Mortality Predictors After Liver Transplant in the Intensive Care Unit

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ABSTRACT

Background. The goal of this study was to evaluate the predictive factors of mortality in patients after liver transplantation in an intensive care unit from the University Hospital.

Methods. This observational study was conducted by using a database analysis of University Hospital. The sample consisted of patients after liver transplantation registered in the database. The study variables of Sequential Organ Failure Assessment score, Acute Physiology and Chronic Health Disease Classification II (APACHE II), Model for End-Stage Liver Disease, and Child-Pugh scores, and the days of hospitalization in intensive care unit, mechanical ventilation time, and reintubation rate, were correlated. Statistical analysis was performed by using the χ^2 test or Fisher exact test, the Mann-Whitney test, and logistic regression analysis.

Results. Fifty-eight individuals were analyzed. In the death group, the days of hospitalization in the intensive care unit were within 12 ± 14 days, the time of mechanical ventilation was 180 ± 148 hours, the APACHE II value was 17.6 ± 7.3, the Sequential Organ Failure Assessment score was 8.2 ± 2.7, and reintubation was 40%. In the multivariate regression, the predictive indexes of mortality were the mortality given by APACHE II (odds ratio, 1.1; CI, 1.03–1.17; $P = .004$), mechanical ventilation time (odds ratio, 1.02; CI, 1.01–1.04; $P = .001$), and reintubation (odds ratio, 9.06; CI, 1.83–44.9; $P = .007$). An increase of 1 unit in APACHE II mortality increases the risk of death by 10.2%, and each hour of mechanical ventilation increases the risk of death by 2.6%.

Conclusions. The time of mechanical ventilation, orotracheal reintubation, and the mortality given by APACHE II were the variables that best predicted death in this study.

MORTALITY rates, adjusted based on mortality predictions provided by prognostic score systems or independent variables, have been increasingly used to compare the quality of care provided by different intensive care units (ICUs) and hospitals. They are also used to evaluate the impact of new therapeutic options or organizational modifications as part of quality improvement initiatives [1]. The objective of the present study was to evaluate possible predictive indexes and independent mortality factors in patients after liver transplantation (TX) who were hospitalized in the ICU and to describe the profile of the treated patients by using epidemiologic data.

MATERIALS AND METHODS

This observational and retrospective cohort study was based on analysis of the records contained in the database of the Transplant Adult ICU of the Clinics Hospital of Unicamp (HC-Unicamp). Data from patients undergoing liver TX with the mortality rate during the ICU stay between the years 2014 and 2015 were analyzed. The HC-Unicamp database is managed by a trained professional, and the information was collected by using medical records to keep the patient's identity confidential. The project was approved by the Ethics Committee of University Medical Science of Campinas for opinion (1,240,556).

To analyze the data, the subjects were divided into 2 groups: the death group, which included patients who died in the ICU after

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0041-1345/18
https://doi.org/10.1016/j.transproceed.2018.02.087

liver TX surgery, and the non-death group, which included patients undergoing liver TX who were discharged from the ICU.

The variables and characteristics of the organ recipients analyzed and correlated with the mortality rate were the general demographic characteristics of the study population. These characteristics included old age, body mass index (BMI), sex, and primary diagnosis of the disease. Other variables included mechanical ventilation (MV), Sequential Organ Failure Assessment (SOFA) score, Model for End-Stage Liver Disease (MELD), Acute Physiology and Chronic Health Disease Classification II (APACHE II), Child-Pugh (CHILD) score, need for orotracheal reintubation, and duration of noninvasive ventilation use.

The variables to evaluate the systemic function of 6 organs, as proposed by Vincent et al [2], were used to calculate SOFA on the first day of ICU admission. For the calculation of APACHE II, the final equation proposed by Knaus et al [3] was used and calculated online by using the Sfar System that integrates the software of the database used. The values of the Glasgow Coma Scale were obtained from medical records of patients who were registered before surgery (ie, the pre-TX period of the liver). The MELD score was obtained by using the values recorded by the physicians in the patients' charts during outpatient follow-up while waiting in transplant row.

Individuals who performed liver TX in adults, who were referred to the ICU, were included in the study. Patients who did not have complete data in the medical records in the database, who died in operating room, and those who underwent liver TX combined with the renal TX were excluded from the study.

For the qualitative variables, absolute (n) and relative (%) frequency were used. For quantitative variables, the mean and SD (minimum and maximum values) were used to indicate the variability of the data. Descriptive analysis in frequency tables for categorical variables and position and dispersion measurements for numerical variables were also used. For comparison of proportions, the χ^2 test or the Fisher exact test was used, when necessary. The Mann-Whitney test was used to compare numerical measurements between the 2 groups. To evaluate the factors related to death, we used the logistic regression analysis, with univariate and multiple models with stepwise criterion of variable selection. To analyze the relationship among numerical variables, the Spearman correlation coefficient was used. The significance level adopted for the statistical tests was 5%.

RESULTS

Demographic and clinical characteristics of the studied population are shown in Table 1. The total number of subjects included in the study was 58; their average (±SD) age was 52.6 ± 12.7 years and body mass index (BMI) was 25.8 ± 5.2 kg/m^2. There was a male prevalence (38 individuals), and the primary diagnosis was hepatocellular carcinoma (53.5%).

The time of MV use in the no death group was statistically lower than in the group of patients who died (34.5 ± 50.9 hours vs 180.9 ± 148.8 hours, respectively; $P < .001$), as shown in Table 2.

Table 3 displays the univariate and multivariate logistic regression analysis. As shown, the time of use of MV and mortality according to APACHE II were the variables that best predicted death for this sample. Increasing 1 unit in the probability by APACHE II increases the risk of death by 10.2% and each hour of MV increases the risk of death by 2.6%. The need for reintubation increases the chance of death by 9 times.

Table 1. Descriptive Analysis of the Variables in Relation to Demographic and Clinical Characteristics of the Study Population

Analyzed Variable	Mean ± SD/No. (%)	No. of Total Individuals
Age, mean ± SD, y	52.6 ± 12.7	58
Body mass index, kg/m^2	25.8 ± 5.2	43
Sex		
Female	10 (20.8)	48
Male	38 (79.2)	48
Primary diagnosis		
Hepatocellular carcinoma	31 (53.5)	58
HC Alcoholic	7 (12.1)	58
HC Vírus C	4 (6.9)	58
HC Vírus C + Alcoholic	2 (3.4)	58
HC Vírus B + Alcoholic	2 (3.4)	58
HC criptogenia	4 (6.9)	58
Others	8 (13.8)	58
Time of MV, h	70 ± 104.6	
RETOT		
Yes	10 (17.2)	54
No	48 (82.8)	58
APACHE II score	16 ± 5	
APACHE II Mortality	25.7 ± 14.3	58
SOFA Total	7.4 ± 2.6	58
CHILD		
1	12 (23.08)	52
2	15 (28.85)	52
3	25 (48.08)	52
MELD	23.9 ± 8.24	52

Mann-Whitney test.

Abbreviations: APACHE II, Acute Physiology and Chronic Health Disease Classification System II; CHILD, Child-Pugh; ICU, intensive care unit; HC, hepatic cirrhosis; MELD, Model for End-Stage Liver Disease; MV, mechanical ventilation; RETOT, orotracheal reintubation; SOFA, Sequential organ failure assessment score.

DISCUSSION

In the last 20 years, the number of liver TXs has grown worldwide. However, the number of candidates awaiting surgery is increasing, maintaining the disproportion between the demand for organs and the availability for TX [4]. The quality of life of the organ recipient after liver TX is independent of the donor's age but may be correlated to the technical aspects of the surgery and characteristics of the transplant candidate. In this study, the average age of recipients was 52.6 ± 12.7 years, which corroborates with most publications in European, Asian, North American, and Brazilian countries related to liver TX [5–7].

In solid organ TXs, donors generally cannot be allocated according to the sex of the candidates, as there are not enough donors available. However, as noted elsewhere, men have more liver diseases than women [8,9], which also agrees with the results of the present study.

The literature also reports that overweight and obese patients have greater morbidity and mortality after liver TX.

Table 2. Comparison Between the Death and No Death Groups in Relation to Age, MV Time, APACHE II, APACHE II Mortality, SOFA and MELD, Use of NIV, and Need for RETOT

Analyzed Variable	Death Group (n = 15)	No Death Group (n = 43)	Total	*P*
Age, mean ± SD, y	52.2 ± 14.1	52.8 ± 12.3	48	.97*
BMI, mean ± SD, kg/m^2	26.6 ± 8.3	25.5 ± 3.8	58	.57*
Length of hospital stay in ICU, mean ± SD, d	12.9 ± 14.5	10.6 ± 10.4	44	.54*
Time of VM, mean ± SD, h	180.9 ± 148.8	34.9 ± 50.9	54	<.001*
APACHE II score, mean ± SD	17.6 ± 7.3	15.4 ± 3.8	58	.50*
APACHE II mortality score, mean ± SD	31.4 ± 21	23.7 ± 10.7	58	.54*
SOFA total, mean ± SD	8.2 ± 2.7	7.1 ± 2.5	58	.14*
MELD score, mean ± SD	24.54 ± 5.8	23.69 ± 8.96	52	.44*
CHILD				
1	2 (15.38%)	10 (25.64%)	52	.54*
2	3 (23.08%)	12 (30.77%)		
3	8 (61.54%)	17 (43.59%)		
NIV (%)				
Yes	6 (40%)	20 (46.5%)	26 (44.8%)	.77†
No	9 (60%)	23 (53.5%)	32 (55.2%)	.77†
RETOT				
Yes	6 (40%)	4 (9.3%)	10 (17.2%)	.013†
No	9 (60%)	39 (90.7%)	48 (82.8%)	

Abbreviations: APACHE II, Acute Physiology and Chronic Health Disease Classification System II; ICU, intensive care unit; MELD, Model for End-Stage Liver Disease; MV, mechanical ventilation; NIV, noninvasive ventilation; RETOT, orotracheal reintubation; SOFA, Sequential Organ Failure Assessment score.
*Mann-Whitney test.
†Fisher test.

Some centers consider these comorbidities as contraindications for surgery [7]. In the population of the present study, the average BMI of the transplanted individuals indicated body overweight (25.8 ± 5.2 kg/m^2). Ayloo et al [10] reported that patients with a BMI between 18.5 and 29.9 kg/m^2 had 5-year survival rates clinically comparable to normal-weight recipients.

The main most-used prognostic indicators of mortality in ICUs, regardless of clinical status, are APACHE II and SOFA. These tools predict the mortality of critically ill patients in the short term [11]. In addition to the group of individuals with liver disease, the MELD and CHILD scores were included in this study because of the use of these indicators.

The findings of this study suggest that APACHE II was a predictive mortality score after liver TX ($P = .0046$) in the multivariate analysis. Thus, Elsayed et al [12], in comparing 2 groups of survivors and nonsurvivors of liver TX, found that APACHE II presented a high level of significance on the first and seventh days of ICU admission to predict mortality after TX. Zhang et al [11] also observed that APACHE II was a predictor of patient mortality after liver TX.

In the statistical analysis of the present study, the MELD and CHILD scores were not predictors of mortality in patients after liver TX, agreeing with the results of Aguiar et al [13]. Although the present findings do not demonstrate a good prognosis for mortality with these scores, as described in the literature, patients with a high MELD score and a CHILD C rating may present a worse prognosis after liver TX [14].

The MV time was higher in patients in the death group ($P < .001$). These findings suggest that MV time may be an independent factor for predicting ICU mortality for this patient group. Similar findings are described in the literature. Studies show that there is a need for the use of MV in patients with liver cirrhosis and after liver TX, in addition to increasing the length of ICU stay, has resulted in some complications including multiple organ failure and mortality rates of 59% and 93%, respectively. These studies also showed that the duration of MV can be considered a predictive factor for mortality [8,15,16].

In an attempt to reduce the mortality rate in this group of patients, studies have reported on the benefits of liver TX using live donor TX. This technique is currently being studied by several researchers. Kim et al [17] suggests that there was a decrease in time of MV, length of ICU stay, and mortality in patients who underwent interventricular TX compared with the traditional method.

Physiological and metabolic changes caused by manipulation of the organs during the surgical procedure may result in a greater need for reintubation after TX, and, consequently, the prolongation of MV time. In a systematic

Table 3. Univariate and Multiple Logistic Regression Analysis of Risk Factors Mortality APACHE II, Time of Use of MV and RETOT in Relation to the Occurrence of Death

Analyzed Variable	95% Confidence Interval	Odds Ratio	*P*
APACHE II mortality	1.030–1.178	1.102	.0046
Time of MV	1.011–1.040	1.026	.0004
RETOT	1.831–44.875	9.065	.0069
MELD	0.937–1.094	1.013	.7464
CHILD	0.173–9.019	0.8249	1.25

Abbreviations: APACHE II, Acute Physiology and Chronic Health Disease Classification System II; MV, mechanical ventilation; RETOT, orotracheal reintubation.

review, in 14 studies, the need for orotracheal reintubation, time of MV, and ventilation-acquired pneumonia resulted in an increase in ICU mortality [18]. The rate of reintubated patients was 40% in the death group and 9.3% in the no death group.

The rate of reintubation in the death group was considered as one of the independent factors of mortality in this study. This value was slightly smaller than that found by Gao et al [18], who observed that patients reintubated after live TX had a mortality rate of 51.2%.

The high mortality rates in reintubated patients reflect future understanding of early extubation protocols, identification of these individuals and their disease, predictive short-term mortality, and possible pulmonary complications and prevention techniques.

Lai et al [19,20] observed that the fragility index may predict the mortality of this group of individuals still candidates for liver TX. Interventions aimed at preventing fragility in the pretransplant period are urgently needed to maximize physical health after TX, assisting in better physical performance of the patient to MV, orotracheal intubation, and APACHE II values. However, despite the importance of evaluating and intervening in terms of fragility, it was not possible in the present study to observe these data due to lack of time. Future research is needed to associate the fragility index with the variables used in the ICU after TX.

To better utilize the resources allocated to the ICU, predictive scores can identify patients who are more likely to survive than those who are more likely to die and thus adopt advanced or conservative strategies after liver TX. In the present study, the main predictors of mortality in the ICU after liver TX were the APACHE II score, MV time, and orotracheal reintubation. Therefore, it is suggested, as already proposed by other works, to incorporate variables related to MV into prognostic indexes.

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