Assessment of Sepsis Severity Using SOFA Score and Ultrasonographic Measurement of Optic Nerve Sheath Diameter

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Abstract

Background: This study aimed to compare optic nerve sheath diameter (ONSD) with SOFA score, mortality, and length of stay in the intensive care unit (ICU) among patients with septic shock.

Methods: An interventional study was conducted on 70 patients with sepsis admitted to the Shariati Hospital ICU. Demographic data were first recorded. Bedside ultrasonography through the upper eyelid was then performed to measure ONSD on admission and repeated on days three and six of ICU stay. Simultaneously, C-reactive protein (CRP), serum lactate levels, and SOFA scores were documented. The presence of encephalopathy was also evaluated. Statistical analyses using paired t-test and Pearson correlation were applied to examine associations between ONSD and clinical/laboratory parameters.

Results: The mean age of patients was 60.42 ± 6.06 years, with 39 (54.2%) males. Encephalopathy was observed in 40 patients (55.6%). The mean ICU stay was 7.64 ± 2.40 days, and 39 patients (54.2%) died. ONSD showed a significant correlation with serum lactate, CRP, and SOFA score ($p < 0.05$). The maximum mean ONSD was 6.0 mm on days one and three, decreasing to 5.6 mm by day six.

Conclusions: ONSD, alongside CRP, lactate, and SOFA score, may serve as useful markers for monitoring neurological status, systemic inflammation, hemodynamic improvement, and organ function in septic shock patients. These findings highlight their potential role in guiding timely ICU management, despite limitations such as sample size and demographic variability.

Keywords: Sepsis; SOFA Score; Optic Nerve Sheath Diameter; Encephalopathy; Critical Care

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Introduction

Sepsis is a life-threatening condition characterized by the body's overwhelming and dysregulated response to infection, ultimately leading to systemic inflammation and multi-organ dysfunction [1]. The severity and progression of sepsis are often evaluated using the Sequential Organ Failure Assessment (SOFA) score, which incorporates various clinical parameters to assess the function of vital organs [2]. Among the most affected organs, the brain is particularly vulnerable, and neurological impairment is captured within SOFA scoring through alterations in the Glasgow Coma Scale (GCS) [3].

Sepsis-associated encephalopathy (SAE) is one of the most frequent and severe complications of sepsis, occurring in more than 70% of septic patients, especially those with septic shock [4]. Clinically, SAE manifests as confusion, delirium, reduced levels of consciousness, and, in severe cases, coma [5]. These neurological changes are often accompanied by cerebral edema and raised intracranial pressure (ICP), both of which further worsen prognosis [6].

Although the exact pathophysiology of SAE is not completely understood, several mechanisms are believed to contribute to its development.

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Neuroinflammation plays a central role, as systemic inflammatory mediators cross the blood–brain barrier, activate glial cells, and lead to neuronal injury [7]. In addition, impairment of cerebral autoregulation compromises the brain's ability to maintain constant blood flow, resulting in ischemia or hyperemia that exacerbates neuronal damage [8]. Dysfunction of the brainstem, which controls critical regulatory centers, further intensifies the clinical severity of SAE [9].

Diagnosing SAE is challenging because its clinical features overlap with other forms of encephalopathy. Biomarkers such as S100B and neuron-specific enolase (NSE) provide insight into neuronal damage, while electroencephalography (EEG) and evoked potentials are useful for assessing cerebral function. Advanced neuroimaging with CT or MRI can reveal structural abnormalities but is often impractical in critically ill patients due to their instability and the time required to complete such procedures [10].

In this context, optic nerve sheath diameter (ONSD) measurement has emerged as a promising bedside tool for the non-invasive detection of raised ICP and cerebral edema [11]. ONSD assessment, performed via ocular ultrasound, offers significant advantages in the intensive care unit (ICU). Unlike CT or MRI, ONSD can be repeatedly measured at the bedside, providing real-time monitoring of intracranial dynamics in unstable patients who cannot be transferred for imaging. The optic nerve sheath expands in response to increased ICP, making this measurement a reliable surrogate marker of intracranial pressure. Its non-invasive nature, low cost, and rapid execution make it highly suitable for critical care settings [12, 13].

Early identification of elevated ICP through ONSD measurement allows clinicians to intervene promptly, manage cerebral edema, and potentially improve neurological and overall outcomes.

Considering these aspects, the present study aims to evaluate the relationship between ONSD measurements and clinical outcomes in septic patients, with particular focus on SOFA scores, mortality, and ICU length of stay. By correlating ONSD values with these critical parameters, the study seeks to determine the predictive utility of ONSD in assessing the severity of SAE and the overall prognosis of septic patients. Establishing ONSD as a reliable predictor could significantly enhance bedside monitoring and clinical decision-making, ultimately contributing to improved patient outcomes.

Materials and Methods

Study Design and Execution

This study was designed as a prospective cohort study aimed at investigating the relationship between ONSD measurements and various clinical indices in patients with septic shock, under the ethics code IR.TUMS.MEDICINE.REC.1403.372. A total of 70 patients diagnosed with septic shock, aged under 70 years and with a SOFA score of 2 or higher, were enrolled. Eligible patients meeting the inclusion criteria (age <70 years and SOFA score ≥2) were admitted to the ICU and closely monitored.

ONSD measurements were performed at the bedside using ultrasonography on days 1, 3, and 6 of admission. The ONSD was measured in millimeters, with a normal range defined as 5.05–5.5 mm. An ONSD value exceeding 5.7 mm was considered indicative of raised intracranial pressure (ICP).

In addition to ONSD, SOFA scores were assessed on days 1, 3, and 6 to evaluate disease severity and organ function. The SOFA score served as a validated indicator for predicting clinical outcomes in septic shock patients. Furthermore, C-reactive protein (CRP) and lactate levels were measured on the same days. CRP was used as an inflammatory marker, while lactate served as a metabolic indicator, providing valuable insights into the inflammatory and metabolic responses to septic shock.

ONSD and eye-to-transverse diameter (ETD) measurements were conducted with high precision using ultrasonography. A probe was placed on the patient's closed eyelid to capture images for ONSD and ETD assessment. This non-invasive, rapid technique allowed for repeated bedside measurements. Data collected—including ONSD, the ONSD/ETD ratio, SOFA score, CRP, and lactate levels on days 1, 3, and 6—were analyzed to explore correlations among these variables. Appropriate statistical analyses were applied to examine these relationships.

Study Type

The study was conducted as a prospective cohort study.

Inclusion Criteria

Patients diagnosed with septic shock, younger than 70 years, and with a SOFA score of 2 or higher were included.

Exclusion Criteria

Patients were excluded if they were older than 70 years, had a SOFA score below 2, did not require ICU admission due to a stable condition, declined to participate, had comorbidities (e.g., severe neurological disorders) that could influence study outcomes, or were unable to undergo ultrasonography

Table 1: Variables, measurement methods, and operational definitions used in the study

Row	Variable Name	Variable Type		Quantitative		Qualitative		Scientific-Operational Definition	Measurement Method	Scale
		Independent	dependent	Continuous	Discrete	Nominal	Ordinal			
1	ONSD		*	*					Ultrasound	Millimeters (mm)
2	Lactate Level		*	*					Patient Tests	mmol/L
3	CPR		*	*					Patient Tests	mg/dL
4	Mortality & Morbidity		*			*			Patient Records	Yes/No
5	Length of Hospital Stay		*	*					Patient Records	Number of Days
6	SOFA Score		*	*					Based on Criteria	Yes/No
7	Cerebral Encephalopathy		*			*			Based on Patient Symptoms	Yes/No

for physical or medical reasons.

Sample Size Calculation

The sample size was calculated based on prior studies, using an alpha of 0.05 and a beta of 20%, resulting in a required sample size of 75 patients. The formula used was:

$N=[(z_{(1-\alpha/2)} + z_{(1+\alpha/2)})^2 \delta^2]^2 / d^2$

$D = \mu_1 - \mu_2$

μ_1= the mean of the control group = 90

μ_2 = the mean of the experimental group = 95

standard deviation of control group : 8.9

Data Collection Methods

Data were collected from septic shock patients admitted to the ICU at Shariati Hospital, Tehran, Iran. ONSD measurements were performed using a high-precision ultrasound device equipped with a probe suitable for imaging deep ocular structures. The non-invasive procedure involved placing the probe on the patient's closed eyelid to measure ONSD on days 1, 3, and 6. The normal ONSD range was defined as 5.05–5.5 mm, with values above 5.7 mm considered suggestive of elevated ICP.

In addition to ONSD, clinical indices such as SOFA score (indicating disease severity and organ dysfunction), CRP (inflammatory marker), lactate (metabolic marker), cerebral encephalopathy occurrence, mortality, morbidity, and ICU length of stay were systematically recorded. These measurements were used to assess correlations between ONSD and clinical outcomes. Statistical analyses were conducted to identify significant relationships among these variables (Table 1).

Study Limitations and Mitigation

No significant operational limitations were encountered during the study.

Data Analysis

Data analysis was performed using SPSS version 27. Comparisons of quantitative data were conducted using ANOVA to assess differences in means across groups. The independent t-test was applied to compare means between two independent groups for statistical significance. Pearson correlation analysis was used to evaluate linear relationships and the strength of correlations (positive or negative) between continuous variables. Results were organized and presented in tabular form for clarity.

Statistical Analysis of Data

To perform the statistical analysis, the normality of the data was initially assessed. Accordingly,

Table 2: Examination of Patients' Demographic Findings, N=70.

Age_ mean(SD)	60.42(6.06)
Gender_ No(%)	
Male	39(54.2)
Female	31(43.1)
Encephalopathy_ No(%)	
Yes	40(55.6)
No	30(41.7)
ICU admission day_ mean(SD)	7.64(2.40)

Table 3: Examination of ICU and Laboratory Data, N=70.

Optic nerve sheath diameter_ mean(SD)	
First day	5.85(0.52)
Third day	5.64(0.49)
Sixth day	5.47(0.42)
CRP level_ mean(SD)(mg/l)	
First day	85.34(9.32)
Third day	78.48(9.05)
Sixth day	68.71(9.22)
Lactate level_ mean(SD)(mmol/l)	
First day	4.73(1.90)
Third day	4.03(1.82)
Sixth day	2.64(1.47)
Sofa score_ mean(SD)	
First day	15.11(3.68)
Third day	13.35(3.13)
Sixth day	10.90(2.92)
Death_ No(%)	
Yes	39(54.2)
No	31(43.1)

normally distributed data were presented as mean ± SD, while non-normally distributed data were reported as median (IQR). For the analysis of normally distributed data, statistical tests such as the paired t-test and Pearson correlation were employed.

Based on the analysis, all data were found to be normally distributed. The mean age of patients was 60.42 ± 6.06 years, with 39 patients (54.2%) being male. The average duration of ICU admission was 7.64 ± 2.40 days. Additionally, 40 patients (55.6%) were diagnosed with encephalopathy (Table 2).

The mean values of the optic nerve sheath diameter (ONSD) were evaluated. The findings indicated that the mean ONSD was 5.85 ± 0.52 mm on the first day, 5.64 ± 0.49 mm on the third day, and 5.47 ± 0.42 mm on the sixth day.

CRP levels were also measured, with a mean of 85.34 ± 9.32 mg/L on the first day, 78.48 ± 9.05 mg/L on the third day, and 68.71 ± 9.22 mg/L on the sixth day. Blood lactate levels were assessed, showing a mean of 4.73 ± 1.90 mmol/L on the first day, 4.03 ± 1.82 mmol/L on the third day, and 2.64 ± 1.47 mmol/L on the sixth day.

SOFA scores were calculated, with a mean of 15.11 ± 3.68 on the first day, 13.35 ± 3.13 on the third day, and 10.90 ± 2.92 on the sixth day. The mortality rate was also evaluated, with 39 patients (54.2%) succumbing during their hospital stay (Table 3).

The relationship between ONSD and CRP levels was examined using the paired t-test, revealing significant correlations across all three days (First day vs. CRP first day: $p<0.001$, df=69, t=-71.08; First day vs. CRP third day: $p<0.001$, df=69, t=-66.91; First day vs. CRP sixth day: $p<0.001$, df=69, t=-56.85; Third day vs. CRP first day: $p<0.001$, df=69, t=3.76; Third day vs. CRP third day: $p<0.001$, df=69, t=6.91; Third day vs. CRP sixth day: $p<0.001$, df=69, t=15.70; Sixth day vs. CRP first day: $p<0.001$, df=69, t=-71.58; Sixth day vs. CRP third day: $p<0.001$, df=69, t=-67.42; Sixth day vs. CRP sixth day: $p<0.001$, df=69, t=-57.30).

Similarly, the relationship between ONSD and blood lactate levels was assessed using the paired t-test, showing significant correlations across all three days (First day vs. lactate first day: $p<0.001$, df=69, t=4.56; First day vs. lactate third day: $p<0.001$, df=69, t=7.68; First day vs. lactate sixth day: $p<0.001$, df=69, t=16.37; Third day vs. lactate first day: $p<0.001$, df=69, t=3.76; Third day vs. lactate third day: $p<0.001$, df=69, t=6.91; Third day vs. lactate sixth day: $p<0.001$, df=69, t=15.70; Sixth day vs. lactate first day: $p<0.001$, df=69, t=3.09; Sixth day vs. lactate third day: $p<0.001$, df=69, t=6.24; Sixth day vs. lactate sixth day: $p<0.001$, df=69, t=14.90).

The relationship between ONSD and SOFA scores was also evaluated using the paired t-test, demonstrating significant correlations across all three days (First day vs. SOFA score first day:

p<0.001, df=69, t=-20.66; First day vs. SOFA score third day: p<0.001, df=69, t=-19.64; First day vs. SOFA score sixth day: p<0.001, df=69, t=-13.63; Third day vs. SOFA score first day: p<0.001, df=69, t=-21.09; Third day vs. SOFA score third day: p<0.001, df=69, t=-20.05; Third day vs. SOFA score sixth day: p<0.001, df=69, t=-14.41; Sixth day vs. SOFA score first day: p<0.001, df=69, t=-21.59; Sixth day vs. SOFA score third day: p<0.001, df=69, t=-20.63; Sixth day vs. SOFA score sixth day: p<0.001, df=69, t=-14.98).

The relationship between ONSD and mortality outcomes was assessed using the Pearson correlation test, revealing significant associations on all measured days ($p < 0.05$). In contrast, the relationship between ONSD and the presence or absence of encephalopathy was also evaluated using the Pearson correlation test, but no significant associations were found ($p > 0.05$) (Table 4). As indicated in Chart 1, based on the measured values, the most frequent optic nerve sheath diameter was 6 mm.

Also, as indicated in Chart 2, based on the measured values, the most frequent optic nerve sheath diameter was 6 mm

Furthermore, as shown in Chart 3, based on the measured values, the most frequent optic nerve sheath diameter was 5.60 mm.

Table 4: Investigation of the Relationship Between ONSD, Lactate Levels, SOFA Score, Mortality, and Encephalopathy

N=70	ONSD first day	ONSD third day	ONSD sixth day
CRP level			
First day	<0.001	<0.001	<0.001
Third day	<0.001	<0.001	<0.001
Sixth day	<0.001	<0.001	<0.001
Lactate level			
First day	<0.001	<0.001	0.003
Third day	<0.001	<0.001	<0.001
Sixth day	<0.001	<0.001	<0.001
Sofa score			
First day	<0.001	<0.001	<0.001
Third day	<0.001	<0.001	<0.001
Sixth day	<0.001	<0.001	<0.001
Death	0.014*	0.024*	0.029*
Encephalopathy	0.82	0.94	0.80

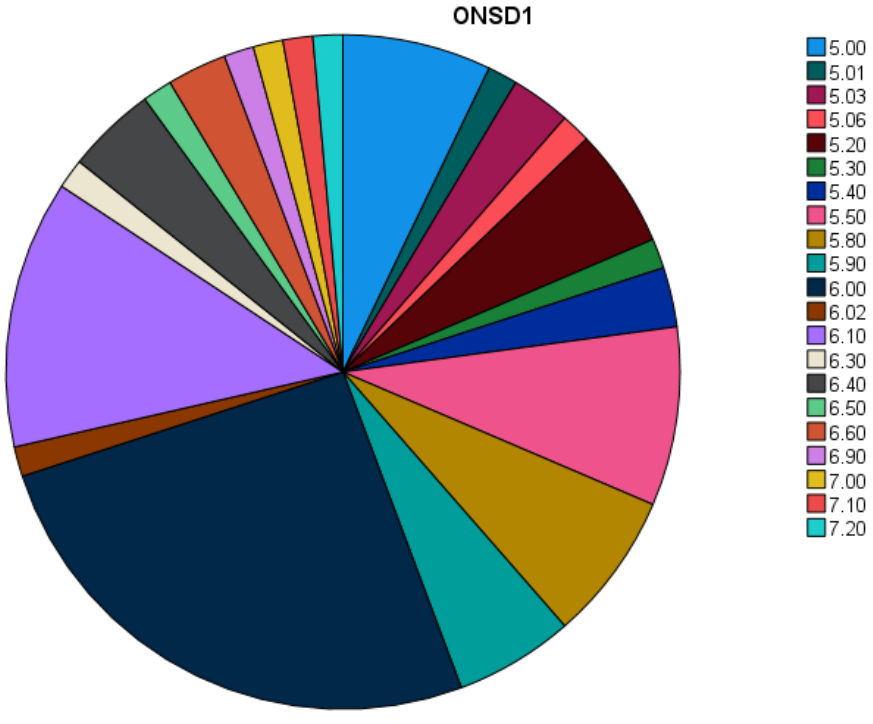

Chart 1: Frequency Analysis of Optic Nerve Sheath Diameter on Day 1

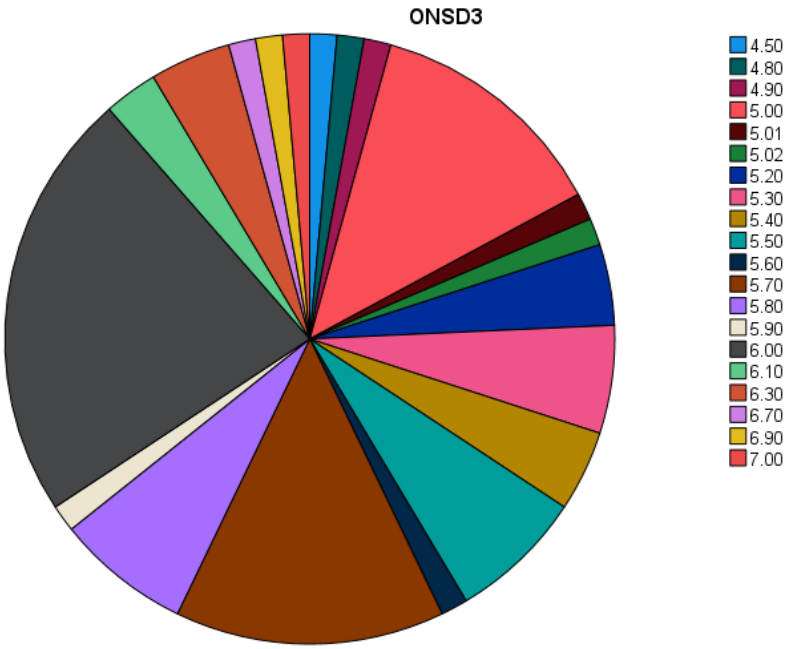

Chart 2: Frequency Analysis of Optic Nerve Sheath Diameter on Day 3

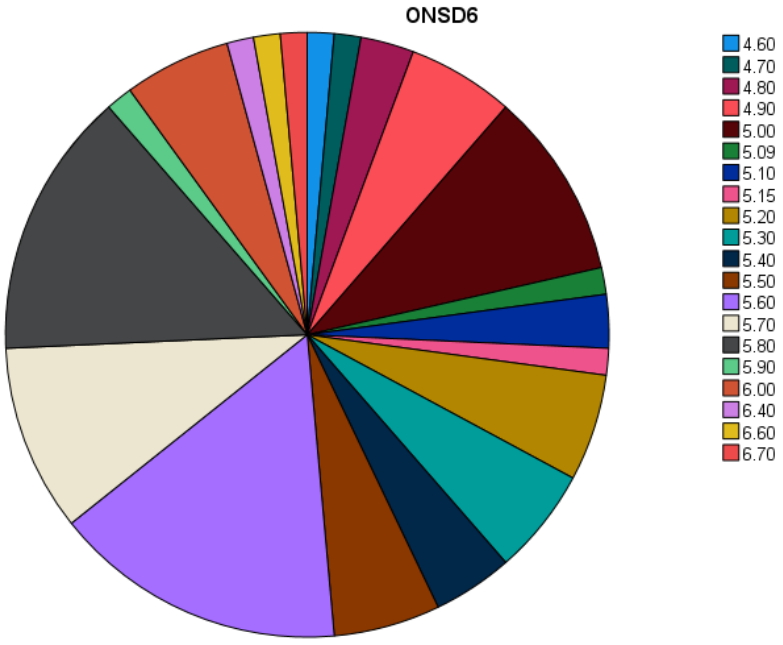

Chart 3: Frequency Analysis of Optic Nerve Sheath Diameter on Day 6

Discussion

The findings of this study highlight the critical role of four key clinical indicators—ONSD, CRP levels, blood lactate, and SOFA score—in assessing the clinical status of patients admitted to the ICU. These parameters provide valuable insights into different aspects of patient health, including neurological status, systemic inflammation, tissue oxygenation, and multi-organ function. Integrating these markers into clinical practice could significantly enhance decision-making and contribute to improved patient outcomes in critical care settings.

Optic Nerve Sheath Diameter (ONSD)

The study confirms that changes in ONSD serve as a reliable non-invasive indicator of intracranial

pressure (ICP). A reduction in ONSD was associated with improved neurological outcomes, consistent with the findings of David Berhanu et al. (2023), who demonstrated that ONSD changes can act as an early marker of elevated ICP in patients with brain injuries [14]. This is particularly valuable in ICU settings, where rapid and accurate assessment of neurological status is crucial for timely interventions.

By monitoring ONSD, clinicians can obtain a clearer picture of a patient's neurological condition without resorting to invasive procedures, which carry inherent risks. However, the study acknowledges that factors such as imaging techniques and operator experience may influence the accuracy of ONSD measurements, underscoring the need for standardized protocols to ensure consistency.

C-reactive Protein (CRP)

The reduction in CRP levels observed in this study indicates successful control of systemic inflammation and infection. This finding is consistent with Tanvi Banait et al. (2022), who reported that elevated CRP levels are associated with severe infections in ICU patients and that a decline in CRP following treatment reflects a positive therapeutic response [15]. The utility of this biomarker lies in its ability to guide clinicians in evaluating the effectiveness of antibiotic or anti-inflammatory interventions.

The study's results suggest that monitoring CRP trends could help identify patients at risk of complications early, thereby allowing tailored therapeutic strategies. Nonetheless, the study acknowledges that CRP is a non-specific marker, and its interpretation must take into account other clinical factors, such as coexisting conditions or immunosuppressive therapies, which may confound results.

Blood Lactate

The observed decrease in blood lactate levels indicates improved tissue oxygenation and metabolic stability. This finding corroborates the work of Brian M. Fuller et al. (2013), who emphasized lactate's role as a marker of hemodynamic restoration in patients with shock [16]. Lactate monitoring provides critical information about the adequacy of oxygen delivery to tissues, making it an essential tool for assessing hemodynamic status in critically ill patients.

The study's findings suggest that a downward trend in lactate levels following intervention is a positive prognostic sign, reflecting improved organ perfusion and metabolic function. However, the study underscores the importance of contextualizing lactate levels, as factors such as liver dysfunction or medication use may influence results, necessitating a comprehensive clinical evaluation.

SOFA Score

The SOFA score proved to be a robust predictor of mortality risk and organ function recovery, with reductions in the score correlating with improved clinical outcomes. This finding aligns with Tiago R. Velho (2022), who underscored the SOFA score's effectiveness in prognosticating ICU patient outcomes [17]. The score's ability to quantify multi-organ dysfunction makes it a versatile tool for guiding clinical decisions, including the need for escalated care or resource allocation.

Integration and Clinical Implications

Overall, these four parameters provide a comprehensive framework for assessing the clinical status of ICU patients. The study's findings underscore the importance of a multimarker approach, as each indicator highlights a different facet of critical illness—neurological, inflammatory, metabolic, and organ-specific. By integrating these markers, clinicians can make more informed decisions and tailor interventions to the patient's condition.

For example, a patient with declining ONSD and lactate levels but persistently elevated CRP may require intensified anti-infective therapy, whereas a rising SOFA score could signal the need for more aggressive organ support.

The consistency of this study's findings with prior research strengthens the case for incorporating these biomarkers into routine ICU practice. However, the study acknowledges certain limitations, including the potential impact of sample size on the generalizability of results and the influence of confounding factors such as age, sex, and comorbidities. These limitations highlight the need for larger, multicenter studies to validate the findings across diverse patient populations.

Future Directions

Moving forward, further research should explore the interplay between these biomarkers and specific therapeutic interventions. For instance, investigating how targeted treatments—such as neuroprotective agents or advanced hemodynamic support—affect ONSD, CRP, lactate, and SOFA scores could provide deeper insights into optimizing patient care.

In addition, the integration of emerging technologies, including advanced imaging modalities and machine learning algorithms, holds promise for enhancing the precision of these biomarkers. Machine

learning, in particular, could enable predictive models that combine these parameters to forecast patient outcomes with greater accuracy, potentially transforming ICU management.

In conclusion, this study underscores the value of ONSD, CRP, lactate, and SOFA scores as complementary tools for monitoring ICU patients. By providing a multifaceted view of a patient's condition, these markers enable clinicians to make timely, evidence-based decisions. While the findings are promising, ongoing research and technological advancements will be essential to refine their application and maximize their impact on patient care. Ultimately, this study serves as a foundation for future investigations aimed at enhancing the quality of critical care and improving patient outcomes.

Conclusion

In this study, we investigated the relationship between optic nerve sheath diameter (ONSD) and key clinical parameters, including SOFA score, mortality, and ICU length of stay, in patients with septic shock. Our findings demonstrated significant correlations between ONSD and markers of systemic inflammation (CRP), hemodynamic instability (serum lactate), and organ dysfunction (SOFA score). These associations suggest that ONSD, as a non-invasive bedside tool, holds considerable promise for monitoring neurological status and intracranial dynamics in critically ill septic patients.

The observed reduction in ONSD by day six of ICU stay, alongside its correlation with clinical parameters, underscores its potential as a dynamic indicator of disease progression and response to treatment. Despite limitations such as a relatively small sample size and demographic variability, our results highlight the utility of ONSD as a complementary tool in the ICU, facilitating timely interventions for sepsis-associated encephalopathy and elevated intracranial pressure. Future studies with larger cohorts and standardized protocols are warranted to further validate ONSD's role in enhancing clinical decision-making and improving outcomes in septic shock management.

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Data Availability

All data generated or analyzed during this study are included within the current article.

Human Ethics and Consent to Participate Declarations

This study was conducted under the ethics approval code IR.TUMS.MEDICINE.REC.1403.372. Participant declarations were not applicable.

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