Research Article
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Analysis of 206 oncohematological patients admitted to the intensive care unit

Abstract

The Intensive Care Unit (ICU) provides support that includes oncohematology (OH) patients. There is tendency to delay admission of this patients to the unit. Currently, advances in the molecular biology of specific mutations; advances in stem cell transplant and immunotherapy have produced a change in the prognosis of patients. A descriptive, retrospective cohort study was carried out in adult patients with oncohematological diseases who were admitted to the ICU, in the period from January 2009 to February 2021 to evaluate mortality in the unit as the main objective as well as associations between epidemiological, clinical variables and others related to the oncohematological situation and mortality during this period.

206 patients were included. The median age was 59years (IQR: 46-68). The median on days of hospitalization was 15 (IQR: 8-28) whilst the median of days in the ICU was 5 (3-8). Mortality was evaluated at the time of discharge from the ICU, reaching 45% (93 patients), 47% at 30days and 49% at 60days, respectively. The median survival of the global population was 15.5days (IQR: 4.25-60). The median APACHE II scored 22 points (IQR: 15-25). A statistically significant relationship was found in the multivariate analysis for mortality with the APACHE II variables (p = 0.0001) and the requirement for mechanical ventilation (p = 0.021). Using the ROC curve method, the APACHE II score value of 22 was obtained as the point of greatest statistical significance. The log rank test method was used to compare patients with a value greater or less than 22. In conclusion, the value of 22 points scored on APACHE II and the requirement for mechanical ventilation served to discriminate between two groups of patients with different prognosis.

Keywords: intensive care unit, oncohematology patients, apache, mechanical ventilation, mortality

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Abbreviations: ICU, intensive care unit; OH, oncohematology; IQR, interquartile range; ROC Curve, receiver operating characteristic curve; MV, mechanical ventilation; NTP, neutropenia; HD, Hemodialysis

Introduction

The critical care unit (ICU) provides resuscitation and support to a varied population that included *oncohematology* (OH) patients. There is a tendency to delay admission of OH patients to the ICU. However, delaying admission to the ICU or rejecting patients based on the type and stage of the OH pathology does not seem to be justified.[1–3] In recent years, many of these diseases have achieved better survival rates due to advances in treatment and prophylaxis strategies along with the development of support therapies.[3] In addition, currently, advances in the diagnosis and treatment of OH diseases have produced a radical change in the prognosis of patients; advances in the molecular biology of specific mutations manage to achieve particular and selective therapeutic options. Along with this, advances in stem cell transplant technology and immunotherapy constitute a paradigm shift during the evolution of these patients.[4,5] In addition the development of supportive therapies in intensive care, numerous changes have occurred regarding the evolution and admission to the ICU of OH patients. Although the initial studies showed an ominous prognosis, recent data suggest that a greater number of patients with this type of neoplasm benefit from intensive care support, with lower mortality rates than those reported in the literature.[6] As described in the study published by Cornish in 2016, ICU survival approaches 40%,[5] in part due to advances in the management of underlying hematologic disorders as well as supportive therapies for organ dysfunction and management of life-threatening complications that this population develops, related or not to the cancer treatment itself.[7,8] Historically, OH patients have a poor prognosis when admitted to the ICU.[3] Advances in critical care through different pharmacological therapies, together with improvements in equipment, have increased the survival of these patients and the criteria for admitting them to the ICU are currently under review since the literature shows that there are patients who benefit from cancer interventions.[1,9,10] We have carried out a study that describes the current situation of adult patients with OH diseases in the ICU, to identify those variables that may have prognostic utility with respect to mortality.

Objective

Primary objective

Assess mortality in the ICU.

Secondary objectives

Assess mortality at 30 and 60 days. Describe the epidemiological and clinical variables and life support therapy requirements of patients with oncohematological diseases admitted to the ICU of a university hospital. Evaluate the association between clinical variables and mortality in the ICU. Evaluate the association between the variables related to the oncohematological diagnosis and mortality in the ICU.

Material and methods

A descriptive single-center retrospective cohort study was carried out on patients with OH diseases admitted to the ICU of a university hospital (CEMIC) within the period between January 2009 and

February 2021 to evaluate mortality in the ICU and associations between epidemiological, clinical variables and others related to the OH situation and mortality in the ICU.

Population

Patients were consecutively included 18-year-old with oncohematological diagnosis of leukemia, lymphoma, plasma cell dyscrasia and myelodysplasia according to the World Health Organization criteria, admitted to the ICU between January 2009 and February2021.[11,12]

Evaluated variables

Clinical, biochemical, and microbiological characteristics, length of stay and complications in the ICU were retrospectively analyzed, through the review of computerized and non-computerized medical records. The risk APACHE II score was calculated according to the work published in 1985 by Knaus et al.[13] risk assessment system APACHE II is used to estimate in-hospital mortality and uses the initial values of 12 routine physiological measurements, age and previous health status, generating an increasing score that correlates closely with the subsequent risk of hospital death[13] It considers various parameters that jointly influence mortality, such as age, body temperature, urgent non-elective hospitalization, mean arterial pressure, heart rate, respiratory rate, alveolar-arterial oxygen gradient, arterial pH, sodium and potassium plasma, creatinine, hematocrit, and leukocytes.

Mortality in the ICU was evaluated with respect to all variables and mortality at 30 and 60days.

The causes of admission to the ICU were acute respiratory failure, sepsis, acute kidney injury, and sensorium impairment, studied according to the following definitions:

i. Acute respiratory failure was defined as those situations in which patients met any of the following criteria: tachypnea, use of accessory respiratory muscles, muscle exhaustion, arterial oxygen saturation less than 90% on room air, oxygen requirement, or MV.

ii. The diagnosis of sepsis was made according to the consensus of Sepsis 1, 2 and 3 according to the criteria used at the time of hospitalization of the patient. Although in all of them sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection, in each of them different parameters were used to define it respect to the period.[14,15]

iii. Acute kidney injury was defined as any of the following parameters: an increase in serum creatinine by ≥0.3mg/dl within 48h, or an increase serum creatinine to ≥1.5times baseline.

iv. Sensory impairment was defined as the presence of neurological deficit with a Glasgow Coma Scale less than or equal to 8. The Glasgow Coma Scale is used to identify neurological dysfunction and progression of the level of consciousness, being a predictor of prognosis.[16]

v. In those patients in whom it was not possible to determine a clear cause for admission to the ICU, they were classified as "other causes".

vi. The complications presented during the ICU stay were defined by the following aspects: shock, mechanical ventilation requirement (MV), neutropenia (NTP) and hemodialysis (HD).

vii. Shock was defined as persistent hypotension requiring vasopressors to maintain mean arterial pressure ≥65mmHg or serum lactate level >2mmol/L, despite adequate intravascular volume resuscitation.

viii. MV, as the need for mechanical ventilation with orotracheal intubation.

ix. NTP was defined as a neutrophil count less than 1000/mm^3.

x. HD was defined as the use of continuous hemofiltration or hemodialysis.

xi. Microbiological data were collected retrospectively on patients in who isolates of bacteria and/or viruses and/or fungi were obtained.

To estimate the severity, the APACHE II score has been realized to patients during the first 24 hours of admission to the ICU by the treating physician. The APACHE II value with the highest statistical significance (using the ROC curve method) was taken as the cut-off point.

Data collection

Demographic, diagnostic and clinical evolution data were collected retrospectively and from medical records. Biochemical and microbiological data were obtained from software of the laboratory. Mortality was assessed during the ICU stay and at 30 and 60days.

Ethics

No informed consent was obtained because it was a retrospective study that kept the anonymity of the patients.

Statistical

Statistical analysis was carried out with the CEMIC University Hospital research methodology team. The t-test was used for continuous variables, while the Chi2 test and Fisher's test were used for nominal variables. The dependent variable was survival in the ICU stay. Univariate and multivariate analyzes (logistic regression) were performed to relate the descriptive variables to mortality in the ICU. The statistical significance established for the p value was less than 0.05. The Kaplan-Meier methods were used for survival calculation and the log Rank test were used for comparison between groups. All analysis was performed using STATA (version 12.1).

Results

206 patients with OH diseases who were admitted to the ICU were included. The median age was 59 years (IQR: 46-68), with a slight male predominance. The median number of hospital days was 15days (IQR: 8-28), while for days in the ICU it was 5 (3-8). The median APACHE II score was 22 (IQR: 15-25). The most frequent diagnoses were leukemias 85 (41%), lymphomas 70 (33%), plasmatic cell dyscrasias 32 (15%) and myelodysplasias 19 (9%)). Half of the patients were admitted with neutropenia 103 (50%) to the ICU. While 46 (22%) patients had at least one episode of bacteremia in the ICU. Mortality was evaluated at the time of discharge from the ICU, where it reached 45% (93 patients), while this number increased at 30 and 60days after admission to the ICU (Table 1).

No significant differences in mortality were observed according to oncohematological diagnosis (Chi2=0.111) (Table 2). A univariate analysis was performed to relate the descriptive variables to mortality in the ICU. Significant results were obtained for the variables: age, APACHE II, MV, use of inotropes, HD and NTP. (Table 3)

All those variables that were significant in univariate analysis analysis were included in the the multivariate analysis by logistic regression. The value of the APACHE II score higher than 22 and the requirement of MV were the only variables with statistical significance (Table 4). The evaluation of survival at day 60 of the general population was performed using the Kaplan-Meier method (Figure 1).

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Table 1 Demographic variables of the population

Patients (number)	(n=206)
Sex (Male) (%)	113 (54)
Age, (median, years) (IQR)	59 (46-68)
Days hospital stay (median) (IQR)	15 (8-28)
Days in ICU (median) (IQR)	5 (3-8)
APACHE II (median) (IQR)	22 (15-25)
ICU mortality (%)	93 (45)
Mort. 30 days (%)	98 (47)
Mort. 60 days (%)	102 (49)

Table 2 ICU mortality, according to diagnosis

Diagnosis	n	Alive	Dead
Leukemia	85	41	44
Lymphoma	70	36	34
Plasma cell dyscrasias	32	23	9
Myelodysplasias	19	8	11

Table 3 Univariate analysis

Variable	n	Alive	Dead	p value	Test
Age (years) (IQR)	206	59 (57-62)	54 (51-57)	**0.0179**	ttest
Male Sex (%)	206	59 (57)	54 (53)	0.96	chi2
Days of ICU hospitalization (IQR)	206	8 (6-10)	7 (6-8)	0.43	**ttest**
APACHE II score (IQR)	206	15 (11-18)	26 (22-31)	**0**	**ttest**
Mechanical ventilation (%)	108 (52%)	32	76	**0.0001**	chi2
Use of inotropes (%)	87 (42%)	36	51	**0.007**	chi2
Hemodialysis (%)	31(15%)	7	24	**0.0001**	chi2
Neutropenia at admission (%)	103 (50%)	36	67	**0.0001**	chi2
Bacteremia (%)	46 (22%)	15	24	**0.03**	Fisher

Table 4 Multivariate analysis

Variable	Odds ratio (adjusted)	95% CI	p value
APACHE II score	1,33	1,21-1,47	**0,0001**
MV Assistance	2,91	1,17-7,17	**0,021**
Neutropenia at admission	2,21	0,98-5,31	0,061
Use of inotropes	0,975	0,73-1,11	0,121
Hemodialysis	2,68	0,66-10,88	0,167
Bacteremia	1,16	0,32-3,74	0,791
Age	0,98	0,96-1,01	0,149

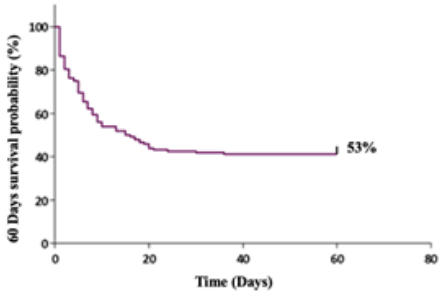

Figure 1 Median Survival at 60 days for the global population.

Using the ROC curve method, the APACHE II score value of 22 was obtained as the point of greatest statistical significance (Figure 2). The log Rank test method was used to compare patients with a value greater or less than 22. The Median Survival for patients with APACHE II score higher than 22 was 5.5days, and was 8.423 for patients with APACHE II lower than 22 points (CI 95% 5.414 – 13.1, p<0.0001).

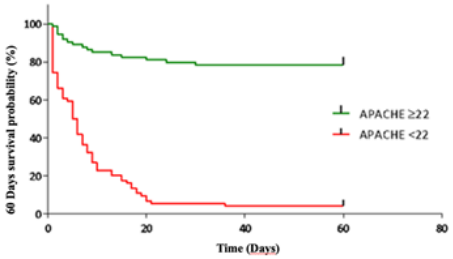

Figure 2 Survival according to APACHE II score.

Discussion

In this study we present the largest series of OH patients admitted to the ICU in the Argentine Republic. In previous international studies, the mortality was 26% to 62% in these patients, while in our study it was 47% during their stay in the ICU.[6] Mortality for global population in the ICU of our center is 11%, comparable with the mortality in the ICU in the literature. Mortality in OH patients present marked variability; this may be due to the heterogeneity that exists in terms of the conditions of admission to the ICU. In our study, we obtained average APACHE II score at admission of 22.2±9.82; the APACHE II analysis showed a significant difference in mortality in the ICU, which was also confirmed in the multivariate analysis. Among the prognostic factors evaluated, the APACHE II risk score scale was the one that showed the greatest correlation with mortality. Although the APACHE II is a scale that has been validated for estimating in-hospital mortality for the population of the original Knaus study, its validity has not been measured in Argentina. Despite the discrepancies between the works listed, including the present one, most agree on the benefit of early admission to the ICU, thus allowing admission with a lower value on the APACHE II scale and earlier indication of support measures to avoid the development of organ failure and thus a higher APACHE II value.

APACHE II is widely used and an excellent predictor of mortality in OH patients in the ICU, due to the evaluation of organ failure among other variables, it is not exempt from limitations since it does not consider some vital organs and systems such as the liver and coagulation. On the other hand, it confers excessive value for age. Scoring system could be evaluated in the future with SOFA score (Sequential Organ Failure Assessment score), frequently used in ICU. It includes the evaluation of the respiratory system through the relationship between arterial oxygen pressure and the inspired oxygen fraction (PaO^2 /FiO^2), coagulation system with the number of platelets, the liver through the value of bilirubin, the cardiovascular system through the control of blood pressure and the requirement of vasoactive drugs, the central nervous system through the Glasgow coma scale and renal function through the measurement of the creatinine value plasmatic. One limitation of our work is that it has not been able to count on the value of the SOFA due to its retrospective nature and the lack of data necessary to reconstruct it.

In this study the main cause of ICU admission was respiratory failure, which produced a large group of patients with mechanical ventilation requirements. This is a recognized factor for a worse prognosis in the ICU.[17] In addition, the association between the

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requirement for mechanical ventilation and mortality was significant in the multivariate analysis.

Another risk factor identified was the state of neutropenia at admission to the ICU, without obtaining significant relevance in the multivariate analysis with an odds ratio of 2.21 (95% CI: 0.98-5.31). This variable is described in the literature, however, we identified its relevance in a group of patients with oncohematological diseases only, not including those with neutropenia due to solid tumors or chemotherapy treatments. While in the univariate analysis a significant difference was obtained for the variables age, use of inotropes, hemodialysis, and bacteremia, in multivariate analysis they lack statistical significance. It is possible that this report does not have enough power to demonstrate the significant relevance of these variables, but it allows us to observe a trend of these items as risk factors.

A sensitivity of 67% was observed, together with a specificity of 88% to predict mortality in the ICU, when associating the two significant variables in the multivariate statistical analysis. This number is like that reported in the work of Jirateep Khwankeaw et al. Therefore, the association of these two variables are a good indicator to evaluate the taking of invasive behaviors in this group of patients with OH diseases.[6] The strength of this study lies in describing the current situation of hospitals that include a bone marrow transplant unit and an ICU. From this, it is possible to generate evidence on which patients benefit from support measures in the ICU and in which it is important to avoid invasive measures that do not improve the prognosis and entail a high economic and human resource cost.

Conclusion

We determined that mortality was 47% during ICU stay in OH patients. A significant association was observed between the APACHE II and ARM variables with ICU mortality. The cut-off points of an APACHE II value of 22 served to discriminate between two populations with different prognosis. There were no differences in mortality according to the OH diagnosis. We suggest that patients be promptly treated. However, prospective and multicenter studies are needed to make recommendations.

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Conflicts of interest

The authors state that there is no conflict of interest.

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