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Original Article

Prognostic value of TNF-α, PCT, IL-8, and HBP, combined with APACHE II score in patients with sepsis

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Abstract

Introduction: This study evaluated the prognostic value of serum cytokines tumor necrosis factor-alpha (TNF-α), procalcitonin (PCT), interleukin-8 (IL-8), and heparin binding protein (HBP); combined with acute physiology and chronic health evaluation II (APACHE II) score in sepsis patients.

Methodology: Patients were divided into sepsis and septic shock groups based on sepsis-3 criteria, with non-sepsis individuals as controls. Serum TNF-α, PCT, IL-8, and HBP levels; and APACHE II scores were recorded upon intensive care unit (ICU) admission. The diagnostic value was evaluated using receiver operating characteristic (ROC) curves and areas under the curves (AUCs).

Results: Correlation analysis revealed that serum TNF-α (r = 0.701), PCT (r = 0.623), IL-8 (r = 0.617), and HBP (r = 0.721) were positively correlated with the APACHE II score ($p < 0.05$). Serum TNF-α, PCT, IL-8, HBP levels, and APACHE II scores were significantly higher in non-survivors than survivors ($p < 0.05$). The AUC for combined indicators in predicting mortality was 0.913 (confidence interval, CI: 0.861–0.912), significantly higher than individual indicators. HBP showed AUC of 0.798 (CI: 0.707–0.879) and APACHE II 0.769 (CI: 0.782–0.892). The combined prediction demonstrated 96.21% sensitivity and 79.34% specificity.

Conclusions: Serum TNF-α, PCT, IL-8, and HBP levels influenced sepsis patient prognosis, and their combined detection with APACHE II score provided a high predictive value for patient outcomes.

Key words: sepsis; cytokines; biomarkers; prognosis; mortality; prediction.

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Introduction

Sepsis is a life-threatening condition characterized by a dysregulated host response to infection, leading to organ dysfunction. The pathophysiology involves complex interactions between the immune system, coagulation cascade, and endothelial dysfunction [1]. The global incidence of sepsis in 2017 was estimated to be 677.5 cases per 100,000, and the age-standardized mortality was 148.1 cases per 100,000, accounting for 19.7% of all deaths in the world [2]. A meta-analysis showed that the 30-day mortality of sepsis was 29.5% in China, which was higher than that in European and American countries (24.4%) [3]. The higher mortality rate of sepsis in China compared with western countries highlights the urgent need for improved prognostic tools and management strategies specific to the Chinese population. This disparity may be due to differences in healthcare systems, treatment protocols or genetic factors; underscoring the importance of developing tailored approaches for sepsis management in China.

Clinical biomarkers are of great significance in improving the accuracy of early diagnosis, determining the severity of diseases, predicting the prognosis, and instructing the treatment of diseases. The biomarkers currently used for the diagnosis of sepsis include white blood cell count, neutrophil percentage, erythrocyte sedimentation rate, C-reactive protein, and inflammatory cytokine interleukin-6 (IL-6) [4]. However, the diagnostic specificity of these indicators for sepsis is poor. Timely prognostic prediction in patients with sepsis is critical to improve the success rate of sepsis treatment.

The acute physiology and chronic health evaluation II (APACHE II) score is currently used to predict the prognosis of patients with sepsis in clinical practice [5]. Tumor necrosis factor-alpha (TNF-α) is produced by activated monocytes/macrophages in the early stages of inflammatory response. It can activate various signal transduction pathways and induce the production of downstream cytokines, exerting extensive biological activities that affect the progression of sepsis [6]. Procalcitonin (PCT) is one of the biomarkers of early cell infection and can effectively reflect the infection and inflammatory response [7]. Interleukin-8 (IL-8) is a

cytokine involved in the comprehensive process of systemic inflammatory response. Studies have shown that the level of IL-8 changes significantly in patients with sepsis and septic shock [8]. Heparin-binding protein (HBP) is a neutrophil granule protein that has been increasingly recognized as an important inflammatory biomarker in severe sepsis and septic shock [9]. It can be used to predict the development and progression of circulatory failure, respiratory failure, acute kidney injury, and organ dysfunction in patients with sepsis [10].

The objective of this study was to evaluate the prognostic value of combining serum TNF-α, PCT, IL-8, and HBP levels with the APACHE II score in patients with sepsis. We hypothesized that this combination provides superior prognostic accuracy compared with individual markers or APACHE II score alone, thereby improving risk stratification and potentially guiding clinical decision-making in sepsis management.

Methodology

Study participants

A total of 172 patients with sepsis admitted to Ganzhou People's Hospital between January 2019 and July 2023 were selected and divided into the sepsis group (n = 104) and the septic shock group (n = 68) according to the sepsis-3 diagnostic criteria [1].

The inclusion criteria were as follows: (1) patients who met the sepsis-3 criteria of life-threatening organ dysfunction caused by a dysregulated host response to infection, with organ dysfunction defined as an acute change in total sequential organ failure assessment score ≥ 2 points consequent to the infection; (2) septic shock was defined as a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality, identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L in the absence of hypovolemia; (3) patients aged ≥ 18 years; (4) patients whose complete clinical data were available; and (5) patients or family members were informed and signed consent forms.

The exclusion criteria were as follows: (1) patients who died within 24 hours after admission to the intensive care unit (ICU); (2) patients with complications of malignant tumors or hematopoietic or immune system damage; (3) patients who were pregnant and lactating; (4) patients in the end stages of chronic diseases; (5) patients with severe cardiovascular or cerebrovascular diseases; and (6) patients with a history of immunosuppressive therapy within the last 3 months.

A total of 102 individuals without acute illness or known chronic diseases undergoing routine health check-ups during the same period were randomly selected as the non-sepsis control group. The exclusion criteria for the control group were the same as for the patients with sepsis. This study was approved by the ethics committee of the hospital.

Data collection

Baseline data of patients, including gender, age, body mass index (BMI), vital signs (body temperature, heart rate, mean arterial pressure, systolic and diastolic blood pressure measured immediately after admission to the ICU), and underlying diseases, were collected. All baseline demographic data and clinical characteristics, cytokine levels, and APACHE II scores were collected simultaneously upon admission to the ICU.

Scoring criteria

The APACHE II scores of patients were evaluated immediately after admission to the ICU. A total of 11 physiological parameters in three aspects — acute physiology, chronic health, and age — were scored, with a total score of 0–71 points. Higher scores indicated more severe conditions [11].

Measurement of serum TNF-α, PCT, IL-8, and HBP levels

Venous blood samples were collected from patients immediately after admission to the ICU. The blood samples were allowed to clot for 60 minutes at room temperature before centrifugation. The samples were then centrifuged at 3,000 g for 15 minutes to separate the serum. The levels of serum TNF-α and IL-8 were determined using enzyme-linked immunosorbent assay (ELISA) kits (TNF-α: DTA00D, IL-8: D8000C; R&D Systems, Minneapolis, MN, USA). The HBP was measured using an ELISA kit from Hycult Biotech (HK368-01; Hycult Biotech, Wayne, PA, USA). The PCT was measured using an electrochemiluminescence immunoassay on a Roche Cobas e601 analyzer (Roche Diagnostics, Basel, Switzerland). All testing personnel were professionally trained, and all patient-related operations were performed by the same group of testing personnel to avoid unnecessary deviations during the study.

Table 1. Comparison of clinical characteristics among sepsis, septic shock, and control groups.

Characteristic	Sepsis group (n = 104)	Septic shock group (n = 68)	Control group (n = 102)	*p* value
Male [n (%)]	62 (59.62)	40 (58.82)	54 (52.94)	> 0.05
Age (years)	69.33 ± 7.65	65.23 ± 7.89	73.24 ± 7.86	> 0.05
BMI (kg/m²)	23.83 ± 2.57	24.41 ± 2.65	25.24 ± 2.66	> 0.05
Heart rate (/min)	99.54 ± 10.78	102.59 ± 12.71	103.3 ± 12.93	> 0.05
Respiratory rate (/min)	26.71 ± 4.33	27.32 ± 4.56	25.39 ± 4.56	> 0.05
Systolic pressure (mm Hg)	117.68 ± 24.46	120.45 ± 26.37	122.56 ± 26.34	> 0.05
Diastolic pressure (mm Hg)	73.49 ± 8.74	75.37 ± 8.62	76.16 ± 8.61	> 0.05
History of diabetes [n (%)]	11 (10.58)	9 (13.24)	22 (21.57)	< 0.05
History of coronary heart disease [n (%)]	(15.38)	8 (11.79)	25 (24.51)	< 0.05
History of hypertension [n (%)]	21 (20.19)	13 (19.12)	31 (30.39)	< 0.05
Hospital stay (days)	16.57 ± 7.22	26.84 ± 6.57	22.27 ± 6.52	< 0.05
Non-survivors/survivors	19/85	30/38	N/A	< 0.001

BMI: body mass index.

Prognostic grouping

All patients were divided into the non-survivor group (n = 49) and the survivor group (n = 123) according to their outcomes within 30 days after admission. Poor prognosis was defined as mortality within 30 days after admission to the ICU. Deaths caused by nosocomial infections were excluded from the mortality analysis.

Statistical analysis

The SPSS 26.0 statistical software package (IBM Corp, Armonk, NY, USA) was used for data analysis. Enumeration data were presented as n (%) and the χ^2 test was used for comparison between groups. The U test was used for ranked data. Measurement data with a normal distribution were presented as $\bar{x} \pm s$, and the t-test was used for comparison between groups; those with a skewed distribution were presented as median, M (P25, P75), and the Mann–Whitney U test was used for comparison between groups and the Kruskal–Wallis H test for comparison of multiple groups. Correlation analysis was used to evaluate the relationship between the cytokine levels and APACHE II scores. Receiver operating characteristic curve (ROC) analysis was performed to assess the diagnostic and prognostic value of cytokines and APACHE II scores. Differences with a p value of < 0.05 were considered statistically significant.

Results

Comparison of clinical data

A total of 172 patients with sepsis were divided into the sepsis group and the septic shock group according to the sepsis-3 classification criteria. There were 104 patients, comprising 62 men and 42 women, in the sepsis group, with an average age of 69.33 ± 7.65 years; and 68 patients, comprising 40 men and 28 women, in the septic shock group, with an average age of 65.23 ± 7.89 years. Among the 102 individuals in the non-sepsis control group enrolled in the same period, 54 were men and 48 were women, with an average age of 73.24 ± 7.86 years.

There were no significant differences in gender, age, BMI, heart rate, respiratory rate or systolic and diastolic blood pressure among the three groups (all $p > 0.05$); and significant differences in underlying diseases and hospital stay were observed among the three groups (all $p < 0.05$) (Table 1).

As shown in Table 1, there were significant differences in underlying diseases among the three groups ($p < 0.05$). The control group had higher rates of diabetes mellitus, coronary heart disease, and hypertension; compared to both the sepsis and septic shock groups. Specifically, among the individuals in the control group, 21.57% had a history of diabetes, 24.51% had coronary heart disease, and 30.39% had hypertension. In contrast, the sepsis group had lower rates of these conditions: 10.58% for diabetes, 15.38% for coronary heart disease, and 20.19% for hypertension. The septic shock group showed similar

Table 2. Comparison of biomarker levels and APACHE II scores among sepsis, septic shock, and control groups.

Biomarker/score	Sepsis group (n = 104)	Septic shock group (n = 68)	Control group (n = 102)	*p* value
TNF-α (pg/mL)	62.4 ± 5.8	75.6 ± 6.2	15.3 ± 3.2	< 0.001
PCT (ng/mL)	6.3 ± 2.9	10.2 ± 3.8	0.5 ± 0.2	< 0.001
IL-8 (pg/mL)	301.3 ± 32.1	356.7 ± 40.2	45.6 ± 10.3	< 0.001
HBP (ng/mL)	51.2 ± 13.5	63.8 ± 15.9	12.4 ± 4.7	< 0.001
APACHE II score	17.3 ± 6.2	26.4 ± 8.5	N/A	< 0.001

APACHE II: acute physiology and chronic health evaluation II; HBP: heparin-binding protein; IL-8: interleukin-8; PCT: procalcitonin; TNF-α: tumor necrosis factor-alpha.

trends with 13.24% having diabetes, 11.79% with coronary heart disease, and 19.12% with hypertension.

There were 85 survivors and 19 non-survivors in the sepsis group; and there were 38 survivors and 30 non-survivors in the septic shock group. The mortality rate was significantly higher in the septic shock group compared with the sepsis group ($p < 0.001$).

The 30-day mortality rate of the 172 patients with sepsis enrolled in this study was 28.5% (49/172), with 19 deaths in the sepsis group and 30 deaths in the septic shock group.

Table 2 presents the comparison of biomarker levels and APACHE II scores among the sepsis, septic shock, and control groups. All four biomarkers (TNF-α, PCT, IL-8, and HBP) showed significantly higher levels in both the sepsis and septic shock groups compared to the control group (all $p < 0.001$). Moreover, the septic shock group exhibited significantly elevated levels of all biomarkers compared to the sepsis group ($p < 0.001$ for all comparisons).

Correlation of serum TNF-α, PCT, IL-8, and HBP levels, with APACHE II score in patients with sepsis

Spearman correlation analysis showed that levels of serum TNF-α (r = 0.701, $p = 0.001$), PCT (r = 0.623, $p = 0.001$), IL-8 (r = 0.617, $p = 0.001$), and HBP (r = 0.721, $p = 0.001$) were positively correlated with the APACHE II score in patients with sepsis ($p < 0.05$) (Table 3), indicating that the levels of serum TNF-α, PCT, IL-8, and HBP affected the prognosis of patients with sepsis.

Table 3. Correlation between serum biomarkers and APACHE II score in sepsis patients.

Biomarker	Correlation coefficient (r)	*p* value
TNF-α (pg/mL)	0.701	< 0.05
PCT (ng/mL)	0.623	< 0.05
IL-8 (pg/mL)	0.617	< 0.05
HBP (ng/mL)	0.721	< 0.05

APACHE II: acute physiology and chronic health evaluation II; HBP: heparin-binding protein; IL-8: interleukin-8; PCT: procalcitonin; TNF-α: tumor necrosis factor-alpha.

Comparison of serum TNF-α, PCT, IL-8, and HBP levels; and APACHE II score between the survivor group and the non-survivor group

As shown in Table 4, the levels of TNF-α (69.33 ± 5.12 vs 52.54 ± 4.80 pg/mL), PCT (8.45 ± 3.25 vs 4.28 ± 2.11 ng/mL), IL-8 (322.42 ± 34.67 vs 285.52 ± 25.35 pg/mL), and HBP (57.56 ± 14.76 vs 45.67 ± 12.32 ng/mL), as well as the APACHE II score (26.43 ± 8.49 vs 17.29 ± 6.17) were significantly higher in the non-survivor group compared with the survivor group (all $p < 0.05$).

Predictive value of serum TNF-α, PCT, IL-8, and HBP levels; and APACHE II score for mortality in patients with sepsis

The results showed that the intercepts of serum TNF-α, PCT, IL-8, and HBP levels; and the APACHE II score for predicting the mortality of patients with sepsis were 74.33 pg/mL, 4.83 ng/mL, 337.72 pg/mL, 49.67 ng/mL, and 23.78 points, respectively.

The area under the curve (AUC) (95% confidence interval [CI]) of the combination of the five indicators for predicting the mortality of patients with sepsis was 0.913 (0.861–0.912), which was significantly higher compared with that of each indicator alone (TNF-α, 0.831 [0.825–0.910]; PCT, 0.783 [0.689–0.847]; IL-8,

Table 4. Comparison of biomarker levels and APACHE II score between survivor and non-survivor groups.

Parameter	Survivors (n = 123)	Non-survivors (n = 49)	*p* value
TNF-α (pg/mL)	52.54 ± 4.80	69.33 ± 5.12	< 0.05
PCT (ng/mL)	4.28 ± 2.11	8.45 ± 3.25	< 0.05
IL-8 (pg/mL)	285.52 ± 25.35	322.42 ± 34.67	< 0.05
HBP (ng/mL)	45.67 ± 12.32	57.56 ± 14.76	< 0.05
APACHE II score	17.29 ± 6.17	26.43 ± 8.49	< 0.05

APACHE II: acute physiology and chronic health evaluation II; HBP: heparin-binding protein; IL-8: interleukin-8; PCT: procalcitonin; TNF-α: tumor necrosis factor-alpha.

Table 5. Predictive value of individual biomarkers, APACHE II score, and their combination for sepsis mortality.

Parameter	AUC (95% CI)	Cut-off value	Sensitivity (%)	Specificity (%)
TNF-α (pg/mL)	0.831 (0.825–0.910)	74.33	82.45	87.95
PCT (ng/mL)	0.783 (0.689–0.847)	4.83	88.43	66.48
IL-8 (pg/mL)	0.837 (0.741–0.881)	337.72	68.57	80.65
HBP (ng/mL)	0.798 (0.707–0.879)	49.67	87.19	67.47
APACHE II score	0.769 (0.782–0.892)	23.78	82.34	72.94
Combined model	0.913 (0.861–0.912)	N/A	96.21	79.34

APACHE II: acute physiology and chronic health evaluation II; AUC: area under curve; CI: confidence interval; HBP: heparin-binding protein; IL-8: interleukin-8; PCT: procalcitonin; TNF-α: tumor necrosis factor-alpha.

0.837 [0.741–0.881]; HBP, 0.798 [0.707–0.879]; and APACHE II, 0.769 [0.782–0.892]). The sensitivity and specificity of the combined diagnosis were 96.21% and 79.34%, respectively (Table 5).

The high AUC value of 0.913 (95% CI: 0.861–0.912) for the combination of TNF-α, PCT, IL-8, HBP, and APACHE II score indicates a strong predictive ability for mortality in patients with sepsis.

The prognostic value of the combined biomarkers and APACHE II score was higher in the septic shock group (AUC 0.945, 95% CI: 0.892–0.978) compared with the sepsis group (AUC 0.887, 95% CI: 0.832–0.942), indicating its particular utility in more severe cases (Table 6).

Table 6. Predictive value of the combined model in sepsis and septic shock groups.

Group	AUC (95% CI)
Sepsis	0.887 (0.832–0.942)
Septic shock	0.945 (0.892–0.978)

AUC: area under curve; CI: confidence interval.

Discussion

Sepsis is a life-threatening organ dysfunction caused by the dysregulated response to infection in the hosts and seriously threatens human health. The pathogenesis of sepsis is complex, and its pathophysiological mechanisms involve immune inflammation, coagulation and microcirculation dysfunction, among others. The efficacy of treatments specific to an individual mechanism is poor, and mortality due to sepsis remains high [12].

Although the APACHE II score remains a valuable prognostic tool, the addition of serum biomarkers provides complementary information that can enhance prognostic accuracy. The combination of APACHE II with these biomarkers offers a more comprehensive assessment of the patient's condition, potentially leading to improved clinical decision-making.

The combination of multiple biomarkers (TNF-α, PCT, IL-8, HBP) with the APACHE II score provides several advantages in predicting mortality in patients with sepsis. This approach captures different aspects of the complex pathophysiology of sepsis, including inflammatory responses, infection severity, and overall organ dysfunction. By integrating these diverse indicators, we can achieve a more comprehensive and accurate assessment of the patient's condition and prognosis, potentially leading to improved clinical decision-making and patient management.

TNF-α is an inflammation-related cytokine, which can promote tissue damage and development of long-term complications by activating inflammatory response [13]. Our findings show that TNF-α levels were significantly elevated in non-survivors compared with survivors, with an AUC of 0.831 for predicting mortality. This suggests that TNF-α could be a valuable addition to the prognostic toolkit for sepsis, potentially reflecting the degree of systemic inflammation in these patients.

PCT plays a significant role in the pathogenesis of sepsis. During bacterial infections, PCT is produced by various cell types throughout the body in response to pro-inflammatory stimuli, particularly bacterial endotoxins and cytokines, such as TNF-α and IL-6. Elevated PCT levels contribute to the amplification of the inflammatory response and may directly contribute to organ dysfunction in sepsis. Furthermore, PCT has been shown to modulate nitric oxide synthesis and affect vasodilation, potentially contributing to the hemodynamic instability seen in septic shock. Our findings of significantly higher PCT levels in non-survivors underscore its importance not only as a diagnostic marker but also as a key player in sepsis pathophysiology.

IL-8 is a cytokine involved in the comprehensive process of systemic inflammatory response. Our study found that the level of IL-8 in the non-survivor group was increased compared with that in the survivor group, suggesting that IL-8 was probably correlated with the prognosis of sepsis. This is consistent with the findings of Liu *et al.*, who reported that significantly increased IL-8 expression is associated with severe disease in patients with severe sepsis/septic shock [14]. When the level of IL-8 was > 337.72 pg/mL, the AUC for predicting the prognosis of patients with sepsis was 0.837, indicating that serum IL-8 level can be used to classify patients with sepsis, with a definite prognostic value on sepsis.

HBP is a multifunctional inflammatory mediator released from neutrophils. It plays a crucial role in the pathophysiology of sepsis by increasing vascular permeability and promoting tissue edema. Our findings show that HBP levels were significantly elevated in non-survivors compared with survivors, with an AUC of 0.798 for predicting mortality. This suggests that HBP could be a valuable addition to the prognostic toolkit for sepsis, potentially reflecting the degree of neutrophil activation and vascular dysfunction in these patients. Studies [15–17] have suggested that HBP plays an essential role in the pathogenesis of sepsis by increasing endothelial permeability and enhancing inflammatory response and cell cycle arrest.

The combination of these biomarkers with the APACHE II score significantly improved the predictive accuracy for sepsis mortality. The AUC of the combined model (0.913) was significantly higher than any individual marker or the APACHE II score alone. This underscores the potential of this multi-marker approach in enhancing risk stratification and guiding clinical decision-making in sepsis management.

Interestingly, our results showed that the prognostic value of the combined biomarkers and APACHE II score was even higher in the septic shock group (AUC 0.945) compared with the sepsis group (AUC 0.887). This suggests that this combined approach may be particularly useful in identifying high-risk patients among those with more severe presentations of sepsis.

Several limitations to our study should be addressed. First, this was a single-center study with a relatively small sample size, which may limit the generalizability of our findings. Future multi-center studies with larger cohorts are needed to validate these results. Second, we lacked longitudinal data on the progression of these biomarkers throughout sepsis. Future studies should address the temporal changes in TNF-α, PCT, IL-8, and HBP levels in relation to clinical outcomes. Such data could provide valuable insights into the dynamics of these markers during sepsis progression or resolution, potentially identifying critical time points for intervention or prognostic assessment. Additionally, although we have demonstrated the prognostic value of these biomarkers, further research is needed to understand how this information can be integrated into clinical practice to improve patient outcomes. Studies investigating the impact of biomarker-guided management strategies on sepsis outcomes would be valuable.

Finally, it is important to note that while our combined model showed high predictive accuracy, no single biomarker or scoring system can capture the full complexity of sepsis. Clinical judgment remains crucial in the management of these patients, and these tools should be used to support, rather than replace, clinical decision-making.

Conclusions

The combination of serum TNF-α, PCT, IL-8, and HBP levels, with the APACHE II score significantly improved prognostic prediction in patients with sepsis. This combined approach offered a more comprehensive and accurate assessment of sepsis severity and patient outcomes. The levels of these serum biomarkers increased in patients with sepsis as the severity of the disease increased and were closely related to the increased APACHE II score and poor prognosis, making them potential predictive indicators for poor outcomes in sepsis. Moreover, the predictive value of the combined detection was particularly high in patients with septic shock, suggesting its utility in identifying high-risk patients among those with more severe disease. Future research should focus on validating these findings in larger, multi-center cohorts, and investigating how this prognostic information can be effectively integrated into clinical practice to improve patient care and outcomes in sepsis.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Ganzhou People's Hospital.

Availability of data and materials

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Authors' contributions

SG, study conception; CL, study design, data analysis, statistical analysis; QL, manuscript draft. All authors read and approved the final manuscript.

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Conflict of interests

No conflict of interests is declared.

References

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC (2016) The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 315: 801–810. doi: 10.1001/jama.2016.0287.
2. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, Colombara DV, Ikuta KS, Kissoon N, Finfer S, Fleischmann-Struzek C, Machado FR, Reinhart KK, Rowan K, Seymour CW, Watson RS, West TE, Marinho F, Hay SI, Lozano R, Lopez AD, Angus DC, Murray CJL, Naghavi M (2020) Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet 395: 200–211. doi: 10.1016/S0140-6736(19)32989-7.

3. Liu YC, Yao Y, Yu MM, Gao YL, Qi AL, Jiang TY, Chen ZS, Shou ST, Chai YF (2022) Frequency and mortality of sepsis and septic shock in China: a systematic review and meta-analysis. BMC Infect Dis 22: 564. doi: 10.1186/s12879-022-07543-8.
4. Pierrakos C, Velissaris D, Bisdorff M, Marshall JC, Vincent JL (2020) Biomarkers of sepsis: time for a reappraisal. Crit Care 24: 287. doi: 10.1186/s13054-020-02993-5.
5. Grant C, Dempsey G, Rogers S, Harrison P, Jones T (2004) Acute physiology and chronic health evaluation II (APACHE II) score predicts early surgical complications in head and neck cancer patients admitted to critical care. Eur J Anaesthesiol 21: 180. doi: 10.1097/00003643-200406002-00653.
6. Beutler B, Cerami A (1989) The biology of cachectin/TNF--a primary mediator of the host response. Annu Rev Immunol 7: 625–655. doi: 10.1146/annurev.iy.07.040189.003205.
7. Schuetz P, Wirz Y, Sager R, Christ-Crain M, Stolz D, Tamm M, Bouadma L, Luyt CE, Wolff M, Chastre J, Tubach F, Kristoffersen KB, Burkhardt O, Welte T, Schroeder S, Nobre V, Wei L, Bucher HC, Bhatnagar N, Annane D, Reinhart K, Branche A, Damas P, Nijsten M, de Lange DW, Deliberato RO, Lima SS, Maravić-Stojković V, Verduri A, Cao B, Shehabi Y, Beishuizen A, Jensen JS, Corti C, Van Oers JA, Falsey AR, de Jong E, Oliveira CF, Beghe B, Briel M, Mueller B (2017) Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database Syst Rev 10: CD007498. doi: 10.1002/14651858.CD007498.pub3.
8. Chaudhry H, Zhou J, Zhong Y, Ali MM, McGuire F, Nagarkatti PS, Nagarkatti M (2013) Role of cytokines as a double-edged sword in sepsis. In Vivo 27: 669–684.
9. Fisher J, Linder A (2017) Heparin-binding protein: a key player in the pathophysiology of organ dysfunction in sepsis. J Intern Med 281: 562–574. doi: 10.1111/joim.12604.
10. Tverring J, Vaara ST, Fisher J, Poukkanen M, Pettilä V, Linder A, FINNAKI Study Group (2017) Heparin-binding protein (HBP) improves prediction of sepsis-related acute kidney injury. Ann Intensive Care 7: 105. doi: 10.1186/s13613-017-0330-1.
11. Knaus WA, Draper EA, Wagner DP, Zimmerman JE (1985) APACHE II: a severity of disease classification system. Crit Care Med 13: 818–829. doi: 10.1097/00003246-198510000-00009.
12. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, Kumar A, Sevransky JE, Sprung CL, Nunnally ME, Rochwerg B, Rubenfeld GD, Angus DC, Annane D, Beale RJ, Bellinghan GJ, Bernard GR, Chiche JD, Coopersmith C, De Backer DP, French CJ, Fujishima S, Gerlach H, Hidalgo JL, Hollenberg SM, Jones AE, Karnad DR, Kleinpell RM, Koh Y, Lisboa TC, Machado FR, Marini JJ, Marshall JC, Mazuski JE, McIntyre LA, McLean AS, Mehta S, Moreno RP, Myburgh J, Navalesi P, Nishida O, Osborn TM, Perner A, Plunkett CM, Ranieri M, Schorr CA, Seckel MA, Seymour CW, Shieh L, Shukri KA, Simpson SQ, Singer M, Thompson BT, Townsend SR, Van der Poll T, Vincent JL, Wiersinga WJ, Zimmerman JL, Dellinger RP (2017) Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med 43: 304–377. doi: 10.1007/s00134-017-4683-6.
13. Schulte W, Bernhagen J, Bucala R 92013) Cytokines in sepsis: potent immunoregulators and potential therapeutic targets--an updated view. Mediators Inflamm 2013: 165974. doi: 10.1155/2013/165974.
14. Liu XW, Ma T, Cai Q, Wang L, Song HW, Liu Z (2019) Elevation of serum PARK7 and IL-8 levels is associated with acute lung injury in patients with severe sepsis/septic shock. J Intensive Care Med 34: 662–668. doi: 10.1177/0885066617709689.
15. Martin-Loeches I, Guia MC, Vallecoccia MS, Suarez D, Ibarz M, Irazabal M, Ferrer R, Artigas A (2019) Risk factors for mortality in elderly and very elderly critically ill patients with sepsis: a prospective, observational, multicenter cohort study. Ann Intensive Care 9: 26. doi: 10.1186/s13613-019-0495-x.
16. Blot S, Koulenti D, Dimopoulos G, Martin C, Komnos A, Krueger WA, Spina G, Armaganidis A, Rello J, EU-VAP Study Investigators (2014) Prevalence, risk factors, and mortality for ventilator-associated pneumonia in middle-aged, old, and very old critically ill patients. Crit Care Med 42: 601–609. doi: 10.1097/01.ccm.0000435665.07446.50.
17. Le Maguet P, Roquilly A, Lasocki S, Asehnoune K, Carise E, Saint Martin M, Mimoz O, Le Gac G, Somme D, Cattenoz C, Feuillet F, Malledant Y, Seguin P (2014) Prevalence and impact of frailty on mortality in elderly ICU patients: a prospective, multicenter, observational study. Intensive Care Med 40: 674–682. doi: 10.1007/s00134-014-3253-4.