ORIGINAL ARTICLE

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An analysis of lactate/albumin, procalcitonin/albumin, and blood urea nitrogen/albumin ratios as a predictor of mortality in uroseptic patients

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SUMMARY

OBJECTIVE: The aim of this study was to investigate the ratios of lactate/albumin, procalcitonin/albumin, and blood urea nitrogen/albumin to predict 14- and 28-day mortality in uroseptic patients. Urosepsis is a disease with high mortality, and early diagnosis and treatment are important.

METHODS: Patients with urosepsis who were admitted to the intensive care unit between January 2021 and September 2022, had a follow-up of at least 28 days, and met the inclusion criteria were evaluated retrospectively.

RESULTS: The mean age was 70.23 (15.66) years and 84 (53.85%) were males. The number of non-survivors were 75 (48%) in the 14-day mortality group and 97 (62.1%) in the 28-day mortality group. Based on the 14-day mortality data, the blood urea nitrogen/albumin ratio was higher in non-survivors vs. survivors (median, 15.88 vs. 9.62), and the lactate/albumin ratio was higher (median, 0.96 vs. 0.52, p<0.01, all). Based on the 28-day mortality data, the blood urea nitrogen/albumin ratio was higher in non-survivors vs. survivors (median, 14.78 vs. 8.46), and the lactate/albumin ratio was higher (median, 0.90 vs. 0.50, p<0.01, all).

CONCLUSION: It is very difficult to determine the prognosis of patients admitted to the emergency department with the diagnosis of urosepsis. The lactate/albumin ratio and the blood urea nitrogen/albumin ratio can be used as early prognostic markers for both 14-day and 28-day mortality until more reliable markers are identified.

KEYWORDS: Mortality. Blood urea nitrogen. Lactate.

INTRODUCTION

Urosepsis is a serious infection of the urinary tract accompanied by systemic inflammatory response syndrome, which manifests in various forms such as pyelonephritis, cystitis, renal abscess, acute prostatitis, or acute epididymo-orchitis. Urosepsis constitute approximately 30% of all cases of sepsis, which may vary based on geographical regions[1]. It entails a high mortality rate, in the range of 30–40%. Its high mortality rate, its potential to cause sequelae, and the rising cost of hospitalized care warrant rapid and detailed evaluation of patients diagnosed with urosepsis[2].

It should also be remembered that early detection and the therapeutic approach used affect the patient's survey[3]. It is necessary to identify reliable and high-performing clinical indices that can be used in clinical practice to predict development of urosepsis in adults. It will also be useful to have a set of biomarkers that can be reliably used in a clinical setting to estimate prognosis.

Serum lactate (L) is a marker of tissue hypoxia and is associated with mortality in sepsis[4]. Albumin (A), a negative acute phase reactant, is a prognostic indicator of inflammation severity in septic patients[5]. Procalcitonin (PCT) is a peptide precursor of calcitonin. It has been shown that serum PCT levels are notably elevated in bacterial infections[6]. BUN level may be associated with poor prognosis and is a major risk factor indicator in septic patients[7,8].

Therefore, the aim of this single-center, retrospective, observational study was to determine the ratios of lactate/albumin (L/A), procalcitonin/albumin (PCT/A), and blood urea nitrogen/albumin (BUN/A) in evaluating 14- and 28-day mortality and prognosis-relevant factors in uroseptic patients and to investigate the specific L/A, PCT/A, and BUN/A values that may be useful in predicting mortality as a future prognostic factor.

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METHODS

Patients and data collection

A total of 156 patients diagnosed with urosepsis who presented at tertiary-care adult intensive care units at Dr. Ersin Arslan Training and Research Hospital over the period of January 2021 to September 2022 were included in this study. A diagnosis of sepsis was made using the criteria of "Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2012"[9]. The inclusion criteria were the presence of sepsis and a proven diagnosis of urinary infection. The exclusion criteria were as follows:

1. Culture results indicating polymicrobial infection
2. Patients aged less than 18 years
3. Patients not diagnosed with urosepsis
4. Lack of medical documentation precluding inclusion in statistical analysis
5. A negative urine culture.

Data on patients' age, gender, underlying conditions, duration of intensive care unit stay, invasive procedures, clinical particulars, and blood and urine culture evaluations, and prognostic data were collected and analyzed. The 14- and 28-day mortality rates were defined as death within 14 or 28 days, respectively, from the onset date of urosepsis. This study complied with the standards of medical ethics as endorsed by decision 184.22.09, dated 01.26.2023, of the Ethics Committee of Gaziantep Islam Science and Technology University.

Statistical analysis

Descriptive statistics of study data were expressed as mean for numerical variables and as frequency and percentage analysis for standard deviation and categorical variables. The consistency of biochemical and hemogram variables with the normal distribution was evaluated using the Shapiro-Wilk test. It was found that the variables were not consistent with the normal distribution ($p<0.05$). The Mann-Whitney U test was used for comparing the variables on mortality at day 14 vs. day 28. The analytical results for variables outlying the normal distribution were given as median (Q1–Q3). Moreover, the differences between categorical variables were analyzed using the Chi-square test. The receiver operating characteristic (ROC) curve was used for determining the cutoff points for the L/A, BUN/A, C-reactive protein/albumin (CRP/A), PCT/A, and neutrophil/lymphocyte (N/L) ratios. ROC analysis was performed to identify the best cutoff value for mortality prediction. The univariate/multivariate logistic regression analysis was used for evaluating variables which could impact on 14-day and 28-day mortality. Statistical analysis was performed using IBM SPSS 22.0 version (IBM SPSS, Chicago, IL). A significance level of $p<0.05$ was adopted.

RESULTS

Demographic data and clinical characteristics

A total of 156 patients who met the diagnostic criteria of urosepsis at hospitalization were included in the study in a total population of 2,332 patients who had been followed up at the tertiary care adult intensive care unit over the period of January 2021 to September 2022. Patients who were non-uroseptic, aged less than 18 years, or with missing study data were excluded. Notably, 84 (53.85%) of the patients were males, and 72 (46.15%) were females. A statistically significant difference in age or gender was absent between the survivor and the non-survivor groups. A total of 105 (67.31%) of the patients received mechanical ventilation support, and 51 (32.69%) did not need it. The number of non-survivors were 75 (48%) in the 14-day mortality group and 97 (62.1%) in the 28-day mortality group.

Based on the 14-day mortality data, the BUN/A ratio was higher in non-survivors vs. survivors [median, 15.88 (9.06–27.27) vs. 9.62 (5.48–16.50)], and the L/A ratio was higher [median, 0.96 (0.64–1.67) vs. 0.52 (0.39–0.71), $p<0.01$, all]. Similarly, based on the 28-day mortality data, the BUN/A ratio was higher in non-survivors vs. survivors [median, 14.78 (8.28–24.29) vs. 8.46 (5.48–14.58)] and the L/A ratio was higher [median, 0.90 (0.59–1.52) vs. 0.50 (0.37–0.67), $p<0.01$, all].

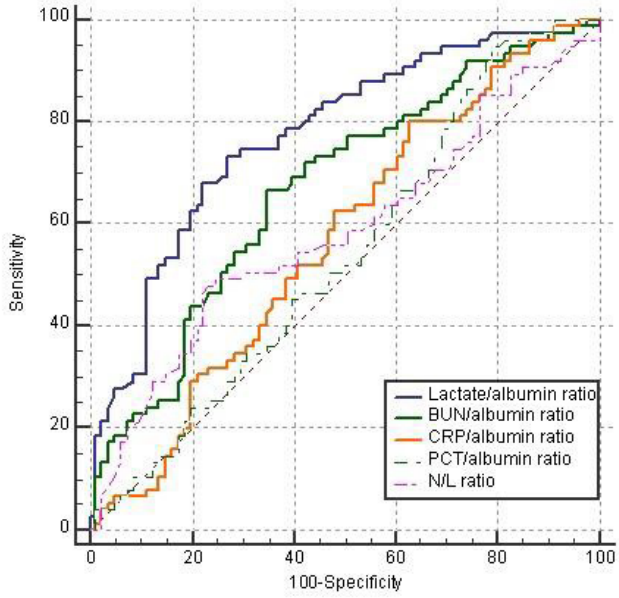
Significant independent risk factors identified by logistic regression analysis in the 14-day mortality data were the L/A ratio, BUN/A ratio, BUN, ferritin, international normalized ratio (INR), protrombin time (PT), D-dimer, platelet, mean corpuscular volume (MCV), and mean platelet volume (MPV). Also, the L/A ratio (OR=7.220, 95%CI 3.249–16.044, $p<0.001$) and the BUN/A ratio (OR=2.672, 95%CI 1.240–5.760, $p=0.012$) were identified as independent risk factors of mortality by multivariate and last model regression analysis (Table 1).

The ROC curves were plotted to predict 14-day mortality using the L/A ratio, BUN/A ratio, CRP/A ratio, PCT/A ratio, and N/L ratio. The area under the curve (AUC) for ROC was 0.771 for the L/A ratio (95%CI 0.697–0.835, $p=0.001$), 0.669 for the BUN/A ratio (95%CI 0.589–0.742, $p=0.001$), 0.567 for the CRP/A ratio (95%CI 0.486–0.646, $p=0.144$), 0.540 for the PCT/A ratio (95%CI 0.459–0.620, $p=0.385$), and 0.584 for the N/L ratio (95%CI 0.502–0.662, $p=0.072$) (Figure 1). For 28-day mortality, AUC for ROC was 0.772 for the L/A ratio (95%CI 0.698–0.835, $p=0.001$), 0.664 for

Table 1. Univariate, multivariate, and last model logistic regression analyses of various features associated with fatal outcomes for 14-day mortality.

Variable	Univariate OR	95%CI	p-value	Multivariate OR	95%CI	p-value	Last model OR	95%CI	p-value
L/A ratio	6.935	3.431–14.016	**<0.001**	6.006	2.488–14.497	**<0.001**	7.220	3.249–16.044	**<0.001**
BUN/A ratio	3.786	1.950–7.350	**<0.001**	2.652	1.196–5.882	**0.016**	2.672	1.240–5.760	**0.012**
BUN	1.020	1.007–1.034	**0.004**						
AST	1.002	0.998–1.005	0.365						
Ferritin	1.001	1.000–1.002	**0.009**	1.000	1.000–1.001	0.324			
INR	2.568	1.025–6.435	**0.044**	1.455	0.104–20.421	0.781			
PT	1.080	1.002–1.164	**0.043**	0.969	0.767–1.224	0.792			
D-dimer	1.096	1.006–1.193	**0.035**	1.047	0.959–1.142	0.303			
Platelet	1.000	1.000–1.000	**0.014**	1.000	1.000–1.000	0.068			
MCV	1.069	1.019–1.120	**0.006**	1.085	1.023–1.150	**0.006**	1.096	1.036–1.159	**0.001**
MPV	1.283	1.012–1.626	**0.039**	1.026	0.756–1.393	0.869			
Neutrophil	1.009	0.985–1.034	0.478						

Statistically significant values are denoted in bold. AST: aspartate aminotransferase.



Variable	AUC	95% CI	p	cutoff
L/A ratio	0.771	0.697 – 0.835	0.001	0.684
BUN/A ratio	0.669	0.589 – 0.742	0.001	12
CRP/A ratio	0.567	0.486 – 0.646	0.144	24.44
PCT/A ratio	0.540	0.459 - 0.620	0.385	0.036
N/L ratio	0.584	0.502 – 0.662	0.072	15.167

Figure 1. Analysis of receiver operating characteristic curve to predict 14-day mortality of uroseptic patients. The area under the curve was 0.771 for lactate/albumin ratio (p=0.001), 0.669 for blood urea nitrogen/albumin ratio (p=0.001), 0.567 for C-reaktive protein/albumin ratio (p=0.144), 0.540 for procalcitonin/albumin ratio (p=0.385), and 0.584 for neutrophil/lymphocyte ratio (p=0.072), respectively. The cutoff point of lactate/albumin ratio to predict 14-day mortality was 0.684 and 12 for blood urea nitrogen/albumin ratio.

the BUN/A ratio (95%CI 0.584–0.738, p=0.001), 0.600 for the CRP/A ratio (95%CI 0.519–0.678, p=0.037), 0.579 for the PCT/A ratio (95%CI 0.497–0.657, p=0.108), and 0.621 for the N/L ratio (95%CI 0.540–0.697, p=0.008) (Figure 2).

A cutoff value of 0.684 was determined for predicting both 14-day and 28-day mortality by L/A, and the survival rates of patients with a value above 0.684 were lower than in those with values below the threshold (p=0.001). Similarly, a cutoff value of 12 was used for predicting 14- and 28-day mortality rates by BUN/A. The survival rates were higher in patients in whom this value was below 12 (p=0.001) (Figures 1 and 2).

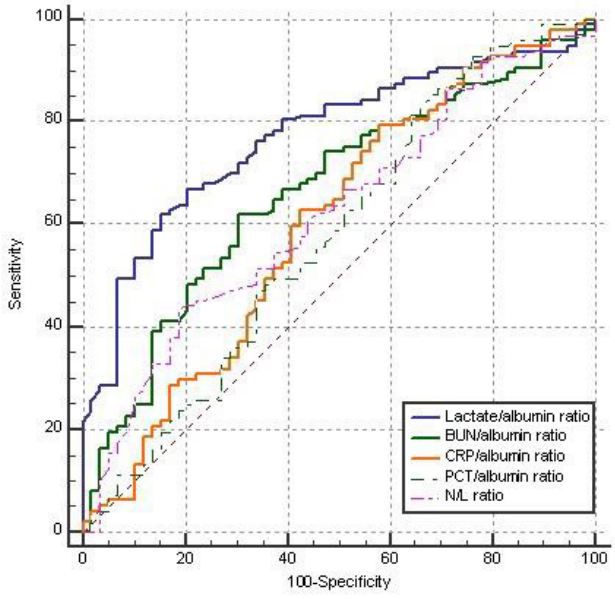
DISCUSSION

Early and accurate identification of sepsis is crucial, particularly in intensive care patients who are at high-risk for mortality. In this study, we investigated the independent risk factors which may potentially impact on prognosis and 14- and 28-day mortality, based on an analysis of clinical characteristics of uroseptic patients.

The 14-day mortality rate was 48% in this study. However, the mortality rate increased with the duration of stay, and the 28-day mortality rate was 62.1%. Our findings were consistent with the mortality rates reported by other studies, ranging from 40–58.3%[10,11].

The L/A ratio is a better prognostic marker of multi-organ failure and mortality in septic patients. Furthermore, a normal or low L/A ratio is associated with better prognosis[12,13]. Some studies have shown the L/A ratio to be a better predictor of mortality in septic patients[14-16].

Moreover, a cutoff value of 0.684 for the L/A ratio was determined for all uroseptic patients to differentiate survivors from non-survivors. In other studies with septic patients, the cutoff



Variable	AUC	95% CI	p	cutoff
L/A ratio	0.772	0.698 – 0.835	0.001	0.684
BUN/A ratio	0.664	0.584 – 0.738	0.001	12
CRP/A ratio	0.600	0.519 – 0.678	0.037	24.44
PCT/A ratio	0.579	0.497 – 0.657	0.108	0.077
N/L ratio	0.621	0.540 – 0.697	0.008	17.8

Figure 2. Analysis of receiver operating characteristic curve to predict 28-day mortality of uroseptic patients. The area under the curve was 0.772 for lactate/albumin ratio (p=0.001), 0.664 for blood urea nitrogen/albumin ratio (p=0.001), 0.600 for C-reaktive protein/albumin ratio (p=0.037), 0.579 for procalcitonin/albumin ratio (p=0.108), and 0.621 for neutrophil/lymphocyte ratio (p=0.008), respectively. The cutoff point of lactate/albumin ratio to predict 28-day mortality was 0.684 and 12 for blood urea nitrogen/albumin ratio.

values used included 1.01, 1.15, and 1.32, respectively[12,17,18]. We believe that the difference originates from the number of included patients. The optimal cutoff values vary between studies, and further investigation is necessary.

Some studies in the literature have suggested that the BUN/A ratio may be inversely related to survival, i.e., survival declines with this ratio increasing[19,20]. In our study, we have also shown that the BUN/A ratio may be used for predicting survey in uroseptic patients. We have determined an optimal cutoff value of 12 for predicting both 14- and 28-day mortality. In a Chinese study on 801 patients, a cutoff threshold of 5.27 was used for predicting 7-day mortality, while in a study on more than 10,000 patients, the cutoff was set to 7.93[19,21]. In a retrospective cohort study of 7,656 patients with sepsis, the cutoff value was 8 to predict 30-day mortality[22]. We believe that this difference between the cutoff values may be due to the differences in population size and the number of days used for mortality assessment.

In our study, in the 14-day mortality evaluation, the PCT/A ratios were higher in non-survivors vs. survivors [median, 0.68 (0.13–3.86) vs. 0.55 (0.6–3.2); p=0.386]. The results were similar for the 28-day mortality evaluation [median, 0.7 (0.14–3.86) vs. 0.36 (0.4–3.2); p=0.1]. Some recent reports in the literature have associated the PCT/A ratio with patient prognosis. A neonatal sepsis study has shown that an increased ratio was predictive of septic shock[23], while another study has suggested that it may be used for differentiating septic and non-septic urinary tract infections[24]. Our study differed from others in that we compared survivors with non-survivors in a population of uroseptic patients. While a statistically significant difference between the two groups was not found, the PCT/A ratios were higher in the non-survivor group.

Compared to the BUN/A ratio, the L/A ratio was a better prognostic marker based on 14-day mortality data (AUC of L/A ratio 0.771, 95%CI 0.697–0.835 vs. BUN/A ratio AUC=0.669, 95%CI 0.589–0.742) (p=0.001) (Figure 1). A similar observation was made in the 28-day mortality data (AUC of L/A ratio 0.772, 95%CI 0.698–0.835 vs. BUN/A ratio AUC=0.664, 95%CI 0.584–0.738) (p=0.001) (Figure 2). Our study has shown that the L/A and BUN/A ratios may be used as prognostic indicators in uroseptic patients. Increases in both of these ratios were independently associated with lower survival.

CONCLUSION

The L/A ratio and the BUN/A ratio may be used as early prognostic markers for both 14-day and 28-day mortality. We recommend using certain ratios as prognostic markers until reliable, affordable, and widely practicable biomarkers, shown to be so in studies, become broadly available.

AUTHORS' CONTRIBUTIONS

AŞ: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Writing – original draft, Writing – review & editing. **SB:** Conceptualization, Data curation, Formal Analysis, Supervision, Validation, Writing – original draft, Writing – review & editing. **SA:** Conceptualization, Data curation, Formal Analysis.

REFERENCES

1. Levy MM, Artigas A, Phillips GS, Rhodes A, Beale R, Osborn T, et al. Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study. Lancet Infect Dis. 2012;12(12):919-24. https://doi.org/10.1016/S1473-3099(12)70239-6
2. Brun-Buisson C. The epidemiology of the systemic inflammatory response. Intensive Care Med. 2000;26(Suppl 1):S64-74. https://doi.org/10.1007/s001340051121
3. Moyer MW. New biomarkers sought for improving sepsis management and care. Nat Med. 2012;18(7):999. https://doi.org/10.1038/nm0712-999
4. Mikkelsen ME, Miltiades AN, Gaieski DF, Goyal M, Fuchs BD, Shah CV, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med. 2009;37(5):1670-7. https://doi.org/10.1097/CCM.0b013e31819fcf68
5. Yin M, Si L, Qin W, Li C, Zhang J, Yang H, et al. Predictive value of serum albumin level for the prognosis of severe sepsis without exogenous human albumin administration: a prospective cohort study. J Intensive Care Med. 2018;33(12):687-94. https://doi.org/10.1177/0885066616685300
6. Charles PE, Ladoire S, Aho S, Quenot JP, Doise JM, Prin S, et al. Serum procalcitonin elevation in critically ill patients at the onset of bacteremia caused by either Gram negative or Gram positive bacteria. BMC Infect Dis. 2008;8:38. https://doi.org/10.1186/1471-2334-8-38
7. Li X, Zheng R, Zhang T, Zeng Z, Li H, Liu J. Association between blood urea nitrogen and 30-day mortality in patients with sepsis: a retrospective analysis. Ann Palliat Med. 2021;10(11):11653-63. https://doi.org/10.21037/apm-21-2937
8. Li X, Li T, Wang J, Dong G, Zhang M, Xu Z, et al. Higher blood urea nitrogen level is independently linked with the presence and severity of neonatal sepsis. Ann Med. 2021;53(1):2192-8. https://doi.org/10.1080/07853890.2021.2004317
9. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39(2):165-228. https://doi.org/10.1007/s00134-012-2769-8

10. Purba AKR, Mariana N, Aliska G, Wijaya SH, Wulandari RR, Hadi U, et al. The burden and costs of sepsis and reimbursement of its treatment in a developing country: an observational study on focal infections in Indonesia. Int J Infect Dis. 2020;96:211-8. https://doi.org/10.1016/j.ijid.2020.04.075
11. Suranadi IW, Sinardja CD, Suryadi IA. Role of procalcitonin in predicting mortality and organ dysfunction at intensive care admission. Int J Gen Med. 2022;15:4917-23. https://doi.org/10.2147/IJGM.S362558
12. Bou Chebl R, Geha M, Assaf M, Kattouf N, Haidar S, Abdeldaem K, et al. The prognostic value of the lactate/albumin ratio for predicting mortality in septic patients presenting to the emergency department: a prospective study. Ann Med. 2021;53(1):2268-77. https://doi.org/10.1080/07853890.2021.2009125
13. Wang B, Chen G, Cao Y, Xue J, Li J, Wu Y. Correlation of lactate/albumin ratio level to organ failure and mortality in severe sepsis and septic shock. J Crit Care. 2015;30(2):271-5. https://doi.org/10.1016/j.jcrc.2014.10.030
14. Wang R, He M, Qu F, Zhang J, Xu J. Lactate albumin ratio is associated with mortality in patients with moderate to severe traumatic brain injury. Front Neurol. 2022;13:662385. https://doi.org/10.3389/fneur.2022.662385
15. Guo W, Zhao L, Zhao H, Zeng F, Peng C, Guo W, et al. The value of lactate/albumin ratio for predicting the clinical outcomes of critically ill patients with heart failure. Ann Transl Med. 2021;9(2):118. https://doi.org/10.21037/atm-20-4519
16. Moustafa AA, Antonios MA, Abdellatif EM, Hussain AH. Association of lactate/albumin ratio level to organ failure and mortality in severe sepsis in a pediatric intensive care unit in Egypt. Turk J Pediatr. 2018;60(6):691-701. https://doi.org/10.24953/turkjped.2018.06.010
17. Shin J, Hwang SY, Jo IJ, Kim WY, Ryoo SM, Kang GH, et al. Prognostic value of the lactate/albumin ratio for predicting 28-day mortality in critically ill sepsis patients. Shock. 2018;50(5):545-50. https://doi.org/10.1097/SHK.0000000000001128
18. Gharipour A, Razavi R, Gharipour M, Mukasa D. Lactate/albumin ratio: an early prognostic marker in critically ill patients. Am J Emerg Med. 2020;38(10):2088-95. https://doi.org/10.1016/j.ajem.2020.06.067
19. Han T, Cheng T, Liao Y, Tang S, Liu B, He Y, et al. Analysis of the value of the blood urea nitrogen to albumin ratio as a predictor of mortality in patients with sepsis. J Inflamm Res. 2022;15:1227-35. https://doi.org/10.2147/JIR.S356893
20. Cai S, Wang Q, Chen C, Guo C, Zheng L, Yuan M. Association between blood urea nitrogen to serum albumin ratio and in-hospital mortality of patients with sepsis in intensive care: a retrospective analysis of the fourth-generation Medical Information Mart for Intensive Care database. Front Nutr. 2022;9:967332. https://doi.org/10.3389/fnut.2022.967332
21. Min J, Lu J, Zhong L, Yuan M, Xu Y. The correlation study between blood urea nitrogen to serum albumin ratio and prognosis of patients with sepsis during hospitalization. BMC Anesthesiol. 2022;22(1):404. https://doi.org/10.1186/s12871-022-01947-4
22. Wang Y, Gao S, Hong L, Hou T, Liu H, Li M, et al. Prognostic impact of blood urea nitrogen to albumin ratio on patients with sepsis: a retrospective cohort study. Sci Rep. 2023;13(1):10013. https://doi.org/10.1038/s41598-023-37127-8
23. Li T, Li X, Liu X, Zhu Z, Zhang M, Xu Z, et al. Association of procalcitonin to albumin ratio with the presence and severity of sepsis in neonates. J Inflamm Res. 2022;15:2313-21. https://doi.org/10.2147/JIR.S358067
24. Luo X, Yang X, Li J, Zou G, Lin Y, Qing G, et al. The procalcitonin/albumin ratio as an early diagnostic predictor in discriminating urosepsis from patients with febrile urinary tract infection. Medicine (Baltimore). 2018;97(28):e11078. https://doi.org/10.1097/MD.0000000000011078