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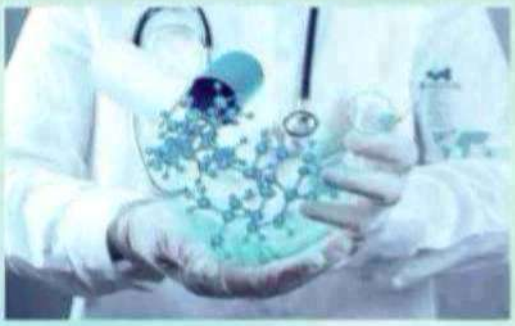

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SEPTIK SHOK BO'LGAN BEMORLARDA 28 KUNLIK O'LIMNING DASTLABKI BASHORATCHILARI QUYIDAGILAR: ISTIQBOLLI KUZATUV TADQIQOTI

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✓ ***Rezyume***

Septik shok butun dunyo bo'ylab intensiv terapiya bo'limlarida (ICU) o'limning asosiy sababi bo'lib qolmoqda, 28 kun davomida o'lim holatlari 30% dan 50% gacha o'zgaradi, reanimatsiya va organlarni qo'llab-quvvatlash strategiyalaridagi yutuqlarga qaramay. Markaziy Osiyodagi intensiv terapiya populyatsiyalaridan maxsus olingan bashoratli modellar hozirda yo'q.

Kalit so'zlar: septik shok, intensiv terapiya bo'limi, 28 kunlik o'lim, laktat, SOFA balli, prokalsitonin, ventilyatsiyaning mexanik ventilyatsiyasi, vazopressor terapiyasi, organ yetishmovchiligi, bashoratli model.

РАННИЕ ПРЕДИКТОРЫ 28-ДНЕВНОЙ СМЕРТНОСТИ У ПАЦИЕНТОВ С СЕПТИЧЕСКИМ ШОКОМ: ПРОСПЕКТИВНОЕ НАБЛЮДАТЕЛЬНОЕ ИССЛЕДОВАНИЕ

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✓ ***Резюме***

Септический шок остаётся ведущей причиной смертности в отделениях интенсивной терапии (ICU) по всему миру, при этом зарегистрированная смертность за 28 дней варьируется от 30% до 50%, несмотря на достижения в реанимации и стратегиях поддержки органов. Раннее и точное выявление пациентов с наибольшим риском смертельного исхода крайне важно для своевременного эскалации терапии и рационального распределения ресурсов отделения интенсивной терапии. Однако проверенные многопараметрические прогнозные модели, специально полученные из популяций реанимации Центральной Азии, в настоящее время отсутствуют.

Ключевые слова: септический шок, отделение интенсивной терапии, 28-дневная смертность, лактат, балл SOFA, прокальцитонин, механическая вентиляция вентиляций, терапия вазопрессорами, органная недостаточность, предиктивная модель.

EARLY PREDICTORS OF 28-DAY MORTALITY IN PATIENTS WITH SEPTIC SHOCK: A PROSPECTIVE OBSERVATIONAL STUDY

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✓ ***Resume***

Septic shock remains the leading cause of mortality in intensive care units (ICU) worldwide, with reported 28-day mortality rates ranging from 30% to 50% despite advances in resuscitation and organ support strategies. Early and accurate identification of patients at highest risk of fatal outcome is essential for timely escalation of therapy and rational allocation of ICU resources. However, validated multiparameter predictive models specifically derived from Central Asian ICU populations are currently lacking.

Keywords: septic shock, intensive care unit, 28-day mortality, lactate, SOFA score, procalcitonin, mechanical ventilation, vasopressor therapy, organ failure, predictive model.

Relevance

Sepsis and septic shock represent a life-threatening dysregulation of the host response to infection, resulting in organ dysfunction and circulatory failure that substantially increases the risk of death.[1] According to the third international consensus definitions (Sepsis-3, 2016), septic shock is defined as a subset of sepsis in which underlying circulatory, cellular, and metabolic abnormalities are profound enough to substantially increase mortality, identified clinically by the need for vasopressor therapy to maintain a mean arterial pressure (MAP) ≥65 mmHg and a serum lactate level >2 mmol/L in the absence of hypovolemia.[2]

Globally, sepsis affects an estimated 48.9 million patients annually and accounts for approximately 11 million deaths — representing nearly 20% of all global mortality.[1] In ICU settings, septic shock constitutes the most severe presentation, carrying a 28-day mortality of 30–50% and a hospital mortality exceeding 40% in many centers.[3] Despite significant advances in understanding of sepsis pathophysiology and widespread adoption of evidence-based resuscitation bundles, mortality rates have remained persistently high, underscoring the need for improved risk stratification tools.

Multiple scoring systems have been developed to assess severity and predict outcomes in critically ill patients, including the Sequential Organ Failure Assessment (SOFA), the Acute Physiology and Chronic Health Evaluation II (APACHE II), and the Simplified Acute Physiology Score (SAPS II).[4,5] However, these scores were developed and validated predominantly in Western European and North American ICU populations. Their performance in Central Asian patients — who may differ in baseline characteristics, comorbidity profiles, and patterns of microbial resistance — has not been prospectively validated.[6]

The objective of this study was to prospectively assess the early clinical and laboratory predictors of 28-day mortality in patients with septic shock admitted to an ICU in Tashkent, Uzbekistan, and to evaluate the discriminatory performance of a combined predictive model in comparison with established scoring systems.

Materials and methods

Study design and patient selection

A prospective observational study was conducted at the Department of Intensive Care, Republican Clinical Hospital No. 1 (Tashkent, Uzbekistan) from January 2021 to December 2023. The study protocol was approved by the Institutional Ethics Committee (Protocol No. 4, dated 10.01.2021). Written informed consent was obtained from patients or their legal representatives prior to enrollment.

Inclusion criteria: age ≥18 ears; diagnosis of septic shock according to Sepsis-3 criteria (vasopressor requirement to maintain MAP ≥65 mmHg and serum lactate >2 mmol/L despite adequate fluid resuscitation[2]); ICU admission within 24 hours of septic shock onset. Exclusion criteria: age <18 ears; do-not-resuscitate order at admission; ICU stay <24 hours (early discharge or death within 24 hours); terminal malignancy with life expectancy <3 months; chronic immunosuppressive therapy; pregnancy.

Data collection and clinical assessment

At ICU admission (Hour 0), the following variables were recorded: age, sex, source of infection, SOFA score, APACHE II score, need for mechanical ventilation (MV) and vasopressor therapy, fluid balance at 6 hours, urine output. SOFA score was calculated as described by Vincent et al.[4] and APACHE II as described by Knaus et al.[5] The primary source of infection was classified as pulmonary, abdominal, urological, soft tissue, or other/unknown.

Laboratory investigations

Blood samples were collected at ICU admission (Hour 0) and at 24 and 72 hours for the following parameters: arterial blood lactate (ABL), procalcitonin (PCT, electrochemiluminescence immunoassay), C-reactive protein (CRP), serum creatinine, total bilirubin, platelet count, international normalized ratio (INR), partial pressure of arterial oxygen to fraction of inspired oxygen ratio (PaO_2/FiO_2), serum albumin, and white blood cell count (WBC). Lactate clearance at 6 hours was calculated as: $[(Lactate_0 - Lactate_6) / Lactate_0] \times 100\%$.

Primary endpoint and follow-up

The primary endpoint was all-cause 28-day mortality. Secondary endpoints included ICU length of stay, duration of mechanical ventilation, and duration of vasopressor therapy. All patients were followed

until death or day 28, whichever occurred first. For patients discharged before day 28, vital status was confirmed by telephone contact.

Statistical analysis

Statistical analyses were performed using SPSS Statistics 27.0 (IBM Corp.) and R 4.3.0. Continuous variables are expressed as median [Q1; Q3] or mean ± SD. Categorical variables are reported as absolute numbers and percentages. Between-group comparisons used the Mann–Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. Multivariable logistic regression was applied to identify independent predictors of 28-day mortality; variables with $p<0.10$ in univariable analysis were entered into the model. Discriminatory performance was assessed by the area under the receiver operating characteristic curve (AUC-ROC). The optimal cutoff for each predictor was determined by the Youden index. A p-value <0.05 was considered statistically significant.

Results end discussion

Baseline characteristics

A total of 186 patients with septic shock were enrolled. The median age was 58 [46; 67] ears; 112 patients (60.2%) were male. The most common sources of infection were pulmonary (68 patients, 36.6%), abdominal (54, 29.0%), and urological (34, 18.3%). Mechanical ventilation was required in 134 patients (72.0%) and vasopressor therapy in all 186 (100%) by definition. The 28-day mortality rate was 42.5% (79 patients). Baseline characteristics stratified by outcome are presented in Table 1.

Independent predictors of 28-day mortality

In univariable analysis, the following variables were significantly associated with 28-day mortality ($p<0.10$): age, SOFA score, APACHE II score, admission lactate, 6-hour lactate clearance, PCT, PaO_2/FiO_2 ratio, serum creatinine, bilirubin, platelet count, serum albumin, need for mechanical ventilation, and norepinephrine dose. These were entered into the multivariable logistic regression model. Four variables emerged as independent predictors (Table 2).

The combined four-predictor model demonstrated AUC = 0.88 (95% CI 0.83–0.93), sensitivity 81.0%, specificity 83.2% at the optimal cutoff — significantly superior to SOFA alone (AUC 0.79; p=0.018) and APACHE II alone (AUC 0.77; p=0.012). Each additional predictor present increased predicted 28-day mortality from 14.2% (0 predictors) to 31.8% (1 predictor), 58.4% (2 predictors), 78.6% (3 predictors), and 91.4% (all 4 predictors).

Discussion

The present prospective study identified four independent early predictors of 28-day mortality in patients with septic shock: admission lactate ≥6.0 mmol/L, 6-hour lactate clearance <10%, SOFA score ≥11, and PCT ≥35 ng/mL. The combined model demonstrated excellent discriminatory capacity (AUC = 0.88), surpassing the performance of SOFA and APACHE II scores used individually — findings consistent with the established principle that septic shock mortality is driven by a convergence of hemodynamic, metabolic, and inflammatory derangements that no single parameter can fully capture.[3,4]

Admission lactate emerged as the strongest predictor (OR 4.82), which is in agreement with a large body of evidence implicating hyperlactatemia as a central marker of tissue hypoperfusion and mitochondrial dysfunction in septic shock.[7] Serum lactate reflects not only impaired oxygen delivery but also accelerated aerobic glycolysis driven by catecholamine excess and impaired hepatic lactate clearance — mechanisms particularly pronounced in the most severely ill patients. The Surviving Sepsis Campaign guidelines recommend lactate measurement at initial assessment and at 2 hours in patients with lactate >2 mmol/L, underscoring its fundamental role in sepsis management.[8]

The independent predictive value of 6-hour lactate clearance <10% (OR 3.64) is equally well supported in the literature. Lactate clearance reflects the capacity of the cardiovascular and metabolic systems to recover from the initial insult in response to resuscitation. Studies by Nguyen et al. and Casserly et al. demonstrated that failure to achieve ≥10% lactate clearance at 6 hours is associated with substantially higher ICU mortality, independent of absolute lactate values.[7,9] Our findings reinforce the clinical utility of serial lactate monitoring not merely as a static measurement but as a dynamic resuscitation target.

A SOFA score ≥11 at admission (OR 3.18) reflects the degree of multiorgan dysfunction, encompassing respiratory, cardiovascular, hepatic, renal, coagulation, and neurological systems. The SOFA score was originally developed by Vincent et al. as a tool for longitudinal tracking of organ dysfunction in ICU patients, and subsequent studies have validated its predictive value for ICU and in-hospital mortality in sepsis.[4] In

the Sepsis-3 consensus framework, an acute increase in SOFA score ≥2 points serves as the diagnostic criterion for sepsis, highlighting its centrality in contemporary intensive care practice.[2]

Table 1. Baseline characteristics of patients with septic shock stratified by 28-day outcome (n=186)

Parameter	Survivors (n=107)	Non-survivors (n=79)	p-value
Age, ears	54 [42; 64]	63 [51; 71]	0.002
Male sex, n (%)	66 (61.7%)	46 (58.2%)	0.631
Pulmonary source, n (%)	36 (33.6%)	32 (40.5%)	0.328
Abdominal source, n (%)	34 (31.8%)	20 (25.3%)	0.341
SOFA score (Day 0)	8 [6; 10]	12 [9; 14]	<0.001
APACHE II score	22 [17; 27]	30 [24; 35]	<0.001
Lactate, mmol/L (Hour 0)	3.8 [2.6; 5.2]	7.4 [5.1; 10.8]	<0.001
Lactate clearance at 6h, %	28.4 [14.2; 42.6]	8.6 [−4.2; 18.8]	<0.001
PCT, ng/mL (Hour 0)	18.4 [8.6; 42.2]	48.6 [22.4; 98.4]	<0.001
PaO_2/FiO_2 ratio	224 [168; 286]	148 [102; 198]	<0.001
Serum creatinine, μmol/L	164 [118; 228]	284 [198; 412]	<0.001
Total bilirubin, μmol/L	28.4 [16.8; 48.2]	62.8 [34.4; 118.6]	<0.001
Platelets, $\times 10^9$/L	148 [96; 218]	84 [48; 136]	<0.001
Serum albumin, g/L	28.4 [24.2; 32.6]	22.8 [18.4; 26.4]	<0.001
Mechanical ventilation, n (%)	68 (63.6%)	66 (83.5%)	0.004
Norepinephrine dose, μg/kg/min	0.18 [0.10; 0.32]	0.48 [0.28; 0.84]	<0.001
ICU length of stay, days	9 [6; 14]	6 [3; 10]	0.008

SOFA — Sequential Organ Failure Assessment; APACHE II — Acute Physiology and Chronic Health Evaluation II; PCT — procalcitonin; PaO_2/FiO_2 — partial pressure of arterial oxygen to fraction of inspired oxygen ratio; ICU — intensive care unit.

Table 2. Independent predictors of 28-day mortality (multivariable logistic regression)

Predictor	OR	95% CI	p-value
Admission lactate ≥6.0 mmol/L	4.82	2.41–9.64	<0.001
6-hour lactate clearance <10%	3.64	1.88–7.04	<0.001
SOFA score ≥11 (Day 0)	3.18	1.64–6.16	<0.001
PCT ≥35 ng/mL (Hour 0)	2.44	1.28–4.64	0.007

OR — odds ratio; CI — confidence interval; SOFA — Sequential Organ Failure Assessment; PCT — procalcitonin.

Procalcitonin ≥35 ng/mL (OR 2.44) was identified as the inflammatory biomarker most predictive of fatal outcome. PCT is synthesized by multiple organs in response to bacterial endotoxins and pro-inflammatory cytokines; in septic shock, markedly elevated PCT reflects overwhelming bacterial burden, systemic inflammatory dysregulation, and failure of host immune containment.[10] While CRP was also significantly elevated in non-survivors, it did not retain independent significance in the multivariable model, likely due to its slower kinetics and lower specificity compared to PCT. Serial PCT measurement has been proposed not only for prognostication but also for antibiotic stewardship — a dual utility that makes it particularly valuable in the ICU setting.[10,11]

The 28-day mortality in our cohort (42.5%) is consistent with published rates for septic shock from both high- and middle-income countries.[3,6] Several factors may account for this persistently high mortality, including delayed ICU referral, limited availability of advanced organ support modalities, and a high prevalence of multidrug-resistant pathogens in Central Asian hospitals.[6] The combined predictive model described here — based entirely on parameters available within the first 6 hours of ICU admission — offers a practical, low-cost risk stratification framework applicable in resource-constrained settings.

This study has several limitations. The single-center design and the absence of microbiological speciation data (source pathogen and susceptibility profiles) limit the generalizability of findings. Furthermore, the study period encompassed the COVID-19 pandemic, during which ICU case-mix and resource availability were altered, potentially introducing confounding. Multicenter validation is required before the proposed model can be recommended for routine clinical implementation.

Conclusion

In patients with septic shock admitted to the ICU, four variables measured within the first 6 hours independently predicted 28-day mortality: admission lactate ≥6.0 mmol/L, 6-hour lactate clearance <10%, SOFA score ≥11 at Day 0, and procalcitonin ≥35 ng/mL. A combined predictive model based on these parameters achieved excellent discriminatory performance (AUC = 0.88) and outperformed established scoring systems used in isolation.

Routine serial lactate measurement, early SOFA calculation, and PCT assessment within the first hours of ICU admission are strongly recommended in patients with septic shock to identify the highest-risk individuals requiring immediate escalation of organ support, intensified hemodynamic monitoring, and early goal-directed resuscitation. Multicenter prospective validation of the proposed model in Central Asian ICU populations is warranted.

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