



## Factors Affecting Mortality in Hematology Patients Accepted to the Intensive Care Unit

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### ABSTRACT

**Objective:** Patients with hematologic diseases can have increased life expectancy with newly developed chemotherapeutic agents, hematopoietic stem-cell transplantation, and further supportive therapy. However, intensive therapies lead to more life-threatening complications that require intensive care unit (ICU) admission. Therefore, understanding the factors affecting mortality is important when accepting these patients to the ICU. This study was conducted to explore the factors affecting the mortality of patients admitted to medical ICUs with a diagnosis of hematologic disease.

**Materials and Methods:** The medical records of patients with diagnoses of hematologic diseases hospitalized in the medical ICU between March 2013 and March 2019 were retrospectively reviewed. Age, gender, subgroup of hematologic disease, APACHE II scores, admission diagnoses, mechanical ventilation requirement, renal replacement therapy, vasopressor therapy, and ICU and hospital outcomes were recorded. The factors affecting mortality were evaluated.

**Results:** Patients with acute leukemia [29 (30%)], multiple myeloma [20 (21%)], lymphoma [22 (23%)], chronic leukemia [8 (9%)], and other hematologic diseases [15 (16%)] were identified and included during the 6-year study period. The median age of patients was 60 (27.5) years, and 50 (53%) patients were women. Bone marrow transplantation was performed in 20% of patients, and 75 (79%) patients required invasive mechanical ventilation. Vasopressor treatment was required in 49 (52%) of patients. The mortality rate was 55%. APACHE II scores were higher in nonsurvivors. Moreover, they required more mechanical ventilation, vasopressor treatment, and renal replacement therapy. According to regression analysis, high APACHE II scores, vasopressor therapy requirement, and presence of respiratory failure were the risk factors for mortality.

**Conclusion:** High APACHE II scores, need for vasopressor therapy, and respiratory failure were identified as independent risk factors for mortality in patients with hematologic diseases admitted to the medical ICU.

**Keywords:** ICU; hematology; respiratory failure

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### INTRODUCTION

Cancer is a leading cause of death, and hematologic malignancies account for 20% of all cancer diagnoses (1, 2). Survival rates have increased due to recently developing pharmacologic treatments and increased autologous or allogeneic bone marrow transplantation rates (3). However, there is also an increase in the rate of complications due to the use of intensive treatments. Deeper neutropenia is associated with more critical conditions, especially more severe infections (4). Despite supportive therapies, mortality is higher in patients with hematologic diseases than in those with other critical illnesses (5).

Due to these advances in treatment strategies, patients with hematologic disease are more frequently encountered in the intensive care unit (ICU). The most common ICU admission diagnoses include acute organ failure, especially respiratory failure, and neutropenia and related infections. Although the mortality of patients with hematologic diseases followed up in ICUs has decreased over the years (3), it is not known whether the risk factors for mortality in this process also vary.

This study was conducted to determine mortality rates in patients with hematologic diseases admitted to the ICU and to explore the risk factors for mortality.

### MATERIALS and METHODS

This study was conducted in a tertiary medical ICU of a university hospital. Data were collected by reviewing the prospective database retrospectively. Ethical approval was received from the local ethics committee before conducting the study. The data of patients admitted to the ICU between March 2013 and March 2019 were examined. Those diagnosed with hematologic diseases, aged >18 years, and with a hospitalization period of >24 h in the ICU were included in this study.

**Table 1.** General characteristics of patients

	Nonsurvivors (n=52)		Survivors (n=42)		Total (n=94)		p
	n	%	n	%	n	%	
Age (median, IQR)	54.73±2.56		58.78±3.16		56.54±2.00		0.27
Female (%)	24	46	26	61	50	53	0.12
Apache II (median, IQR)	29.5 (13.5)		20.5 (10)		25 (13.25)		<0.01
Diagnosis							0.60
Acute leukemia	19	36	10	24	29	30	
Multiple myeloma	11	21	9	21	20	21	
Lymphoma	12	23	10	23	22	23	
Chronic leukemia	3	5	5	11	8	9	
Others	7	13	8	19	15	16	
Admission diagnosis							
Sepsis	33	63	20	47	53	56	0.12
Respiratory failure	44	85	25	60	69	73	<0.01
Infection	28	54	26	57	54	57	0.43
Hemorrhage	1	2	3	7	4	4	0.21
Cardiac failure	2	4	3	7	5	5	0.47
Bone marrow transplantation	13	25	6	14	19	20	0.19
Mechanical ventilation							<0.01
Invasive	51	98	24	57	75	79	
Noninvasive	1	2	6	14	7	7	
Vasopressor therapy	38	73	11	26	49	52	<0.01
Renal replacement therapy	22	42	8	19	30	31	0.01
Length of ICU stay (median, IQR)	12.5 (22)		10 (17)		10 (18.75)		0.91

IQR: Interquartile range; ICU: Intensive care unit

The following data were recorded: age, gender, hematologic disease subtypes, bone marrow transplantation status, APACHE II scores calculated within the first 24 h in the ICU, admission diagnoses, mechanical ventilation support, vasopressor requirement, need for renal replacement therapy, length of ICU stay, and ICU and hospital outcomes.

The patients were divided into two groups as survivors and nonsurvivors. These groups were examined in terms of the factors affecting mortality, with an aim to determine the possible risk factors.

### Statistical Analysis

The research data were evaluated using “SPSS (Statistical Package for Social Sciences) 25.0 (SPSS Inc, Chicago, IL).” Descriptive variables were expressed as mean±standard deviation, median [interquartile range (IQR)], frequency distribution, and percentage. Categorical variables were evaluated using Pearson’s chi-square test and Fisher’s exact test. The suitability of variables to normal distribution was evaluated using histogram, probability plots, and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk test). For variables that did not conform to normal distribution, the Mann–Whitney U test was used in between two independent groups as a statistical method. For variables that conformed to normal dis-

tribution, the independent samples t-test was used between two independent groups.

The possible risk factors identified in the univariate analyses were further entered into logistic regression analysis for determining the independent predictors of patient outcome.

### RESULTS

During the study period, 969 patients were admitted to the ICU, of whom 94 (9.7%) patients with hematologic diseases were included in this study. Of these 94 patients, 29 (30%) with acute leukemia, 20 (21%) with multiple myeloma, 22 (23%) with lymphoma, 8 (9%) with chronic leukemia, and 15 (16%) patients with other hematologic diseases were admitted to the ICU. Of the 94 included patients, 19 (20%) underwent allogeneic or autologous bone marrow transplantation. Table 1 shows the general characteristics of the patients. The median age of the patients was 60 (27.5) years, and 50 (53%) were women. The most common diagnoses for ICU admission were respiratory failure (73%) and infection (57%). The median APACHE II score was 25, and the median length of ICU stay was 10 days.

A total of 82 (87%) patients needed mechanical ventilation support, of whom 75 (79%) underwent invasive and 7 (7%) under-

**Table 2.** Effects of risk factors on ICU survival

Risk factor	RR (95% CI)*	p**
Respiratory failure	4.82 (1.23–18.82)	0.02
Invasive mechanical ventilation	2.52 (0.51–12.26)	0.25
Noninvasive mechanical ventilation	0.55 (0.03–8.70)	0.67
Vasopressor therapy	6.45 (2.07–20.12)	<0.01
Apache II score	1.11 (1.02–1.21)	<0.01

ICU: Intensive care unit; CI: Confidence interval; \*: Estimated relative risk represented by odds ratio; \*\*: p<0.05

went noninvasive mechanical ventilation. Vasopressor treatment was required in 49 (52%) patients. Renal replacement therapy was performed in 30 (31%) patients.

The study patients were divided into two groups according to their ICU outcome, 52 (55%) patients in the nonsurvivor group and 42 (45%) patients in the survivor group. There was no difference between the groups in terms of age and gender distribution. The median APACHE II scores were higher in the nonsurvivor group. No differences were detected in the subtypes of hematologic diseases between the two groups. The rates of bone marrow transplantation were similar.

Regarding admission diagnoses, respiratory failure was more common among nonsurvivors than survivors ( $p<0.01$ ). Other admission diagnoses were similar between the two groups. When the patients were evaluated for the rate of mechanical ventilation support, it was observed that the need for mechanical ventilation support was more frequent in nonsurvivors ( $p<0.01$ ).

Vasopressor treatment was used more frequently in nonsurvivors ( $p<0.01$ ). The need for RRT was also higher among nonsurvivors ( $p=0.01$ ).

The length of ICU stay was found to be similar between the two groups.

Logistic regression analysis was conducted to determine the effect of these differences on mortality in nonsurvivors, which revealed the presence of respiratory failure [RR: 4.82 (1.23–18.82),  $p=0.02$ ], vasopressor treatment [RR: 6.45 (2.07–20.12),  $p<0.01$ ], and high APACHE II scores [RR: 1.11 (1.02–1.21),  $p<0.01$ ] as risk factors for mortality (Table 2).

Regarding the hospital outcomes of the study patients, it was observed that 33 (35%) were discharged from the hospital.

## DISCUSSION

Among patients admitted to the ICU in the 6-year period, 94 patients with hematologic diseases were included in this investigation. The ICU mortality rate in this study was 55%. In a previous study conducted by Yau E et al. (6) in 1991, this rate was reported as 65%. However, a study conducted by Yeo et al. (7) in 2012 reported an ICU mortality rate as high as 84%. In another recently conducted study in our country, the mortality rate was found to be 70% (8). The mortality rate observed in the present study was similar to that of recently published studies (9). The different

mortality rates may be attributed to the differences in patient admission criteria.

The role of high APACHE II scores in determining ICU mortality has been demonstrated in several studies. Similarly, elevation of APACHE II scores was found to be a risk factor for ICU mortality in patients with hematologic diseases (RR: 1.11 (1.02–1.21),  $p<0.01$ ). The average APACHE II scores and mortality rates in the present study are similar to those reported by Medić et al. (9). In another study, Ćamendys-Silva SO et al. (10) reported a mortality rate of 47%. However, the mean APACHE II score of the patients included in this study was 17.5, and it can be clearly observed that the difference in mortality rate was due to the difference in disease severity. In the study conducted by Benoit et al. (11), although the mortality rates were lower, the ICU mortality rate was found to be 42%. The low mortality rates in this study were believed to be due to the status of the patients' hematologic diseases who were admitted to the ICU. All patients who were admitted to the ICU in the study of Benoit et al. (11) were in remission. In our study, patients with refractory disease were also accepted and followed up in the ICU.

This study covered a 6-year period, and the mortality rate reflects the total duration. It was evaluated in terms of changes in mortality rates over the years. Consequently, the mortality rate decreased from 75% in 2013 to 30% in 2017–2018. This difference may first be due to the early recognition of critically ill patients by hematology doctors and the early consultation and transfer to the ICU. Second, it was believed that the indication for ICU admission was based on more objective criteria. Moreover, the recently developed treatment opportunities are another important aspect. As mentioned in the large review by Azoulay E. et al. (4), the development of chemotherapeutic agents, more potent and targeted therapies and supportive therapies applied in the ICU, and advanced therapies have prolonged the life expectancy of patients with hematologic diseases admitted to the ICU.

Acute respiratory failure was the most common ICU admission diagnosis. The majority of these patients required invasive mechanical ventilation. Similarly, several studies have reported respiratory failure as the most common cause of ICU admission (2, 9–13). When the factors affecting the ICU outcome were evaluated, the mortality rate was found to be higher in patients with respiratory failure. This finding was also observed in studies wherein similar investigations were conducted (9, 13, 14). Cornish M et al. (15) reported that the need for invasive mechanical ventilation was a risk factor for mortality in critically ill patients diagnosed with hematologic disease. However, in our study, although the need for invasive mechanical ventilation support was high among nonsurvivors, it was not detected as a risk factor.

Multiple organ failure and severity of dysfunction are the other indicators of mortality in this patient group (2, 11). Vasopressor therapy requirement was reported as a risk factor for mortality in all the studies conducted in this patient group (11, 15, 16). Similarly, in our analyses, the need for vasopressor treatment was found to be a risk factor on mortality. The regression analysis revealed vasopressor treatment as a risk factor (RR: 6.45 (2.07–20.12),  $p<0.01$ ).

Age, sex, and subtype of hematologic disease were not determined as risk factors for mortality. Patients undergoing bone marrow

transplantation are known to have higher mortality rates. However, in our study, although the rate of bone marrow transplantation was higher among nonsurvivors, no difference was observed in the analysis. This result was believed to be due to the low number of ICU-admitted patients who underwent bone marrow transplantation.

### Conclusion

Advances in treatment modalities and early recognition of critical illnesses can increase the ICU life expectancy of patients with hematologic diseases. However, in this patient group, those with respiratory failure, requiring vasopressor treatment, and high APACHE II scores have higher mortality rates than others.

**Ethics Committee Approval:** The Ankara University Faculty of Medicine Clinical Research Ethics Committee granted approval for this study (date: 10.10.2019, number: 14-141-19).

**Informed Consent:** Informed consent was obtained from patients' first degree relatives.

**Peer-review:** Externally peer-reviewed.

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**Conflict of Interest:** The authors have no conflict of interest to declare.

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