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ORIGINAL RESEARCH INTENSIVE CARE

Evaluation of prognostic factors associated with intensive care unit mortality in patients with hematopoietic stem cell transplantation

Burcu Tunay[1], Sevil Sadri[2]

Author affiliations:

1. Department of Anesthesiology and Reanimation, Istanbul Medipol University School of Medicine, Goztepe, Metin Sk. No:4, 34214 Bagcilar/Istanbul, Turkey; E-mail: bhizarci@medipol.edu.tr
2. Department of Hematology, Istanbul Medipol University School of Medicine, Goztepe, Metin Sk. No:4, 34214 Bagcilar/Istanbul, Turkey; E-mail: sevilsadri@hotmail.com

Correspondence: Burcu Hizarci, MD, **E-mail:** bhizarci@medipol.edu.tr; **Phone:** +905327065196

Abstract

Background & objective: Although the outcome of patients admitted to ICUs have considerably improved in recent years, hematopoietic stem cell transplantation (HSCT) continues to be significantly associated with mortality.

We studied the prognostic factors associated with ICU mortality after HSCT. The Acute Physiological and Chronic Health Evaluation II (APACHE II) was used as a prognostic scoring system.

Methods: Within the scope of the research, the clinical and laboratory data of 52 patients who were admitted to the ICU after undergoing HSCT between 2013 and 2019 were analyzed retrospectively.

Results: Mortality risk was found to be 4.22 times higher in patients who received mechanical ventilation (MV) within the first 24 h (P = 0.047), 18.37 times higher in patients who received total parenteral nutrition (TPN) support (P = 0.007), and 158.17 times higher in recipients of vasopressor drug support compared to those who did not (P < 0.001). It was found that a one unit increase in GCS score decreased mortality risk by 0.58 fold (P = 0.015). Additionally, a one unit increase in heart rate was found to increase mortality risk by 1.03 fold (P = 0.010). Whereas, one unit increases in systolic blood pressure or diastolic blood pressure decreased the mortality risk by 0.91 and 0.92 fold, respectively (P = 0.001 and P = 0.002). Mortality was not associated with APACHE II or graft-versus-host disease.

Conclusion: Receiving MV, TPN or vasopressor treatment, and having lower GCS, higher heart rate, lower systolic and diastolic blood pressure were associated with an increase in the risk of ICU mortality in HSCT recipients admitted to the ICU.

Abbreviations: HSCT - hematopoietic stem cell transplantation; TPN - total parenteral nutrition; APACHE II - Acute Physiological and Chronic Health Evaluation II: GVHT - graft-versus-host disease; ICU - intensive care unit; GCS – Glasgow Coma Scale; MODS - Multiple organ dysfunction syndrome

Key words: Hematopoietic stem cell transplantation; Intensive care; Mortality; Mechanical ventilation, parenteral nutrition; MV- mechanical ventilation;

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1. Introduction

Hematopoietic stem cell transplantation (HSCT) using peripheral blood or bone marrow is the standard treatment method for both congenital and acquired hematological disorders.[1] An important limitation of HSCT is the increased risk of organ toxicity and transplant-related death in the first 100 days after transplantation.[2] In addition, secondary critical illnesses, such as graft-versus-host disease (GVHD) and overlapping infections, compromise the prognosis of

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these patients, often necessitating intensive care unit (ICU) admission.[1,3]

The most common indications for ICU admission among patients undergoing HSCT are respiratory failure and septic shock. Pulmonary infections can cause both respiratory failure and septic shock at the same time. However, non-infectious lung diseases such as widespread alveolar hemorrhage and acute respiratory distress syndrome (ARDS) can also lead to respiratory failure after HSCT. There are other frequently reported reasons for admission to ICU among HSCT recipients, including cardiac dysfunction, neurological disorders and gastrointestinal bleeding.[4]

Although the outcome of patients admitted to ICUs have considerably improved in the recent years, HSCT continues to be significantly associated with high mortality.[5,6] There are many variables associated with increased patient morbidity and mortality in patients admitted to the ICU. The most common of these is respiratory failure requiring mechanical ventilation (MV) and multiple organ dysfunction syndrome (MODS).[3] It has been reported that other predictors of survival in the ICU include hemodynamic imbalances, GVHD, hyperbilirubinemia, Acute Physiological and Chronic Health Evaluation II (APACHE II) score and transplantation type.[7]

Despite advances in the understanding of factors associated with ICU mortality in select patient groups, there is a great need to identify strong prognostic factors associated with mortality in the short term. Such indicators can guide ICU admission policy and therapeutic decisions. In this context, the aim of the study was to retrospectively examine clinical and laboratory findings associated with mortality in patients admitted to the ICU after undergoing HSCT.

APACHE II is a common scoring system used to determine ICU mortality risk in the adult age group. It was developed in 1981 by Knaus et al., and consists of three components: Acute Physiology Score, Age and Chronic Health Status.[8] The web application is used to calculate APACHE II scores.[9]

2. Methodology

This retrospective study was conducted in our Hospital between January 2013 and December 2019.

Ethics committee approval was received to conduct the study. The study was conducted in accordance with Good Clinical Practice Guidelines and the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

Within the scope of the study, patients aged 18 or older who had been transferred to the ICU during the treatment process after HSCT (auto + allo) between January 2013 and December 2019 were retrospectively analyzed. The study group was comprised of patients diagnosed with Acute Myeloid Leukemia (AML), Acute Lymphoblastic Leukemia (ALL), Myelodysplastic Syndrome (MDS), Non-Hodgkin Lymphoma (NHL) and Hodgkin Lymphoma (HL). At the ICU, there is a disciplined collaboration between hematologists and intensive care specialists that allows regular, almost-routine reassessment of patients' conditions. The decision to admit this group of patients to the ICU in our hospital is routinely made by both the attending hematologist and the on-duty intensive care specialist.

For patients admitted to the ICU more than once during their treatment, only the first occurrence was considered to be eligible for the study in order to maintain the independence of observations. Patients demographic data, the results of the treatments, laboratory results during ICU stay and various clinical characteristics were obtained and recorded from patients' medical files. These included: diagnoses, relapse (presence/absence, time until relapse), conditioning regimens; e.g., (myeloablative, TBI (traumatic brain injury), Thiotepa, BEAM [a combination of chemotherapy drugs that includes carmustine, etoposide, Ara-C (cytosine arabinoside) and melphalan], BeEAM ((bendamustine, etoposide, cytarabine, melphalan), RIC (resistance to inhibitors of cholinesterase), transplantation types, e.g., matched unrelated donor (MUD), HLA-matched (identical) sibling donor (MSD), haplogeneic, and autologous types. The time until ICU admission from HSCT treatment (days) was also noted. Patients' clinical features and treatment requirements in the ICU were recorded, and included the following: total parenteral nutrition (TPN), and respiratory support parameters including type of ventilation (NIV or MV), tracheostomy, duration, intubation and extubation times, transition/non-transition from NIV, and GVHD.

Diagnoses related to ICU admission were classified as sepsis, respiratory failure, cardiac arrest, postoperative indications, neurological symptoms and bleeding. We monitored and recorded arterial blood gas values (PaO_2, $PaCO_2$, pH, lactate, bicarbonate), creatinine, albumin,

procalcitonin, C-reactive protein (CRP), and neutrophil/platelet engraftment levels.

All physiological and clinical data at the time of admission to ICU were recorded. Body Mass Index (BMI) was calculated. Patient files that lacked any of the examined variables were excluded from the study group. The ICU mortality was defined as death due to any cause in the ICU before discharge. Patients were grouped for mortality outcome (survivors, non-survivors) and comparisons were performed between these groups.

Statistical analysis

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Table 1: Comparison of mortality rates according to the characteristics of the patients.

Variable	ICU-Nonsurvivor (n = 37)	ICU-Survivor (n = 15)	Total (n = 52)	p
Gender				
Male	25 (67.6)	8 (53.3)	33 (63.5)	0.334
Female	12 (32.4)	7 (46.7)	19 (36.5)	
Age	41 (18-70)	39 (18-56)	39.50 (18.00-70.00)	0.413
BMI (kg/m^2)	1.80 (1.41-2.35)	1.74 (1.45-2.40)	1.79 (1.41-2.40)	0.571
Diagnosis				
AML	12 (32.4)	3 (20.0)	15 (28.8)	0.319
ALL	11 (29.7)	9 (60.0)	20 (38.5)	
MDS	2 (5.4)	0 (0.0)	2 (3.8)	
HL	1 (2.7)	0 (0.0)	1 (1.9)	
NHL	11 (29.7)	3 (20.0)	14 (26.9)	
Relapse				
Present	10 (27.0)	3 (20.0)	13 (25.0)	0.596
Absent	27 (73.0)	12 (80.0)	39 (75.0)	
Preparation regimen				
Myeloablative	14 (37.8)	8 (53.3)	22 (42.3)	0.577
TBI	10 (27.0)	5 (33.3)	15 (28.8)	
Thiopeta	4 (10.8)	0 (0.0)	4 (7.7)	
BEAM	3 (8.1)	0 (0.0)	3 (5.8)	
BeEAM	4 (10.8)	1 (6.7)	5 (9.6)	
RIC	2 (5.4)	1 (6.7)	3 (5.8)	
Transplantation type				
MUD	8 (21.6)	0 (0.0)	8 (15.4)	**0.034**
MSD	14 (37.8)	11 (73.3)	25 (48.1)	
Haplo	2 (5.4)	2 (13.3)	4 (7.7)	
Autologous	13 (35.1)	2 (13.3)	15 (28.8)	
Relapse time (month)	12.0 (3.0-36.0)	16.0 (15.0-24.0)	15.0 (3.0-36.0)	0.287
Transition time to ICU (day)	19.0 (1.0-53.0)	13.0 (1.0-60.0)	17.0 (1.0-60.0)	0.206

**ICU:Intensive care unit, BMI:Body mass index, AML: Acute Myeloid Leukemia, ALL: Acute Lymphoblastic Leukemia, MDS: Myelodysplastic Syndrome, NHL: Non-Hodgkin Lymphoma, HL: Hodgkin Lymphoma, TBI: Total body irradiation, BEAM: Carmustine-Cytarabine-Etoposide-Melphalan, BeEAM: Bendamustine-EAM, RIC: Reduced-intensity conditioning, MUD: Matched unrelated donor, MSD: Matched sibling donor*

All analyses were performed on SPSS v15 (SPSS Inc., Chicago, IL, USA). Number, percentage, mean, standard deviation, median, minimum and maximum values were used in the evaluation of the descriptive data. The Shapiro-Wilk test was used to determine whether variables were normally distributed. Non-normally distributed variables were analyzed with the Mann–Whitney U test. Categorical variables were analyzed with Chi-squared tests. Univariate Logistic Regression Analysis was used to evaluate factors affecting mortality rate. Two-tailed P-values of less than 0.05 were considered statistically significant.

3. Results

The study group consisted of 52 patients, 33 (63.5%) males and 19 (36.5%) females. Mean age of the patients was 40.3 ± 14.5 y. The ICU mortality rate of the patients

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Table 2: Distribution of clinical parameters according to survival in ICU

Parameter	ICU-Nonsurvivor (n = 37)	ICU-Survivor (n = 15)	Total (n = 52)	p
Extubation	1 (2.7)	2 (13.3)	3 (5.8)	0.136
TPN	21 (56.8)	1 (6.7)	22 (42.3)	**0.001**
Vasopressor medication	34 (91.9)	1 (6.7)	35 (67.3)	**<0.001**
Duration of NIV (day)	2.0 (0.0-5.0)	5.0 (2.0-8.0)	3.0 (0.0-8.0)	0.001
Duration of MV (day)	2.5 (0.0-30.0)	2.5 (2.0-6.0)	2.5 (0.0-30.0)	0.778
Reasons for being accepted to the ICU				
Sepsis	16 (43.2)	6 (40.0)	22 (42.3)	0.830
Respiratory failure	21 (56.8)	11 (73.3)	32 (61.5)	0.266
Cardiac arrest	2 (5.4)	0 (0.0)	2 (3.8)	0.358
Postop causes	2 (5.4)	0 (0.0)	2 (3.0)	0.358
Neurological symptoms	6 (16.2)	1 (6.7)	7 (13.5)	0.361
Bleeding	0 (0.0)	1 (6.7)	1 (1.9)	0.113
GVHD	13 (35.1)	7 (46.7)	20 (38.5)	0.439
Noninvasive on the first day in ICU	18 (48.6)	10 (66.7)	28 (53.8)	0.238
Tracheostomy on the first day in ICU	1 (2.7)	0 (0.0)	1 (1.9)	0.520
Extubation on the first day in ICU	2 (5.4)	2 (13.3)	4 (7.7)	0.331
Extubation on the first day in ICU	2 (5.4)	2 (13.3)	4 (7.7)	0.331
MV on the first day in ICU	19 (51.4)	3 (20.0)	22 (42.3)	**0.038**
MV from NIV on the first day in ICU	15 (40.5)	0 (0.0)	15 (28.8)	**0.003**
APACHE II	27.0 (10.0-96.0)	19.0 (8.0-42.0)	26.0 (8.0-96.0)	0.072
GCS	4.0 (3.0-15.0)	15.0 (11.0-15.0)	10.0 (3.0-15.0)	**<0.001**
Heart rate	122 (48-180)	95 (55-160)	114 (48-180)	**0.003**
Systolic blood pressure	88 (40-130)	122 (100-143)	100 (40-143)	**<0.001**
Diastolic blood pressure	50 (10-99)	68 (55-85)	55.5 (10-99)	**<0.001**

NIV: Noninvasive mechanical ventilation, MV: Mechanical ventilation, GVHD: Graft versus host disease, APACHE II: Acute Physiological and Chronic Health Evaluation II, GCS: Glaskow Coma Scale

Table 3. Distribution of laboratory parameters according to survival in ICU

	ICU-Nonsurvivor (n = 37)	ICU-Survivor (n = 15)	Total (n = 52)	p
PaO2	80.0 (40.0-236.0)	65.0 (56.0-196.0)	79.5 (40.0-236.0)	0.179
PaCO2	40.4 (28.2-61.1)	41.7 (30.3-79.8)	40.9 (28.2-79.8)	0.437
pH	7.4 (6.9-7.8)	7.4 (7.1-7.5)	7.4 (6.9-7.8)	0.425
Creatinine	1.0 (0.3-3.8)	0.9 (0.4-1.6)	1.0 (0.3-3.8)	0.298
Lactate	3.0 (0.8-24.0)	2.7 (1.0-3.5)	2.9 (0.8-24.0)	0.172
Albumin	2.7 (1.4-4.0)	2.8 (2.1-3.9)	2.8 (1.4-4.0)	0.280
Bicarbonate	24.9 (17.0-36.5)	22.6 (19.1-25.2)	24.3 (17.0-36.5)	0.442
Procalcitonin	2.8 (0.1-224.7)	3.5 (0.1-61.7)	3.2 (0.1-224.7)	0.709
CRP	192.5 (7.8-483.5)	134.3 (10.0-524.3)	190.8 (8.0-524.3)	0.976
Neutrophil engraftment	15.0 (0.0-35.0)	17.0 (11.0-42.0)	15.0 (0.0-42.0)	0.159
Platelet engraftment	13.0 (0.0-42.0)	17.0 (11.0-42.0)	15.0 (0.0-42.0)	0.296

**CRP:C-reactive protein*

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was determined to be 71.2% (n = 37). The most common diseases in the study group were acute lymphoblastic leukemia (ALL) (38.5%) and acute myeloid leukemia (AML) (28.8%). While relapse was detected in 25% of the patients, the mean time until relapse was found to be 15.8 ± 9.0 months. Among the HSCT patients treated in the ICU, survivors and non-survivors were found to be comparable in terms of age, gender, BMI, diagnosis, presence of relapse, preparation regimen, time until relapse (months) and transition time to ICU after hospitalization (days). It was found that transplantation type was significantly different between the groups; the majority of non-survivors had undergone MSD transplant (37.8%) and autologous transplant (35.1%) (P = 0.034). This data is presented in Table 1.

The frequency of TPN and vasopressor use was significantly higher in the non-survivor group compared to the survivor group (P = 0.001 and P < 0.001). It was also found that MV application within the first 24 h of ICU stay was significantly more common among subjects who died (P = 0.038). Glasgow Coma Scale (GCS) score was significantly lower in non-surviving patients compared to survivors (P < 0.001). Finally, pulse rate was higher in non-survivors (P = 0.003), while systolic (P < 0.001) and diastolic blood pressures (P < 0.001) were significantly lower in non-surviving HSCT patients admitted to the ICU. There were no significant relationships between mortality and any of the other factors examined (Table 2).

Laboratory findings including PaO_2, $PaCO_2$, pH, creatinine, lactate, albumin, bicarbonate, procalcitonin, CRP, neutrophil engraftment and platelet engraftment levels of patients were comparable in survivors and non-survivors (Table 3).

Transplantation type (P = 0.999) and transition from NIV to MV in the first 24 h (0.998) had no effect on mortality in logistic regression analysis performed with variables found to be significant in the Chi-Square and Mann–Whitney U analyses. Significant variables were as follows: mortality risk was 4.22 times higher in those who used MV within the first 24 h compared to those who did not (P = 0.047), 18.37 times higher in patients who received TPN support compared to those who did not (P = 0.007), and 158.17 times higher in recipients of vasopressor support compared to non-recipients (p < 0.001). A one unit increase in GCS score was determined to decrease mortality risk by 0.58 fold (P = 0.015). Furthermore, in continuous variables, a one-unit increase in heart rate increased mortality risk 1.03 times (p = 0.010); whereas, one unit of increase in systolic and diastolic pressure decreased mortality risk by 0.91 and 0.92 fold respectively (P = 0.001 and P = 0.002) (Table 4).

Table 4: Univariate logistic regression analysis of factors affecting mortality

Parameter	Exp (B)	%95 Confidence Interval	p
Transplantation type	-	-	0.999
MV on the first day in ICU	4.22	1.02-17.47	**0.047**
MV from NIV on the first day in ICU	-	-	0.998
TPN	18.37	2.18-154.69	**0.007**
Vasopressor medication	158.17	15.17-1659.05	**<0.001**
GCS	0.58	0.38-0.90	**0.015**
Heart rate	1.03	1.01-1.06	**0.010**
Systolic blood pressure	0.91	0.86-0.96	**0.001**
Diastolic blood pressure	0.92	0.87-0.97	**0.002**

**MV: Mechanical ventilation, ICU: Intensive care unit, TPN: Total parenteral nutrition, NIV: Noninvasive mechanical ventilation, GCS: Glaskow Coma Scale*

4. Discussion

Patients who undergo HSCT are known to have high morbidity and mortality, especially in the presence of ICU requirement in the peri-transplant period.[10] Our data suggests relationships between a number of patient characteristics, including transplantation type, the use of TPN, vasopressor use and MV, GCS score, and vital signs such as heart rate and systolic/diastolic blood pressure. However, none of the laboratory parameters were found to be associated with mortality.

According to the results of various studies reported previously, ICU mortality in this group was 39–48.3%.[10-12] In a recent metanalysis aggregating the data of 2342 patients, ICU mortality rate after HSCT was reported as 51.7%.[13] However, in the present study, the mortality rate was found to be 71.2% – indicating a considerable adverse deviation from the literature. Most of the patients in our hospital were diagnosed and were treated with chemotherapy at an external center. Also, our data showed that the most common diagnosis was ALL (38.5%), followed by AML (28.8%). Other researchers have reported the main indication for HSCT was AML followed by ALL,[6] or as NHL, AML and ALL, in that order.[11] The increased mortality rate in our study may have been due to the time elapsed from HSCT to ICU admission. This time varies greatly according to circumstances and is reported to range from 12-156 days.[6] A transition period from transplantation to ICU of 30 days or less may be a factor to reduce the risk of

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mortality.[12] Michel et al., however, concluded that the duration of this period was not associated with mortality.[10] In the current study there was no difference between the two groups in terms of time until ICU admission. Access to an ICU, the presence and use of advanced treatment facilities and the disease characteristics of the patients will have significant effect on the mortality rates, as will the design of each research and their inclusion/exclusion criteria.

The most common ICU indications in this study were respiratory failure (61.5%) and sepsis (42.3%), which is in agreement to numerous earlier studies.[1,7,10]

Our data did not yield any statistically significant relationships between ICU indications and mortality. Townsend et al. and Orvain et al. examined patients with allogeneic transplants, and reported that admission to ICU due to respiratory failure and neurological reasons had no effect on mortality.[14,16] In contrast, Saillard et al. evaluated the results of 18 studies, and reported that the mortality was increased in cases where admission to the ICU was caused by acute respiratory failure.[13] We believe that it will be greatly beneficial to closely monitor patients after HSCT for respiratory risks through various methods, including clinical and laboratory characteristics, in order to swiftly recognize the need for ICU treatment.

As GVHD causes tissue damage and its treatment suppresses the immune system, it is likely that there exists a cause-effect relationship between GVHD and ICU mortality.[4] Acute GVHD is thought to negatively affect survival in HSCT recipients admitted to the intensive care unit.[12,16] In the study by Hayani et al., it was reported that the risk for ICU mortality increased in relation with the risks associated with immune complications such as GVHD.[2] Contrary to these results, no relationship was found between GVHD and ICU mortality in our study, because we included autologous patients in our study. There are other studies reporting similar results.[15,17] It is important to consider that the severity of GVHD cases may be different from study to study; thereby affecting final outcomes and statistical analyses.There was no significant relationship between laboratory parameters measured in the study and the survival. Since the number of beds is high in our ICU and the cooperation between the hematologist and intensive care specialist is very good, we can transfer our patients to ICU early so we did not determine a significant difference in our patients between laboratory measurement. A study reported higher lactate levels in non-surviving patients, while there were no differences in terms of other laboratory parameters.[10] In the present study, we found that mortality did not change according to NIV duration or use of MV on the first day in ICU; whereas, receiving TPN support, lower GCS, higher heart rate, lower systolic and diastolic blood pressure were associated with increased risk of ICU mortality. According to the results of various studies reported previously, it has been confirmed that the use of MV is one of the factors that is associated with increased risk of mortality.[3,10,12,13,14,18,19] However, Townsend et al. noted that MV duration had no effect on ICU mortality, as was observed in our study. Interestingly, although Van Vliet et al. found that prolonged MV increased mortality, but NIV had no effect on mortality.[17] In this study, it was found that the use of vasopressor drugs had a negative effect on mortality, in accordance with the results reported in the literature.[2,4,10,12,14,15,17,19,20] A study by Michel et al. it was reported that heart rate was significantly higher and mean arterial pressure was significantly lower in non-surviving patients, and it was consistent with our results.[10]

Scoring systems such as Acute Physiology and Chronic Health Assessment (APACHE) and Sequential Organ Failure Assessment (SOFA) are widely used in clinical practice.[4] Orvain et al. found that three different ICU

prognostic scores (SOFA, LODS and APACHE II) were effective in determining mortality.[15] Lamia et al. reported that the SOFA score on the first and third days, was useful in predicting mortality in patients admitted to the ICU after HSCT.[21] ICU prognostic scores (SOFA or APACHE II) have been reported to distinguish between survivors and non-survivors based on the results of other previously reported studies.[2,10,14,22] In the current study, the APACHE II score was comparable between survivors and non-survivors, as shown by many other studies.[11,14,17,20] When taken together, these findings further indicate the limited value of scoring systems in detecting the prognosis of patients with HSCT; therefore, patient care decisions should not be made solely on the basis of these scores.

In general, our results prove that transplantation characteristics (other than transplantation type), prognostic scores and laboratory parameters do not provide any benefit in predicting the survival. Nonetheless, use of MV, TPN, vasopressor medication, and the GCS scores, pulse rate, systolic and diastolic blood pressure were useful in the survival prediction. Close monitoring of these parameters in HSCT recipients admitted to the ICU may be helpful in identifying patients on high risk.

5. Limitations

The study was of retrospective type, so scoring of data and comorbidities was based on medical records, and it is possible that some data might not be complete. In addition, the possibility that patients who were in need of critical care but were not transferred to the ICU (due to a selection bias by the attending physician or patient / family approvals) may have affected our results.

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The small number of patients in the study group and the fact that it was carried out in a single center may have reduced the potential power of our study and could have limited the ability to detect differences.

Another limitation of the study is that mortality was evaluated only during the ICU process without long-term analysis.

Finally, the outcomes of HSCT recipients was not compared with a group of patients admitted to the ICU for reasons other than HSCT in the same period. Nevertheless, our study is valuable in terms of sharing the descriptive features affecting ICU mortality in HSCT recipients during a 7-year period and demonstrating the lack of relationships between mortality and laboratory results.

6. Conclusions

The ICU mortality after HSCT was 71.2% in our study, representing a considerably higher ratio compared to other studies. It was found that the APACHE II prognostic score and laboratory parameters had no effect in predicting ICU mortality in HSCT patients. The use of MV, TPN and vasopressor drugs, lower GCS score, higher heart rate and lower systolic and diastolic blood pressure were found to be associated with higher ICU mortality in HSCT patients. It is concluded that close monitoring of these factors during ICU stay, as well as signs of respiratory distress, would be beneficial for patients. More comprehensive studies are needed to investigate prognostic factors related to clinical and laboratory results in HSCT patients.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Conflict of interest

The authors declare no conflict of interest.

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10. Authors' contribution

BT: Concept, training program and system models, data acquisition, final editing
SS: Literature search, formatting and editing the manuscript

11. References

1. Naeem N, Eyzaguirre A, Kern J, Lazarus H, Hejal R, Laughlin M, et al. Outcome of adult umbilical cord blood transplant patients admitted to a medical intensive care unit. Bone Marrow Transplant. 2006;38(11):733-8. [PubMed] DOI: 10.1038/sj.bmt.1705502
2. Hayani O, Al-Beihany A, Zarychanski R, Chou A, Kharaba A, Baxter A, et al. Impact of critical care outreach on hematopoietic stem cell transplant recipients: a cohort study. Bone Marrow Transplant. 2011;46(8):1138-44. [PubMed] DOI: 10.1038/bmt.2010.248
3. Naeem N, Reed M, Creger R, Youngner S, Lazarus H. Transfer of the hematopoietic stem cell transplant patient to the intensive care unit: does it really matter? Bone Marrow Transplant. 2006;37(2):119-33. [PubMed] DOI: 10.1038/sj.bmt.1705222
4. Bayraktar UD, Nates JL. Intensive care outcomes in adult hematopoietic stem cell transplantation patients. World J Clin Oncol. 2016;7(1):98. [PubMed] DOI: 10.5306/wjco.v7.i1.98
5. Gooley TA, Chien JW, Pergam SA, Hingorani S, Sorror ML, Boeckh M, et al. Reduced mortality after allogeneic hematopoietic-cell transplantation. N Engl J Med. 2010;363(22):2091-101. [PubMed] DOI: 10.1056/NEJMoa1004383
6. Saillard C, Blaise D, Mokart D. Critically ill allogeneic hematopoietic stem cell transplantation patients in the intensive care unit: reappraisal of actual prognosis. Bone Marrow Transplant. 2016;51(8):1050-61. [PubMed] DOI: 10.1038/bmt.2016.72
7. Bayraktar UD, Shpall EJ, Liu P, Ciurea SO, Rondon G, De Lima M, et al. Hematopoietic cell transplantation-specific comorbidity index predicts inpatient mortality and survival in patients who received allogeneic transplantation admitted to the intensive care unit. J Clin Oncol. 2013;31(33):4207-14. [PubMed] DOI: 10.1200/JCO.2013.50.5867
8. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818-29. [PubMed]
9. Moon JW, Chae HD. Vaginal Approaches Using Synthetic Mesh to Treat Pelvic Organ Prolapse. Ann Coloproctol. 2016;32(1):7-11. [PubMed] DOI: 10.3393/ac.2016.32.1.7
10. Michel CS, Teschner D, Schmidtmann I, Theobald M, Hauptrock B, Wagner-Drouet EM, et al. Prognostic factors and outcome of adult allogeneic hematopoietic stem cell transplantation patients admitted to intensive care unit during transplant hospitalization. Sci Rep. 2019;9(1):1-7. [PubMed] DOI: 10.1038/s41598-019-56322-0
11. Agarwal S, O'donoghue S, Gowardman J, Kennedy G, Bandeshe H, Boots R. Intensive care unit experience of haemopoietic stem cell transplant patients. Intern Med J. 2012;42(7):748-54. [PubMed] DOI: 10.1111/j.1445-5994.2011.02533.x
12. Pène F, Aubron C, Azoulay E, Blot F, Thiéry G, Raynard B, et al. Outcome of critically ill allogeneic hematopoietic stem-cell transplantation recipients: a reappraisal of indications for organ failure supports. J Clin Oncol. 2006;24(4):643-9. [PubMed] DOI: 10.1200/JCO.2005.03.9073
13. Saillard C, Darmon M, Bisbal M, Sannini A, Chow-Chine L, Faucher M, et al. Critically ill allogenic HSCT patients in the intensive care unit: a systematic review and meta-analysis of prognostic factors of mortality. Bone Marrow Transplant. 2018;53(10):1233-41. [PubMed] DOI: 10.1038/s41409-018-0181-x
14. Townsend WM, Holroyd A, Pearce R, Mackinnon S, Naik P, Goldstone AH, et al. Improved intensive care unit survival for

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critically ill allogeneic haematopoietic stem cell transplant recipients following reduced intensity conditioning. Br J Haematol. 2013;161(4):578-86. [PubMed] DOI: 10.1111/bjh.12294

15. Orvain C, Beloncle F, Hamel J-F, Thépot S, Mercier M, Kouatchet A, et al. Different impact of the number of organ failures and graft-versus-host disease on the outcome of allogeneic stem cell transplantation recipients requiring intensive care. Transplantation. 2017;101(2):437-44. [PubMed] DOI: 10.1097/TP.0000000000001143
16. Lengliné E, Chevret S, Moreau AS, Pène F, Blot F, Bourhis JH, et al. Changes in intensive care for allogeneic hematopoietic stem cell transplant recipients. Bone Marrow Transplant. 2015;50(6):840-5. [PubMed] DOI: 10.1038/bmt.2015.55
17. Van Vliet M, Van Der Burgt M, Van Der Velden W, Van Der Hoeven J, De Haan A, Donnelly J, et al. Trends in the outcomes of Dutch haematological patients receiving intensive care support. Neth J Med. 2014;72(2):107-12. [PubMed]
18. Lindgaard SC, Nielsen J, Lindmark A, Sengeløv H. Prognosis of allogeneic haematopoietic stem cell recipients admitted to the intensive care unit: a retrospective, single-centre study. Acta Haematologica. 2016;135(2):72-8. [PubMed] DOI: 10.1159/000440937
19. Mayer S, Pastores SM, Riedel E, Maloy M, Jakubowski AA. Short-and long-term outcomes of adult allogeneic hematopoietic stem cell transplant patients admitted to the intensive care unit in the peritransplant period. Leuk Lymphoma. 2017;58(2):382-90. [PubMed] DOI: 10.1080/10428194.2016.1195499
20. Gilli K, Remberger M, Hjelmqvist H, Ringden O, Mattsson J. Sequential Organ Failure Assessment predicts the outcome of SCT recipients admitted to intensive care unit. Bone Marrow Transplant. 2010;45(4):682-8. [PubMed] DOI: 10.1038/bmt.2009.220
21. Lamia B, Hellot M-F, Girault C, Tamion F, Dachraoui F, Lenain P, et al. Changes in severity and organ failure scores as prognostic factors in onco-hematological malignancy patients admitted to the ICU. Intensive Care Med. 2006;32(10):1560-8. [PubMed] DOI: 10.1007/s00134-006-0286-3
22. Neumann F, Lobitz O, Fenk R, Bruns I, Köstering M, Steiner S, et al. The sepsis-related Organ Failure Assessment (SOFA) score is predictive for survival of patients admitted to the intensive care unit following allogeneic blood stem cell transplantation. Ann Hematol. 2008;87(4):299-304. [PubMed] DOI: 10.1007/s00277-008-0440-9

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