolic blood pressure, reveals immediate cardiovascular strain [6]. The DSI modifies this concept by focusing on diastolic pressure to sharpen the predictive precision of the calculation [7]. The medical literature suggests that both SI and DSI can flag circulatory failure before clear, severe hypotension sets in [6, 7]; however, a thorough evaluation comparing their performance side-by-side has been lacking. Separately, CRT measures peripheral blood flow and has been directly linked to in-hospital survival in critically ill populations [8]. Finally, the MS grades skin discoloration to reveal microcirculatory collapse [9]. Each technique helps clinicians identify deteriorating patients early, enabling faster medical intervention.

While these noninvasive tests have demonstrated merit individually, no rigorous research has compared their performance in predicting sepsis fatalities across short- and long-term windows. This investigation was therefore designed to measure and contrast the predictive accuracy of the SI, DSI, CRT, and MS regarding 24-hour, 7-day, and 28-day mortality in septic cohorts. By running direct pairwise comparisons of these metrics, we aimed to identify which examination provides the highest clinical utility during the earliest phases of emergency care. Ultimately, this data seeks to guide clinical choices and optimize survival outcomes for individuals battling sepsis and septic shock.

Materials and Methods

Ethics statement

This protocol received formal approval from the Ethics Committee of the Area Vasta Emilia Centro (Protocol No. 301/2023/Oss/AOUFe). Researchers secured written informed consent from all participants or their legal proxies before enrollment. The study adhered strictly to the ethical mandates established by the institutional review board on human subjects research as well as the 1975 Declaration of Helsinki.

Study design and setting

This prospective, noninterventional observational study was conducted at a single tertiary medical facility from January through September 2024. The hosting hospital maintains approximately 600 beds and an emergency department that handles more than 70,000 annual patient presentations. To be enrolled, patients had to fulfill the following criteria: (1) age ≥18 years; (2) clinical suspicion of an active infection; (3) a triage NEWS-2 score of ≥5; and (4) signed consent from the patient (or from family members if the patient's critical health state prevented them from providing it). Sepsis diagnoses were validated using standard Sepsis-3 criteria [1]. The NEWS-2 threshold was used for screening because it is widely accepted in modern medicine for flagging early sepsis risk [2, 5].

The dataset included age, biological sex, and core vital signs (systolic and diastolic blood pressure, pulse rate, breathing rate, blood oxygen saturation, supplemental oxygen delivery, body temperature, and level of consciousness), along with baseline CRT and MS measurements. Sepsis-related fatalities at 24 hours, 7 days, and 28 days were confirmed using official hospital charts. All noninvasive metrics (SI, DSI, CRT, MS) were recorded during the initial emergency room evaluation, before any medical treatments were initiated. CRT was tested by compressing the finger tip for 5 seconds and timing the return of normal skin color [8]. Skin mottling was evaluated using an established five-tier system **(Figure 1)** [9], though consistency among observers was not assessed in this trial. Notably, the MS was checked exclusively on the front of the knee, mirroring the protocol of the original validation paper [9]. While the knee provides a highly consistent and easy-to-access area for tracking, mottling is a systemic issue that can also appear on the hands, feet, or torso. This localized approach may lower the test's sensitivity in individuals with unusual blood flow patterns or darker skin tones, where discoloration is naturally harder to spot. Future studies should evaluate multiple skin sites to help improve overall diagnostic accuracy.

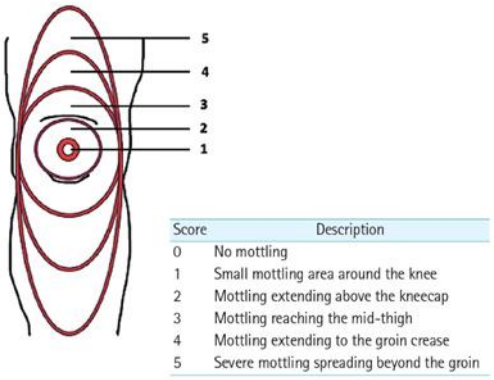


Figure 1. A graphical representation of the mottling score. As the severity increases, in-hospital mortality rises accordingly.

Statistical analysis

Continuous parameters are reported as medians with corresponding interquartile ranges (IQRs), whereas counts and percentages are used to represent categorical data. To evaluate differences between two distinct, unpaired cohorts, the Mann-Whitney test was used for continuous variables, and the chi-square test was used to analyze the distribution of categorical variables. Correlations between pairs of continuous metrics were explored using Spearman's rank correlation coefficients. To account for prospective clinical confounders, a multivariable logistic regression model targeting 24-hour mortality was generated to adjust for age, the Charlson Comorbidity Index [CCI], and changes in mental status. A separate multivariable logistic regression model evaluated the same endpoints, controlling for baseline SOFA scores and circulating lactate levels. The discriminative power of each diagnostic score was calculated using the area under the curve (AUC) derived from a receiver operating characteristic (ROC) graph. Direct statistical comparisons between pairs of ROC curves were performed using the DeLong method.

To provide a deeper exploration of how these noninvasive bedside clinical assessments perform, several secondary statistical models were created. First, the Youden index was used to determine the optimal diagnostic cutoffs for the SI, DSI, CRT, and MS to predict survival at 24 hours, 7 days, and 28 days. Working from these operational thresholds, researchers determined the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall predictive accuracy for each metric. Additionally, the interactions among the four bedside assessments were examined using a Kendall tau-b correlation analysis to determine whether these instruments capture overlapping biological processes or represent unique physiological axes. Finally, a subgroup analysis by age was conducted, stratifying participants into four age groups: < 65, 65–75, 75–85, and > 85 years. Because no deaths occurred in the cohort aged under 65 years, calculating comparative survival outcomes for that specific age group was impossible. All computations were performed using Jamovi version. 2.5 (the jamovi project) and MedCalc version. 19.8 (MedCalc Software Ltd).

Results and Discussion

A total of 135 individuals were prospectively enrolled in the investigation; the median age of this cohort was 85 years (IQR, 79–90 years), and 60 (44.4%) of the participants were female. The observed mortality rates were 15.6% at 24 hours, 25.2% at 7 days, and 35.6% at 28 days. Additional baseline specifications and tracking records are organized in **Table 1**.

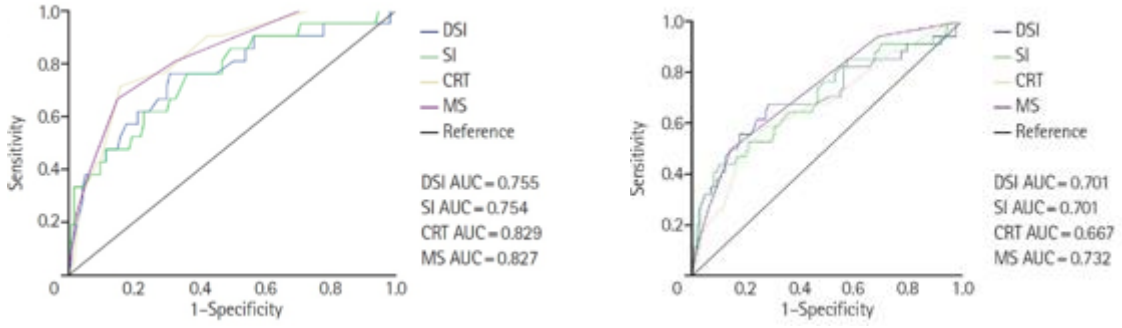
Table 1. Overview of baseline clinical indicators, patient demographics, and survival endpoints.

Characteristic	28-day mortality		7-day mortality		24-hr mortality		Total (n=135)
	Nonsurvivors (n = 48, 35.6%)	Survivors (n = 87, 64.4%)	Nonsurvivors (n = 34, 25.2%)	Survivors (n = 101, 74.8%)	Nonsurvivors (n = 21, 15.6%)	Survivors (n = 114, 84.4%)	
Age (years)	86 (78–90)	86 (79–90)	85 (79–90)	87 (79–91)	83 (80–89)	86 (79–91)	85 (79–90)
Female sex	29 (64.4)	31 (35.6)	21 (61.4)	39 (38.6)	11 (52.4)	49 (43.0)	60 (44.4)
CCI	3 (1–5)	3 (1–4)	3 (1–4)	3 (2–5)	2 (1–3)	3 (2–5)	3 (1–4)
SBP (mmHg)	90 (75–110)	110 (95–135)	90 (70–110)	110 (95–135)	85 (70–100)	105 (95–130)	100 (90–130)
DBP (mmHg)	60 (40–70)	60 (60–80)	50 (40–60)	60 (60–80)	50 (40–60)	60 (60–80)	60 (50–80)

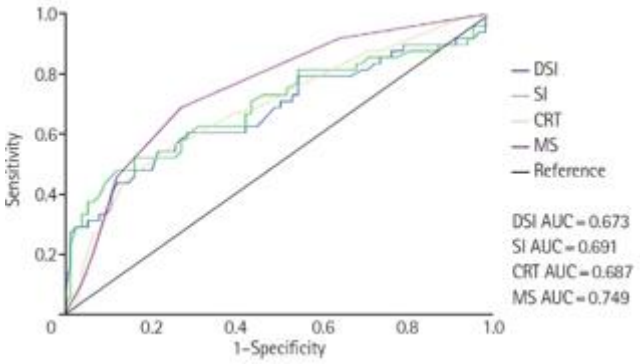
HR (bpm)	105 (90–120)	100 (90–110)	105 (90–120)	101 (90–112)	105 (90–125)	100 (90–113)	102 (90–115)
RR (breaths/min)	27 (22–30)	24 (18–28)	24 (20–28)	24 (20–28)	28 (22–32)	24 (20–28)	24 (20–28)
SpO_2 (%)	93 (90–96)	94 (91–97)	93 (90–96)	94 (91–97)	92 (90–96)	94 (91–96)	93 (90–96)
FiO_2 (%)	0.28 (0.21–0.60)	0.21 (0.21–0.35)	0.29 (0.21–0.60)	0.21 (0.21–0.36)	0.40 (0.21–0.80)	0.21 (0.21–0.35)	0.24 (0.21–0.40)
GCS score	11 (9–14)	14 (13–15)	10 (8–13)	14 (12–15)	9 (8–12)	14 (12–15)	14 (11–15)
Body temperature (°C)	37.8 (36.7–38.3)	38.0 (36.9–38.3)	38.0 (37.0–38.4)	37.9 (36.9–38.4)	37.8 (37.0–38.2)	38.0 (36.9–38.5)	38.0 (36.9–38.5)
DSI	1.8 (1.4–2.5)	1.5 (1.3–1.8)	2.0 (1.4–2.6)	1.5 (1.3–1.8)	2.0 (1.8–2.9)	1.5 (1.3–1.8)	1.5 (1.3–1.9)
SI	1.1 (0.9–1.5)	0.9 (0.7–1.1)	1.1 (0.9–1.6)	0.9 (0.7–1.1)	1.2 (1.0–1.9)	0.9 (0.7–1.1)	0.9 (0.7–1.1)
CRT (sec)	5.0 (3.0–7.0)	3.0 (2.0–4.5)	5.0 (3.0–7.0)	3.3 (2.5–5.0)	6.0 (5.0–8.0)	3.0 (2.5–5.0)	3.5 (3.0–5.0)
MS	2 (1–3)	1 (0–2)	3 (1–4)	1 (0–2)	3 (2–4)	1 (0–2)	1 (1–2)
SOFA score	7 (5–9)	4 (3–6)	8 (6–9)	4 (3–6)	8 (6–9)	5 (3–6)	5 (4–7)

Data are presented as median (interquartile range) or number (%).
Abbreviations: CCI = Charlson Comorbidity Index; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate; bpm = beats per minute; RR = respiratory rate; SpO_2 = peripheral oxygen saturation; FiO_2 = fraction of inspired oxygen; GCS = Glasgow Coma Scale; DSI = diastolic shock index; SI = shock index; CRT = capillary refill time; MS = mottling score; SOFA = Sequential Organ Failure Assessment.

When comparing the diagnostic metrics, CRT proved to be the most accurate indicator of short-term 24-hour mortality, yielding an AUC of 0.829 (compared to MS = 0.827; SI = 0.754; DSI = 0.755; $P < 0.001$), which highlights its strong prognostic value during the initial presentation of sepsis **(Figure 2a)**. For longer tracking intervals, the MS demonstrated the highest prognostic reliability, yielding the most accurate AUC values at both 7 days (MS = 0.732; SI = 0.701; DSI = 0.701; CRT = 0.667; $P < 0.001$) **(Figure 2b)** and 28 days (MS = 0.749; SI = 0.691; CRT = 0.687; DSI = 0.673; $P < 0.001$) **(Figure 2c)**. No statistically significant differences in performance were found when making direct pairwise comparisons between the four diagnostic tools **(Table 2)**.
In univariable analyses, all four bedside metrics were independent risk factors for mortality at 24 hours, 7 days, and 28 days **(Table 3)**. These associations were investigated further using an adjusted multivariable logistic regression model **(Table 4)**, which tested each noninvasive index (SI, DSI, CRT, and MS) individually while controlling for age, CCI, and altered mental status. All four bedside tools maintained a statistically independent association with mortality across all three time intervals.
Specifically, the SI demonstrated odds ratios (ORs) of 10.949 (95% confidence interval [CI] = 4.065–29.480) for 24-hour mortality, 7.299 (95% CI = 3.012–17.689) for 7-day mortality, and 10.379 (95% CI = 4.070–26.467) for 28-day mortality. The DSI generated OR values of 4.492 (95% CI = 2.402–8.638), 3.960 (95% CI = 2.225–7.045), and 4.116 (95% CI = 2.317–7.312), respectively, across the identical observation markers. CRT also retained its statistical significance in all adjusted models, producing ORs of 1.810 (95% CI = 1.451–2.258), 1.422 (95% CI = 1.195–1.692), and 1.358 (95% CI = 1.149–1.605), respectively. Similarly, higher MS values were significantly associated with increased mortality risk, yielding ORs of 3.007 (95% CI = 2.117–4.270) at 24 hours, 2.203 (95% CI = 1.679–2.890) at 7 days, and 2.103 (95% CI = 1.609–2.748) at 28 days.



a) b)



c)

Figure 2. Discriminative performance graphs showing receiver operating characteristic (ROC) curves for the diastolic shock index (DSI), SI, capillary refill time (CRT), and mottling score (MS) across three distinct observation periods: (a) immediate 24-hour mortality, (b) intermediate 7-day mortality, and (c) long-term 28-day mortality resulting from severe sepsis or septic shock. AUC, area under the curve.

Table 2. Comparison of area under the curve (AUC) metrics and direct head-to-head testing of ROC trajectories for DSI, SI, CRT, and MS across all survival intervals.

Outcome	Predictor	Pairwise ROC curve comparison (P-value)				Overall P-value	95% confidence interval	AUC
		MS	CRT	SI	DSI			
24-hour mortality						<0.001		
	DSI	0.259	0.168	0.948	–		0.672–0.824	0.754
	SI	0.244	0.132	–	0.948		0.674–0.825	0.755
	CRT (sec)	0.970	–	0.132	0.168		0.755–0.889	0.829
	MS	–	0.970	0.244	0.259		0.753–0.887	0.827
7-day mortality						<0.001		
	DSI	0.592	0.622	>0.999	–		0.614–0.779	0.701
	SI	0.579	0.606	–	>0.999		0.614–0.779	0.701
	CRT (sec)	0.174	–	0.606	0.622		0.579–0.748	0.667
	MS	–	0.174	0.579	0.592		0.646–0.806	0.732
28-day mortality						<0.001		
	DSI	0.180	0.818	0.488	–		0.582–0.756	0.673
	SI	0.317	0.955	–	0.488		0.601–0.772	0.691
	CRT (sec)	0.140	–	0.955	0.818		0.597–0.769	0.687
	MS	–	0.140	0.317	0.180		0.662–0.823	0.749

The P-values refer to pairwise comparisons of the ROC curves for the different tools (DSI, SI, CRT, and MS) in predicting 24-hour, 7-day, and 28-day mortality. These P-values indicate whether the tools differ significantly in their predictive performance.
Abbreviations: AUC = area under the curve; DSI = diastolic shock index; SI, shock index; CRT = capillary refill time; MS = mottling score; ROC = receiver operating characteristic; CI = confidence interval.

Table 3. Unadjusted univariable testing evaluating the separate correlations between each clinical index and mortality at 24 hours, 7 days, and 28 days.

Variable	P-value	OR (95% CI)
24-hr mortality		
DSI	< 0.001	4.911 (2.182–11.056)
SI	< 0.001	13.657 (3.869–48.211)
CRT (sec)	< 0.001	1.896 (1.435–2.504)
MS	< 0.001	2.371 (1.643–3.422)
7-day mortality		
DSI	< 0.001	3.949 (1.907–8.177)
SI	< 0.001	8.549 (2.766–26.428)
CRT (sec)	0.002	1.375 (1.120–1.688)
MS	< 0.001	1.817 (1.353–2.440)
28-day mortality		
DSI	< 0.001	3.638 (1.769–7.481)

SI	< 0.001	8.911 (2.790–28.458)
CRT (sec)	0.001	1.438 (1.171–1.764)
MS	< 0.001	1.889 (1.399–2.553)

Abbreviations: OR = odds ratio; CI = confidence interval; DSI = diastolic shock index; SI = shock index; CRT = capillary refill time; MS = mottling score.

Table 4. Fully adjusted multivariable logistic regression frameworks tracking the statistical correlation between individual noninvasive metrics and survival outcomes at 24 hours, 7 days, and 28 days.

Model	28-day mortality		7-day mortality		24-hr mortality	
	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)
Shock index	< 0.001	10.379 (4.070–26.467)	< 0.001	7.299 (3.012–17.689)	< 0.001	10.949 (4.065–29.480)
Age (yr)	0.449	1.012 (0.981–1.043)	0.848	1.003 (0.972–1.036)	0.776	1.005 (0.970–1.042)
CCI	0.070	1.135 (0.990–1.301)	0.901	0.992 (0.868–1.113)	0.890	0.990 (0.853–1.148)
Altered mentation	0.002	3.662 (1.596–8.400)	0.001	6.881 (2.240–21.139)	0.006	17.914 (2.283–140.564)
Diastolic shock index	< 0.001	4.116 (2.317–7.312)	< 0.001	3.960 (2.225–7.045)	< 0.001	4.492 (2.402–8.638)
Age (yr)	0.509	1.010 (0.980–1.042)	0.901	1.002 (0.970–1.035)	0.799	1.005 (0.969–1.042)
CCI	0.092	1.122 (0.982–1.283)	0.901	0.992 (0.868–1.113)	0.928	0.993 (0.856–1.152)
Altered mentation	0.002	3.820 (1.659–8.795)	0.001	7.248 (2.342–22.425)	0.006	18.214 (2.341–141.698)
Capillary refill time (sec)	< 0.001	1.358 (1.149–1.605)	< 0.001	1.422 (1.195–1.692)	< 0.001	1.810 (1.451–2.258)
Age (yr)	0.669	1.006 (0.977–1.036)	0.966	0.999 (0.968–1.032)	0.904	1.002 (0.964–1.042)
CCI	0.172	1.096 (0.961–1.249)	0.523	0.957 (0.836–1.095)	0.321	0.923 (0.787–1.080)
Altered mentation	0.015	2.720 (1.214–6.095)	0.005	4.899 (1.613–14.882)	0.028	9.979 (1.277–77.962)
Mottling score	< 0.001	2.103 (1.609–2.748)	< 0.001	2.203 (1.679–2.890)	< 0.001	3.007 (2.117–4.270)
Age (yr)	0.856	1.003 (0.973–1.034)	0.805	0.996 (0.963–1.029)	0.925	0.998 (0.958–1.040)
CCI	0.106	1.122 (0.976–1.291)	0.622	0.964 (0.835–1.114)	0.450	0.936 (0.789–1.111)
Altered mentation	0.013	2.960 (1.259–6.957)	0.003	6.040 (1.847–19.752)	0.008	21.039 (2.199–201.259)

Each model was stratified by age, CCI, and altered mentation.
Abbreviations: OR = odds ratio, CI = confidence interval, and CCI = Charlson Comorbidity Index.

To evaluate whether these clinical instruments track overlapping physiological pathways or provide distinct, complementary data, a Kendall tau-b correlation analysis was executed. The macrohemodynamic variables, SI and DSI, shared strong statistical connections with indices such as the $\text{PaO}_2/\text{FiO}_2$ ratio, shifting platelet counts, and liver dysfunction markers. In contrast, peripheral tissue assessments, namely CRT and MS, demonstrated distinct associations with mean arterial pressure trends and Glasgow Coma Scale scores.

In addition to the primary models, a secondary multivariable regression analysis was performed for each independent noninvasive metric, adjusting for overall SOFA scores and baseline blood lactate concentrations. Both CRT and MS remained independent predictors of 24-hour mortality risk, maintaining their statistical significance despite accounting for these traditional prognostic scores. Conversely, the SI and DSI failed to maintain independent predictive significance within these highly adjusted frameworks, indicating that their prognostic accuracy may be conditional upon concurrent hemodynamic variables.

Finally, an age-stratified ROC analysis was conducted to assess the stability of these prognostic indicators across demographic cohorts. The study population was separated into four predefined age cohorts (< 65, 65–75, 75–85, and > 85 years); however, due to the absence of any mortality events in the youngest bracket (< 65 years), the ROC curve generation was restricted to the upper three categories. At the same time, the MS consistently offers stronger predictive capacity at later observation windows.

The findings of this investigation demonstrate that CRT achieved the highest AUC for predicting 24-hour mortality, whereas MS achieved the highest AUC for predicting 7-day and 28-day survival outcomes.

Additionally, head-to-head pairwise testing between these parameters revealed no statistically significant variations. This indicates that each diagnostic instrument has clinical utility and can be used interchangeably in emergency settings without any single modality establishing clear superiority over the others.

Nevertheless, it is critical to recognize that the indices evaluated in this clinical trial monitor distinct physiological pathways: SI and DSI primarily serve as metrics of macrocirculatory performance [6, 7], whereas CRT and MS primarily track microcirculatory tissue perfusion [8, 9]. Our primary objective was to compare these modalities side by side to contrast their relative prognostic accuracy, despite their focus on different circulatory compartments. This analytical strategy helps clinicians ascertain whether one specific physiological domain delivers superior predictive utility in daily practice. Even so, we acknowledge that subsequent investigations would benefit from clustering these assessment methods by their underlying physiological targets or from creating composite risk scores that merge macrohemodynamic and microhemodynamic parameters to optimize risk tiering.

The elevated prognostic precision of CRT at 24 hours highlights its clinical value as a rapid screening instrument in high-acuity emergency care. As a straightforward bedside evaluation, CRT assesses peripheral blood flow and can be executed within seconds, offering a highly accessible monitoring option for frontline healthcare professionals [8, 10, 11]. Among individuals with sepsis, an abnormal CRT signal indicates impaired peripheral perfusion and has been consistently linked to higher in-hospital mortality and unfavorable clinical trajectories [8, 10]. Prior research indicates that a prolonged CRT following initial fluid resuscitation correlates with an elevated probability of experiencing major adverse events, such as extended stays in the intensive care unit, the requirement for invasive mechanical ventilation, and the initiation of renal replacement therapy [10]. Furthermore, a meta-analysis synthesizing data across multiple clinical trials confirmed that delayed capillary return serves as a reliable predictor of in-hospital death in septic cohorts, particularly among individuals experiencing acute circulatory collapse [11]. The notable correlation observed in this study between baseline CRT and subsequent in-hospital mortality underscores the critical importance of evaluating circulatory status early in the development of sepsis. Delayed or insufficient tissue perfusion represents a key warning sign of systemic deterioration [10], and CRT functions as a rapid, timely alert for clinical teams.

Conversely, the superior performance of MS for predicting 7-day and 28-day mortality demonstrates its effectiveness in determining mid-term and long-term outcomes in septic patients. This suggests that while immediate resuscitation decisions guided by initial CRT are essential, sequential monitoring using the MS provides deeper insight into a patient's evolving clinical status. Cutaneous mottling develops as a direct consequence of microcirculatory failure, mirroring the systemic physiological impact of sepsis, and serves as a major clinical indicator of high-severity illness progression [9, 12–14]. The capacity of MS to maintain its predictive value over extended time horizons stems from its direct assessment of skin blood flow and systemic hemodynamic equilibrium. Published reports have confirmed that elevated mottling scores are strongly associated with worsening clinical outcomes in septic shock [12]. For instance, a previous trial showed that patients with more severe skin mottling exhibited significantly lower cutaneous oxygen saturation levels and higher 28-day mortality rates [12]. The MS framework, graded from 0 (no visible mottling) to 5 (extensive mottling), serves as a rapid bedside metric for assessing septic shock severity and predicting in-hospital mortality. Patients who present with a mottling score of 3 or higher typically face an unfavorable prognosis [12, 13].

In addition, the total duration of skin mottling represents another crucial clinical factor. The persistence of visible mottling for more than 6 hours is strongly associated with increased in-hospital mortality, underscoring the importance of rapidly detecting and treating circulatory failure in individuals with septic shock [14]. Nevertheless, the clinical utility of MS has inherent boundaries; it exhibits reduced diagnostic accuracy in patients with darker skin pigmentation and demands structured clinical training to ensure consistent interpretation among different observers [12–14].

Both the SI and DSI generally track the onset of low blood pressure. However, while systemic hypotension typically manifests as a late stage of circulatory shock, both indices are widely used as early screening markers for sepsis due to their capacity to identify cardiovascular impairment before overt hypotension becomes clinically apparent [6, 7]. These computational metrics supply vital data regarding a patient's overall cardiovascular state, facilitating rapid diagnosis and accelerated intervention in septic populations, which is essential for improving overall survival rates.

The advanced median age of our study cohort (85 years) is a major factor that may influence how these statistics are interpreted. Geriatric patients routinely present with highly complex clinical profiles, frequently shaped by multiple pre-existing comorbidities that can alter both the initial presentation and outcomes of a septic event [5, 15, 16]. The physiological frailty and reduced compensatory reserves typical of older populations also contribute to a higher underlying risk of in-hospital mortality [15]. Other confounding elements that can negatively influence the prognosis of geriatric individuals include age-related declines in organ system function and delayed clinical detection caused by atypical, non-classic symptom patterns [17]. Our data accentuates the critical need to design tailored triage algorithms for older patient populations, in whom classic physiological markers may fail to fully capture the subtle nuances of sepsis onset and progression.

Furthermore, the small sample size raises valid concerns about how broadly these insights can be applied. While our current results offer meaningful data, larger multi-center trials are required to validate these patterns and increase the statistical power of the analysis. The absence of statistically significant differences in our pairwise comparisons indicates that both CRT and MS are highly promising clinical options; however, subsequent trials enrolling a larger sample might reveal subtle differences in predictive accuracy that our study was underpowered to detect.

The clinical implications derived from these findings are highly meaningful. Promptly identifying individuals who face a high probability of in-hospital death is essential for optimizing therapeutic pathways in sepsis management. Although this investigation did not find wide variations in the individual predictive capacities of the evaluated parameters, the strong performance profiles of both CRT and MS suggest they can function effectively as sequential, complementary tests. For example, CRT could be deployed during the initial triage to rapidly tier risk, with the MS subsequently used to monitor evolving circulatory risks over time. Embedding these noninvasive metrics into routine emergency protocols could help medical staff flag deteriorating individuals and trigger rapid therapeutic changes. Furthermore, because these tools are easy to perform at the bedside, they are exceptionally valuable in resource-limited medical settings, particularly in environments where advanced hemodynamic monitoring infrastructure is unavailable.

In the multivariable models, each parameter retained a significant association with mortality across all three distinct tracking intervals, demonstrating that they serve as valuable indicators of patient outcomes during sepsis. Despite evaluating different elements of physiology—ranging from core cardiovascular dynamics to distal tissue perfusion—all four diagnostic methods successfully and consistently flagged patients at high risk of death at specific intervals. This consistency confirms that, in daily clinical settings, any of these scoring systems can be used effectively to stratify patient risk in sepsis, supporting rapid, targeted interventions to improve survival rates.

Our primary findings are further validated by our secondary statistical models. The adjusted multivariable logistic regression models confirm that each bedside metric is an independent predictor of mortality at all evaluation intervals, even after controlling for major confounding factors such as age, total comorbidity burden, and neurological impairment. This reinforces the overall robustness of their prognostic utility in active clinical environments. Additionally, we calculated optimal diagnostic cutoffs for each score to provide actionable, practical thresholds for frontline medical decision-making. The correlation matrices showed moderate interdependence among the tools, particularly between scores within the same underlying physiological domain, but no total redundancy was observed. This suggests that blending macrocirculatory indices (SI, DSI) with microcirculatory indicators (CRT, MS) could provide a cumulative, additive prognostic benefit. Finally, a subgroup analysis across distinct elderly cohorts confirmed that these predictive patterns remain highly reproducible even within very old patient groups, reinforcing the potential value of these tools for geriatric sepsis evaluations.

A major advantage of this investigation is its exclusive focus on entirely noninvasive tools that demand zero laboratory processing or specialized mechanical equipment. In contrast to traditional biomarkers like serum lactate, which require invasive blood draws and laboratory infrastructure, the bedside parameters analyzed here can be measured in any medical environment (including prehospital and emergency transit care) at no cost. This makes them highly useful in low-resource environments, where immediate risk classification is critical but access to advanced diagnostic laboratories may be delayed or unavailable.

Several limitations of this research should be noted. First, the trial was conducted at a single medical center, limiting the generalizability of our findings. Patient demographics, hospital resources, and standard clinical practices differ widely across separate healthcare institutions, particularly between nations with different medical systems. Second, our relatively small sample size could reduce the overall statistical power of our datasets and limit our ability to detect minor differences among the individual prognostic tools. Additionally, a formal a priori power calculation was not executed for this study protocol. Enrolling a larger patient cohort would yield more stable and widely generalizable conclusions. Finally, the median age of the study group was 85 years. While this demographic accurately mirrors the heightened vulnerability of older individuals to severe infections, it restricts the direct translation of these findings to younger or middle-aged patient populations, who frequently demonstrate different physiological responses and survival trajectories. Independent external validation using more heterogeneous, age-balanced cohorts is necessary to verify that our conclusions hold across broader patient groups.

Future research designs should aim to recruit larger, multi-institutional patient cohorts to further validate these initial observations. Additionally, our study design did not include a non-septic control cohort, which limits certain comparative analyses; however, our primary clinical goal was to evaluate the predictive accuracy of these scores within confirmed septic populations. Exploring how to embed these tools directly into automated clinical decision trees could provide fresh insights into how they might actively improve patient survival rates. Investigating potential multi-tool diagnostic combinations or using them in tandem with traditional severity scoring systems (such as the comprehensive SOFA framework) could also yield valuable clinical breakthroughs.

Conclusion

In conclusion, this investigation highlights the strong prognostic accuracy of noninvasive bedside metrics for evaluating sepsis mortality. CRT showed the highest AUC at the 24-hour mark, whereas MS showed the highest AUC at the 7-day and 28-day intervals. Although our statistical analyses did not reveal significant performance differences among the four tools, the complementary nature of these scoring methods provides a clear pathway to optimize clinical screening protocols. Furthermore, because every independent parameter predicted mortality across all three tested observation points, subsequent research should examine whether integrating these tools into a hybrid framework (potentially combining both macrocirculatory and microcirculatory signs) could improve overall prognostic sensitivity. These findings provide further support for the hypothesis that microcirculatory markers, such as CRT and MS, retain independent prognostic value during the early phases of sepsis care, even when accounting for comprehensive laboratory-based scores such as the SOFA index and serum lactate concentrations. The lack of independent predictive power observed for the SI and DSI in these adjusted models may stem from their high correlation with hemodynamic factors already factored into the standard SOFA score, suggesting multicollinearity within those multivariable frameworks. Future studies should focus on evaluating hybrid triage strategies that blend macrohemodynamic and microhemodynamic parameters to achieve optimal, early risk stratification. Continued research remains necessary to deepen our understanding of how to maximize the utility of these tools during sepsis management, particularly when treating highly vulnerable patient groups such as the elderly.

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