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# OUTCOME AND PROGNOSTIC FACTORS IN PATIENTS WITH HEMATOLOGICAL MALIGNANCY ADMITTED TO AN INTENSIVE CARE UNIT: A SINGLE-CENTER STUDY

# YOĞUN BAKIM ÜNİTESİNE KABUL EDILEN HEMATOLOJIK MALIGNITELI HASTALARIN SONUÇLARI VE PROGNOSTIK FAKTÖRLERI: TEK MERKEZLI ÇALIŞMA

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## ABSTRACT

**Objective:** This study aimed to determine if the prognostic factors associated with intensive care unit (ICU) outcomes in patients with hematological malignancy help determine the course of treatment.

**Materials and Method:** In this study, 107 adult patients with hematological malignancies, requiring ICU admission in 2014–2020 at Medipol University Hospital, were retrospectively screened. The collected data included: demographic characteristics, sepsis-related organ failure assessment (SOFA) score, and the use of noninvasive/invasive mechanical ventilation during the ICU stay. The prognostic factors of the patients that received blood transfusions and those that did not receive blood transfusions as part of their treatment were compared.

**Results:** Among the 107 patients with hematological malignancy that were admitted to the ICU, 67 (62.6%) were men. Of the patients admitted to the ICU, 39.3% had acute myeloid leukemia. The non-survivor rate was significantly higher in patients with a SOFA score>=2 (87.7%) and those that were intubated (98.7%) ($p<0.05$). The Acute Physiology and Chronic Health Evaluation (APACHE) score and creatinine levels were significantly higher in the non-survivor group ($p<0.05$). The pH values and base deficit values were significantly lower in the non-survivor group ($p<0.05$). The mean hemoglobin values on the first day of admittance to the ICU were 8.57±1.68 (4.9-13.6) and during the ICU stay average of 3 units were transfused. The C-reactive protein (CRP) levels and length of ICU stay (days) were significantly higher in the patients that received blood transfusions ($p<0.05$). The non-survivor rate (87.7%) was significantly higher in the patients with a SOFA score of ($p<0.05$).

**Conclusion:** If the prognostic factors of ICU outcomes in patients with a hematological disease are known, they can be used to help determine if mechanical ventilation, renal replacement, or blood transfusions are appropriate for patients with multiorgan failure. This multidisciplinary approach helps provide optimal treatment.

**Keywords:** Hematology malignancy, Intensive care unit, Transfusion

## ÖZ

**Amaç:** Bu çalışmada, tedavileri esnasında yoğun bakım ünitesine (YBÜ) yatırılması gereken hematolojik maligniteli hastalarla ilgili prognostik faktörlerin, tedavi sürecini belirlemeye yardımcı olup olmadığını belirlemeyi amaçladık.

**Gereç ve Yöntem:** Bu çalışmada, Medipol Üniversite Hastanesi'nde 2014-2020 yılları arasında YBÜ'ye yatırılması gereken hematolojik maligniteli 107 erişkin hasta retrospektif olarak tarandı. Toplanan veriler şunları içeriyordu: demografik özellikler, hematolojik malignite türü, sepsisle ilişkili organ yetmezliği değerlendirme (SOFA) skoru ve YBÜ'de kalış sırasında noninvaziv/invaziv mekanik ventilasyon kullanımı. Kan transfüzyonu alan ve tedavisinin bir parçası olarak kan transfüzyonu almayan hastaların prognostik faktörleri ve sonuçları karşılaştırıldı.

**Bulgular:** Yoğun bakım ünitesine başvuran 107 hematolojik maligniteli hastanın 67'si (%62.6) erkekti. Yoğun bakım ünitesine kabul edilen hastaların %39.3'ünde akut miyeloid lösemi ve %60.7' sinde solunum yetmezliği vardı. SOFA skoru>=2 olanlarda (% 87.7) ve entübe edilenlerde (%98.7) hayatta kalmayan oranı anlamlı olarak yüksekti ($p<0.05$). Hayatta kalmayan grupta Acute Physiology and Chronic Health Evaluation (APACHE) skoru ve kreatinin düzeyleri anlamlı olarak yüksekti ($p<0.05$). Hayatta kalmayan grupta pH değerleri ve baz açığı değerleri anlamlı olarak düşüktü ($p<0.05$). YBÜ' ye kabulün ilk gününde ortalama hemoglobin değerleri 8.57±1.68 (4.9-13.6) idi ve YBÜ'de kalış süresi boyunca ortalama 3 ünite transfüze edildi. Kan transfüzyonu yapılan hastalarda C-reaktif protein (CRP) düzeyleri ve YBÜ' de kalış süresi (gün) anlamlı olarak yüksekti ($p<0.05$). SOFA skoru ($p<0.05$) olan hastalarda hayatta kalmayan oranı (%87.7) anlamlı olarak daha yüksekti.

**Sonuç**: Hematolojik hastalığı olan hastalarda mekanik ventilasyon uygulanması, renal replasman tedavisi veya kan transfüzyonlarının yoğun bakım yatış sürecini arttığı ve mortalite için risk faktörü olduğu unutulmamalıdır. Bu hastalara uygulanacak multidisipliner yaklaşım, optimum tedavinin sağlanmasına yardımcı olur.

**Anahtar Kelimeler:** Hematolojik malignite, Yoğun bakım ünitesi, Transfüzyon

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## INTRODUCTION

Sepsis and septic shock are inflammatory responses to infection; thus, treatment of septic patients aims to remedy the infection and provide organ support [1]. The increase in treatment options and an increase in life expectancy have led studies to focus on prognostic factors, outcomes, and management strategies [2]. Patients with hematological malignancy have a risk of high risk of multiorgan failure and mortality due to chemotherapy, bone marrow involvement, and chronic anemia [3]. Management of sepsis consists of delivering oxygen to the tissue to avoid hypoxia and multiorgan dysfunction syndrome [1]. Early goal-directed therapy (EDGT) trails have emphasized the importance having a hematocrit value of 30% in patients with sepsis during the first hours of admission to an intensive unit care (ICU) [4]. Randomized trials have suggested a more restrictive strategy of transfusion in critically ill patients [5, 6]. According to the Surviving Sepsis Campaign guidelines, patients with a hemoglobin concentration <7g/dL should receive a blood transfusion, with a target concentration of 7-9g/dL [7]. In our study, we retrospectively evaluated the results of hematology patients hospitalized in the intensive care unit. We also compared the prognostic factors and outcomes of the patients that received transfusions to those that did not.

## MATERIAL AND METHODS

A total of 107 adult patients with hematological malignancies, who need to be admitted to an intensive unit care in period of 2014-2020 at Medipol University Hospital in Istanbul, Turkey, were screened, retrospectively. This study was conducted with the approval of the ethics committee at Medipol University. The collected data included the patients' demographic characteristics, type of hematological malignancy, sepsis-related organ failure assessment (SOFA) score, and the use of noninvasive/invasive mechanical ventilation during the ICU stay. Ordering a blood transfusion is an independent decision of the treating physician that is based on clinical considerations. We used leucocyte depleted blood as the clinical consideration in all the patients for blood transfusions.

### Statistical Analysis

The data obtained in this study were analyzed using the SPSS version 21 package program. The dependency between categorical variables using the chi-square dependency test. Comparisons between groups were analyzed using the Mann-Whitney U test. 0.05 was used as the level of significance and it was stated that there is a significant difference when $p<0.05$, and there is no significant difference if $p>0.05$.

## RESULTS

Of the 107 patients with hematological malignancy admitted to the ICU, 67 (62.6%) were men. The median (interquartile range) age was 56 (19-93). Of the 107 patients, 39.3% had acute myeloid leukemia, 25.2% had non-Hodgkin lymphoma, and 22.5% had acute lymphoblastic leukemia (Table 1). A total of 65 (60.7%) patients who had applied to the ICU due to respiratory failure, 18 (17%) for septic shock, 13 (12.1%) for severe sepsis, 6 (5.6%) for cardiac arrest, 3 (2.8%) for hemorrhagic shock, 1 (0.9%) for intracerebral hemorrhage, and 1(0.9%) for generalized convulsive seizure (Table 1). The ICU hemoglobin levels of the patients on the first day of admission to the ICU are presented in Table 2. Twenty-nine patients (27.1%) were extubated and 78 (72.9%) required endotracheal intubation. Only 2 (6.9%) of the extubated patients died, but 77 (98.7%) of the intubated patients died ($p=0.0001$). The duration of hospitalization in the ICU was 6.64±8.44 days. Twenty-eight (26.2%) patients were discharged from the ICU to the hematology service and 79 patients (73.8%) died. The non-survivor rate was higher in patients with a SOFA score>=2 (87.7%) and in patients that were intubated (98.7%) ($p<0.05$). On the first day in the ICU, the patients with a hemoglobin level <7 mg/dL had a higher non-survivor rate (56.3%) ($p<0.05$) than those with higher hemoglobin levels because they required more blood transfusions. The APACHE II score and creatinine levels were

**Table 1.** Hematological Malignancies of the Patients Admitted to the ICU

| **Pathology** | n | **%** |
|---|---|---|
| Acute myeloid leukemia | 43 | 40.2 |
| Non-Hodgkin lymphoma | 27 | 25.2 |
| Acute lymphoblastic leukemia | 24 | 22.5 |
| Myelodysplastic syndrome | 5 | 4.7 |
| Chronic lymphocytic leukemia | 4 | 3.7 |
| T-lymphoblastic lymphoma | 2 | 1.9 |
| Multiple myeloma | 1 | 0.9 |
| Burkitt lymphoma | 1 | 0.9 |
| **Conditions of the Patients Admitted to the ICU** | **n** | **%** |
| Acute respiratory failure | 65 | 60.7 |
| Septic shock | 18 | 17 |
| Sepsis | 13 | 12.1 |
| Cardiac arrest | 6 | 5.6 |
| Hemorrhagic shock | 3 | 2.8 |
| Cerebral hemorrhage | 1 | 0.9 |
| Generalized convulsive seizure | 1 | 0.9 |

significantly higher in with the patients in the non-survivor group ($p<0.05$). The pH values and base deficit values were significantly lower in the non-survivor group ($p<0.05$). No significant difference was found between the other variables ($p>0.05$). A comparison of the characteristics of the non-survivor and survivor patients are presented in Table 3. In this study, we compared the parameters between the non-transfused group and the blood transfused group during ICU hospitalization. The mean hemoglobin values on the first day of being admitted to the ICU were 8.57±1.68 (4.9-13.6) The C-reactive protein (CRP) values and length of stay in ICU (days) were significantly higher in the patients who received blood transfusions ($p<0.05$). No significant difference between the other variables was observed for the non-transfused and transfused patients (Table 4). Patients with a SOFA score of 2 had a significantly higher non-survivor rate (87.7%) ($p<0.05$), and no significant difference was found for blood transfusion replacement between the non-survivor and survivor patients ($p>0.05$), as seen in Table 5.

**Table 2.** Hemoglobin Levels on the First Day of Admission to the ICU

| **Hemoglobin levels** | **Status** | | | | | **p value** |
|---|---|---|---|---|---|---|
| | **Survivor** | | **Non-survivor** | | **Total** | |
| | **n** | **%** | **n** | **%** | **n** | |
| **<7** | 7 | 43.8 | 9 | 56.3 | 16 | 0,0001 |
| **7–9** | 11 | 22.0 | 39 | 78.0 | 50 | |
| **>9** | 10 | 24.4 | 31 | 75.6 | 41 | |
| **Total** | 28 | 26.2 | 79 | 73.8 | 107 | |

### Discussion

In recent years, the increase in the treatment modalities for hematology malignancies has increased the need for intensive care of patients, and these malignancies have one of the poorest prognoses and highest mortality rates. Knowing unfavorable prognostic factors helps physicians predict the course of treatment and enables them to provide more supportive care [8]. Our study included 107 patients admitted to the ICU over a six-year period. We did not find a significant association between age, gender, procalcitonin, albumin, and lenght of stay in the ICU. Medic et al. [9] reported a 53% mortality rate and the average

APACHE II score in their patients on the first day was 25.9. In our study, the overall mortality was 73.8% and the APACHE II score was 22.2±10.68. Medic et al. [9] included patients with allogeneic transplantation in their study; thus, most of their patients were in remission. In contrast, in our study, the patients that were admitted to the ICU were newly diagnosed or relapsed patients, so this can explain the higher rate of ICU admission. In both studies, the APACHE II score on the day of admission was significantly associated with ICU mortality. Ferra et al. [10] reported that 80% of the patients in their study required orotracheal intubation; in our study, 72.9% of the patients required endotracheal intubation, and we found that the prognosis for patients undergoing noninvasive mechanical ventilation was better.

**Table 3.** Comparison of the Characteristics of the Non-survivor and Survivor Patients

| Variables | Non-survivor (n=79) Mean (Min-Max) | Survivor (n=28) Mean (Min-Max) | P value |
|---|---|---|---|
| **Day (in ICU)** | 7.31±9.64 (0.2-62) | 4.75±2.53 (0.4-10) | 0.806 |
| **Base deficit** | -3.64±7,67 (-22.4-14.7) | -0.1±5.28 (-7.7-10.4) | 0.035 |
| **Lactate** | 4.6±4.9 (0-24) | 2.6±1.3 (0.7-7) | 0.139 |
| **$PaO_2$** | 140.4±139.4 (32-295) | 107±48.1 (43-272) | 0.769 |
| **pH** | 7.334±0.15 (6.658-7.57) | 7.409±0.061 (7.29-7.525) | 0.013 |
| **Creatinine** | 1.43±0.85 (0.3-3.85) | 1.16±1.18 (0.26-6.82) | 0.032 |
| **GFR** | 82.3±71.6 (16-350) | 94.3±63.2 (9-316) | 0.052 |
| **Procalcitonin** | 25.55±60.33 (0.88-382) | 20.03±44.35 (0.028-222) | 0.384 |
| **CRP** | 202.4±161.9 (4.55-582.9) | 190.5±161.4 (5.53-524.3) | 0.747 |
| **Albumin** | 2.789±0.612 (0.36-4.05) | 16.07±68.84 (2.21-3.67) | 0.041 |
| **APACHE II score** | 35.25±20.41 (7.62-96.08) | 22.2±10.68 (11-56.9) | 0.0001 |
| **Age** | 58.7±18.2 (22-93) | 54.5±20.6 (19-91) | 0.989 |
| **Hematocrit %** | 25.4±5 (14.9-40.3) | 24.8±6.1 (16.9-38.3) | 0.419 |

Staudinger et al. [11]. reported an overall ICU mortality of 47% in their study; it was 73.8% in our study. Moreover, they included data on post-surgery solid cancer and those patients had a better prognosis than patients with a hematological malignancy [11]. Maqsood et al. [12] reported a 55.9% mortality rate, and acute respiratory failure was the main reason for admission to the ICU. In our study, respiratory failure was also the main reason for ICU admission (60.7%). Demandt et al. [13] emphasized that disease characteristics were not associated with ICU mortality; they reported that the APACHE II score and SOFA score were both associated with poor prognosis. Their study included stem cell transplantation patients. In our study, our patients were newly diagnosed or relapsed but also their APACHE II scores and SOFA scores on the first day of ICU admission were significantly higher than the respective scores of the non-survivor patients. In their cohort study, Yeo et al. [14] found that invasive ventilation and the APACHE II score, inotropic agents, and acute myeloid leukemia were associated with poor prognosis. They explained this by noting that intensive chemotherapy treatment results in a poor acute myeloid leukemia prognosis. They also reported that the prognosis for acute respiratory failure was poor, so they highlighted the importance of respiratory

**Table 4.** Comparison of the Parameters for the Transfused and Non-transfused Patients during the ICU Stay

| Variables | Transfused (n=82) Mean (Min-Max) | Non-transfused (n=25) Mean (Min-Max) | P value |
|---|---|---|---|
| **Day (in ICU)** | 7.81± 9.23 (0.4-62) | 2.79± 2.68 (0.2-8) | 0.0001 |
| **Base deficit** | -2.42±6.90 (-21.23-14.7) | -3.84± 8.64 (-22.4-10.6) | 0.579 |
| **Lactate** | 3.8± 3.8 (0-23) | 5.0± 6.0 (0.7-4) | 0.472 |
| **$PO_2$** | 117.1±85.67 (32.2-295) | 188.1± 209.3 (63-272) | 0.066 |
| **pH** | 7.359±0.133 (6.658-7.537) | 7.332±0.152 (6.901-7.571) | 0.446 |
| **Creatinine** | 1.38±0.96 (0.26-6.82) | 1.31±0.92 (0.3-3.84) | 0.609 |
| **GFR** | 81.6±64.2 (9-316) | 97.9±84.6 (16-350) | 0.437 |
| **Procalcitonin** | 21.9±43.933 (0.88-246.84) | 21.9±43.93 (0.028-382) | 0.231 |
| **CRP** | 214.06±157.32 (7.97-582.9) | 147.59±166.84 (4.55-571.5) | 0.017 |
| **Albumin** | 2.90±0.521 (1.78- 4.40) | 19.28±77.72 (0.368-3.67) | 0.784 |

treatment in hematological patients. They also reported that the differences in pH between survivors and non-survivors were significant. However, differences in the $CO_2$ and $HCO_3$ levels were not significant between the two groups. They suggested the need to study the acid-base balance in these patients. They suggested that the APACHE II score was a good independent factor for predicting mortality in an ICU. In our study, in the acute myeloid leukemia (40.2%) patients that were transferred to the ICU, the pH and base deficit values were significantly lower in the non-survivor group (7.334±0.15 and -3.64±7.67, respectively) than the survivor group (7.409±0.061 and -0.1±5.28, respectively). There was no significant difference in $PO_2$ between the two groups. In patients with a hematology malignancy, anemia has a multifactorial etiology, including chemotherapy, bone marrow infiltrated with the disease, and

**Table 5.** SOFA Scores for the Survivor and Non-Survivor Groups

| SOFA Score | Survivor | | Non-survivor | | Total | | Analysis | |
|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | Chi-square | P value |
| **<2** | 18 | 69.2 | 8 | 30.8 | 26 | 100.0 | | |
| **≥2** | 10 | 12.3 | 71 | 87.7 | 81 | 100.0 | 30.1 | 0.0001 |
| **Total** | 28 | 26.2 | 79 | 73.8 | 107 | 100.0 | | |

a decrease in the production of erythropoietin due to inflammatory cytokines, such as interleukin-6 (IL-6), interferon-gamma, and IL-1 [15]. In our study, the transfusion group had significantly higher CRP values (p=0.017). In our hospital, physicians decide on whether to prescribe a blood transfusion based on the Surviving Sepsis Campaign guidelines (2012). Blood transfusion target values of hemoglobin are 7-9 g/dL [7]. Hebert et al. [16] reported that blood transfusion was effective in helping to maintain a hemoglobin level >7 g/dL as the hemoglobin levels in critically ill patients are usually >10g/dL. Furthermore, two studies reported that blood transfusion was associated with improved survival in patients with septic shock [17, 18]. In our study, we compared the transfused group and the non-transfused group and found that the duration of hospitalization was significantly less in the non-transfused group (p=0.0001). Oxygen delivery to tissues is important for maintaining cellular function, and a blood transfusion increases the oxygen delivery to tissues. In sepsis and septic shock, microcirculatory dysfunction causes less oxygenation in tissues. [20]. As in our study, the non-transfused patients had a high level of hemoglobin; thus, they had a higher level of oxygenation. Similar to these studies, our study emphasized that hematological malignancies are too risky for admission to the ICU and patients with those conditions have a high mortality risk. Understanding the predictor factors of ICU outcomes in patients with a hematological disease enables intensivists to determine the appropriate treatment options, including mechanical ventilation, renal replacement, or blood transfusion for patients with multiorgan failure.

In conclusion it is very important that hematologists and intensivists work together to follow these patients. This multidisciplinary approach helps provide optimal treatment. This study had some limitations.

The main limitation is that it was a single-center study that reviewed data retrospectively, which limits the ability to generalize the findings to other patient populations. Moreover, we focused on laboratory data from the hospital's medical records archives.

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