Araştırma Makalesi *Research Article*

Pamukkale Tıp Dergisi
Pamukkale Medical Journal

doi:https://dx.doi.org/10.31362/patd.938235

The effect of fluid balance on outcomes in patients with sepsis; experience of a tertiary hospital

Sepsisli hastalarda sıvı dengesinin sonuçlara etkisi; üçüncü basamak bir hastane deneyimi

Deniz Uysal Sönmez, Hülya Dirol, Abdullah Erdoğan

Gönderilme tarihi:17.05.2021 Kabul tarihi:28.07.2021

Purpose: Fluid replacement is vital for stabilizing hemodynamic status in sepsis. However, the positive fluid balance may result in pulmonary edema and may be associated with increased mortality.
Materials and methods: This is a single-center, retrospective study in which the patients, supported with mechanical ventilation (MV) due to sepsis, were enrolled. All the data about the demographic features, medications, MV duration, vital signs, blood gas analysis, blood tests, the fluid balance were obtained from the patient files and nursing reports. Patients were subclassed positive, negative and balanced according to fluid balance and compared to each other.
Results: A total of fifty patients with sepsis were included in the study. Twenty-six (52%) of the patients were male and the mean age was 66.58±3.25 years. The mortality rate was 90%. The mean fluid intake and output were 3481.8±1002.7, 1877.6±921.3 milliliters, respectively. Forty-two (84%) were in positive fluid balance, 6 (12%) in negative fluid balance, and 2 (4%) in balance. There was no significant difference between the fluid balance subgroups in terms of length of stay in the ICU, duration of mechanical ventilation, and mortality. The use of diuretics was significantly higher in patients with positive fluid balance (p=0.023). CRP was significantly higher while serum albumin was lower in patients with positive fluid balance (respectively, p=0.003, p=0.034). There was no difference between the mean GCS, SOFA scores of survivors and nonsurvivors but the mean APACHE II scores in nonsurvivors were significantly higher than in survivors (p=0.026).
Conclusion: Our study showed that positive fluid balance did not affect the length of stay in the ICU, duration of mechanical ventilation and mortality, and that APACHE II was better than SOFA and GCS in predicting mortality.

Key words: Fluid therapy, sepsis, shock, mechanical ventilation, intensive care.

Uysal Sonmez D, Dirol H, Erdoğan A. The effect of fluid balance on outcomes in patients with sepsis; experience of a tertiary hospital. Pam Med J 2022;15:87-94.

Öz
Amaç: Sıvı replasmanı, sepsiste hemodinamik durumu stabilize etmek için hayati öneme sahiptir. Bununla birlikte, pozitif sıvı dengesinin olumsuz etkileri olabilir.
Gereç ve yöntem: Ağustos 2016-Nisan 2017 tarihleri arasında üçüncü basamak bir hastanede sepsise bağlı mekanik ventilasyonla desteklenen hastaları içeren tek merkezli, retrospektif bir çalışmadır. Demografik özellikler, ilaçlar, mekanik ventilasyon süresi, yoğun bakımda kalış süresi, kan biyokimyasal testleri, sıvı dengesi ile ilgili tüm veriler hasta dosyaları ve hemşire çizelgelerinden elde edildi. Hastalar sıvı dengesine göre pozitif, negatif ve dengeli olarak alt sınıflandırılarak birbirleriyle karşılaştırıldı.
Bulgular: Çalışmaya toplam 50 sepsisli hasta alındı. Hastaların yirmi altısı (%52) erkekti ve yaş ortalaması 66,58±3,25 yıl idi. Ölüm oranı %90 idi. Ortalama sıvı alımı ve çıkışı sırasıyla 3481,8±1002,7, 1877,6±921,3 mililitre idi. Kırk ikisi (%84) pozitif sıvı dengesinde, 6'sı (%12) negatif sıvı dengesinde ve 2'si (%4) dengede idi. Sıvı dengesi alt grupları arasında yoğun bakımda kalış süresi, mekanik ventilasyon süresi ve mortalite açısından anlamlı fark yoktu. Pozitif sıvı dengesi olan hastalarda diüretik kullanımı anlamlı olarak daha yüksekti (p=0,023). Pozitif sıvı dengesi olan hastalarda CRP anlamlı olarak daha yüksek, serum albümini ise daha düşüktü (sırasıyla, p=0,003, p=0,034). Sağ kalanların ve sağ kalmayanların ortalama GCS, SOFA skorları arasında fark yoktu ancak sağ kalmayanlarda ortalama APACHE II skorları sağ kalanlardan anlamlı derecede yüksekti (p=0,026).
Sonuç: Çalışmamız, pozitif sıvı dengesinin yoğun bakımda kalış süresi, mekanik ventilasyon süresi ve mortaliteyi etkilemediğini ve APACHE II'nin mortaliteyi öngörmede SOFA ve GKS'ye göre daha iyi olduğunu gösterdi.

Anahtar kelimeler: Sıvı tedavisi, sepsis, şok, mekanik ventilasyon, yoğun bakım.

Uysal Sönmez D, Dirol H, Erdogan A. Sepsisli hastalarda sıvı dengesinin sonuçlara etkisi; üçüncü basamak bir hastane deneyimi. Pam Tıp Derg 2022;15:87-94.

Deniz Uysal Sönmez, Chest Physiotherapist, Akdeniz University Hospital, Chest Department, Antalya, Turkey, e-mail: denizuysalsonmez@hotmail.com (https://orcid.org/0000-0001-7168-361X)

Hülya Dirol, M.D. Pulmonolog, Ass. Prof. Akdeniz University Hospital Chest Department, Dumlupınar Boulevard Akdeniz University Hospital, Antalya, Turkey, e-mail: hulyadirol@akdeniz.edu.tr (https://orcid.org/0000-0002-7712-6467) (Corresponding Author)

Abdullah Erdoğan, M.D. Professor, Akdeniz University Hospital, Chest Surgery Department, Antalya, Turkey, e-mail: abdullaherdogan@akdeniz.edu.tr (https://orcid.org/0000-0002-5299-441X)

Introduction

Sepsis is a syndrome characterized by organ dysfunction, hypoperfusion, and hypotension due to infection [1]. Although treatment options for sepsis have improved over the years, the mortality rate is still quite high [2]. Various factors related to mortality in sepsis have been reported so far [3]. Fluid replacement therapy is supposed to improve tissue oxygenation and stabilize the hemodynamic status and thereby decrease mortality in sepsis. However, results regarding the effect of this treatment on mortality are contradictory. Moreover, the concern is also common that excessive fluid replacement in sepsis will lead to increased hydrostatic pressure in vessels prone to extravasation due to increased vascular permeability and, consequently, pulmonary edema and this may increase the length of mechanical vantilation and hospital stay and even mortality.

In this study, we evaluated the effect of fluid balance on the patients supported by mechanical ventilation due to sepsis.

Methods

Study population

The patients, supported with invasive mechanical ventilation due to sepsis or septic shock between August 2016 and April 2017 in the intensive care unit of Akdeniz University Hospital, were involved in the study. The patients with chronic heart failure and/or chronic renal failure and who stayed lesser than 72 hours in ICU, were excluded from the study. All the data about the demographic features, medications, IMV duration and modes, sedation supports, vital signs, blood gas analysis, blood tests, the fluid balance were obtained from the patients' files, nurse observation charts, and intensive care unit electronic records. APACHE II score, Glasgow coma score (GCS) and Sequential organ failure assessment (SOFA) score in the first 24-hour were used in the study.

We used "The Third International Consensus Definitions for Sepsis and Septic Shock-2016" for the diagnosis of sepsis [4]. The patients not eligible for this consensus were excluded from the study. We calculated the patient's 24-hour total intake (intravenous infusion, blood transfusion, albumin replacement, feeding) and total output (urine, feces, colostomy, drainage, vomiting, and the amount of fluid obtained during dialysis) and then we classified them according to the fluid balance. The classification criteria were as follows i) positive fluid balance; intake was at least more than 400 ml higher than output. ii) negative fluid balance; output was at least more than 400 ml higher than intake. iii) balanced; intake was <400 ml higher than output or equal to output.

The study was approved by the Clinical Research Ethics Committee of Akdeniz University Medical Faculty. Written informed consent was obtained from all participants.

Statistical analysis

For the statistical analysis, Statistical Package for Social Science (SPSS) 21.0 was used. Descriptive statistics were presented with frequency, percentage, mean, standard deviation (SD), median, minimum (min.), and maximum (max.) values. Fisher's Exact Test and Pearson chi-square test were used to analyze the relationships between categorical variables. Kolmogorov Smirnov test was used for the distribution of numerical measurements. T-test, Mann Whitney U test, ANOVA, and Sidak test were used for comparison of the groups. The cutoff value for significance was accepted as 0.05 in the study.

Results

Demographic-clinical features of the patients

A total of 50 patients supported by mechanical ventilation because of sepsis were included in the study. Of these patients, 26 (52%) were male and the mean age was 66.58±5.25 years (Table 1). The mean fluid intake of the patients was 3481.8±1002.7 milliliter (ml) and the mean output was 1877.6±921.3 ml. Of the patients, 42 (84%) were in positive fluid balance, 6 (12%) were in negative fluid balance and 2 (4%) were in balance. The mean intensive care unit stay length was 9.80±7.14 days and the mean mechanical ventilation duration was 7.50±3.24 days. The mean APACHE II score, GCS, and SOFA score were 25.9±4.7, 6.7±2.2, 7.9±1.9, respectively. Forty-five of the patients were expired and the mortality rate was 90 percent.

There was no significant difference in intensive care unit stay length and mechanical ventilation duration between the fluid balance subgroups (balance, positive and negative).

Table 1. Baseline characteristics of the patients

	All n=50
Age (mean±SD)	66.58±5.25
Gender (n; %) Male Female	 26 (52%) 24 (48%)
Comorbidities (n; %) DM COPD HT Other	 11 (27.5%) 8 (16.33%) 13 (32.5%) 8 (16.33%)
Fluid balance Positive Negative Balance	 42 (84%) 6 (12%) 2 (4%)
Fluid intake ml (mean±SD) Fluid output	3481.88±1002.68 1877.62±921.25
Diuretic drug use Yes No	 49 (%98) 1 (2%)
Vasoactive support (%) Yes No	 49 (98%) 1 (2%)
Steroid Yes No	 35 (70%) 15 (30%)
Sedative drug use Yes No	 47 (94%) 3 (6%)
MV modality A/C Spontaneous	 38 (76%) 12 (24%)
Mechanical ventilation settings (mean±SD) FiO2 PEEP Frequency Tidal Volume ml	 48.37±11.39 4.75±1.49 14.93±3.05 458.54±51.18
Weaning Yes No	 12 (24%) 38 (76%)
GCS (mean±SD) APACHE II SOFA	6.7±2.2 25.9± 4.7 7.9±1.9
Survivor nonsurvivor	5 (10%) 45 (90%)

DM: Diabetes Mellitus, COPD: Chronic Obstructive Pulmonary Disease, HT: Hypertension
MV: Mechanical Ventilation. FiO2: Fraction of inspired oxygen. PEEP: Positive End Expiratory Pressure. GCS: Glasgow coma score
APACHE II: Acute physiology and chronic health evaluation II, SOFA: Sequential organ failure assessment, N: Number, Sd: Standart deviation

Among the biochemical blood tests, C- reactive protein (CRP) was significantly higher (p=0.003) and albumin level was significantly lower (p=0.034) in patients with positive fluid balance than those with a negative balance (Table 2). There was no significant difference in creatinine level between the fluid balance subgroups. The diuretic use was significantly more common in patients with positive fluid balance than those with a negative balance (p=0.02). There was no significant difference in mechanical ventilation setting features (FiO2, PEEP, frequency, tidal volume) and in APACHE II, GCS, SOFA scores, between the fluid balance subgroups. There was no significant difference in the fluid balance between survivors and nonsurvivors.

Survivors and nonsurvivors were similar in respect to gender and comorbidity but the survivors were significantly older than the nonsurvivors (p=0.021) (Table 3). The survivors required significantly less vasoactive support than nonsurvivors (p=0.0024). All the survivors were supported with spontaneous mechanical ventilator mode, and there was a significant difference in the MV modality between survivors and nonsurvivors (p=0.0001). There was no difference between the mean GCS and SOFA scores of survivors and nonsurvivors but the mean APACHE II scores of nonsurvivors were significantly higher than those of the survivors (p=0.026).

Table 2. Demographic and clinical features of the patients according to fluid balance

	Fluid balance Positive	Fluid balance Negative	Fluid balance Balance	*p*
Age (mean±SD)	66.24±2.16	63.28±2.25	64.42±2.16	0.997
Creatine (mean±SD)	2.04±1.44	3.67±2.5	1.03±0.65	0.098
CRP (mean±SD)	16.52±4.62	10.84±3.4	5.49±0.95	**0.003**
Albumine (mean±SD)	2.47±0.36	2.85±0.2	2.70±0.43	**0.034**
Diuretic drug use				**0.0237**
Yes	42 (100%)	5 (83.3%)	2 (100%)	
No	0	1 (16.7%)	0	
Steroid use				0.2045
Yes	28 (66.7%)	6 (100%)	1 (50%)	
No	14 (33.3%)	0	1 (50%)	
Vasopressor/inotrop use				0.9074
Yes	41 (97.6%)	6 (100%)	2 (100%)	
No	1 (2.4%)	0	0	
Central Venous Pressure (mean±SD)	11.09±2.91	10.33±1.0	-	0.772
GCS	6.66±2.33	6.43±1.0	8.93±0.81	0.221
APACHE II	26.37±4.54	25.19±4.83	20.41±6.24	0.255
SOFA	7.91±1.89	8.22±1.17	5.53±2.16	0.296
Mechanical ventilation settings (mean±SD)				
FiO2	48.63±12.08	49.09±7.13	40.74±1.04	0.276
PEEP	4.72±1.46	5.49±1.42	3.21±1.71	0.230
Frequency	14.84±3.14	14.58±2.53	18.03±0.04	0.291
Tidal Volume ml	455.29±52.28	466.67±40.82	530.00±38.03	0.255
Weaning				0.25
Yes	11 (26.2%)	-	1 (50%)	
No	31 (73.8%)	100	1 (50%)	
Mechanical ventilation duration	9.20±1.34	9.44±2.24	9.10±1.36	0.534
Intensive care unit stay duration	10.60±1.88	10.34±3.46	10.95±1.20	0.644
Survivor	3 (7.1%)	1 (16.7%)	1 (50%)	0.1205
nonsurvivor	39 (92.9%)	5 (83.3%)	1 (50%)	

CRP: C-reactive protein. FiO2: Fraction of inspired oxygen. PEEP: Positive End Expiratory Pressure. GCS: Glasgow coma score
APACHE II: Acute physiology and chronic health evaluation II, SOFA: Sequential organ failure assessment

Table 3. Demographic and clinical features of the survivors and nonsurvivors

	Survivor n=5	Non-survivor n=45	*p*-value
Age (mean±SD)	75.40±7.37	61.56 ±3.73	0,021
Gender (n; %)			0.6613
Male	2 (40%)	24 (53.33%)	
Female	3 (60%)	21 (46.67%)	
Comorbidities (n; %)			0.3926
DM	-	11 (29.73%)	
COPD	-	8 (21.62%)	
HT	2 (66.67%)	11 (29.73%)	
Other	1 (33.33%)	7 (18.92%)	
Fluid balance			0.1205
Positive	3 (60%)	39 (86.67%)	
Negative	1(20%)	5 (11.11%)	
Balance	1(20%)	1 (2.22%)	
Vasoactive support (%)			**0.0024**
Yes	4 (80%)	45 (100%)	
No	1 (20%)	-	
MV modality			**0.0001**
A/C	-	38 (84.44 %)	
Spontaneous	5 (100%)	7 (15.56%)	
GCS	9.00±2.45	6.78±2.02	0.067
APACHE II	20.40±4.62	25.98±4.27	**0.026**
SOFA	6.40±1.95	7.11±1.65	0.497

DM: Diabetes Mellitus, COPD: Chronic Obstructive Pulmonary Disease, HT: Hypertension, MV: Mechanical Ventilation
GCS: Glasgow coma score, APACHE II: Acute physiology and chronic health evaluation II,
SOFA: Sequential organ failure assessment, N: Number, Sd: Standart deviation

Discussion

In our study, we observed that fluid balance had no significant effect on the length of ICU stay and on both the mechanical ventilation duration and the settings. The assessment tests for the severity and the prognosis of the disease, such as APACHE II, SOFA, and GCS were not significantly different between the fluid balance subgroups. Based on this finding, we suggest that the results of these tests in the first 24-hour could not predict the fluid balance or requirements. Additionally, we found that diuretic drugs were more frequently used and CRP was significantly higher while albumin was lower in patients with positive fluid balance than in those with negative fluid balance. There was no significant difference in fluid balance between survivors and nonsurvivors. The survivors required fewer vasoactive drugs and all the survivors were supported with spontaneous mechanical ventilator mode. Among the disease severity assessment tests (APACHE II, GCS, SOFA), only APACHE II was significantly higher in nonsurvivors than the survivors.

The fluid balance is the basis of critical patient management in the intensive care unit. In sepsis and septic shock, characterized by infection-related organ dysfunction, hypoperfusion, and low blood pressure, fluid replacement is often required at high volumes to cope with organ hypoperfusion and hypotension. However, microvascular endothelial injury related to sepsis increases the extravasation of intravascular fluid, which may result in pulmonary edema. The effects of positive fluid balance on patients are controversial. In a previous study, no relationship was found between positive fluid balance and weaning [5]. Similarly, we did not find a significant difference in weaning between the patients with positive fluid balance and the patients with negative fluid balance. Moreover, we found that there was no significant difference in the duration of mechanical ventilation and intensive care unit stay. But contrary to our study, Diaz et al. [6] reported that the positive fluid balance was associated with the duration of mechanical ventilation and the duration of intensive care stay. This difference may be related to the participants in their study because

they performed this research in children, not in adults.

Although the treatment options for sepsis and septic shock are improved every day, the mortality rate is still over 50%. There are some scoring systems that can predict the mortality rate and prognosis, like APACHE II, SOFA, and GCS. Significant long mechanical ventilation and weaning failure were detected in patients with high APACHE II scores at the time of intensive care unit admission and it was previously reported to be lower in sepsis-survivors than in sepsis-non-survivors [7-9]. Moreover, APACHE, and SOFA scores, within the first 24 hours of intensive care unit admission, were higher in nonsurvivors in a recent study [10]. In order to estimate the mortality rate in patients with sepsis, the APACHE II score is the one that is strongly recommended [11]. Wang et al. [12] reported that both SOFA and APACHE II score, are independent prognostic factors in sepsis. In our study, we observed that only the APACHE II score was significantly higher in survivors than in the nonsurvivors. Based on this finding, we suggest that APACHE II may be better in predicting mortality, than SOFA and GCS.

Moreover, there was no significant difference between the creatine levels of the patients in respect to fluid balance in our study. Similarly, De Oliveira FSV et al. [13] reported no association between positive fluid balance and acute renal failure. But the need for diuretic drugs was significantly more common in patients with positive fluid balance than those with negative fluid balance in our study. Recently, loop diuretic was not associated with severe acute renal damage [14]. Based on these findings, the diuretic drug requirement seems to be high in patients with positive fluid and can be safely applied without increasing creatine levels.

The other significant difference between the patients with positive fluid balance and those with negative balance was the albumin level in our study. The albumin levels in patients with positive fluid balance were significantly lower than in patients with negative fluid balance. Hypoalbuminemia may be an indicator of malnutrition with inadequate amount and content. It may be dilutional or a result of a negative acute phase response also. Hypoalbuminemia may cause muscle weakness and extend intensive care unit stay, thus increase mortality [15]. Previously, hypoalbuminemia was associated with mortality and prolonged mechanical ventilation [15, 16]. Although, statistically not significant we also observed in our study that albumin levels tended to be lower in survivors than in nonsurvivors.

Furthermore, we observed that there was no significant difference in the fluid balances of survivors and nonsurvivors. Similarly, no association was reported between the fluid intake within the first 24 hours and 90 days mortality previously [17, 18]. However, there are some reports contrary to these studies [2, 19, 20]. Recently, the negative fluid balance was associated with lower mortality [21]. Positive fluid balance was independently associated with mortality in sepsis accompanied by ARDS in another study [12]. The reason for the difference in our result about the effect of fluid balance on survival may be the small number of survivors. While the effect of positive fluid balance on survival remains uncertain, recently, it was reported that fluid replacement therapy applied according to hemodynamic parameters provided less fluid burden but didn't reduce the total 30-day mortality [19].

There are some limitations to our study. Major limitations are the small sample size and missing data. The number of patients in survivor and nonsurvivor subgroups and the number of patients in positive and negative/balanced fluid balance subgroups were very different and quite a few. In order to avoid obvious numerical differences between subgroups, the study parameters should be investigated prospectively and with sufficient number of patient subgroups. Moreover, in this study, the survivor group and the nonsurvivor group were not similar in respect to age. We don't know whether the positive fluid balance is the cause or the effect with respect to all these parameters. Lastly, there may be many different parameters that may affect survival, and some of these parameters may be overlooked based on the retrospective study design.

In conclusion, we observed in this study that there was no effect of positive fluid balance on the length of intensive care unit stay, the mechanical ventilation duration and the mortality. Diuretic drugs were more frequently required in patients with positive fluid balance but they didn't result in renal parenchymal damage so

they can be safely applied as needed in patients with sepsis. Only APACHE II was significantly higher in nonsurvivors, so seems to be better in predicting mortality than SOFA and GCS. This was a retrospective study from a tertiary hospital, with significant numerical difference between patient subgroups. The findings of the study need to be supported by better designed, randomized, controlled prospective studies.

Conflict of interest: No conflict of interest was declared by the authors.

References

1. Napolitano LM. Sepsis 2018: Definitions and Guideline Changes. Surg Infect 2018;19:117-125. https://doi.org/10.1089/sur.2017.278
2. Acheampong A,Vincent JL. A positive fluid balance is an independent prognostic factor in patients with sepsis. Crit Care 2015;19:251. https://doi.org/10.1186/s13054-015-0970-1
3. Brink A, Alsma J, Verdonschot RJCG, et al. Predicting mortality in patients with suspected sepsis at the Emergency Department; a retrospective cohort study comparing qSOFA, SIRS and National Early Warning Score. PLoS One 2019;14:e0211133. https://doi.org/10.1371/journal. pone.0211133
4. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:801-810. https://doi.org/10.1001/jama.2016.0287
5. Upadya A, Tilluckdharry L, Muralidharan V, Amoateng Adjepong Y, Manthous CA. Fluid balance and weaning outcomes. Intensive Care Med 2005;31:1643-1647. https://doi.org/10.1007/s00134-005-2801-3
6. Diaz F, Benfield M, Brown L, Hayes L. Fluid overload and outcomes in critically ill children: a single center prospective cohort study. J Crit Care 2017;39:209-213. https://doi.org/10.1016/j.jcrc.2017.02.023
7. Lasen HC. A preliminary report on the 1952 epidemic of poliomyelitis in Copenhagen with special reference to the treatment of acute respiratory insufficiency. Lancet 1953;1:37-42. https://doi.org/10.1016/s0140-6736(53)92530-6
8. Lee J, de Louw E, Niemi M, et al. Association between fluid balance and survival in critically ill patients. J Intern Med 2015;277:468-477. https://doi.org/10.1111/joim.12274
9. Yang PH, Hung JY, Yang CJ, et al. Successful weaning predictors in a respiratory care center in Taiwan. Kaohsiung J Med Sci 2008;24:85-91. https://doi.org/10.1016/S1607-551X(08)70102-5
10. Miranda AC, de Menezes IAC, Junior HC, Luy AM, do Nascimento MM. Monitoring peripheral perfusion in sepsis associated acute kidney injury: Analysis of mortality. PLoS ONE 2020;15:e0239770. https://doi.org/10.1371/journal.pone.0239770
11. Rezende E, Silva Junior JM, Isola AM, Campos EV, Amendola CP, Almeida SL. Epidemiology of severe sepsis in the emergency department and difficulties in the initial assistance. Clinics 2008;63:457-464. https://doi.org/10.1590/s1807-59322008000400008
12. Wang YM, Zheng YJ, Chen Y, et al. Effects of fluid balance on prognosis of acute respiratory distress syndrome patients secondary to sepsis. World J Emerg Med 2020;11:216-222. https://doi.org/10.5847/wjem.j.1920-8642.2020.04.003
13. De Oliveira FSV, Freitas FGR, Ferreira EM, et al. Positive fluid balance as a prognostic factor for mortality and acute kidney injury in severe sepsis and septic shock. J Crit Care 2015;30:97-101. https://doi.org/10.1016/j.jcrc.2014.09.002
14. Liborio AB, Barbosa ML, Sa VB, Leite TT. Impact of loop diuretics on critically ill patients with a positive fluid balance. Anaesthesia 2020;75:134-142. https://doi.org/10.1111/anae.14908
15. Dasgupta A, Rice R, Mascha E, Litaker D, Stoller JK. Four-year experience with a unit for long-term ventilation (respiratory special care unit) at the Cleveland Clinic Foundation. Chest 1999;116:447-455. https://doi.org/10.1378/chest.116.2.447
16. Modawal A, Candadai NP, Mandell KM, et al. Weaning success among ventilator-dependent patients in a rehabilitation facility. Arch Phys Med Rehabil 2002;83:154-157. https://doi.org/10.1053/apmr.2002.29614
17. Carlsen S, Perner A, East Danish Septic Shock Cohort I. Initial fluid resuscitation of patients with septic shock in the intensive care unit. Acta Anaesthesiol Scand 2011;55:394-400. https://doi.org/10.1111/j.1399-6576.2011.02399.x
18. Smith SH, Perner A. Higher vs. lower fluid volume for septic shock: clinical characteristics and outcome in unselected patients in a prospective, multicenter cohort. Crit Care 2012;16:76. https://doi.org/10.1186/cc11333
19. Douglas IS, Alapat PM, Corl KA, et al. Fluid response evaluation in sepsis hypotension and shock a randomized clinical trial. Chest 2020;158:1431-1445. https://doi.org/10.1016/j.chest.2020.04.025
20. Niels M, Bart FG, Jan MB, et al. A higher fluid balance in the days after septic shock reversal ıs associated with ıncreased mortality: an observational cohort study. Crit Care Explor 2020;2:219. https://doi.org/10.1097/CCE.0000000000000219

21. Tsering D, Jong Chie T, Alberto M, Cassie CK, Ognjen G, Kianoush BK. Association of negative fluid balance during the de-escalation phase of sepsis management on mortality: a cohort study. J Crit Care 2020;55:16-21. https://doi.org/10.1016/j.jcrc.2019.09.025

Ethics committee approval: Approval was obtained from Akdeniz University Faculty of Medicine Clinical Research Ethics Committee Presidency with the date of 11.12.2019 and the number 1165.

Contributions of the authors

D.S., H.D. and A.E. set up the main idea and hypothesis of the study. H.D. and D.S. developed the main idea and organized the materials and methods section. D.S. and H.D. evaluated the data in the results section and wrote the discussion section of the article. A.E. reviewed the article and made necessary corrections. In addition, all authors discussed the entire study and approved its final version.