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Effect of treatment applied in sepsis on intensive care unit and hospital stay: how effective are albumin/steroid/vasopressor agents?

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Abstract

Background: The incidence and prevalence of sepsis have increased in recent years and it is the most common cause of intensive care admission. The aim of this study was to determine the effects of albumin, steroid, and vasopressor agents and other possible factors on the duration of intensive care unit and hospital stay in sepsis patients. Open access data set obtained from Tohoku Sepsis Registry database was used. Four hundred sixty-two patients admitted to intensive care unit with the diagnosis of sepsis were divided into four groups according to their intensive care unit (≤ 5 or > 5 days) and hospital length of stay (≤ 24 or > 24 days). Demographic data, vital signs, laboratory values, mechanical ventilation requirement, and treatment protocols such as albumin, steroid, and vasopressor agent use were used in the evaluation of the groups.

Results: The use of albumin (odds ratio [OR] = 3.76 [95% confidence interval (CI), 2.16–6.56]; $p < 0.001$), steroids (OR = 2.85 [95% CI, 1.67–4.86]; $p < 0.001$), and vasopressor agents (OR = 3.56 [95% CI, 2.42–5.24]; $p < 0.001$) were associated with an increasing risk of prolonged intensive care unit length of stay. Also, it was found that the use of albumin (OR = 3.43 [95% CI, 2.00–5.89]; $p < 0.001$), steroids (OR = 2.81 [95% CI, 1.66–4.78]; $p < 0.001$), and vasopressor agents (OR = 4.47 [95% CI, 3.02–6.62]; $p < 0.001$) were associated with an increasing risk of prolonged hospital length of stay. In addition, prognostic scoring systems, body temperature, mean arterial pressure, pH, PaO_2/FiO_2 ratio, and mechanical ventilation requirement in the first 24 h were also found to be associated with length of stay in intensive care unit and hospital. There was a significant relationship between platelet count, creatinine, Na, lactic acid, and time between diagnosis of sepsis and source control and intensive care unit length of stay, and between hematocrit and C-reactive protein and hospital length of stay.

Conclusions: The use of albumin, steroid, and vasopressor agents has been found to be significantly correlated with both intensive care unit and hospital length of stay. Further studies are needed to determine in what order or at what dosage these agents will be administered in sepsis treatment.

Keywords: Critical care, Intensive care unit, Length of stay, Risk factors, Sepsis

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Background

The incidence and prevalence of sepsis, the most common cause of admission to intensive care unit (ICU) for critically ill patients, are increasing globally (Perner et al. 2016). However, sepsis mortality has decreased by 20–30% with advances in sepsis treatment (Gaieski et al. 2013; Kaukonen et al. 2014). This issue has been the concern of the studies conducted in recent years. The studies investigating the long-term outcomes of sepsis are of great interest because of the decrease in mortality and insufficient sensitivity to demonstrate the effect of acute interventions.

The predictability of intensive care unit length of stay (ICULOS) and hospital length of stay (HLOS) is important for both the intensive care unit physicians and patients and their relatives. ICULOS/HLOS has been used in the evaluation of various diseases or surgical procedures in many publications in recent years. ICULOS is affected by the severity of the disease and the rapid and on-site interventions (Knaus et al. 1993). In the literature, there are limited studies investigating the factors affecting ICULOS and HLOS in sepsis. Especially in the treatment of sepsis, the effect of albumin use, vasopressor agents, or steroid use on prognosis is still controversial. Knowing these factors will help to reduce the length of stay in the ICU. Therefore, the aim of this study is to determine the effects of albumin, steroid, and vasopressor agents and other possible factors on ICULOS and HLOS in 462 patients followed up with the diagnosis of sepsis in the ICU.

Methods

The data set (Kudo et al. 2018b) obtained from Tohoku Sepsis Registry database (UMIN000010297) which includes data from patients with sepsis in ICUs of 3 university and 7 community hospitals in Tohoku region in the northern part of Japan and utilized by Kudo et al. (2018a) was used in our study. The study of Kudo et al. (2018a) has been approved by the institutional review board of each institution. All institutional review boards concluded that there was no need for patient information and consent form, as it was an observational study that did not require any treatment other than treatment administered in daily clinical routine according to Japanese guidelines (Kudo et al. 2018a).

Patients who were admitted to the ICU with the diagnosis of sepsis or who were diagnosed as sepsis after being admitted to the ICU between January and December 2015 were included prospectively in the study (Kudo et al. 2018a). The diagnosis of severe sepsis or septic shock was established according to the international sepsis guidelines published in 2012 (Dellinger et al. 2013). A total of 616 patients were enrolled in the Tohoku Sepsis Registry. In our study, patients younger than 18 years of age, patients who received aggressive treatment for the first 4 days (n = 43), and patients who died during the hospitalization (n = 111) were not included in the present analysis. Data analysis was performed with 462 patients.

These data included demographic data such as age, gender, body mass index (BMI), and comorbidities. Scoring values such as Acute Physiology and Chronic Health Evaluation (APACHE II), Glasgow coma scale (GCS), and sequential organ failure assessment (SOFA) at admission were also included. In addition, vital signs of the first day (body temperature, pulse rate, mean arterial pressure (MAP), and respiration rate), laboratory results (leukocyte, platelet count, hematocrit (HCT), blood glucose, creatinine, Na, K, lactic acid, C-reactive protein (CRP), procalcitonin, bilirubin, pH, and PaO_2/FiO_2 ratio) were included. The patients' need for mechanical ventilation (MV) in the first 24 h, and such treatment data as the time from the diagnosis of sepsis to the source control or the start of antibiotics were present in the recorded sets. Treatment information data include the use of albumin during fluid resuscitation, vasopressor agents, and steroid for hypotension. Total ICULOS and HLOS data were obtained from the records.

In our study, the median value was used instead of the mean for the cut-off value, since the ICULOS and HLOS were not normally distributed. The median time for ICULOS was 5.5 days and for HLOS 24 days. Four hundred sisty-two patients were divided into four groups according to ICULOS (≤ 5 or > 5 days) and HLOS (≤ 24 or > 24 days). The flow chart of our study was presented in Fig. 1. Our study was conducted in accordance with the Helsinki Declaration Principles.

Statistical analysis

Mean, standard deviation (SD), median, minimum, maximum, frequency, and ratio values were used in the descriptive statistics of the data. Distribution of variables was measured by Shapiro-Wilk test. T test and Mann-Whitney U test were used for the analysis of quantitative independent data; chi-square test, Fisher's exact test when chi-square test conditions were not met, was used for the analysis of qualitative independent data. Univariate binary logistic regression analysis was used to determine risk factors. Data with missing values were excluded from the analysis. Significance level was accepted as $p < 0.05$ in 95% confidence interval for all analyses. SPSS 22.0 (Statistical Package of Social Sciences Inc., Chicago, IL, USA) software was employed to analyze the data.

Results

A total of 462 patients' data were processed; 277 (59.96%) were male and 185 (40.04%) were female. The age distribution of the patients was minimum 19, maximum 97, and median 75 (mean ± SD 72.07 ± 14.77)

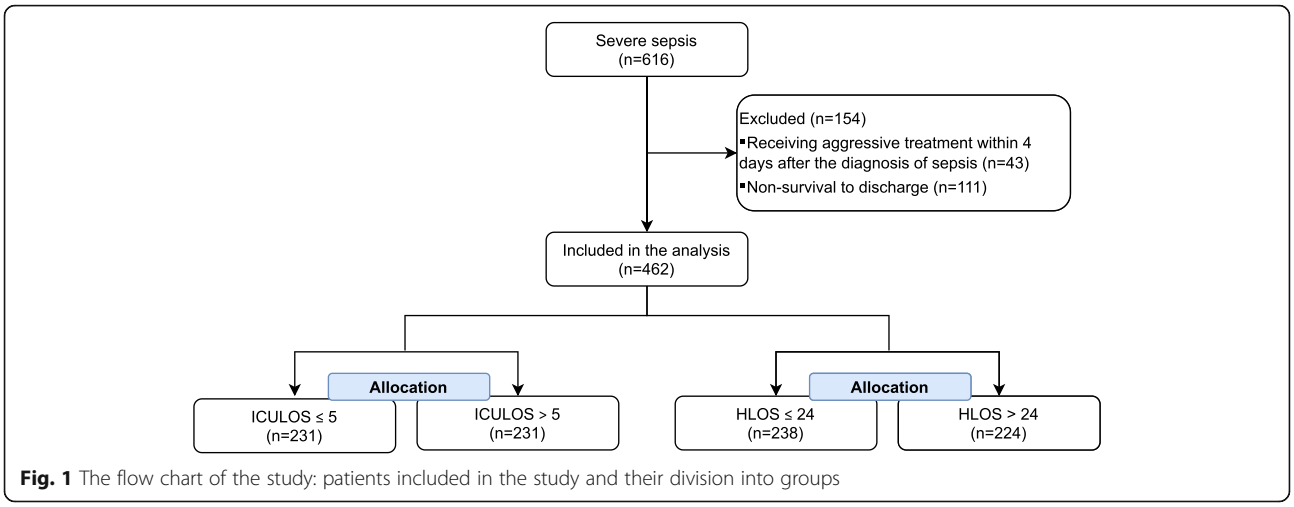

Fig. 1 The flow chart of the study: patients included in the study and their division into groups

years old. The ICULOS was minimum 1, maximum 236, and median 5.5 (mean ± SD 9.44 ± 16.07) days; HLOS was minimum 1, maximum 389, and median 24 (mean ± SD 42.35 ± 50.02) days.

A significant relationship was found between albumin ($p < 0.001$, $p < 0.001$), steroid ($p < 0.001$, $p < 0.001$), and vasopressor agent use ($p < 0.001$, $p < 0.001$) and prolonged ICULOS/HLOS. As for ICULOS and HLOS, there were also significant differences between the groups considering SOFA ($p < 0.001$, $p < 0.001$), APAC HE II ($p < 0.001$, $p < 0.001$), and GCS ($p < 0.001$, $p = 0.004$) scoring systems, body temperature ($p = 0.014$, $p = 0.003$), MAP ($p = 0.001$, $p < 0.001$), pH ($p = 0.002$, $p = 0.012$), PaO_2/FiO_2 ratio ($p < 0.001$, $p = 0.018$), and need for MV in the first 24 h ($p < 0.001$, $p < 0.001$). In addition, significant correlations were found between platelet count ($p = 0.002$), creatinine ($p = 0.011$), Na ($p = 0.002$), lactic acid ($p = 0.030$), and time between diagnosis of sepsis and source control ($p = 0.004$) and ICULOS, and between HCT ($p = 0.002$) and CRP ($p < 0.001$) values and HLOS (Table 1).

Univariate binary logistic regression analysis was performed for each of the risk factors and the coefficients of the risk factors that were significant as a result of the analysis were given in Table 2.

Use of albumin ($p < 0.001$, $p < 0.001$), steroid ($p < 0.001$, $p < 0.001$), and vasopressor agents ($p < 0.001$, $p < 0.001$) increased the probability of prolonged ICULOS and HLOS. Prolonged ICULOS and HLOS probability was high in patients using albumin (odds ratio [OR] = 3.763, OR = 3.429), steroid (OR = 2.845, OR = 2.813), and vasopressor agents (OR = 3.561, OR = 4.466).

Low MAP ($p = 0.002$, $p < 0.001$), body temperature ($p = 0.025$, $p < 0.001$), and pH ($p < 0.001$, $p = 0.005$), high creatinine ($p = 0.003$, $p = 0.013$), and need for MV ($p < 0.001$, $p < 0.001$) in the first 24 h increased the probability of prolonged ICULOS and HLOS. While low PaO_2/FiO_2 ratio ($p < 0.001$) and platelet count ($p = 0.01$) and high Na ($p = 0.004$) increased the probability of prolonged ICULOS, low HCT ($p = 0.002$) and high CRP ($p < 0.001$) increased the probability of HLOS.

Discussion

In this study, we aimed to determine the relationship between ICULOS/HLOS and albumin, steroid, and vasopressor agent use and to identify possible risk factors for prolonged ICULOS/HLOS in 462 patients followed up with the diagnosis of sepsis in the ICU. As a result of our study, there was a significant relationship between application of albumin, steroid, and vasopressor agent and ICULOS/HLOS. In addition to these factors SOFA, APACHE II, and GCS scoring systems, body temperature, MAP, pH, PaO_2/FiO_2 ratio, and need for MV in the first 24 h were found to be significantly related with both ICULOS and HLOS. Moreover, platelet count, creatinine, Na, lactic acid, and time between diagnosis of sepsis and source control were found to be correlated with the prolonged ICULOS, and HCT and CRP were found to be correlated with prolonged HLOS.

It is still controversial whether the use of crystalloid solutions or colloid solutions is better suited for both resuscitation and maintenance in sepsis and septic shock. Albumin has been shown to play a critical role in a variety of diseases and has a serious effect due to its oncotic properties (Caironi and Gattinoni 2009). In a randomized controlled study (Caironi et al. 2014), it was shown that albumin use was not associated with a decrease in mortality, but 20% albumin administration was beneficial in achieving the targeted MAP in the first hour and contributed to improving fluid balance over the next 7 days. In The Saline versus Albumin Fluid Evaluation (SAFE) study (The SAFE Study Investigators 2004), 4% albumin and normal saline applications were compared in intensive care patients, and no difference was found between the groups in terms of mortality. In the CRISTAL study

Table 1 Relationship between ICU and hospital stay and risk factors (frequency (percentage) of categorical variables; mean ± SD of numerical variables showing normal distribution; median values (Min–Max) of numerical variables not normally distributed)

Risk Factors		**ICU Length of Stay ≤ 5 Days**	**ICU Length of Stay > 5 Days**		**Hospital Length of Stay ≤ 24 Days**	**Hospital Length of Stay > 24 Days**	
		Median (Min–Max) Mean ± SD *n* (%)	**Median (Min–Max) Mean ± SD n (%)**	***p***	**Median (Min–Max) Mean ± SD *n* (%)**	**Median (Min–Max) Mean ± SD *n* (%)**	***p***
Number of patients		231 (%50.00)	231 (%50.00)		238 (%51.52)	224 (%48.48)	
Age (year)		74 (19–97)	76 (22–95)	0.529	76 (22–97)	74 (19–94)	0.122
Gender	Male	136 (%58.87)	141 (%61.04)	0.704	137 (%57.56)	140 (%62.50)	0.297
	Female	95 (%41.13)	90 (%38.96)		101 (%42.44)	84 (%37.50)	
BMI (kg/m^2)		22.23 (7.70–38.56)	22.04 (11.39–49.50)	0.471	22.28 (7.70–41.42)	21.88 (11.39–49.50)	0.122
Number of accompanying diseases		1 (0–3)	1 (0–5)	0.231	1 (0–5)	1 (0–4)	0.571
SOFA score		5 (0–15)	9 (1–18)	**<0.001**	6 (0–17)	8 (0–18)	**<0.001**
APACHE II score		16 (2–41)	20 (5–42)	**<0.001**	16 (2–40)	21 (4–42)	**<0.001**
GCS score		15 (3–15)	14 (3–15)	**<0.001**	14 (3–15)	14 (3–15)	**0.004**
Body temperature (°C)		37.8 (21.2–42.0)	37.5 (27.1–41.6)	**0.014**	37.9 (35.1–42.0)	37.5 (21.2–40.7)	**0.003**
Pulse rate (bpm)[a]		104.93 ± 23.62	106.01 ± 22.35	0.612	104.04 ± 22.20	106.99 ± 23.73	0.168
MAP (mmHg)		82.67 (29.67–156.67)	74.67 (32.33–157.00)	**0.001**	83.67 (44.00–156.67)	75 (29.67–157.00)	**<0.001**
Respiratory rate/min		24 (6–42)	24 (6–50)	0.687	24 (6–50)	24 (6–44)	0.822
Number of leukocytes × $10\text{^}3/mm^3$		11.90 (0.30–43.30)	11.50 (0.10–73.30)	0.986	11.80 (1.10–54.30)	11.65 (0.10–73.30)	0.942
HCT (%)[a]		35.09 ± 6.67	34.48 ± 7.21	0.347	35.75 ± 6.07	33.74 ± 7.65	**0.002**
Platelet count × $10\text{^}4/mm^3$		17.5 (1.2–63.7)	14.7 (0.7–73.3)	**0.002**	16.8 (1.2–54.8)	15.05 (0.7–73.3)	0.259
Creatinine (mg/dl)		1.04 (0.30–10.25)	1.23 (0.13–11.02)	**0.011**	1.08 (0.30–11.02)	1.17 (0.13–9.89)	0.121
Blood glucose (mg/dl)		150.50 (53–819)	154.50 (11–1706)	0.964	152 (33–927)	152 (11–1706)	0.889
Na (mmol/l)		136 (117–158)	137 (110–175)	**0.002**	136 (118–174)	137 (110–175)	0.379
K (mmol/l)		3.9 (2–8.4)	4.1 (2–9)	0.091	3.9 (2.3–8.4)	4.1 (2–9)	0.203
Bilirubin (mg/dl)		0.9 (0.1–22.0)	0.9 (0.1–15.7)	0.458	0.9 (0.1–15.7)	0.9 (0.1–22.0)	0.991
pH		7.41 (6.67–7.74)	7.39 (6.81–7.56)	**0.002**	7.41 (6.67–7.74)	7.39 (6.81–7.58)	**0.012**
Lactic acid (mmol/l)		2.20 (0–30.50)	2.40 (0–28.00)	**0.030**	2.40 (0–30.50)	2.20 (0–28.00)	0.478
PaO_2/FiO_2 ratio		277.14 (6.29–3176.19)	206 (19.94–1388)	**<0.001**	256 (6.29–3176.19)	236.88 (19.94–1388)	**0.018**
C–reactive protein (mg/dl)		10.56 (0.03–61.89)	13.59 (0.01–45.14)	0.128	9.84 (0.03–46.70)	15.34 (0.01–61.89)	**<0.001**
Procalcitonin (ng/ml)		7.94 (0.18–205.55)	10 (0–459.14)	0.820	7.33 (0.19–223.48)	10 (0–459.14)	0.398
Use of albumin	No	212 (%91.77)	172 (%74.78)	**<0.001**	216 (%91.14)	168 (%75)	**<0.001**
	Yes	19 (%8.23)	58 (%25.22)		21 (%8.86)	56 (%25)	

Table 1 Relationship between ICU and hospital stay and risk factors (frequency (percentage) of categorical variables; mean ± SD of numerical variables showing normal distribution; median values (Min–Max) of numerical variables not normally distributed) *(Continued)*

Risk Factors		ICU Length of Stay ≤ 5 Days	ICU Length of Stay > 5 Days		Hospital Length of Stay ≤ 24 Days	Hospital Length of Stay > 24 Days	
		Median (Min–Max) Mean ± SD *n* (%)	Median (Min–Max) Mean ± SD n (%)	*p*	Median (Min–Max) Mean ± SD *n* (%)	Median (Min–Max) Mean ± SD *n* (%)	*p*
Application of vasopressor agents	No	156 (%68.42)	87 (%37.83)	**<0.001**	166 (%70.34)	77 (%34.68)	**<0.001**
	Yes	72 (%31.58)	143 (%62.17)		70 (%29.66)	145 (%65.32)	
Steroid use	No	209 (%90.48)	177 (%76.96)	**<0.001**	214 (%90.30)	172 (%76.79)	**<0.001**
	Yes	22 (%9.52)	53 (%23.04)		23 (%9.70)	52 (%23.21)	
Immunosuppressive use	No	224 (%96.97)	222 (%96.94)	>0.999	232 (%97.48)	214 (%96.40)	0.592
	Yes	7 (%3.03)	7 (%3.06)		6 (%2.52)	8 (%3.60)	
Time between diagnosis of sepsis and source control (h) [b]	NDD	115 (%50.44)	136 (%59.13)	**0.004**	136 (%57.87)	115 (%51.57)	0.405
	<12	100 (%43.86)	69 (%30.00)		80 (%34.04)	89 (%39.91)	
	12–24	10 (%4.39)	13 (%5.65)		13 (%5.53)	10 (%4.48)	
	24<=	3 (%1.32)	12 (%5.22)		6 (%2.55)	9 (%4.04)	
Time between diagnosis of sepsis and onset of antibiotics (h) [b]	None	1 (%0.44)	3 (%1.36)	0.061	1 (%0.43)	3 (%1.40)	0.241
	<1	73 (%32.02)	90 (%40.91)		78 (%33.48)	85 (%39.53)	
	1–3	120 (%52.63)	90 (%40.91)		119 (%51.07)	91 (%42.33)	
	3<=	34 (%14.91)	37 (%16.82)		35 (%15.02)	36 (%16.74)	
The need for MV in the first 24 hours	No	169 (%73.16)	101 (%44.30)	**<0.001**	181 (%76.69)	89 (%39.91)	**<0.001**
	Yes	62 (%26.84)	127 (%55.70)		55 (%23.31)	134 (%60.09)	

BMI body mass index, *GCS*: Glasgow coma scale, *MAP* mean arterial pressure, *MV* mechanical ventilation, *NDD* no drainage or debridement
[a]Normally distributed data
[b]Fisher exact test results

Table 2 Coefficient estimation of risk factors in univariate binary logistic regression model for prolonged ICULOS/HLOS

	Risk Factors	B	S.E.	Wald	df	Sig.	Odd ratio/ Exp (B)	95% C.I. for EXP(B)	
								Lower	Upper
ICU length of stay	SOFA score	0.251	0.033	56.631	1	< 0.001	1.285	1.204	1.372
	APACHE II score	0.082	0.015	29.625	1	< 0.001	1.085	1.054	1.118
	GCS score	− 0.156	0.033	22.857	1	< 0.001	0.855	0.802	0.912
	Body temperature (°C)	− 0.136	0.06	5.056	1	0.025	0.873	0.775	0.983
	MAP (mmHg)	− 0.014	0.004	9.600	1	0.002	0.987	0.978	0.995
	Platelet count $\times 10^4/mm^3$	− 0.023	0.009	6.552	1	0.010	0.977	0.96	0.995
	Creatinine (mg/dl)	0.174	0.060	8.552	1	0.003	1.190	1.059	1.338
	Na	0.041	0.014	8.315	1	0.004	1.042	1.013	1.072
	pH	− 3.441	0.869	15.671	1	< 0.001	0.032	0.006	0.176
	PaO_2/FiO_2 ratio	− 0.003	0.001	14.239	1	< 0.001	0.997	0.995	0.999
	Albumin use	1.325	0.284	21.838	1	< 0.001	3.763	2.158	6.559
	Application of vasopressor agents	1.270	0.197	41.592	1	< 0.001	3.561	2.421	5.239
	Steroid use	1.045	0.273	14.620	1	< 0.001	2.845	1.665	4.861
	Need for MV in the first 24 h	1.232	0.200	38.106	1	< 0.001	3.427	2.318	5.068
Hospital Length of Stay	SOFA score	0.173	0.030	32.926	1	< 0.001	1.188	1.120	1.261
	APACHE II score	0.073	0.015	24.687	1	< 0.001	1.076	1.045	1.108
	GCS score	− 0.095	0.030	10.139	1	0.001	0.909	0.858	0.964
	Body temperature (°C)	− 0.240	0.067	12.651	1	< 0.001	0.787	0.689	0.898
	MAP (mmHg)	− 0.020	0.005	20.239	1	< 0.001	0.980	0.971	0.988
	HCT (%)	− 0.043	0.014	9.482	1	0.002	0.958	0.933	0.985
	Creatinine (mg/dl)	0.143	0.057	6.228	1	0.013	1.154	1.031	1.291
	pH	− 2.241	0.803	7.793	1	0.005	0.106	0.022	0.513
	C-reactive protein (mg/dl)	0.029	0.008	13.132	1	< 0.001	1.030	1.014	1.046
	Albumin use	1.232	0.276	19.961	1	< 0.001	3.429	1.997	5.887
	Application of vasopressor agents	1.496	0.200	55.713	1	< 0.001	4.466	3.015	6.615
	Steroid use	1.034	0.271	14.613	1	< 0.001	2.813	1.655	4.780
	Need for MV in the first 24 hours	1.600	0.206	60.397	1	< 0.001	4.955	3.309	7.418

MAP mean arterial pressure, *MV* mechanical ventilation, *GCS* Glasgow coma scale

(Annane et al. 2013), there was no significant difference in 28/90 days mortality between 4 and 20% colloid solutions and normal saline applied groups. In the Albumin Italian Outcome Sepsis (ALBIOS) study (Caironi et al. 2014) in which a serum albumin level of 3 g/dl was targeted for 28 days in septic patients, although higher serum albumin levels were obtained in the treatment group (albumin replacement with a 20% solution), there was no difference in 28/90 day mortality. In addition, these studies showed that albumin administration does not benefit organ failure or mechanical ventilation duration. In a meta-analysis (Delaney et al. 2011) evaluating a total of 17 studies, it was reported that albumin use was associated with lower mortality in patients with sepsis. As a result, there is no clear information about the benefit or harm of albumin in sepsis, so the Surviving Sepsis Campaign (SSC) (Rhodes et al. 2017) guideline recommends adding albumin if there is a significant amount of crystalloid requirement. As a result of our study, it was also found that there was a significant relationship between albumin use and ICULOS/HLOS. In patients with sepsis, albumin replacement was associated with approximately 4-fold increase in the risk of prolonged ICULOS; increased the risk of prolonged HLOS approximately 3.5-fold.

Vasopressor agents increase blood pressure by increasing peripheral vascular resistance. Vasopressor agents can be utilized in patients who are hypotensive despite adequate fluid treatment and who develop cardiogenic or pulmonary edema (Keeley et al. 2017). Auchet et al.

(2017) aimed to evaluate patients receiving high-dose vasopressor agent therapy for survival. They determined that high-dose vasopressor agent therapy increased survival by 40% on 28th day in patients with septic shock. A meta-analysis (Avni et al. 2015) reported an 11% reduction in 28-day all-cause mortality with norepinephrine. Cochrane systematic review (Gamper et al. 2016), the efficacy of vasopressor agents for the treatment of any circulatory failure was evaluated, and the mortality benefit was not demonstrated in all direct comparisons between different vasopressor agents or vasopressor agent combinations. In another review (De Backer et al. 2012), focusing only on the comparison of norepinephrine and dopamine in septic shock, it has been shown that norepinephrine has an advantage over dopamine in 28-day all-cause mortality. Clinical outcomes other than mortality have been rarely reported, so it was not possible to obtain strong evidence for ICULOS/HLOS. Due to the lack of detailed information about the applied vasopressor agents in the data set used in our study, the differences between agents could not be evaluated, but as a result of our study, the probability of prolonged ICULOS/HLOS was found to be significantly higher in patients receiving vasopressor agent compared to patients not receiving it.

The 2016 SSC guideline (Rhodes et al. 2017) recommends the use of intravenous hydrocortisone (200 mg/day) in patients whose hemodynamic stability cannot be achieved with vasopressor agents. When the related literature is inquired, between 1976 and 2018, 24 randomized clinical trials were published examining the association between steroid use and 28-day mortality in sepsis or septic shock. These studies have conflicting results. The use of steroids has been found to be advantageous in terms of survival in some studies, while no survival benefit has been shown in others (Vandewalle and Libert 2020). Annane et al. (2002) found in 2002 that the steroid use in septic shock reduced mortality. However, in the CORTICUS (Sprung et al. 2008) study conducted in 2008, it was found that steroid use did not provide any benefit on mortality In 2016, in the HYPR ESS study (Keh et al. 2016), it was found that hydrocortisone did not prevent the development of septic shock in hospital acquired sepsis patients. In a review of steroid use in sepsis (Gibbison et al. 2017), 22 studies were examined, and only 2 studies indicated that steroid use reduced ICULOS, but there was insufficient data regarding HLOS. In addition to these studies, large-scale studies such as Adjunctive Corticosteroid Treatment in Critically Ill Patients with Septic Shock (ADRENAL) (Venkatesh et al. 2018) and Activated Protein C and Corticosteroids for Human Septic Shock (APROCCHSS) (Annane et al. 2018) have been carried out to clarify the use of steroids. While there was no reduction in 90-day mortality in the ADRENAL study with steroid use, a 6.1% decrease was found in the APROCCHSS study. In addition, in these two studies, the duration of shock resolution, weaning time from mechanical ventilation, and hospital stay were found to be lower in patients receiving steroid therapy. In our study, the probability of prolonged ICULOS/HLOS was found to be approximately 3 times higher in patients receiving steroids. This may be attributed to the difference in the patient population (age, concomitant disease, etc.) or the steroid agent/dose difference used.

The relationship between the need for MV and ICULOS/HLOS has been shown in some previous studies (Cislaghi et al. 2007; Güler 2009). Cislaghi et al. (2007) showed that, in patients with coronary artery by-pass grafting, prolongation of MV duration was significantly correlated with both ICULOS and HLOS. In another study dealing with patients undergoing coronary artery surgery, MV duration was found to be one of the factors affecting ICULOS (Güler 2009). Unlike these studies, in our study, it was shown that not the duration of MV but the need for MV on the first day of the patients' diagnosis of sepsis had a significant impact on ICULOS/HLOS.

CRP is a protein produced in the acute phase of inflammation. Khaled et al. (2014) found that the first day CRP value was significantly higher in the general ICU patients than the group staying in the ICU more than 7 days. Farah et al. (2018) showed that significant decreases in CRP levels in pneumonia patients on day 2 were associated with shorter HLOS and rapid recovery. Similar to these studies, HLOS and CRP levels were found to be correlated in our study as well.

Thrombocytopenia is a common condition with high mortality in ICUs. In a study excluding hematological diseases, sepsis was reported to be one of the most important causes of thrombocytopenia in patients in ICU (Levi and Löwenberg 2008). Coşkun et al. (2016) found, too, that ICULOS was higher in patients with thrombocytopenia than in those without thrombocytopenia, similar to our study.

In a study investigating the prognostic value of HCT and its utility in the decision of erythrocyte transfusion of anemic patients, Mudumbai et al. (2011) detected an increase in long-term mortality in patients with HCT values less than 25% without transfusion. As a result of our study, low HCT values were found to be associated with prolonged ICULOS/HLOS too. Toptas et al. (2018) targeted to determine the factors affecting the ICULOS in patients followed up in the ICU. Similar to our study, they found a negative correlation between HCT levels and ICULOS in their study.

The 2016 SSC guideline (Rhodes et al. 2017) recommends that 30 ml/kg intravenous crystalloid fluid be administered within the first 3 h. Since the data on fluid

replacement was not sufficient in the data set we used in our study, the effect of differences in fluid replacement on ICULOS/HLOS could not be evaluated.

Conclusions

As a result of our study, in patients with sepsis followed up in ICU, the use of albumin, steroid, and vasopressor agents causes a significant increase in ICULOS and HLOS. In addition, it was found that the need for MV in the first 24 h and GCS, APACHE II, and SOFA scoring systems can be used in the prediction of prolonged ICULOS/HLOS. If it is desired to create scoring systems that allow the calculation of the estimated length of stay, in addition to these parameters, platelet count, respiratory rate (admission to the intensive care unit), and PaO_2/FiO_2 ratio can be used for prolonged ICULOS and MAP, HCT, and CRP can also be used for prolonged HLOS.

Abbreviations

APACHE II: Acute Physiology and Chronic Health Evaluation; BMI: Body mass index; CI: Confidence interval; CRP: C-reactive protein; GCS: Glasgow coma scale; HCT: Hematocrit; HLOS: Hospital length of stay; ICU: Intensive care unit; ICULOS: Intensive care unit length of stay; MAP: Mean arterial pressure; MV: Mechanical ventilation; OR: Odds ratio; SD: Standard deviation; SOFA: Sequential organ failure assessment; SSC: Surviving Sepsis Campaign

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Authors' contributions

SK designed the study, revised the literature, wrote, and critically revised the manuscript. ÖK analyze the data, wrote, and critically revised the manuscript. All authors approved the final version of the manuscript.

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Availability of data and materials

A public and up-to-date data set in the Mendeley data website was used. The data set can be downloaded from https://data.mendeley.com/datasets/vvv89kw3k5/1.

Ethics approval and consent to participate

Not applicable. The study does not require ethical approval and consent to participate because data are anonymous.

Consent for publication

Not applicable.

Competing interests

There is no competing interest.

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