Outcomes of critical illness in patients with haematological malignancy who were hospitalized in the intensive care unit and the evaluation of predictors of mortality

Rania Bouneb, Kmira Zahra, Aliaa Yaacoubi, Imed Chouchène, Jamila Baroudi, Khelif Abderrahim, Slah Bouchoucha

Abstract

Aim— We studied outcomes and prognostic factors in critically ill patients with haematological malignancies admitted to the intensive care unit (ICU).

Methods— It was a retrospective cohort study in an eight-bed medical ICU of a university hospital. One hundred and five critically ill patients with haematological malignancies treated over a 20-year period were included. Patients' clinical characteristics and outcomes were examined. Multivariate analysis was performed to identify prognostic factors.

Results— The underlying malignancies were predominantly acute leukaemia (45.7%), non-Hodgkin's lymphoma (37.1%), Hodgkin's lymphoma (6.7%) and multiple myeloma (6.7%). The mean length of stay in the ICU was 4.77±6.14 days. All patients were on ventilation (78%with invasive ventilation and 22% with non-invasive ventilation). ICU mortality was 73.3%, with significantly higher mortality in invasively ventilated patients (74%) vs. non-invasive ventilated patients (12%), p<0.001. The mean of Simplified Acute Physiology Score II (SAPS II) was 47.35±15.57.The aetiology of acute respiratory failure was infectious disease in 75% of patients, neutropenia in 53.3%of patients and septic shock in 38.1%of patients. Multivariate analysis identified the SAPS II score, catecholamine use in the first 24-hours and ventilator support immediately prior to or at admission to the ICU as independent prognostic factors of ICU mortality.

Conclusion— The overall outcomes for critically ill patients with haematological malignancies were poor. SAPS II score, catecholamine use and mechanical ventilation were independent prognostic factors.

Key words: Haematological malignancy; critical illness; outcome; predictors of mortality.

INTRODUCTION

In recent decades, the prognosis of patients with haematologic malignancies has improved substantially, particularly because of new intensive chemotherapeutic regimens, haematopoietic stem cell transplantation, and better supportive measures [1, 2]. Unfortunately, more intense cancer treatment has led to increasing rates of therapy-associated complications, which may be life-threatening and often necessitate transfer to an intensive care unit (ICU).

- *Rania Bouneb, Imed Chouchène, Slah Bouchoucha: Department of Medical Intensive Care Unit, Farhat Hached University Hospital. Sousse, Tunisia.*
- *Kmira Zahra, Khelif Abderrahim: Department of Clinical Hematology, Farhat Hached University Hospital. Sousse, Tunisia*
- *Aliaa Yaacoubi : Parasitology laboratory,Farhat Hached, Sousse University Hospital. Sousse, Tunisia*

Although favourable intensive-care survival rates have been reported in critically ill patients with cancer in recent decades [3,4],survival remains very low among patients with haematologic malignancies. In these patients, ICU mortality rates are 30% to 82% and the in-hospital and long-term mortality rates are even higher [5, 6].

As a result, the decision to transfer a severely ill patient to the ICU presents an ethical dilemma to haematologists and intensive-care specialists. Preferably, these decisions should be based on prognoses tailored to individual patients. Although several studies have identified prognostic factors to maximize survival and limit unnecessary suffering and costs, few of those studies have been published in the last five years [5, 7, 8, 9,10].

This study identified prognostic factors associated with mortality in a cohort of critically ill patients with haematologic malignancies admitted to a Tunisian ICU.

MATERIALS AND METHODS

This is a retrospective study including 105 patients with haematological malignancies who were admitted to the medical ICU of the University Hospital Farhat Hached Sousse from 1January 1994 to 31 December 2014. Patients over 15 years of age with haematological malignancies treated in the clinical haematology department of the hospital and who were or became critically ill were eligible. Critical illness for the purpose of study entry was defined according to the criteria in Table 1. All of the admissions to the ICU were for medical reasons; there were no postoperative surgical admissions.

Enrolled patients were followed throughout their hospital stays. Information recorded included patient demographics, haematological diagnosis and treatment, details of acute illness at admission and during the ICU stay and the outcome at ICU. Only clinically indicated investigations were performed. The Simplified Acute Physiology Score II (SAPS II)[11] was calculated for all patients using the worst physiological variables within 24 hours of study enrolment. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score [12] in the first 24 hours after ICU admission was also calculated for patients admitted to the ICU.

If a patient had more than one hospital admission complicated by critical illness, only the first admission or the one that lasted more than 24 hours was considered for outcome analysis. The data were analysed using Microsoft Excel XP (Microsoft Corporation, Redmond, WA) and SPSS for Windows (SPSS Inc., Chicago, IL) version 18.0. Continuous, non-normally distributed data are presented as the median, interquartile range (IQR) and [range]. The groups were compared using the chi-square test. Logistic regression analyses were then performed using all the statistically significant associations found in univariate analysis to determine which factors were independently associated with hospital survival. Continuous data were dichotomized into categorical variables using the median as the threshold to calculate the odds ratios (OR) by logistic regression analysis. The results were considered statistically significant if the p-value was less than 0.05.

RESULTS

During the study period, 420 patients with haematological malignancies were proposed for admission to the ICU, but only 105 patients were accepted because of the limited ICU capacity.

Critically ill patients and treatment.

There were 105 admissions to the ICU for critical illness. The median age of the critically ill patients was 49 years (IQR 32 [range 15–86] years), and 64 patients (60%) were male. The comorbidities, the underlying haematological diagnoses, the status of the disease and the type of the acute illnesses are shown in Table 2. The median time from the diagnosis of haematological malignancy to the onset of critical illness was one year (IQR 3 [range 0–10 years] years). Seventy-six patients had received at least one course of chemotherapy prior to ICU admission. Thirty-seven patients (35.2%) had neutropenia with a neutrophil count of less than 1000/mm3at admission. A neutrophil count of less than 500/mm3 was found in 30 of the 37 patients.

Upon ICU admission, the median SAPS II was 46 (IQR 28), and the median APACHE II was 32 (IQR 18).Twenty-seven patients received non-invasive respiratory support; 47 patients underwent tracheal intubation and mechanical ventilation (MV); and 31 patients did not need ventilation. Forty-two ICU patients received vasopressors, and twenty-one patients received renal replacement therapy.

Hospital survival

The hospital mortality rate for all patients who became critically ill was 73.3% (77/105).According to univariate analysis, the predictors of mortality were age, haematological diagnosis, disease status, disease severity at admission, number of organs in failure, use of invasive mechanical ventilation (IMV), administration of catecholamines and severe hypoxemia at admission (Table 3).

Upon multiple logistic regression analysis, the SAPS II score, (OR=4.2; CI 95% [0-20] (p=0,00)), the use of IMV (OR=5.6; IC95% [0,4-86] (p=0,015)) and the use of catecholamines (OR=12; IC95% [1.6-190] (p=0,038)) were independently associated with hospital mortality.

DISCUSSION

In this study, we found that IMV, use of vasopressors, and SAPSIII score were independently associated with a poor prognosis. These results are consistent with those of previous studies, suggesting that IMV is a strong predictor of mortality in patients with haematologic malignancies[5,13].Other factors thought to be associated with high mortality upon admission to the ICU include old age, the presence of

haemodynamic instability, neutropenia, and number of failing organs[5,6,7,9,14].

Our cohort showed relatively high mortality compared with cohorts in previous studies[5,6,15].These results could be partially explained by the poor prognostic factors of the patients transferred to our institution (old age[16,17], relapse[18], and previous treatment failure). Therefore, we postulate that the relatively high mortality in these results might be attributable to the severity of the haematologic malignancies.

Our data showed that the type of haematologic malignancy does not predict the prognosis. These results are consistent with those of some previous studies [13, 15, 19, 20, 21]: the type of haematologic malignancy does not predict mortality. However, two reports [22,23]suggested an association between underlying AML and high mortality.

Neutropenia has been suggested to be associated with hospital mortality and poor outcomes [9, 15, 24, 25]. However, several studies suggest that neutropenia did not affect outcome, and our data failed to show that neutropenia is an independent predictor of a poor prognosis [7, 6].These conflicting findings warrant further larger studies to confirm this relationship.

Our study revealed that patients requiring IMV and inotropics/vasopressors had worse prognoses. Patients with respiratory distress and haemodynamic instability have high organ-failure scores. Our data highlight the importance of respiratory and haemodynamic status in predicting outcomes for patients with haematologic malignancies [6, 21].

The intended use of the SAPS II score and similar scoring systems is to predict outcomes for critically ill patients [10].For patients with malignancies who were transferred to the ICU, SAPSII could be a good basis for evaluating these verity of organ dysfunction [26]. Our data were consistent with prior results, suggesting that SAPSII is an independent predictor of outcome and survival in critically ill patients with haematologic malignancies [8, 25]. However, scoring systems such as APACHE II, the SAPS II, and Sequential Organ Failure Assessment do not perform well in this specific group of patients [26, 27]; they predict relatively high mortality rates in survivors and low rates in non-survivors [28]. Therefore, the SAPS II score alone should not be used for individual decision-making [21], and other factors predicting mortality in patients with haematologic malignancy in the ICU should be considered. The SAPSII score, it should be noted, gives a risk of in-hospital mortality rather than ICU mortality.

Moreover, many previous studies also used ICU mortality as an end point [19, 20].Our study has several limitations. First, it was a retrospective observational study. However, using a single cohort whose treatment was based on the same protocol, we carefully evaluated all patients admitted to the ICU who were enrolled in the study. The aim of this study was to identify factors predicting the ICU outcome, and therefore, the setting of our study may not have greatly differed from that of a prospective observational study. Second, our study was conducted in a single institution, which limits the generalizability of our findings to other patient populations.

In conclusion, increased mortality in patients with haematologic malignancies admitted to the ICU is associated with more severe illness, as reflected in higher organ-failure scores or respiratory or haemodynamic instability. Further study of the prognostic factors in patients with haematologic malignancies admitted to the ICU is needed.

Table 1. Definition of critical illness**.**

Critical illness was defined by one or more of the following criteria
Respiratory
-Pa02 < 60 mmHg
-SaO_2 < 90% in ambient air
-Pa02/Fi02<300 mmHg
Cardiovascular
- Systolic blood pressure <90 mmHg or falling>40 mmHg from premorbid readings despite fluid resuscitation
-Average blood pressure < 65 mm Hg
-Diastolic blood pressure < 40 mmHg associated with hyperlactatemia>2 mmol/l
Neurological
- Glasgow Coma Score <14
-Uncontrolled seizures
Renal
- Serum creatinine >177 µmol.l−1
-Oliguria <0.5 ml /kg persisting for 3 hours despite fluid resuscitation
Severe sepsis
- Systemic inflammatory response syndrome (SIRS) + suspected infection + at least one organ dysfunction

Table 2. Patient characteristics.

Characteristics (n=105)	Total number of patients (%)
Comorbidities	
No comorbidity	54 (51.4)
Diabetes	16 (15.2)
Hypertension	12 (11.4)
Heart disease	7 (6.7)
Chronic lung disease	6 (5.7)
Diabetes + hypertension	4 (3.8)
Renal impairment	4 (3.8)
Liver injury	2 (1,9)
Haematologic diagnoses	
Non-Hodgkin's lymphoma (NHL)	39 (37.1)
Acute myeloid leukaemia (AML)	30 (28.6)
Chronic lymphocytic leukaemia (CLL)	10 (9.5)
Acute lymphoblastic leukaemia (ALL)	8 (7.6)
Hodgkin lymphoma (HL)	7 (6.7)
Multiple myeloma (MM)	7 (6.7)
Others	4 (3.8)
Status of the haematological disease	
Complete remission	19 (18.1)
Relapse or progression	54 (51.4)
Initial phase	32 (30.5)
Acute illness	48 (45.7)
Respiratory failure	20 (19)
Primary cardiac event	17 (16.2)
Sepsis	7 (6.7)
Neurological failure	9 (8.6)
Renal failure	4 (3.8)
Bleeding	
Number of organ failures at admission	28 (26)
1	30 (29)
2	29 (27)
3	19 (18)
≥4	

Table 3. Patient characteristics according to vital status at ICU discharge**.**

	Survivors (n=28)	**Deaths** (n=77)	p-value
Age (yrs) (mean±SD)	41±16	49±19	0.04*
Sex (Male)n (%)	15 (53)	49 (63)	0.35
Diseasen (%)			0.25
ALL	0 (0)	8 (10)	
AML	11 (39)	19 (24)	
NHL	12 (42)	27 (35)	
Hodgkin's	2 (7)	5 (6)	
CLL	2 (7)	8 (10)	
CML	1 (3)	3 (3)	
Myeloma	0 (0)	7 (9)	
Comorbidities n (%)			0.06
Congestive heart failure	2 (7)	5 (6)	
Chronic pulmonary disease	1 (3)	5 (6)	
Renal failure	0 (0)	4 (5)	
Diabetes mellitus	5 (17)	11 (14)	
Hypertension	4 (14)	8 (10)	
Diseasestage n (%)			0.15
Diagnosis	13 (46)	19 (24)	
Remission	5 (18)	14 (18)	
Progression	1 (3)	53 (69)	0.0010.0002
APACHEII	20±3	38±8	*
SAPSII	39±8	53±9	
Diagnosis at admission n (%)			0.002*
ARF	18 (64)	39 (51)	
Shock	6 (21)	31 (40)	
Neutropenia n (%)	11 (39)	26 (33)	
Infection n (%)	19 (67)	54 (70)	
Invasive MV n (%)	8 (28)	39 (50)	0.68
PaO2/Fio2 n (%)			0.82
>200	26 (64)	43 (56)	0.0001*
<200	10 (36)	34 (44)	0.000*
Catecholamines n (%)	8 (28)	34 (44)	0.000*
Hemodialysisn (%)	4 (14)	17 (22)	0.38
Organfailuren (%)			0.000
≤2	27 (96)	30 (38)	
≥3	1 (3)	47 (61)	

Abbreviations: ALL, acute lymphoblastic leukaemia; **AML**, acute myeloid leukaemia; **NHL**, non Hodgkin's lymphoma; **CLL**,chronic lymphoblastic leukaemia; **CML**, chronic myeloid leukaemia; **ARF**, acute respiratory failure

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