



RESEARCH

The factors affecting survival in patients followed up with the diagnosis of lymphoma in the intensive care unit

Yoğun bakım ünitesinde lenfoma tanısı ile takip edilen hastalarda sağkalımı etkileyen faktörler

Kaniye Aydın¹, Ömer Doğan²

¹Çukurova University, Faculty of Medicine, Department of Internal Medicine, Division of Intensive Care Unit, ² Department of Anesthesiology and Reanimation, Adana, Türkiye

Abstract

Purpose: This retrospective analysis aimed to elucidate the key factors influencing survival outcomes in patients diagnosed with lymphoma and admitted to an Intensive Care Unit (ICU).

Materials and Methods: The study cohort comprised individuals aged 18 or older diagnosed with lymphoma and admitted to the ICU between November 2015 and February 2023. Data were collected on patients' demographic characteristics, primary hematological diagnoses, reasons for ICU admission, laboratory parameters, Acute Physiology and Chronic Health Evaluation (APACHE) II scores, Sequential Organ Failure Assessment (SOFA) scores, clinical trajectory, and 28-day mortality rates. Patients were stratified into two categories based on their mortality outcomes: Survivors and non-survivors.

Results: A total of 165 patients were included in the study, with a mean age of 52.41 ± 17.99 years; 63% were male. Table 1 summarizes the demographic characteristics, clinical trajectories, and 28-day mortality rates. The APACHE II and SOFA scores of the patients were 34 (7–53) and 12 (10–14), respectively. The predominant reasons for ICU admission were sepsis (58.2%) and acute respiratory failure (57.6%). Vasopressor necessity prior to and during ICU stay was 23.6% and 92.4%, respectively. During ICU monitoring, thrombocytopenia, and acute kidney injury (AKI) were observed in 77.6% and 66.4% of patients, respectively; 10% required renal replacement therapy. The 28-day mortality rate was 84.8%. Kaplan-Meier analysis revealed that patients with a SOFA score ≥ 9 had a significantly reduced survival time of 4.5 ± 0.4 days compared to those with lower SOFA scores (14.3 ± 2.6 days). Patients with AKI and those requiring invasive mechanical ventilation (IMV) exhibited reduced survival times of 4.7 ± 0.5 days and 5.6 ± 0.5 days, respectively.

Öz

Amaç: Bu retrospektif analiz, lenfoma tanısı konan ve Yoğun Bakım Ünitesine (YBÜ) yatırılan hastalarda sağkalım sonuçlarını etkileyen temel faktörleri aydınlatmayı amaçlamıştır.

Gereç ve Yöntem: Çalışma grubu, Kasım 2015 ile Şubat 2023 arasında lenfoma tanısı konan ve YBÜ'ye kabul edilen 18 yaş ve üzeri bireylerden oluşmaktadır. Hastaların demografik özellikleri, birincil hematolojik tanıları, YBÜ'ye kabul nedenleri, laboratuvar parametreleri, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi (APACHE) II skorları, Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) skorları, klinik seyirleri ve 28 günlük mortalite oranları hakkında veriler toplanmıştır. Hastalar mortalite sonuçlarına göre iki kategoriye ayrılmıştır: Hayatta kalanlar ve ölenler.

Bulgular: Ortalama yaşı $52,41 \pm 17,99$ yıl olan toplam 165 hasta çalışmaya dahil edilmiştir; hastaların %63'ü erkektir. Tablo 1 demografik özellikleri, klinik seyirleri ve 28 günlük mortalite oranlarını özetlemektedir. Hastaların APACHE II ve SOFA skorları sırasıyla 34 (7-53) ve 12 (10-14)'di. YBÜ'ye kabulün başlıca nedenleri sepsis (%58,2) ve akut solunum yetmezliği (%57,6). YBÜ'de kalış öncesinde ve sırasında vazopressör ihtiyacı sırasıyla %23,6 ve %92,4 idi. YBÜ izlemi sırasında hastaların sırasıyla %77,6 ve %66,4'ünde trombositopeni ve akut böbrek hasarı (ABH) gözlemlendi; %10'unda renal replasman tedavisi gerekti. 28 günlük mortalite oranı %84,8 idi. Kaplan-Meier analizi, SOFA skoru ≥ 9 olan hastaların sağkalım süresinin SOFA skoru daha düşük olanlara kıyasla ($14,3 \pm 2,6$ gün) $4,5 \pm 0,4$ gün daha kısa olduğunu ortaya koymuştur. Akut böbrek hasarı olan ve invaziv mekanik ventilasyon (IMV) gerektiren hastalarda sırasıyla $4,7 \pm 0,5$ gün ve $5,6 \pm 0,5$ günlük azalmış sağkalım süreleri görülmüştür. Yüksek SOFA skorları (HR 2.355, %95 CI 1.485-3.734), AKI varlığı (HR 1.511, %95 CI 1.055-2.163) ve IMV ihtiyacı (HR 5.721, %95 CI 1.377-23.770) artmış 28 günlük

Address for Correspondence: Kaniye Aydın, Çukurova University, Faculty of Medicine, Department of Internal Medicine, Department of Intensive Care, Adana, Turkey E-mail adresi: kaydin@cu.edu.tr

Received: 17.08.2023 Accepted: 11.09.2023

Elevated SOFA scores (HR 2.355, 95% CI 1.485–3.734), presence of AKI (HR 1.511, 95% CI 1.055–2.163), and the need for IMV (HR 5.721, 95% CI 1.377–23.770) were significantly correlated with increased 28-day mortality. Receiver Operating Characteristic (ROC) curve analysis identified the optimal SOFA cut-off point for predicting 28-day mortality as nine, with an Area Under the Curve (AUC) of 0.897, sensitivity 83.6% and specificity 92%.

Conclusions: The findings of this study underscore the elevated mortality rates among lymphoma patients admitted to the ICU. Our data suggest that several factors serve as significant predictors of 28-day mortality in this patient population. Specifically, elevated APACHE II scores, SOFA scores, the presence of AKI, and the requirement for IMV emerged as crucial indicators associated with adverse survival outcomes. Consequently, these factors warrant meticulous monitoring and could inform targeted interventions to improve survival rates among lymphoma patients in critical care settings.

Keywords: Lymphoma, intensive care unit, APACHE II score, SOFA score, mortality

INTRODUCTION

Patients diagnosed with cancer are highly susceptible to life-threatening diseases and complications. Among these, hematological malignancies such as leukemia and lymphomas are most frequently encountered in Intensive Care Units (ICUs)¹⁻³. Individuals with hematological malignancies may necessitate ICU admission during their initial diagnosis or due to complications arising from treatment regimens. The indications for ICU admission can be broadly categorized into three groups: malignancy-related (e.g., critical organ infiltration, pulmonary embolism), treatment-associated (e.g., sepsis, drug toxicity), or complications from concomitant diseases (e.g., kidney injury, cardiac failure, exacerbation of chronic obstructive pulmonary disease).

The primary reason for ICU admission among cancer patients is typically acute organ failure, such as acute respiratory failure (ARF), acute kidney injury (AKI), or shock⁴⁻⁵. Notably, the prognosis for adult patients suffering from critical hematologic malignancies tends to be governed more by their critical condition's etiology than by the underlying malignancy's prognosis⁶⁻⁸.

Several factors are significant predictors of poor outcomes for critically ill patients with hematological malignancies. These include the onset of multiple organ failure, the requirement for invasive mechanical ventilation (IMV) or vasopressors, and

mortalite ile anlamlı şekilde ilişkiydi. Alıcı İşlem Karakteristiği (ROC) eğrisi analizi, 28 günlük ölüm oranını tahmin etmede optimal SOFA kesme noktasını dokuz olarak tanımladı; Eğri Altındaki Alan (AUC) 0,897, duyarlılık %83,6 ve özgüllük %92'di.

Sonuç: Bu çalışmanın bulguları, YBÜ'ye kabul edilen lenfoma hastaları arasındaki yüksek mortalite oranlarının altını çizmektedir. Verilerimiz, bu hasta popülasyonunda çeşitli faktörlerin 28 günlük mortalitenin önemli belirleyicileri olduğunu göstermektedir. Özellikle, yüksek APACHE II skorları, SOFA skorları, AKI varlığı ve IMV gereksinimi, olumsuz sağlık sonuçlarıyla ilişkili önemli göstergeler olarak ortaya çıkmıştır. Sonuç olarak, bu faktörler titiz bir izlem gerektirmektedir ve kritik bakım ortamlarındaki lenfoma hastalarındaki sağlık oranlarını iyileştirmek için hedeflenen müdahaleler hakkında bilgi verebilir.

Anahtar kelimeler: Lenfoma, yoğun bakım ünitesi, APACHE II skoru, SOFA skoru, mortalite

elevated Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores^{2,8-10}. Mortality rates in ICUs for patients with hematological malignancies demonstrate substantial variability, ranging from 25% to 85%⁹. Prior research suggests that early ICU admission for patients at elevated risk of multiple organ failure, in conjunction with prompt and aggressive intervention, may ameliorate in-hospital mortality rates¹¹.

Interpreting the factors influencing survival becomes particularly challenging in studies involving heterogeneous hematological malignancies in ICU settings. Each type of hematological malignancy follows a unique clinical course, adding to the complexity of the analysis. A review of the existing literature reveals a preponderance of studies encompassing a diverse range of hematological malignancies. Despite advancements in treatment modalities, patients with lymphoma continue to constitute a significant fraction of ICU admissions. Few studies have focused exclusively on the factors affecting survival outcomes in critically ill patients diagnosed with lymphoma¹²⁻¹³.

Given this framework, we hypothesized that specific clinical characteristics, disease trajectory, and instances of organ failure could serve as predictors of mortality in critically ill lymphoma patients. The primary objective of this study is to elucidate the determinants influencing survival outcomes in ICU patients diagnosed with lymphoma. Enhancing our

understanding of these factors holds the potential to improve the quality of triage, inform management decisions, and ultimately reduce morbidity and mortality rates.

MATERIALS AND METHODS

Study design

This study is a retrospective, single-center, cross-sectional investigation conducted at the Department of Internal Medicine, Division of Medical ICU, Faculty of Medicine, Cukurova University. The study protocol received approval from the Non-Interventional Clinical Research Ethics Committee of Cukurova University's Faculty of Medicine (Approval Date: July 14, 2023; Reference Number: 19/135). The research was conducted in strict adherence to the ethical guidelines stipulated in the Helsinki Declaration of 1964, along with its subsequent amendments.

Procedure

Following approval from the local Clinical Research Ethics Committee, this retrospective study was conducted in the medical ICU from November 2015 to February 2023. Patient care and clinical follow-up were managed by a multidisciplinary team comprising an attending physician specializing in internal medicine and intensive care, resident physicians in intensive care, and resident physicians in internal medicine. When deemed necessary, consultations were sought from hematology or oncology specialists.

Comprehensive patient data were documented daily, including medical history, physical examination findings, laboratory results, treatment plans, diagnostic assessments, and clinical progress. These records were stored in the patient's physical files and the digital hospital information management system under categories such as intensive care follow-up notes and discharge summaries (epicrisis). Subsequent to patient discharge, physical files were archived, scanned, and integrated into the hospital's digital information management system. For analysis, variables such as patient's demographic and clinical characteristics, administered treatments, clinical trajectories, and 28-day mortality rates were extracted from these comprehensive records.

Participants

Inclusion criteria for the study were set as patients aged 18 years or older with a confirmed lymphoma diagnosis. Exclusion criteria encompassed patients under 18 and those without a lymphoma diagnosis. Of the 4,602 patients admitted to the medical ICU during the designated study period, 171 fulfilled the inclusion criteria. Six patients were subsequently excluded due to incomplete data sets. Patients were stratified into two groups based on 28-day mortality outcomes for analytical purposes: Survivors and non-survivors.

Variables

Demographic variables, including age and gender, along with clinical variables such as the type of lymphoma, disease status (e.g., newly diagnosed, previously diagnosed and treated, in remission, relapsed, or refractory), APACHE II and SOFA scores, were meticulously documented. Laboratory parameters recorded upon ICU admission encompassed complete blood count, C-reactive protein (CRP), procalcitonin, blood urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, International Normalized Ratio (INR), and fibrinogen levels. Admission locations to the ICU were classified into two categories: Emergency rooms and inpatient services. Additionally, variables such as the reasons for ICU admission, pre-ICU use of vasopressors, post-chemotherapy status, presence of ARF, and AKI as per the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 criteria were retrospectively analyzed¹⁴.

Treatments administered during the ICU stay—including vasopressor therapy, IMV, renal replacement therapy (RRT), and therapeutic apheresis—along with the duration of ICU stay (in days) and 28-day mortality rates were also evaluated. For sepsis and septic shock, diagnosis criteria from the 2001 International Sepsis Definitions Conference were applied to patients admitted between 2015 and February 2016¹⁵. For admissions post-February 2016, the Sepsis-3 criteria were employed¹⁶. Acute respiratory failure was characterized as acute and progressive hypoxemia, with or without concomitant hypercapnia. Instances requiring ICU admission due to central nervous system involvement, infection, seizures, or cerebrovascular events were categorized as acute neurological disorders.

Measures

Acute Physiology and Chronic Health Evaluation (APACHE) II Score

The Acute Physiology and Chronic Health Evaluation (APACHE) II is a well-established prognostic tool to assess baseline risk stratification in critically ill patients¹⁷. The scoring system incorporates 12 physiological parameters, alongside additional points allocated for age and pre-existing chronic conditions.

Sequential Organ Failure Assessment (SOFA) Score

The Sequential Organ Failure Assessment (SOFA) score is an evaluative metric for quantifying the degree of organ dysfunction and associated mortality risk in ICU settings¹⁷. The score is derived from a range of physiological variables, including the ratio of arterial oxygen tension to fraction of inspired oxygen ($\text{PaO}_2/\text{FiO}_2$), vasoactive medication requirements for hypotension management, bilirubin levels, platelet counts, Glasgow Coma Scale scores, and either serum creatinine levels or urine output. Each variable is assigned a score ranging from 0 to 4.

Statistical analysis

Continuous variables were summarized using means, standard deviations, medians, and interquartile ranges (Q1–Q3), while categorical variables were presented as frequencies and percentages. Based on 28-day mortality outcomes, patients were classified into two groups: Survivors and non-survivors. Categorical variables between these groups were compared using the Chi-square test. The Kolmogorov-Smirnov test was employed to validate the normal distribution of continuous variables, which were then compared between groups using either the Student's t-test or the Mann-Whitney U test. Kaplan-Meier survival analyses were conducted for univariate analysis, complemented by the log-rank test. Risk factors were identified through univariate analyses and simple statistical evaluations of quantitative variables. Subsequently, Cox regression analysis was conducted on these variables. Predictors of mortality were identified through Cox regression analysis, incorporating variables significant at the $p < 0.25$ level in univariate analyses. Receiver Operating Characteristic (ROC) analysis was employed to assess the SOFA score's predictive capacity for 28-day mortality. All analyses were executed using IBM SPSS Statistics version 20.0 (Armonk, NY: IBM Corp.),

with a significance level set at $p < 0.05$ for all tests

The requisite sample size was estimated based on effect sizes of significant predictors identified in prior literature, in alignment with the study's primary objective of assessing factors affecting survival. Utilizing an effect size ($d = 0.908$) for the SOFA score, 95% statistical power, and a 5% margin of error (α), the calculated sample size was approximately 70 patients. For the APACHE II score with an effect size of ($d = 0.919$), the sample size was estimated to be 68 patients. Calculations were performed using the G*Power 3.1.9.7 software. Ultimately, 165 patients who met the inclusion criteria were enrolled in the study. The study included all consecutive patients who met the predetermined inclusion criteria to mitigate selection bias.

RESULTS

During the study timeframe, 4,602 patients were admitted to our tertiary-level ICU. Out of 557 patients with hematological malignancies, 165 patients diagnosed with lymphoma were included in the study. The cohort had a mean age of 52.41 ± 17.99 years and a predominance of male patients (63%, $n=104$).

The median APACHE II score at admission was 32, ranging from 2 to 53. In contrast, the SOFA score on the day of admission had a median value of 11, with an interquartile range of 8-14. Most patients (81.2%, $n=134$) had received a diagnosis and undergone treatment for their malignancy, while 7.9% ($n=13$) were either in complete or partial remission. The predominant reasons for ICU admission were septic shock (96%) and ARF (95%). Table 1 presents the demographic and baseline clinical characteristics of lymphoma patients in the ICU, segmented according to their 28-day mortality outcomes. Notably, both APACHE II and SOFA scores were statistically and clinically higher in non-survivors compared to survivors ($p < 0.001$).

As outlined in Table 2, neutrophil and platelet counts were clinically and statistically lower in non-survivors compared to survivors, with p-values of 0.031 and 0.001, respectively. Additionally, serum creatinine and procalcitonin levels were statistically elevated in non-survivors compared to survivors ($p < 0.05$).

During the ICU stay, IMV was necessitated for 87.3% of the 147 patients. The overall 28-day mortality rate stood at 84.8%. Table 3 elaborates on

the clinical course of lymphoma patients in the ICU, stratified by 28-day mortality outcomes. Notably, AKI and the requirement for continuous RRT were exclusively observed in non-survivors.

Table 1. The demographic and clinical characteristics of patients with lymphoma according to 28-day mortality in the ICU

	All patients (n=165)	Survivors (n=25)	Non-survivors (n=140)	p- value
Age (years)	52.41±17.99	52.4±16.3	52.4±18.3	0.999
Gender				0.032
Male	104(63)	11(44)	93(66.4)	
Female	61(37)	14(56)	47(33.6)	
APACHE II score	32(2-53)	19(2-35)	34(7-53)	<0.001
SOFA score	11(8-14)	6(5-8)	12(10-14)	<0.001
Admission to ICU				
From emergency department	13(7.9)	2(8)	11(7.9)	0.999
From hematology clinic	152(92.1)	23(92)	129(92.1)	
Disease status				
Newly diagnosed	14(8.5)	2(8)	12(8.6)	0.008
Diagnosed and treated	134(81.2)	19(76)	115(82.1)	
In remission	4(2.4)	3(12)	1(0.7)	
Relapsed/refractory	13(7.9)	1(4)	12(8.6)	
Reason for ICU admission				
Sepsis	96(58.2)	12(48)	84(60)	0.263
Acute respiratory failure	95(57.6)	11(44)	84(60)	0.136
Gastrointestinal bleeding	1(0.6)	1(4)		
Acute neurological disorders	11(154)	2(8)	9(6.4)	0.674
Need for vasopressors before ICU admission	39(23.6)	4(16)	35(25)	0.329
Chemotherapy before ICU admission	121(73.3)	17(68)	104(74.3)	0.513

Values are presented as mean±SD, number(%) or median (Q1-Q3). APACHE II: Acute Physiology Assessment and Chronic Health Evaluation II, SOFA: Sequential Organ Failure Assessment, ICU: Intensive Care unit

Table 2. Laboratory findings of patients with lymphoma according to 28-day mortality in the ICU

	All patients (n=165)	Survivors (n=25)	Non-survivors (n=140)	p- value
Hemoglobine (gr/dL)	9(8-10)	9(8-11)	9(8-10)	0.197
Neutrophil count (10 ³ /mL)	2.4(0.1-8.2)	5(1.45-10.25)	2.1(0.1-7.7)	0.031
Platelet count (x10 ³ /µL)	39(16-107.5)	149(36-268)	31(15-93.25)	0.001
Creatinine (mg/dL)	1.1(0.6-2.2)	0.74(0.34-1.1)	1.32(0.6-2.32)	0.004
AST (U/L)	44(24-73.5)	32(20-48)	46(25-89)	0.300
CRP (mg/dL)	140.5(68.3-250)	119(53-157)	141(70-273)	0.120
Procalcitonin (ng/mL)	5(1-31.3)	1(0.3-16)	6(1-32)	0.006
INR	1(1-2)	1	1(1-2)	0.008
Fibrinogen (mg/dL)	363(261-522)	479(381-638)	352(250-510)	0.009

All values are expressed as numbers (%) or median (Q1-Q3). AST: Aspartate aminotransferase, CRP: C-reactive protein, INR: International normalized ratio

Table 3. The clinical course of lymphoma according to 28-day mortality in the ICU

	All patients (n=165)	Survivors (n=25)	Non-survivors (n=140)	p- value
Acute kidney injury	93(56.4)		93(66.4)	<0.001
Liver failure	42(26)	3(12)	39(28)	0.111
Need for vasopressors during ICU	144(87.3)	8(32)	136(97.1)	<0.001
Need for invasive mechanical ventilation	144(87.3)	6(24)	138(98.6)	<0.001
Need for CRRT	14(8.5)		14(10)	0.131
Plasmapheresis	13(7.9)	1(4)	12(8.6)	0.694
Length of ICU stay (days)	3(1-7)	5(3.5-7)	3(1-7)	0.004

Values are presented as number (%) or median (Q1-Q3). CRRT: Continuous renal replacement therapy, ICU: Intensive care unit

ROC curve analysis was employed to determine the optimal SOFA score cut-off for predicting 28-day mortality. A SOFA score of 9 was identified as the optimal cut-off, with an Area Under the Curve (AUC) of 0.897. Utilizing this threshold yielded a sensitivity of 83.6% and a specificity of 92% ($p < 0.001$).

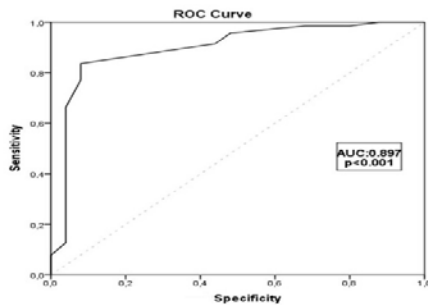


Figure 1. ROC analysis of the SOFA score to predict 28-day mortality AUC: Area under the curve

Kaplan-Meier survival analysis revealed that patients with a SOFA score of 9 or higher had a significantly reduced survival time of 4.5 ± 0.4 days, compared to those with lower SOFA scores with a survival time of 14.3 ± 2.6 days. Similarly, patients with AKI and those requiring IMV had diminished survival times of 4.7 ± 0.5 days and 5.6 ± 0.5 days, respectively. Elevated SOFA scores (Hazard Ratio [HR], 2.355; 95% Confidence Interval [CI], 1.485–3.734; $p < 0.001$), the presence of AKI (HR, 1.511; 95% CI, 1.055–2.163; $p = 0.024$), and the need for IMV (HR, 5.721; 95% CI, 1.377–23.770; $p = 0.016$) were significantly associated with increased 28-day mortality.

DISCUSSION

Morbidity and mortality remain pressing concerns for patients with lymphoma admitted to the ICU. Despite advancements in medical care, these patients, regardless of their disease stage, often require intensive interventions and still face elevated mortality rates. While predictors of mortality have been well-established for ICU patients with hematological malignancies, there exists a paucity of evidence specifically addressing predictors of survival for critically ill lymphoma patients¹²⁻¹³. In an 8-year retrospective review, it was observed that 12.1% of patients with hematologic malignancies received care in our ICU, of which 3.7% were diagnosed with lymphoma. This study aims to elucidate the factors

influencing survival outcomes in a cohort of 165 critically ill lymphoma patients.

Acute respiratory failure (ARF) and AKI are frequently encountered organ dysfunctions in this patient population¹². Various etiological factors can contribute to ARF in lymphoma patients, including mediastinal involvement, opportunistic pulmonary infections, sepsis-induced acute respiratory distress syndrome, acute pulmonary embolism, acute cardiogenic edema, and diffuse intraalveolar hemorrhage. During periods of immunosuppression, patients may exhibit resistance to antimicrobial therapies. Several risk factors, including immunosuppression, underlying malignancy, malnutrition, elevated APACHE II scores, prior use of broad-spectrum antibiotics, opioid exposure, male gender, steroid treatment, and the presence of central venous catheters, contribute to the incidence of nosocomial and ventilator-associated pneumonia¹⁸. Most of these risk factors were prevalent in our lymphoma patient cohort. Consequently, this often necessitates IMV, perpetuating a vicious cycle that leads to prolonged MV duration and heightened mortality rates^{18,19}. More than half of the patients in this study presented with ARF upon ICU admission, and a significant proportion required IMV during their ICU stay. In a survey by Irie et al., the necessity for IMV was markedly higher in non-surviving hematological patients compared to survivors (84.2% vs. 33.9%)¹.

The etiology of AKI in this patient cohort may be multifactorial, including drug toxicity, renal and post-renal events secondary to disease involvement, sepsis, acute tubular necrosis, or prerenal causes. In the current study, AKI was ubiquitously observed in all fatal cases. Our findings underscore AKI as a significant predictor of mortality, with a mortality rate of 100% among patients requiring RRT. Consistently, Park et al. reported elevated mortality in patients necessitating AKI and RRT²⁰.

Cytopenia in patients may result from diverse factors such as bone marrow involvement, post-chemotherapy status, drug side effects, viral or bacterial infections, sepsis, and nutritional deficiencies leading to vitamin deficiencies. Febrile neutropenia constitutes a hematological emergency requiring prompt diagnosis and treatment. A study by Bernal et al. reported higher mortality rates in neutropenic patients²¹. In the current research, neutrophil counts were statistically lower in non-survivors yet remained above $1.5 \times 10^3/\text{mL}$. Various

etiological factors may induce thrombocytopenia, including certain infections like COVID-19 pneumonia and cytomegalovirus infection or antimicrobial agents like linezolid²²⁻²⁴. In our cohort of non-survivors, platelet counts and SOFA scores were clinically significantly low and high, respectively.

Three-quarters of the study participants were in the post-chemotherapy phase. Immunocompromised states, such as post-chemotherapy or underlying diseases like lymphoma, render patients susceptible to opportunistic infections and sepsis, thereby elevating the risk of septic shock and associated morbidity and mortality²⁵. In this study, sepsis was diagnosed in over half of the patients upon ICU admission. The mortality risk escalates by approximately 7.6% for every hour delay in sepsis diagnosis and treatment²⁶. Our study reaffirms that a high SOFA score is an independent predictor of mortality, consistent with prior studies on critically ill patients with various hematological malignancies^{1,9,27}. Factors contributing to poor prognosis include the presence of sepsis, multiple organ failure, the need for IMV, usage of vasopressor agents, and aberrations in hematological and biochemical parameters. Interestingly, the etiology of the critical illness, rather than the prognosis of the underlying hematological malignancy, dictated the 28-day mortality outcomes in our study⁶⁻⁸.

Patel et al. reported an 85.7% mortality rate in critically ill AKI patients with APACHE II scores between 30-34 and 100% mortality for scores exceeding 34²⁸. These findings are consistent with our study, where the APACHE II score for non-survivors was 34. Geerse et al. also reported higher APACHE-II and SOFA scores in non-survivors compared to survivors (34 vs. 19 and 12 vs. 6, respectively)²⁹. Our study outcomes were markedly poorer than those of the general ICU population³⁰. Early therapeutic interventions for critically ill cancer patients have reduced in-hospital mortality^{11,31}. The ICU stay was longer in non-survivors, possibly reflecting their clinical presentations' greater severity and complexity. Delays in ICU admission might also have exacerbated mortality while reducing the length of ICU stay. These findings echo the assertions of Mokart et al., emphasizing the potential benefits of early ICU admission in mitigating morbidity and mortality¹¹.

This study is not without limitations, primarily due to its retrospective nature and confinement to a single center, which may constrain the generalizability and

quality of the findings. However, it is noteworthy that the study benefits from a robust sample size, comprising 165 patients exclusively diagnosed with lymphoma. Additionally, the study uniquely focuses on discerning factors that are predictive of ICU admission and overall survival outcomes for this particular patient demographic.

In conclusion, notwithstanding advancements in treatment methodologies, the mortality rates for lymphoma patients in the ICU remain distressingly high. This elevated mortality carries emotional costs and translates into extended hospital and ICU stays, thereby inflating healthcare costs. The imperative of early and accurate prognostication in lymphoma patients with critical illness conditions cannot be overstated. Parameters such as elevated APACHE II and SOFA scores, AKI occurrence, high dependence on vasopressor therapy, and the requirement for IMV stand out as significant predictors of mortality. Early ICU admission for patients with organ dysfunction can reduce mortality rates. Consequently, timely identification of risk factors and initiation of early, efficacious treatments could substantially improve survival outcomes. This underscores the need for future multicenter, prospective studies examining the benefits of early diagnostic interventions and ICU admissions in enhancing the survival prospects of critically ill lymphoma patients.

Author Contributions: Concept/Design : KA, ÖD; Data acquisition: KA, ÖD; Data analysis and interpretation: KA, ÖD; Drafting manuscript: KA, ÖD; Critical revision of manuscript: KA, ÖD; Final approval and accountability: KA, ÖD; Technical or material support: KA, ÖD; Supervision: KA, ÖD; Securing funding (if available): n/a.

Ethical Approval: Ethical approval was obtained from Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee for this study. (With the date 14.7.2023 and the number 19/135).

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support

Acknowledgement: This study was presented as a poster presentation at the 16th World Intensive and Critical Care Congress (August 26–30, 2023, Istanbul). The authors thank Yusuf Kemal Arslan for contributing to the statistical analysis.

REFERENCES

1. Irie H, Otake T, Kawai K, Hino M, Namazu A, Shinjo Y et al. Prognostic factors in critically ill patients with hematological malignancy admitted to the general intensive care unit: a single-center experience in Japan. *J Anesth.* 2017;31:736-43.
2. Grgić Medić M, Gornik I, Gašparović V. Hematologic malignancies in the medical intensive care unit-- Outcomes and prognostic factors. *Hematology.* 2015;20:247-53.

3. Ferreyro BL, Scales DC, Wunsch H, Cheung MC, Gupta V, Saskin R et al. Critical illness in patients with hematologic malignancy: a population-based cohort study. *Intensive Care Med.* 2021;47:1104-14.
4. Darmon M, Thiery G, Ciroidi M, de Miranda S, Galicier L, Raffoux E et al. Intensive care in patients with newly diagnosed malignancies and a need for cancer chemotherapy. *Crit Care Med.* 2005;33:2488-93.
5. Larché J, Azoulay E, Fieux F, Mesnard L, Moreau D, Thiery G et al. Improved survival of critically ill cancer patients with septic shock. *Intensive Care Med.* 2003;29:1688-95.
6. Massion PB, Dive AM, Doyen C, Bulpa P, Jamart J, Bosly A et al. Prognosis of hematologic malignancies does not predict intensive care unit mortality. *Crit Care Med.* 2002;30:2260-70.
7. Kalicińska E, Kuszczak B, Dębski J, Szukalski Ł, Wątek M, Strzala J et al. Hematological malignancies in Polish population: what are the predictors of outcome in patients admitted to Intensive Care Unit? *Support Care Cancer.* 2021;29:323-30.
8. Bird GT, Farquhar-Smith P, Wigmore T, Potter M, Gruber PC. Outcomes and prognostic factors in patients with haematological malignancy admitted to a specialist cancer intensive care unit: a 5 yr study. *Br J Anaesth.* 2012;108:452-9.
9. Bıkmaz ŞGA, Gökçe O, Haşimoğlu MM, Boyacı N, Türkoğlu M, Yeğin ZA et al. Risk factors for ICU mortality in patients with hematological malignancies: a singlecenter, retrospective cohort study from Turkey. *Turk J Med Sci.* 2023;53:340-51.
10. Rawson JL, Fagan FM, Burrough GC, Tang HM, Cuncannon MA, Ellem KL et al. Intensive care unit outcomes in patients with hematological malignancy. *Blood Sci.* 2020;2:33-7.
11. Mokart D, Lambert J, Schnell D, Fouché L, Rabbat A, Kouatchet A et al. Delayed intensive care unit admission is associated with increased mortality in patients with cancer with acute respiratory failure. *Leuk Lymphoma.* 2013;54:1724-9.
12. Zduniak A, Mihailescu SD, Lequesne J, Lenain P, Contentin N, Pepin LF et al. Outcomes after intensive care unit admission in newly diagnosed diffuse large B-cell lymphoma patients: A real-life study. *Eur J Haematol.* 2021;106:788-99.
13. Qi J, Gu C, Wang W, Xiang M, Chen X, Fu J. Elevated Lactate Dehydrogenase Levels Display a Poor Prognostic Factor for Non-Hodgkin's Lymphoma in Intensive Care Unit: An Analysis of the MIMIC-III Database Combined With External Validation. *Front Oncol.* 2021;11:753712.
14. Stevens PE, Levin A, Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann Intern Med.* 2013;158:825-30.
15. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med.* 2003;31:1250-6.
16. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315:801-10.
17. Quintairo A, Pilcher D, Salluh JIF. ICU scoring systems. *Intensive Care Med.* 2023;49:223-25.
18. Türk Toraks Derneği. Erişkinlerde Hastanede Gelişen Pnömoni Tanı Ve Tedavi Uzlaşı Raporu 2018. Ankara, Türk Toraks Derneği, 2018..
19. Maqsood S, Badar F, Hameed A. Characteristics . *Asian Pac J Cancer Prev.* 2017;18:1833-7.
20. Park MR, Jeon K, Song JU, Lim SY, Park SY, Lee JE et al. Outcomes in critically ill patients with hematologic malignancies who received renal replacement therapy for acute kidney injury in an intensive care unit. *J Crit Care.* 2011;26:107.e1-6.
21. Bernal T, Pardavila EV, Bonastre J, Jarque I, Borges M, Bargay J et al. Survival of hematological patients after discharge from the intensive care unit: a prospective observational study. *Crit Care.* 2013;17:R302.
22. Zong X, Gu Y, Yu H, Li Z, Wang Y. Thrombocytopenia is associated with COVID-19 severity and outcome: an updated meta-analysis of 5637 patients with multiple outcomes. *Lab Med.* 2021;52:10-5.
23. Shragai T, Lebel E, Deshet D, Varon D, Avivi I, Kirgner I et al. Characteristics and outcomes of adults with cytomegalovirus-associated thrombocytopenia: a case series and literature review. *Br J Haematol.* 2020;191:863-7.
24. Maray I, Rodríguez-Ferreras A, Álvarez-Asteinza C, Alaguero-Calero M, Valledor P, Fernández J. Linezolid induced thrombocytopenia in critically ill patients: Risk factors and development of a machine learning-based prediction model. *J Infect Chemother.* 2022;1249-54.
25. Wu TKY, Tang KHK, Hwang YY, Chan TSY, Tse E, Kwong YL. Bendamustine treatment of haematological malignancies: significant risks of opportunistic viral, fungal and bacterial infections. *Hematology.* 2022;27:535-42.
26. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med.* 2006;34:1589-96.
27. Judickas Š, Stasiūnaitis R, Žučenka A, Žvirblis T, Šerpytis M, Šipylaitė J. Outcomes and risk factors of critically ill patients with hematological malignancy.

- prospective single-centre observational study. *Medicina (Kaunas)*. 2021;57:1317.
28. Patel P, Gupta S, Patel H, Bashir MA. Assessment of APACHE II Score to Predict ICU outcomes of patients with AKI: A single-center experience from Haryana, North India. *Indian J Crit Care Med*. 2022;26:276-81.
 29. Geerse DA, Span LF, Pinto-Sietsma SJ, van Mook WN. Prognosis of patients with haematological malignancies admitted to the intensive care unit: Sequential Organ Failure Assessment (SOFA) trend is a powerful predictor of mortality. *Eur J Intern Med*. 2011;22:57-61.
 30. Vandijck DM, Depuydt PO, Offner FC, Nolle J, Peleman RA, Steel E et al. Impact of organ dysfunction on mortality in ICU patients with hematologic malignancies. *Intensive Care Med*. 2010;36:1744-50.
 31. Azoulay E, Mokart D, Pène F, Lambert J, Kouatchet A, Mayaux J et al. Outcomes of critically ill patients with hematologic malignancies: prospective multicenter data from France and Belgium--a groupe de recherche respiratoire en réanimation onc-hématologique study. *J Clin Oncol*. 2013;31:2810-8.