



ARAŞTIRMA / RESEARCH

Factors predicting prognosis with oncology patients followed in the intensive care unit

Yoğun bakım ünitesinde izlenen onkoloji hastalarının prognozunu belirleyen faktörler

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Abstract

Purpose: The aim of the study is to determine the factors affecting the mortality of oncology patients followed in the intensive care unit (ICU).

Materials and Methods: In this study 100 patients who were followed up in the ICU of Cukurova University Faculty of Medicine, Internal Medicine Department between 2012-2014 were prospectively included. Acute Physiology and Chronic Health Evaluation (APACHE) II, 1st and 3rd day Sequential Organ Failure Assessment Score (SOFA) scores were used to determine the factors that were affecting mortality. Lactate, magnesium, phosphorus, potassium, blood urea nitrogen (BUN) and beta 2 microglobulin levels were determined at the time of admission to ICU. The relationship between vasopressor, renal, respiratory support need, neutropenia, infectious agents and mortality was determined during the follow-up period in the ICU. The patients were divided into two groups as patients transferred from ICU to the inpatient clinics (Group 1: 40 patients) and patients who were died in the ICU follow-up (Group 2: 60 patients).

Results: APACHE II and 1st and 3rd day SOFA scores, predictive mortality rate, intensive care admission lactate levels, vasopressor and respiratory support needs, renal support needs, BUN, potassium and magnesium levels, beta 2 microglobulin levels, positive Acinetobacter baumannii culture mean was statistically significant with mortality during intensive care follow up between the Group 1 and 2 patients. In addition, mortality was found to be less in patients who were followed up in the new ICU.

Conclusion: Beta 2 microglobulin level can be used to predict intensive care mortality.

Keywords: Intensive care unit, oncology patients, beta 2 microglobulin, mortality

Öz

Amaç: Çalışmanın amacı yoğun bakım ünitesinde takip edilen onkoloji hastalarının mortalitesine etki eden faktörlerin belirlenmesidir.

Gereç ve Yöntem: Bu çalışmada 2012-2014 yılları arasında Çukurova Üniversitesi Tıp Fakültesi İç Hastalıkları ABD. yoğun bakım ünitesinde takip edilen ardışık 100 hasta prospektif olarak incelenmiştir. Mortaliteyi etkileyen faktörleri saptamak için Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi (APACHE) II, Sıralı Organ Yetmezliği Değerlendirme Puanı (SOFA) 1. gün ve SOFA 3. gün skorları kullanılmıştır. Laktat, magnezyum, fosfor, potasyum, kan üre azotu (BUN) ve beta 2 mikroglobülin düzeyleri belirlenmiştir. Hastaların yoğun bakımda takip edildiği süre boyunca vazopressör, renal, solunumsal destek ihtiyacı, nötropeni ve enfeksiyöz etkenler ile mortalite arasındaki ilişki belirlenmiştir. Yoğun bakım takibinden çıkarılıp servise devredilen hastalar (Grup 1: 40 hasta) ve yoğun bakım takibinde ölen hastalar (Grup 2: 60 hasta) olmak üzere iki grupta incelenmiştir.

Bulgular: Grup 1 ve Grup 2'deki hastaların APACHE II değeri, SOFA 1. Gün ve SOFA 3. Gün skoru, Prediktif mortalite oranı, yoğun bakıma kabul anındaki laktat değerleri, vazopressör destek ihtiyacı, solunumsal destek ihtiyacı, renal destek ihtiyacı, BUN düzeyi, potasyum düzeyi, magnezyum düzeyi, beta 2 mikroglobülin düzeyi ve Acinetobacter baumannii üremesi ile hastaların yoğun bakım takiplerinde kaybedilmesiyle istatistiksel olarak anlamlı bulunmuştur. Ayrıca hastaların izlemi sırasında yeni yoğun bakım ünitesinde izlenen hastalarda mortalite daha az bulunmuştur.

Sonuç: Beta 2 mikroglobülin düzeyi yoğun bakım mortalitesini tahmin etmekte kullanılabilir.

Anahtar kelimeler: Yoğun bakım ünitesi, onkoloji hastası, beta 2 mikroglobülin, mortalite

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INTRODUCTION

Scoring systems in intensive care unit (ICU); It is widely used to predict recovery from disease, determine the severity of the disease and the degree of organ dysfunction, evaluate the treatments administered, standardize patients to participate in clinical trials, and compare the performance of ICUs.¹ Scoring systems that define disease severity were used such as Acute Physiology and Chronic Health Evaluation (APACHE), Simplified Acute Physiology Score (SAPS), Mortality Prediction Model (MPM), Multi Organ Dysfunction Score (MODS), Logistic Organ Dysfunction Score (LODS) and Sequential Organ Failure Assessment Score (SOFA). These scores using physiological measurements were parallel to the prognosis of the disease and the risk of mortality²⁻⁴.

The use of scoring systems in patients hospitalized in the ICU enables the severity of the disease and the intensive care mortality to be scored numerically (usually after the first 28 days). However, they do not provide information on mortality and quality of life after discharge³. The increase in plasma Beta 2 microglobulin level may reflect decreases in various systems and may be responsible for poor phenotype among older adults⁵. It is known that this marker is a non-specific marker and increases in some malignancies and diseases^{6,7}. In this study, 164 patients with a diagnosis of malignancy who were followed up in the ICU between 2012 and 2014 were prospectively evaluated in order to determine the factors affecting the mortality of patients followed in the ICU.

MATERIALS AND METHODS

This study was conducted in the ICU of Cukurova University Faculty of Medicine between 2012 and 2014, with the approval of the Ethics Committee of Cukurova University, dated 03.01.2013, numbered 15. All procedures performed in our study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and ethical standards. Written informed consent forms were obtained from all subjects.

As for inclusion criteria: 100 patients with a history of malignancy and chemotherapy, older than 18 years of age, no previous history of malignancy-related

intensive care hospitalization, followed up in the ICU for at least 24 hours, received the last radiotherapy at least 30 days ago, at least 2 weeks past malignancy-related major surgery were included in the study. As for exclusion criteria: 64 Patients who had a second malignancy, received radiotherapy within the last 30 days, did not receive chemotherapy before, had a major surgery history in the last 2 weeks and died within 24 hours were excluded from the study.

Patients admitted to the ICU for septic shock (at least two of the criteria >100 / min heart rate, >30 / min respiratory rate, $4000 < \text{leukocyte count} < 12000$, body temperature less than 36 C or greater than 38.5 C and proven microorganism), hypovolemic shock (hypotension due to intravascular volume loss due to bleeding or non-bleeding reasons and shock causing tissue perfusion disorder), cardiogenic shock [decreased state of consciousness, heart rate >100 / min, respiratory rate >20 / min or partial pressure of carbon dioxide (PaCO_2) <32 mmhg, base deficit <4 mEq / L or lactate > 4 mmol/L in arterial blood gas, urine output > 0.5 ml / kg / hour, having at least four criteria for arterial hypotension lasting longer than 20 minutes], respiratory failure [at least two of the criteria for $\text{PaCO}_2 >45$ mmhg, $\text{pH} <7.35$ and partial pressure of oxygen (PaO_2) <60 mmhg] and close follow-up (previous seizure, symptomatic electrolyte imbalance, interventional procedures with expected bleeding, etc.) were included in the study. The first intensive care admissions of the patients who had repeated intensive care admissions during the follow-up were evaluated. The patients were divided into two groups as those who were transferred from the ICU to the inpatient clinic (Group 1) and were died in the ICU (Group 2).

During the study period, the location of the ICU was changed. In the old ICU, there were 11 patient beds in total, the number of beds with closed isolation was 3, the monitors of the patients could not be monitored on a single device and they could benefit from sunlight in a small amount. In the new ICU, all the beds were covered with closed isolation, all patients were monitored instantly through the central monitor system, and the use of sunlight was higher than in the old ICU. The old ICU devices continued to be used in the new ICU.

Procedure

Patients' age, gender, chronic organ failure status, malignancy diagnosis, chemotherapy history in the

last two weeks, reason for admission to intensive care, length of stay, need for vasopressor support during hospitalization, need for renal support, need for mechanical ventilation and if any, the type and duration of support, follow-up status in the old or new ICU, duration of stay in the mechanical ventilator, systolic and diastolic blood pressures during ICU admission, mean arterial blood pressure, body temperature, heart rate and respiratory rate per minute were recorded using the patient observation form. From venous blood samples obtained during admission to intensive care, the patients' white blood cell count, hemoglobin, hematocrit, thrombocyte, total protein, albumin, blood urea nitrogen, creatinine, sodium, potassium, serum bicarbonate level, magnesium, ionized calcium, phosphorus, uric acid, Procalcitonin, C-reactive protein and beta-2 microglobulin levels were measured and recorded. For lactate follow-up of the patients, the highest lactate levels detected at the time of admission to intensive care, at the end of the 1st, 2nd and 3rd days of intensive care admission and during the intensive care admission were used and, arterial blood samples were used to measure PaO₂, Alveolar-arterial oxygen gradient [(A-a) O₂] and pH levels, which were used to calculate APACHE II and SOFA scores.

The Glasgow Coma Scale (GCS) scores of patients was recorded using eye opening, motor response and verbal response parameters at admission to ICU. For the APACHE II score, age, chronic organ failure status, body temperature, respiratory rate, serum bicarbonate level, serum potassium level, hematocrit level, mean arterial blood pressure, heart rate, PaO₂ level for non-intubated patients, (A-a) O₂ level for intubated patients, arterial pH, serum sodium level, serum creatinine level, white blood cell count and GCS parameters that deviates the most from normal during the first 24 hours of patients in intensive care were calculated by entering the data to the computer program. At the end of the 1st and 3rd day of admission to the ICU, among the patients' PaO₂ / fraction of inspired oxygen (FiO₂) values, platelet counts, creatinine values, bilirubin values, the presence of inotropic support (if any) and the GCS scores that showed the highest deviation from normal were entered into the computer program, and SOFA 1st and 3rd day scores were calculated. For the predictive mortality rate calculation, heart rate, blood pressure, respiratory rate, body temperature, GCS, arterial Ph, arterial PaCO₂, arterial PaO₂, arterial FiO₂, serum sodium level, potassium level, BUN level, creatinine level, the number of white cells,

hematocrit, thrombocyte, hourly urine output, serum bilirubin level, need for vasopressor support, age and chronic immune system failure conditions that showed the highest deviation from normal were calculated by entering the data to the computer program. GCS, APACHE II, SOFA I and SOFA III scores and predictive mortality rate (PMR) were calculated by clinicians working in the ICU. Urine, blood and respiratory secretion culture (tracheal aspiration culture if the patient was intubated) specimens was obtained from all patients during admission to the ICU. During the follow-up of the patients, culture sampling was repeated in case of clinical necessity.

Among the patients who were followed up, patients with cardiac or respiratory arrest, those with apnea or prolonged bradipnea, those with GCS <8, those with acute respiratory acidosis and impaired consciousness, those with resistant hypoxemia and those who could not provide airway patency due to increased secretion were intubated and followed up. Positive inotropic support was provided to patients with a mean arterial pressure lower than 60 mmHg and concomitant impaired tissue perfusion. Noradrenaline was initiated at a dose of 0.01-0.15 mcg/kg/minute as positive inotropic agent. Dose adjustment was applied in the range of 0.5-3.3 mcg/kg/min in case of refractory shock. In order to determine survival, the death dates of the patients were taken from the Population Directorate.

Statistical analysis

Statistical analysis was performed using the statistical package *SPSS software* (Version 25.0, SPSS Inc., Chicago, IL, USA). If continuous variables were normal, they were describe as the mean±standard deviation ($p>0.05$ in Kolmogorov-Smirnov test or Shapira-Wilk ($n<30$)), and if the continuous variables were not normal, they were described as the median. Comparisons between groups were applied using Student T test and Mann Whitney U test used for the data not normally distributed. The categorical variables between the groups was analyzed by using the Chi square test or Fisher Exc. test. Receiver operating characteristic curves (ROC curves) were constructed and the areas under curve (AUC) as well as the sensitivity (sen.), and the specificity (spe.) were calculated. A multiple logistic regression analysis was used to know associations between measurements with mortality as dependent variable Values of $p < 0.05$ were considered statistically.

RESULTS

A total of 100 patients were included in the study. In the first group, 45% (n: 18) were women, 55% (n: 22) were men, and in the second group, 50% (n: 30) were women and 50% (n: 30) were men. The mean age of the patients included in the study was 54.62 ± 15.4 years. The average age of the patients transferred from the ICU to the inpatient clinic was 55.08 ± 16.7 years, and the average age of the patients who died in the intensive care follow-up was 54.32 ± 14.6 years. When the malignancy diagnoses of the patients were examined, it was found that the majority of both groups were diagnosed with lymphoproliferative malignancy and multiple myeloma ($p > 0.05$). When the indications for admission to the ICU were examined, it was seen that the majority of the patients transferred to the inpatient clinic were admitted for close follow-up, and the majority of the patients who died in the ICU were patients with septic shock

($p < 0.05$). When the need for positive inotrope, renal replacement and respiratory support in the ICU were examined, it was seen that patients who died in intensive care follow-up needed more support ($p < 0.001$, $p < 0.001$, $p < 0.005$, respectively). While 23% of patients (n: 9) transferred from intensive care to the inpatient clinic needed invasive mechanical ventilation (IMV) support, 87.7% (n: 53) of the patients who died in the ICU needed IMV support ($p < 0.001$). 76.7% (n: 46) of the patients who died in the ICU were in the old ICU, while 23.3% (n: 14) were in the new ICU ($p < 0.001$). When positive *Acinetobacter baumannii* culture results were evaluated, while there were in 30% (n: 18) of the patients who died in the ICU, there were in 12.5% (n: 5) of the patients transferred to the inpatient clinic ($p < 0.01$ and $p < 0.05$). 64% of positive *Acinetobacter baumannii* culture was detected in the old ICU, while 36% was found in the new ICU ($p < 0.01$). The clinical and demographic characteristics of the patients were given in Table 1.

Table 1. Characteristics of the patient.

| Variables | Group 1- % (n:40) | Group 2- % (n:60) | P |
|---|-------------------|-------------------|---------------|
| Age (mean±sd) | 55,08±16,7 | 54,32±14,6 | >0,05 |
| Gender, female (%) | 45 | 50 | >0,05 |
| Diagnosis (%) | | | |
| Respiratory system cancer | 20 | 16,7 | >0,05 |
| Gastrointestinal system cancer | 18 | 20 | >0,05 |
| Genitourinary system cancer | 18 | 13,3 | >0,05 |
| Lymphoma and multiple myeloma | 28 | 26,7 | >0,05 |
| Breast cancer | 10 | 16,7 | >0,05 |
| Other malignancies | 8 | 6,7 | >0,05 |
| Chemotherapy history (last 2 weeks) | 62 | 63 | >0,05 |
| Reason for hospitalization (%) | | | |
| Septic shock | 22 | 51,7 | <0,05 |
| Hypovolemic shock | 8 | 3,3 | >0,05 |
| Cardiogenic shock | 5 | 3,3 | >0,05 |
| Respiratory Failure | 25 | 13,3 | <0,05 |
| Close follow-up | 40 | 28,7 | <0,05 |
| Length of stay | 7,33±5,6 | 7,4±7,1 | >0,05 |
| Presence of neutropenia (%) | 15 | 22 | 0,287 |
| Need for vasopressor support (%) | 45 | 95 | <0,001 |
| Renal support need (%) | 15 | 45 | 0,001<p<0,005 |
| Mechanical ventilator requirement (%) | 48 | 90 | <0,001 |
| Invasive Only | 5 | 37 | <0,001 |
| Non-invasive Only | 25 | 5 | <0,001 |
| Invasive and non-invasive | 18 | 53 | <0,001 |
| Follow-up intensive care unit (%) | | | 0.001 |
| Old intensive care unit | 45 | 76.7 | |
| New intensive care unit | 55 | 23.3 | |
| Positive <i>Acinetobacter baumannii</i> culture (%) | 12.5 | 30 | 0.01<p<0.05 |

*APACHE: Acute Physiology And Chronic Health Evaluation; †SOFA: The Sequential Organ Failure Assessment ; ‡GCS: Glasgow Coma Scale

Table 2. Scoring systems, predictive mortality rate, duration of stay in the mechanical ventilator and laboratory parameters of the patients.

| Variables | Mean \pm Standard deviation | | | <i>p</i> |
|--|-----------------------------------|-------------------------------------|-----------------------------------|------------------------|
| | Group 1 (n:40) | Group 2 (n:60) | All patients (n:100) | |
| APACHE II* score | 18.43 \pm 5.7 19(9-30) | 25.18 \pm 8.4 24.5(5-44) | 22.48 \pm 8.1 23(5-44) | <0.001 |
| SOFA I† score | 4.95 \pm 2.09 5(1-11) | 7.67 \pm 3.6 7(1-16) | 6.58 \pm 3.7 6(1-16) | <0.001 |
| SOFA III score | 3.62 \pm 2.7 3(1-12) | 10.89 \pm 3.8 11(3-18) | 7.65 \pm 4.9 7(1-18) | <0.001 |
| GCS ‡ score | 12.9 \pm 3.67 15(3-15) | 10.1 \pm 4.4 12(3-15) | 11.2 \pm 4.3 13(3-15) | 0.001< <i>p</i> <0.005 |
| Predictive mortality rate | 48.69 \pm 20.5 48.2(8-85.2) | 69.08 \pm 21.6 73.6(13.1-97.8) | 60.93 \pm 23.3 65.7(8-97.8) | <0.001 |
| Duration of stay in the mechanical ventilation (hrs) | 69.26 \pm 60.2 54(8-215) | 122 \pm 140.1 72(8-620) | 108.65 \pm 126.5 63(8-620) | <0.05 |
| Blood urea nitrogen | 27.2 \pm 22.5 20(1-117) | 47.5 \pm 37.2 36.5(3-194) | 39.41 \pm 33.6 28(1-194) | 0.001< <i>p</i> <0.05 |
| Creatinine | 1.62 \pm 1.7 0.97(0.1-7.6) | 1.76 \pm 1.46 1.34(0.3-9.3) | 1.7 \pm 1.5 1(0.1-9.3) | >0.05 |
| Sodium | 134.8 \pm 5.31 135(119-147) | 136.9 \pm 7.64 136(124-159) | 136 \pm 6.85 136(119-159) | >0.05 |
| Potassium | 3.82 \pm 0.67 3.7(2.7-5.4) | 4.2 \pm 1.06 4.2(2.4-8.2) | 4.1 \pm 0.95 4(2.4-8.2) | <0.05 |
| Magnesium | 1.79 \pm 0.43 1.7(0.7-2.9) | 2.04 \pm 0.61 1.8(1.2-4.2) | 1.94 \pm 0.57 1.8(0.7-4.2) | <0.05 |
| Ionized calcium | 1.12 \pm 0.25 1.14(0.5-2.1) | 1.07 \pm 0.22 1.07(0.7-1.9) | 1.09 \pm 0.23 1.1(0.5-2.1) | >0.05 |
| Phosphorus | 4.01 \pm 2.1 3.65(1.5-11) | 4.91 \pm 2.67 4.35(1.1-11.3) | 4.55 \pm 2.5 3.7(1.1-11.3) | >0.05 |
| Uric acid | 5.35 \pm 2.55 6(1-11) | 6.57 \pm 4.02 5.25(1.3-21) | 6.08 \pm 3.54 5.7(1-21) | >0.05 |
| Procalcitonin | 14.1 \pm 31.5 0.8(0.1-100) | 17.5 \pm 31.5 1.69(0-100) | 16.2 \pm 31.4 1.44(0-100) | >0.05 |
| C-reactive protein | 15.4 \pm 13.3 10.7(0.1-47.9) | 19.2 \pm 12.5 18.4(0.5-46) | 17.5 \pm 12.9 14.2(0.1-47.9) | >0.05 |
| Beta 2 microglobulin | 7.24 \pm 8.69 3.47(0.6-41.8) | 8.3 \pm 6.55 6.17(1.1-36.5) | 7.8 \pm 7.4 5.32(0.6-41.8) | <0.05 |
| White blood count | 10.6 \pm 8.8 9.5(0.7-49) | 12.8 \pm 11.2 11.5(0.1-42.6) | 11.9 \pm 10.3 10.4(0.1-49) | >0.05 |
| Hemoglobin | 9.1 \pm 2.7 9.3(2-17.4) | 9.4 \pm 1.7 9.3(5.9-15) | 9.3 \pm 2.2 9.3(2-17.4) | >0.05 |
| Hematocrit | 28.5 \pm 8.7 27.6(8.8-55.2) | 29.3 \pm 5.5 29.8(18.2-46) | 28.8 \pm 7.04 28.5(8.8-55.2) | >0.05 |
| Platelet | 169.1 \pm 12.05 151(16-513) | 158.6 \pm 152.8 113(3.2-759) | 162.8 \pm 140.2 126(3.2-759) | >0.05 |
| Total protein | 5.1 \pm 0.97 5.1(3-9) | 4.9 \pm 0.91 4.8(2-7) | 5.0 \pm 0.94 4.9(2-9) | >0.05 |
| Albumin | 2.1 \pm 0.4 2.2(1-3) | 2.1 \pm 0.5 2.1(1-3) | 2.1 \pm 0.47 2.1(1-3) | >0.05 |

*APACHE: Acute Physiology And Chronic Health Evaluation; †SOFA: The Sequential Organ Failure Assessment ; ‡GCS: Glasgow Coma Scale

When the APACHE II, SOFA I, SOFA III, GCS and PMR scores and the duration of stay in the mechanical ventilator and the length of stay in the

ICU of the Group 1 and Group 2 patients were examined, APACHE II, SOFA I, SOFA III, PMR scores and the duration of stay in the mechanical

ventilator were found to be lower in Group 1 patients ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$ and $p > 0.05$, respectively). GCS was found to be lower in Group 2 patients ($0.001 < p < 0.005$). When the levels of BUN, creatinine, uric acid, sodium, potassium, magnesium, phosphorus, ionized calcium, beta 2 microglobulin, procalcitonin, c-reactive protein (CRP), white blood cell, hemoglobin, hematocrit, platelet count, total protein, albumin were examined, there was no statistically significant difference between two groups

except BUN, magnesium and potassium levels ($0.01 < p < 0.05$, $p < 0.05$, $p < 0.05$, respectively). Scoring systems and laboratory parameters were given in Table 2.

When the highest lactate levels were compared on the day of admission to ICU, day 1, day 2, and day 3, it was observed that the lactate levels were higher in Group 2 patients than Group 1 patients ($p < 0.001$). Lactate levels of both groups were given in Table 3.

Table 3. Patients' lactate levels and venous blood pressure values at admission.

| Variables | Mean \pm Standard deviation Median (min-max) | | |
|---------------------------------------|---|---------------------------------|----------------------------------|
| | Group 1 (n:40) | Group 2 (n:60) | All patients (n:100) |
| Lactate (mg/dL) | | | |
| Lactate value at admission* | 2.5 \pm 1.5 2.15(0.3-6) | 5.9 \pm 5.21 3.3(0.3-20) | 4.5 \pm 4.46 2.8(0.3-20) |
| Lactate value on day 1* | 2.3 \pm 1.6 2(0.4-9.1) | 6.1 \pm 5.5 4.4(0.6-28) | 4.6 \pm 4.81 2.6(0.4-28) |
| Lactate value on day 2 * | 1.8 \pm 1.3 1.7(0.2-7.3) | 6.3 \pm 5.08 4.65(0.2-26) | 4.4 \pm 4.53 2.8(0.2-26) |
| Lactate value on day 3* | 1.8 \pm 1.22 1.45(0.5-5.7) | 5.6 \pm 3.22 4.6(1.4-14.5) | 3.9 \pm 3.1 3.1(0.5-14.5) |
| Highest lactate value * | 3.1 \pm 1.86 2.7(0.4-9.1) | 9.6 \pm 5.17 8.55(1.8-28) | 7.04 \pm 5.2 6(0.4-28) |
| Blood pressure (mmHg) | | | |
| Systolic blood pressure at admission | 99.57 \pm 23.55 97.5(42-161) | 91.28 \pm 24.26 91(49-178) | 94.6 \pm 24.2 93(42-178) |
| Diastolic blood pressure at admission | 60.88 \pm 15.28 60.5(37-98) | 51.72 \pm 17.27 47(18-98) | 55.38 \pm 17.03 54.5(18-98) |

* $p < 0.001$

When the factors affecting mortality and ICU survival were examined, high APACHE II score was negatively correlated with ICU survival ($p: 0.004$) in multiple regression analysis, while no statistically significant correlation was found in total survival ($p > 0.05$). BUN level was found to be statistically negatively correlated with both ICU survival ($p < 0.05$) and mortality ($p < 0.05$) in multiple regression analysis. Blood magnesium levels were not found to be statistically significant in ICU mortality ($p > 0.05$) when multiple regression analysis was applied, but it was found to be significant when total mortality was evaluated ($p < 0.05$) and it was found to be twice as effective. According to the survival analysis results of the patients, the estimated average life expectancy was 4.9 ± 1.1 months; The 3-month survival probability was found to be 42.4%, the 6-month survival probability 26.5% and the 12-month survival probability was 10.6%.

While the median beta-2 microglobulin value of the patients in Group 1 was 3.47 (0.6-41.8) mg / L; The median beta-2 microglobulin value of the patients in Group 2 was 6.17 (1.1-36.5) mg / L ($p = 0.014$). Beta-2 microglobulin value of the patients in Group 2 was found to be statistically significantly higher. Therefore, the cut-off value for beta-2 microglobulin level was evaluated. As a result of the ROC analysis, if the beta-2 microglobulin level is ≥ 4.88 mg / L, 65% sensitivity, 60% specificity and 65% probability ($p = 0.014$) the patient is expected to die in the ICU. However, there was no statistically significant effect of beta2 value on the survival of patients who survived after discharged from the ICU.

DISCUSSION

Studies on intensive care follow-up of cancer cases have found different results according to the type of

cancer, the conditions under which they are followed, prospective or retrospective follow-up and the parameters used in follow-up. Siddiqui et al. stated in their study that the APACHE II score was moderately reliable in determining the mortality of 431 cancer patients followed in the ICU. Again, in this study, it was stated that the APACHE II scoring system did not have sufficient reliability in determining mortality in postoperative evaluation⁸. In our study, the APACHE II scores of the patients were statistically significant in detecting mortality in the ICU, however, it was found to be statistically insignificant in determining the mortality of patients transferred from intensive care to the inpatient clinic. Therefore, it was determined that the APACHE II scoring system could not be used in determining the survival of patients after discharge.

In the study conducted by Tseng et al., it was stated that it was sufficient to detect mortality in the six-month period after intensive care hospitalization due to respiratory failure in patients with advanced lung cancer⁹. In our study, the increased SOFA scores of the patients, need for vasopressor support, renal support and mechanical ventilator support were found to be statistically significant with the mortality of the patients in the intensive care follow-up. However, in our study, it was found that the SOFA score was insufficient to detect mortality after discharge. The reason for this may be that only patients who were admitted to intensive care due to respiratory failure were included in the study conducted by Tseng et al.

In a prospective study by Panay et al., lactate levels were found to be insufficient in determining the 30-day mortality of 3589 cancer patients admitted to ICU¹⁰. In our study, a statistically significant difference was found between the lactate levels measured in the intensive care follow-up of the patients, and the lactate levels of the patients who deceased were found to be higher than the patients transferred to the inpatient clinic. In our study, similar to the study by Panay et al., lactate levels were found to be insufficient in determining long-term mortality.

In the United States, annually 125,000 elderly patients need mechanical ventilation, and half of this patient group was re-hospitalized after discharge and 30% to 65% were deceased within 6 months^{11,12}. Free beta 2 microglobulin is physiologically present in body fluids, because it is secreted intracellularly. Beta 2 microglobulin levels are also increased in patients

with hematological malignancies^{13,14}. The increase in plasma beta 2 microglobulin may reflect decline in various systems and may be responsible for the wretched phenotype among older adults⁵. In our study, a statistically significant difference was found between high beta 2 microglobulin levels in patients transferred to the inpatient clinic and patients who died in the intensive care follow-up. In our study, we found that beta 2 microglobulin values higher than 4.88 mg / L determined that the patient would die during intensive care follow-up with 65% sensitivity. Beta 2 microglobulin used to predict the wretched phenotype in elderly patients, can also be used to predict intensive care mortality in oncology patients hospitalized in the ICU.

In the study conducted by Limaye et al. In the ICU, it was found that patients with hypomagnazemia died at a higher rate and needed mechanical ventilator support for a longer time¹⁵. In our study, a statistically significant difference was found between the magnesium levels of the patients transferred to the inpatient clinic and the patients who deceased in the intensive care follow-up, and the magnesium levels of the patients who deceased in the intensive care follow-up were found to be higher than the patients transferred to the inpatient clinic. The reason for this may be that patients who die in intensive care follow-up have renal insufficiency at a level that requires renal support and decreased urinary magnesium excretion. In addition, considering the mortality, we found that magnesium levels outside the limits of 1.2-3.4 mg / dl had a two fold increased risk on the mortality of the patients.

In the study of Arihan et al., it has been shown that high BUN levels are associated with increased intensive care mortality¹⁶. Potentially, mortality appears to increase 7.88-fold in situations with low albumin levels and high BUN levels¹⁷. We also found in our study that high BUN levels during hospitalization in intensive care is associated with mortality.

Acinetobacter baumannii bacteremia was associated with a high mortality rate ranging from 29% to 46.9%¹⁸. Similarly, in our study, it was found that the presence of *Acinetobacter baumannii* infection in patients was associated with increased mortality in the intensive care follow-up of the patient. In addition, the fact that *Acinetobacter baumannii* presence being higher in the older ICU where patients were not able to stay in an isolated room showed that an isolated room opportunity should be provided to reduce the

mortality of oncology patients in intensive care. Sleep problems are more common in ICUs due to more noise than normal wards in hospitals. This appears as a problem in critical patients in intensive care¹⁹. Decreased plasma melatonin levels and disruption of circadian rhythm have been previously detected in adults on mechanical ventilation^{20,21}. Perras et al. showed a relationship between plasma melatonin level and day-night cycle²². In our study, a statistically significant difference was found between the ICUs where the patients were followed in terms of mortality. The reason for this may be the reduced risk of contamination with the isolated room facilities provided by the new ICU, as well as the reduction of continuous exposure to light by providing the day and night cycle to the patients and providing a quieter environment. The possibility to observe all monitors simultaneously in the new ICU, to provide day-night cycle, to have less auditory stimulus and to be able to intervene patients instantly thanks to the camera system may have caused a statistically significant difference between the two ICUs.

In this study, it has been shown for the first time that beta-2 microglobulin level can be used to predict intensive care mortality and improving the intensive care physical conditions reduces mortality.

Yazar Katkıları: Çalışma konsepti/Tasarımı: SP, AO, EK; Veri toplama: AO, MB; Veri analizi ve yorumlama: EK, MB, GŞ; Yazı taslağı: AO, MB, GŞ; İçeriğin eleştirel incelenmesi: GŞ, SP, EK; Son onay ve sorumluluk: AO, SP, EK, MB; Teknik ve malzeme desteği: EK, MB; Süpervizyon: SP; Fon sağlama (mevcut ise): yok.

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REFERENCES

1. Bouch DC, Thompson JP. Severity scoring systems in the critical ill. *Continuing Education in Anesthesia and Critical Care*. 2008;8:181-5.
2. Sakarya M. Yoğun bakımda skorlama sistemleri. *Anestezi Yoğun Bakım Ağrı* (Ed F Tüzüner):1209-1220. Ankara, Nobel Tıp, 2010.
3. Holmes CL, Gregoire G, Russell JA. Assessment of severity of illness. *Principals of Critical Care*. (Eds Hall JB, Schmidt GA, Wood LDH):63-78. New York, The McGraw- Hill Company, 2005.
4. Higgins TL. Severity of illness indices and outcome prediction. *Textbook of Critical Care*. (Eds Fink MP, Abraham E, Vincent JL, Kochanek PM):2195-2206. Philadelphia, Elsevier Saunders, 2005.
5. Cédric A, Régis B, Nicolas F, Delphine D, Bruno F, Olivier B. Plasma beta-2 microglobulin as a marker of frailty in older adults: a pilot study. *J Gerontol*. 2011;66:1077-9.
6. Bataille R, Grenier J, Sany J. Beta-2-microglobulin in myeloma: optimal use for staging, prognosis, and treatment. A prospective study of 160 patients. *Blood*. 1984;63:468-76.
7. Shinkai S, Chaves PH, Fujiwara Y, et al. Beta2-microglobulin for risk stratification of total mortality in the elderly population: comparison with cystatin C and C-reactive protein. *Arch Intern Med*. 2008;168:200-6.
8. Siddiqui SS, Narkhede AM, Kulkarni AP, et al. Evaluation and Validation of Four Scoring Systems: the APACHE IV, SAPS III, MPM0 II, and ICMM in critically ill cancer patients. *Indian J Crit Care Med*. 2020;24:263-9.
9. Tseng HY, Shen YC, Lin YS, Tu CY, Chen HY. Etiologies of delayed diagnosis and six-month outcome of patients with newly diagnosed advanced lung cancer with respiratory failure at initial presentation. *Thorac Cancer*. 2020;11:2672-80.
10. Panay S, Ruiz C, Abarca M, Nervi B, Salazar I, Caro P et al. Mortality of adult patients with cancer admitted to an ICU in Chile: A prospective cohort study. *J Glob Oncol*. 2018;4:1-9.
11. Lieberman D, Nachshon I, Miloslavsky O, Dvorkin V, Shimoni A, Lieberman D. How do older ventilated patients fare? A survival/functional analysis of 641 ventilations. *J Crit Care*. 2009;24:340-46.
12. Dardaine V, Dequin PF, Ripault H, Constans T, Giniès G. Outcome of older patients requiring ventilatory support in intensive care: impact of nutritional status. *J Am Geriatr Soc*. 2001;49:564-70.
13. Goodfellow PN. The Beta 2 microglobulin gene is on chromosome 15 and not in the HLA-A region. *Nature*. 1975;254-7.
14. Chiorazzi N, Rai KR, Ferrarini M. Chronic lymphocytic leukemia. *N Engl J Med*. 2005;352:804-8.

15. Limaye CS, Londhey VA, Nadkart MY, Borges NE. Hypomagnesemia in critically ill medical patients. *J Assoc Physicians India*. 2011;59:19-22.
16. Arihan O, Wernly B, Lichtenauer M, et al. Blood Urea Nitrogen (BUN) is independently associated with mortality in critically ill patients admitted to ICU. *PLoS One*. 2018;13:1-10.
17. Pan SW, Kao HK, Yu WK. Synergistic impact of low serum albumin on ICU admission and high blood urea nitrogen during ICU stay on post-ICU mortality in critically ill elderly patients requiring mechanical ventilation. *Geriatr Gerontol Int*. 2013;13:107–15.
18. Park SY, Choo JW, Kwon SH. Risk factors for mortality in patients with acinetobacter baumannii bacteremia. *Infect Chemother*. 2013;45:325-30.
19. Al-Samsam RH, Cullen P. Sleep and adverse environmental factors in sedated mechanically ventilated pediatric intensive care patients. *Pediatr Crit Care Med*. 2005;5:562-67.
20. ShiloL, DaganY, SmorjikY, Weinberg U, Dolev S, Komptel B et al. Patients in the ICU suffer from severe lack of sleep associated with loss of normal melatonin secretion pattern. *Am J Med Sci*. 1999;317:278-81.
21. Mistraletti G, Sabbatini G, Taverna M, Figini MA, Umbrello M, Magni P et al. Pharmacokinetics of orally administered melatonin in critically ill patients. *J Pineal Res*. 2010;48:142-47.
22. Vaughan GM, Pelham RW, Pang SF, Loughlin LL, Wilson KM, Sandock KL et al. Nocturnal elevation of plasma melatonin and urinary 5-hydroxyindoleacetic acid in young men: attempts at modification by brief changes in environmental lighting and sleep and by autonomic drugs. *J Clin Endocrinol Metab*. 1976;42:752-64.