ORIGINAL ARTICLE

DOI: 10.4274/nkmj.galenos.2024.44712
Nam Kem Med J 2024;12(3):182-189

The Effect of Sepsis Associated Encephalopathy on One-Year Mortality in Patients Aged 65 Years and Over After Discharge: A Retrospective Cohort Study

Sepsis İlişkili Ensefalopatinin 65 Yaş ve Üzeri Hastalarda Taburculuk Sonrası Bir Yıllık Mortalite Üzerine Etkisi: Retrospektif Bir Kohort Çalışması

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ABSTRACT

Aim: Sepsis remains a leading cause of mortality among the older hospitalized patients, particularly those with complex comorbidities. This study investigates the prognostic factors influencing one-year mortality in patients aged 65 years and over, who were hospitalized with sepsis, emphasizing the role of sepsis-associated encephalopathy (SAE) in long-term outcomes.

Materials and Methods: In a retrospective cohort of 207 older patients treated for sepsis, clinical and laboratory data were meticulously recorded. Demographic details, comorbidity indices, and specific treatment interventions were analyzed. The association between these variables and one-year mortality was evaluated using univariate and multivariate Cox regression models. The Kaplan-Meier curves, complemented by the Log-rank test, assessed the survival probabilities.

Results: The cohort consisted of patients with a nearly equal gender distribution, with a mean age of 73.7 years. The study found that SAE, increased international normalized ratio (INR), and advanced age were significantly associated with higher one-year mortality ($p<0.05$). Notably, SAE presented a hazard ratio of 3.41 in the multivariate analysis. Other factors such as gender, Charlson Comorbidity Index, Sequential Organ Failure Assessment score and various laboratory markers did not show significant prognostic value.

Conclusion: SAE and elevated INR are potent predictors of one-year mortality in older sepsis survivors. These findings highlight the importance of close neurological assessment and monitoring of coagulation parameters in this population. Focused strategies on these elements could potentially improve the management and outcomes of sepsis in the older patients.

Keywords: Sepsis, encephalopathy, mortality

ÖZ

Amaç: Sepsis, hastanede yatan yaşlı hastalar arasında, özellikle de karmaşık komorbiditeleri olanlarda önde gelen bir mortalite nedeni olmaya devam etmektedir. Bu çalışmada, sepsis ile hastaneye yatırılan 65 yaş ve üzeri hastalarda bir yıllık mortaliteyi etkileyen prognostik faktörlerin araştırılması ve uzun vadeli sonuçlarda sepsis ilişkili ensefalopatinin (SAE) rolününün vurgulanması amaçlanmaktadır.

Gereç ve Yöntem: Sepsis nedeniyle tedavi edilen 207 yaşlı hastadan oluşan retrospektif bir kohortta, klinik ve laboratuvar verileri kaydedilmiştir. Demografik ayrıntılar, komorbiditeler ve spesifik tedavi müdahaleleri analiz edilmiştir. Bu değişkenler ile bir yıllık mortalite arasındaki ilişki tek değişkenli ve çok değişkenli Cox regresyon modelleri kullanılarak değerlendirilmiştir. Log-rank testi ile tamamlanan Kaplan-Meier eğrileri sağkalım olasılıklarını değerlendirmiştir.

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Received: 08.05.2024 **Accepted**: 29.05.2024

Bulgular: Kohort, ortalama yaşı 73,7 olan ve cinsiyet dağılımı neredeyse eşit olan hastalardan oluşmuştur. Çalışmada ensefalopati, artmış uluslararası normalleştirilmiş oran (INR) ve ileri yaşın daha yüksek bir yıllık mortalite ile anlamlı şekilde ilişkili olduğu bulunmuştur (p<0,05). Özellikle, sepsis ilişkili ensefalopati çok değişkenli analizde 3,41'lik bir oranı sunmuştur. Cinsiyet, Charlson Komorbidite İndeksi, Ardışık Organ Yetmezliği Değerlendirme skoru ve çeşitli laboratuvar belirteçleri gibi diğer faktörler anlamlı prognostik değer göstermemiştir.

Sonuç: Sepsis ilişkili ensefalopati ve yüksek INR, sepsis sonrası sağ kalan yaşlı hastalarda bir yıllık mortalitenin güçlü belirleyicileridir. Bu bulgular, bu popülasyonda yakın nörolojik değerlendirme ve koagülasyon parametrelerinin izlenmesinin önemini vurgulamaktadır. Bu unsurlara odaklanan stratejiler, yaşlı hastalarda sepsis yönetimini ve sonuçlarını potansiyel olarak iyileştirebilir.

Anahtar Kelimeler: Sepsis, ensefalopati, mortalite

INTRODUCTION

Sepsis is a life-threatening organ dysfunction due to dysregulated host response to infection[1]. Atypical presentations can be particularly more common in older patients[2-5]. Although sepsis affects all age groups, older patients are at greater risk as a result of increased frequency of comorbidities, malnutrition, polypharmacy, immunosenescence and inflammaging[6]. Sepsis-related in-hospital mortality varies between 30% and 60% in older patients[3]. Besides that, with the advances in treatment, a decrease in sepsis-related mortality has been reported in older patients likewise the patients under the age of 65 years[7]. Poor prognosis in patients with sepsis is closely associated with advanced age, disease severity, organ failures, and comorbidities[8,9]. Sepsis-associated encephalopathy (SAE) is a diffuse cerebral dysfunction resulted from a dysregulated host response without central nervous system infection[10]. Although the mechanisms are incompletely understood, compromised blood brain barrier, increased central nervous cytokine levels and microglial and astrocytic activation which results in neuroinflammation are the probable pathophysiological and molecular alterations[11]. The clinical course of the patient with SAE is characterized by the changes in patient's consciousness[12]. In the study by Young et al.[13], SAE was reported to be associated with poor prognosis and also mortality was correlated with the severity of SAE. Survivors of the sepsis have been reported to have a tendency to develop cognitive alterations[14,15], however, the data about the long-term survival after an episode of sepsis are limited among older adults. In this retrospective cohort study, we aimed to determine the factors influencing one-year mortality in patients aged 65 years and over, who were hospitalized with sepsis, emphasizing the role of SAE.

MATERIALS AND METHODS

Patient Selection

This retrospective study included patients aged 65 years and above, with a diagnosis of sepsis in accordance with the Sepsis-3 definition[3], who were admitted to the intensive care unit (ICU) of Ege University Faculty of Medicine, Department of Internal Medicine between January 2013 and January 2023. The study was performed with the permission of Ege University Medical Research Ethics Committee (decision no: 24-3.1T/77, date: 21.03.2024), and adhered to the principles of the Declaration of Helsinki. For each patient included in the present study, we retrospectively collected the following data: the medical history, general data including age, gender, comorbidities and laboratory parameters of the patients during ICU admission. The Charlson Comorbidity Index (CCI) was calculated for comorbidity assessment[16]. For detecting acute kidney injury at any stage, the Kidney Disease Improving Global Outcomes criteria were used[17]. The sequential organ failure assessment (SOFA) score on ICU admission was recorded. SAE identification was defined as a Glagow coma score <15 or the presence of delirium confirmed by the confusion assessment method for the intensive care unit (CAM-ICU)[18,19]. Exclusion criteria were as follows: having a history of advanced stage of malignancy, being on palliative care, having central nervous system infections, having sedative-related cognitive effects, the presence of chronic alcohol or drug abuse, and having severe electrolyte imbalances.

Statistical Analysis

In this study, descriptive statistics were used to summarize the collected data. For continuous variables, the data obtained were presented considering their distribution: mean ± standard deviation or median with minimum and maximum values were used and displayed in tables. Categorical variables were represented as counts and percentages. The normality of numerical variables was checked using the Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests.

For the analysis of categorical variables between the groups, the Pearson chi-square test was applied to 2x2 tables with expected observations of five or more. The Fisher's exact test was used for tables where expected observations were fewer than five. For RxC tables with small expected observations, the Fisher Freeman Halton test was utilized.

In comparisons of two independent groups, the Independent Samples t-test was employed for numerical variables with a normal distribution. The Mann-Whitney U test was used when the distribution was not normal.

Cox regression analysis was used to identify factors affecting 1-year mortality, with both univariable and multivariable analyses performed. The univariable Cox regression analysis examined the effect of each independent variable such as gender, encephalopathy, bacteremia, age, CCI, SOFA score, albumin, lactate, hemoglobin, neutrophil/lymphocyte ratio (NLR), international normalized ratio (INR), activated partial thromboplastin time (APTT), and procalcitonin levels on 1-year mortality. Hazard ratio (HR) with 95% confidence intervals (CI) and p values were calculated for each factor. In the multivariable analysis, the combined effect of significant variables from the univariable analysis was evaluated, adjusting for other factors, and HR, 95% CI, and p values were presented.

The Kaplan-Meier survival analysis was used to examine the factors affecting 1-year mortality among patients who survived during the hospital stay. The analysis assessed the impact of variables such as the presence or absence of encephalopathy on 1-year mortality. The log-rank test determined the significance of differences in survival times between the groups.

Statistical analyses were conducted using Jamovi (version 2.3.28) and JASP (version 0.18.3) software. The significance level for all statistical tests was set at 0.05 (p value).

RESULTS

Of the 207 participants, 50.7% were female (n=105) and 49.3% were male (n=102), with a mean age of 73.7±7.2 years. Prevalence of comorbidities was as follows: diabetes mellitus (DM) 35.7% (n=74), hypertension 60.9% (n=126), chronic renal failure 22.7% (n=47), cardiovascular diseases 27.1% (n=56), chronic obstructive pulmonary disease (COPD)/asthma 15.0% (n=31), chronic kidney disease 17.4% (n=36), malignancy 21.3% (n=44). Clinical outcomes during ICU follow-up included a median CCI of 5 points for sepsis patients and a median hospital stay of eight days. Encephalopathy was observed in 40.6% of the patients (n=84). The predominant sources of sepsis were respiratory system infections at 24.6% (n=51), followed by urinary tract infections at 20.3% (n=42), skin and soft tissue infections at 11.1% (n=23), and blood-catheter-related sepsis also at 11.1% (n=23). Other sources included abdominal infections at 8.7% (n=18), multiple foci at 8.7% (n=18), and various other causes at 8.2% (n=17). During ICU follow-up, mortality was recorded at 49.8% (n=103) among hospitalized sepsis patients. At the one-year follow-up of discharged patients, mortality was 25% (n=26). The median survival time over one year was 12 months. In intensive care, 55.6% of patients (n=115) required vasopressor support, and 62.8% (n=130) developed acute kidney injury. Hemodialysis was necessary for 20.3% of patients (n=42). The median SOFA score at the onset of sepsis was 7 points. Bacteremia was identified in 33.2% (n=68) of the cases Table 1.

During the ICU follow-up, analyses of hematologic and biochemical parameters are shown in Table 2.

Table 1. Demographic and clinical variables for patients admitted to intensive care unit for sepsis

	Overall (n=207)
Age†	73.7±7.2
Gender‡	
Female	105 (50.7)
Male	102 (49.3)
Diabetes mellitus, present‡	74 (35.7)
Hypertension, present‡	126 (60.9)
Heart failure, present‡	47 (22.7)
Cardiovascular disease, present‡	56 (27.1)
Chronic obstructive pulmonary disease, present‡	31 (15.0)
Chronic kidney disease, present‡	36 (17.4)
Malignancy, present‡	44 (21.3)
Charlson comorbidity index§	5.0 [1.0-10.0]
Encephalopathy, present‡	84 (40.6)
Source of sepsis‡	
Respiratory system	51 (24.6)
Urinary system	42 (20.3)
Hepatobiliary system	15 (7.2)
Skin/soft tissue	23 (11.1)
Abdomen	18 (8.7)
Blood-catheter	23 (11.1)
Multiple focus	18 (8.7)
Other	17 (8.2)
Length of stay, days§	8.0 [1.0-80.0]
In hospital mortality, yes‡	103 (49.8)
1-year mortality, yes‡	26 (25.0)
Post discharge survival time (months)§	12.0 [1.0-12.0]
Vasopressor support, present‡	115 (55.6)
Acute kidney injury, present‡	130 (62.8)
Need for hemodialysis, present‡	42 (20.3)
SOFA score at onset of sepsis§	7.0 [0.0-16.0]
Bacteremia, present‡	68 (33.2)

†: Values are presented as mean ± standard deviation for continuous variables, ‡: Values for categorical variables are presented as number (percentage) of patients, §: Median values with range (minimum-maximum) are shown for continuous variables, SOFA: Sequential organ failure assessment

In the analysis of demographic and clinical variables between patients with and without mortality at the 1-year follow-up post-discharge, significant findings included a higher mean age in the mortality group (p<0.001). The incidence of COPD/asthma was also significantly greater in the mortality group at 30.8% compared to those without mortality (p=0.011). No statistically significant differences were found between the groups regarding gender, diabetes mellitus, hypertension, chronic renal failure, cardiovascular diseases, chronic kidney disease, and malignancy (p>0.05 for each). At the 1-year follow-up after discharge, patients who died had significantly higher CCI and SOFA scores compared to survivors (p=0.002 and p=0.047, respectively). Additionally, a higher prevalence of encephalopathy was observed among deceased patients (p<0.001), along with longer hospital stays (p=0.013). Formun Üstü On the other hand, no significant differences were observed between the groups regarding the sources of sepsis, the need for vasopressor support, acute kidney injury, the need for hemodialysis, and bacteremia (p>0.05 for each) Table 3.

Laboratory values were analyzed in 104 patients followed up post-discharge. The bilirubin level was 0.6 mg/dL, aspartate aminotransferase 28.5 U/L, INR 1.1, prothrombin time (PT) 13.4 seconds, and APTT 27.3 seconds. Fibrinogen level was 543.0 mg/dL, and baseline creatinine 3.0 mg/dL. The C-reactive protein (CRP) level was 196.0 mg/L, and albumin 3.1 g/dL with a standard deviation of 0.6 at baseline. Hematologic parameters included a neutrophil count of 9535 cells/mm^3, lymphocyte count of 815 cells/mm^3, hemoglobin level of 10.9 g/dL, platelet count of 165.000 cells/mm^3, NLR of 12.1, lactate level of 1.9 mmol/L, and procalcitonin of 5.5 ng/mL. At discharge, CRP and albumin levels were 15.0 mg/L and 2.9±0.7 g/dL, respectively.

According to pairwise comparisons, INR (p=0.031), PT (p=0.038), and lactate levels (p=0.012) were significantly higher in patients with mortality at the 1-year follow-up. Conversely, albumin levels measured at baseline and discharge were significantly lower in patients with mortality (p=0.032 and p=0.004, respectively). Other laboratory parameters, including fibrinogen, creatinine, CRP, neutrophils, lymphocytes, hemoglobin, platelets, NLR, and procalcitonin, values did not show significant differences between the groups (p>0.05 for each) Table 4.

When analyzing factors that might affect 1-year mortality rates post-discharge, univariate Cox regression analysis revealed significantly higher mortality risk in patients with encephalopathy, with a HR of 9.69 (CI: 1.94-48.45, p=0.006). Additionally, each unit increase in INR values raised the mortality risk by nearly threefold (HR: 2.97, CI: 1.20-7.36, p=0.019). An increase in APTT value by each unit was associated with an 8% increase in the 1-year mortality risk (HR: 1.08, CI: 1.01-1.15, p=0.017). However, other variables such as gender, bacteremia, CCI, SOFA score, albumin, lactate, hemoglobin,

Table 2. Laboratory parameters in patients admitted to intensive care unit for sepsis

	Overall (n=207)
Bilirubin[§]	0.7 [0.1-11.0]
INR[§]	1.2 [0.8-4.2]
PT[§]	13.9 [9.9-41.7]
APTT[§]	28.6 [17.0-80.0]
Fibrinogen[§]	483.0 [40.0-1044.0]
Creatinine[§]	2.5 [0.2-9.6]
CRP[§]	184.0 [1.0-619.0]
Albumin[§]	2.9 [1.2-9.0]
Neutrophils[§]	9380.0 [20.0-46600.0]
Lymphocyte[§]	760.0 [9.4-87520.0]
Hemoglobin[§]	10.1 [6.3-570.0]
Platelet count[§]	144000.0 [70.0-570000.0]
NLR[§]	12.2 [0.1-278.0]
Lactate[§]	2.3 [0.5-15.0]
Procalcitonin[§]	4.7 [0.0-100.0]

[§]: Data represents median values with the range (minimum-maximum) for key biochemical and hematologic parameters monitored during the intensive care unit stay of sepsis patients. INR: International normalized Ratio, PT: Prothrombin time, APTT: Activated partial thromboplastin time, CRP: C-reactive protein, NLR: Neutrophil/lymphocyte ratio

NLR, and procalcitonin did not significantly affect mortality risk (p>0.05 for each).

In multivariate analysis, encephalopathy, INR values, and age significantly influenced mortality risk. The 1-year mortality risk in patients with encephalopathy was 3.41 times higher than in those without (HR: 3.41, CI: 1.46-7.95, p=0.005). Each unit increase in age led to a 6% increase in mortality risk (HR: 1.06, CI: 1.01-1.11, p=0.018). Increases in INR levels resulted in a 2.42-fold increase in mortality risk (HR: 2.42, CI: 1.28-4.58, p=0.007) Table 5. Post discharge mortality outcomes in sepsis patients with and without encephalopathy are shown in Figure 1.

Discussion

In the current study, we found that patients with encephalopathy exhibited significantly higher one-year mortality rates, underscoring the need for intensive neurological monitoring and management in older sepsis survivors. Elevated INR levels were associated with increased one-year mortality,

Table 3. Comparison of demographic and clinical characteristics in terms of 1-year mortality in discharged sepsis patients

	Overall (n=104)	1-year mortality		p value
		Yes (n=26)	No (n=78)	
Age†	73.6±7.7	78.7±6.2	71.9±7.4	**<0.001**
Gender‡				
Female	49 (47.1)	15 (57.7)	34 (43.6)	0.307
Male	55 (52.9)	11 (42.3)	44 (56.4)	
Diabetes mellitus, present‡	40 (38.5)	10 (38.5)	30 (38.5)	0.999
Hypertension, present‡	66 (63.5)	13 (50.0)	53 (67.9)	0.158
Heart failure, present‡	25 (24.0)	9 (34.6)	16 (20.5)	0.233
Cardiovascular disease, present‡	30 (28.8)	11 (42.3)	19 (24.4)	0.134
Chronic obstructive pulmonary disease, present‡	15 (14.4)	8 (30.8)	7 (9.0)	**0.011**
Chronic kidney disease, present‡	17 (16.3)	7 (26.9)	10 (12.8)	0.125
Malignancy, present‡	15 (14.4)	2 (7.7)	13 (16.7)	0.346
Charlson comorbidity index§	5.0 [1.0-10.0]	6.0 [3.0-9.0]	5.0 [1.0-10.0]	**0.002**
Encephalopathy, present‡	29 (27.9)	15 (57.7)	14 (17.9)	**<0.001**
Source of sepsis‡				
Respiratory system	21 (20.2)	7 (26.9)	14 (17.9)	0.780
Urinary system	29 (27.9)	9 (34.6)	20 (25.6)	
Hepatobiliary system	11 (10.6)	2 (7.7)	9 (11.5)	
Skin/soft tissue	8 (7.7)	2 (7.7)	6 (7.7)	
Abdomen	7 (6.7)	1 (3.8)	6 (7.7)	
Blood-catheter	11 (10.6)	3 (11.5)	8 (10.3)	
Multiple focus	10 (9.6)	2 (7.7)	8 (10.3)	
Other	7 (6.7)	0 (0.0)	7 (9.0)	
Length of stay, days§	10.0 [3.0-80.0]	13.0 [3.0-58.0]	9.0 [3.0-80.0]	**0.013**
Vasopressor support, present‡	47 (45.2)	15 (57.7)	32 (41.0)	0.211
Acute kidney injury, present‡	66 (63.5)	18 (69.2)	48 (61.5)	0.638
Need for hemodialysis, present‡	17 (16.3)	3 (11.5)	14 (17.9)	0.552
SOFA score at onset of sepsis§	7.0 [0.0-14.0]	7.5 [2.0-10.0]	6.0 [0.0-14.0]	**0.047**
Bacteremia, present‡	26 (25.0)	7 (26.9)	19 (24.4)	0.999

†: Mean ± standard deviation, ‡: n (%), §: Median (min.-max.), SOFA: Sequential organ failure assessment

emphasizing the importance of monitoring coagulation states as part of post-sepsis patient care. Advanced age was found to incrementally increase the risk of mortality within one year after sepsis, highlighting the necessity for age-adapted therapeutic strategies in elderly patients. Common comorbidities such as DM, hypertension, along with traditional inflammatory markers like CRP and procalcitonin, did not significantly predict mortality, suggesting that specific post-sepsis conditions such as encephalopathy and coagulation disturbances may be more relevant predictors in this population. Kaplan-Meier analysis revealed that variables such as the presence or absence of encephalopathy distinctly affected survival outcomes, providing a clear direction for targeted interventions. The use of both univariate and multivariate Cox regression analyses helped to identify the most critical determinants of mortality, offering actionable insights for clinicians focusing on the long-term recovery and management of older sepsis patients.

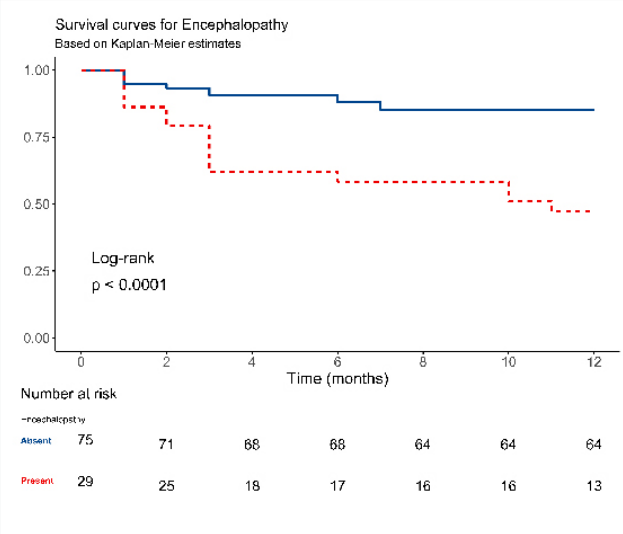

Figure 1. 1-Year post-discharge mortality outcomes in sepsis patients with and without encephalopathy

Sepsis can be complicated with SAE. In the current literature, SAE was reported in up to 40-70% of patients[20,21]. In our study, SAE frequency was 40.6% which is consistent with literature. In hospital mortality was 49.8%, which is also similar with reports in the current data[3].

When compared in terms of one-year mortality, SAE was significantly higher in non-survivors. Long-term sequel including neurocognitive dysfunction was reported in many studies[22-24], however, data about the mortality are limited. In our study, one-year mortality was 25% and presence of SAE during ICU increased the one-year mortality. Many older sepsis survivors develop chronic critical illness, which results in hospital readmissions and possibly death[25]. In a prospective cohort study, one-year mortality was 63.3% and severely frail group was associated with worse outcomes[26]. Our mortality results were lower than the literature data. Although it is difficult to compare the populations, sociocultural characteristics may be one of the reasons. We did not compare the frailty, which may be an also possible explanation.

Table 4. Comparison of biochemical and hematologic characteristics in terms of 1-year mortality in discharged sepsis patients

	Overall (n=104)	1-Year Mortality		p value
		Yes (n=26)	No (n=78)	
Bilirubin§	0.6 [0.2-10.1]	0.6 [0.2-10.1]	0.6 [0.2-10.1]	0.895
INR§	1.1 [0.8-3.9]	1.2 [0.9-3.9]	1.1 [0.8-2.0]	**0.031**
PT§	13.4 [9.9-39.0]	14.9 [10.7-39.0]	13.2 [9.9-23.3]	**0.038**
APTT§	27.3 [17.0-64.9]	28.8 [21.0-64.9]	27.0 [17.0-47.0]	0.091
Fibrinogen§	543.0 [40.0-900.0]	503.0 [40.0-610.0]	577.0 [214.0-900.0]	0.263
Creatinine§	3.0 [0.4-9.6]	2.8 [1.0-8.2]	3.2 [0.4-9.6]	0.647
CRP§	196.0 [1.0-619.0]	208.5 [24.0-550.0]	184.0 [1.0-619.0]	0.785
Albumin†	3.1±0.6	2.9±0.4	3.2±0.6	**0.032**
Hemoglobin§	10.9 [6.6-124.0]	11.3 [7.3-14.0]	10.6 [6.6-124.0]	0.893
NLR§	12.1 [0.1-109.6]	15.2 [3.3-46.9]	11.8 [0.1-109.6]	0.331
Lactate§	1.9 [0.5-9.4]	2.5 [0.6-9.4]	1.5 [0.5-8.4]	**0.012**
Procalcitonin§	5.5 [0.0-100.0]	2.6 [0.3-100.0]	8.3 [0.0-100.0]	0.391
Discharge CRP§	15.0 [0.4-110.0]	22.0 [2.3-110.0]	12.5 [0.4-100.0]	0.157
Discharge albumin†	2.9±0.7	2.5±0.7	3.0±0.7	**0.004**

†: Mean ± standard deviation, §: Median (min.-max.), INR: International normalized ratio, PT: Prothrombin time, APTT: Activated partial thromboplastin time, CRP: C-reactive protein, NLR: Neutrophil/lymphocyte ratio

Table 5. Factors affecting 1-year survival in discharged sepsis patients

Dependent: 1-year Mortality, Time: Survival time (Months)	HR (univariable)	HR (multivariable)
Gender: Male vs. Female	0.84 (0.20-3.52, p=0.813)	-
Encephalopathy: Present vs. absent	9.69 (1.94-48.45, p=0.006)	3.41 (1.46-7.95, **p=0.005**)
Bacteremia: Present vs. absent	0.84 (0.17-4.19, p=0.836)	-
Age	1.08 (1.00-1.16, p=0.065)	1.06 (1.01-1.11, **p=0.018**)
Charlson comorbidity index	1.09 (0.78-1.53, p=0.602)	-
SOFA score	1.08 (0.88-1.33, p=0.481)	-
Albumin	0.72 (0.17-2.99, p=0.655)	-
Lactate	0.96 (0.63-1.47, p=0.842)	-
Hemoglobin	1.15 (0.82-1.60, p=0.423)	-
NLR	0.99 (0.96-1.03, p=0.728)	-
INR	2.97 (1.20-7.36, **p=0.019**)	2.42 (1.28-4.58, **p=0.007**)
APTT	1.08 (1.01-1.15, **p=0.017**)	-
Procalcitonin	0.98 (0.96-1.01, p=0.218)	-

Depicts hazard ratios (HR) from univariable and multivariable Cox regression analyses assessing factors influencing 1-year mortality among discharged sepsis patients. SOFA: Sequential organ failure assessment, NLR: Neutrophil/lymphocyte ratio, INR: International normalized ratio, APTT: Activated partial thromboplastin time, HR: Hazard ratios

Age was associated with increased in-hospital mortality in older sepsis patients[27,28]. Additionally, we found that increased age was a risk factor for one-year mortality. Albumin, both on admission and at discharge, were significantly higher in survivors. Low albumin is a well-known poor prognostic factor in sepsis[29]. Our study also reveals the effect of discharge albumin value on one-year mortality, for which there are limited data in the literature.

The presence of sepsis-associated coagulopathy predicts hospital mortality, with increasing INR values at higher risk[30]. In addition to current literature, we determined that INR level was also associated with long-term mortality.

Study Limitations

This study, while shedding light on significant prognostic factors for one-year mortality post-sepsis, is not without limitations. The retrospective design limits the ability to infer causality from the associations found. Data were derived from a single-center, which may limit the generalizability of the findings to different healthcare settings or populations. Another limitation lies in the variability of clinical presentations and the complexity of sepsis, which may influence the recorded variables. The potential for unrecognized confounders, despite meticulous data collection and analysis, cannot be entirely ruled out. Moreover, some variables of interest, such as detailed functional status post-discharge or quality of life assessments, were not available for analysis.

Future studies should aim to include prospective designs, multi-center data, and a broader patient demographics to validate and expand upon these findings. Longitudinal studies that track the recovery trajectory of sepsis survivors beyond the one-year mark could provide further insights into the chronic impact of sepsis and its management. Additionally, the integration of qualitative data reflecting patient and caregiver experiences could offer a more holistic understanding of the post-discharge journey for sepsis survivors.

CONCLUSION

The present study comprehensively explored the factors influencing one-year mortality in patients over the age of 65 years, who were hospitalized with sepsis, with a particular focus on the role of encephalopathy. The findings reveal that encephalopathy is an independent predictor of mortality within one year following hospital discharge. This association highlights the critical importance of neurological assessment in the management of sepsis, which could significantly affect patient outcomes. Age, a non-modifiable risk factor, was also found to be incrementally associated with higher mortality, underscoring the need for heightened vigilance and potentially different therapeutic strategies in the older sepsis patient population. The study's findings support the necessity for a multidisciplinary approach to sepsis treatment, considering both the immediate and long-term implications of this condition in the older sepsis patients.

These insights are instrumental for clinicians who are tasked with providing care for this vulnerable patient population. They indicate a pivotal shift towards including comprehensive neurological evaluations in routine sepsis management protocols. Integrating such parameters into the prognostic models for sepsis may improve the ability to identify high-risk patients and tailor interventions more effectively, potentially improving survival outcomes.

Ethics

Ethics Committee Approval: The study was conducted after obtaining the necessary permissions from Ege University Medical Research Ethics Committee (decision no: 24-3.1T/77, date: 21.03.2024). The study was conducted in accordance with Good Clinical Practice Guidelines and adhered to the principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: Ş.M.K.B., İ.A.K., C.A., Z.T.K., R.Y., H.D.A., M.D.E., D.B., Concept: M.K.B., İ.A.K., C.A., D.B., Design: M.K.B., İ.A.K., C.A., D.B., Data Collection or Processing: Z.T.K., R.Y., H.D.A., M.D.E., D.B., Analysis or Interpretation: Z.T.K., R.Y., H.D.A., M.D.E., D.B., Literature Search: Z.T.K., R.Y., H.D.A., M.D.E., D.B., Writing: Ş.M.K.B., İ.A.K., C.A., D.B.

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

Financial Disclosure: The authors declared that this study received no financial support.

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