ORIGINAL ARTICLE

Predictors of Death and Discharge in Intensive Care Units: A Competing Risks Model

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Abstract

Background: Many risk factors are associated with death in and discharge from the Intensive Care Unit (ICU). This study aimed to evaluate the risk factors associated with death and discharge among ICU patients.

Methods: This historical cohort study was conducted on 712 patients admitted to the ICU of Namazi hospital in Shiraz between 2013 and 2015. The competing risks regression model was suitable for assessing the risk factors associated with death and discharge in ICU. Data analysis was performed using STATA 13.0 and R software.

Results: The mean age of the participants was 53.3±20.7 years. Out of 712 patients, 436 (61.2%) were male and 121 (17.8%) died. In the competing risks model, death was considered as the event of interest, and age and total days of Central Venous Catheter (CVC) and mechanical ventilation use increased the risk of death (all Sub-distribution Hazard Ratios (SHRs) >1).

Conclusion: The findings indicated that increase in age, use of CVC and mechanical ventilation, and female sex caused an increase in death in ICU. However, the risk of death decreased or the chance of discharge increased when the patients were admitted due to surgical reasons.

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Keywords: Mortality, Patient Discharge, Intensive care units

Introduction

There are various reports on the mortality rate and complications of admission in Intensive Care Units (ICUs). However, there is disagreement about the causes of death and discharge and their relationship with the length of stay in this unit.[1] Hospital-Acquired Pneumonia (HAP) has been reported to account for 15-20% of all nosocomial infections, which are associated with high mortality rate in ICUs.[2] Given the increasing tendency towards prediction models for post-admission mortality, many authors have attempted to determine the factors related to ICU mortality and discharge. However, these studies have achieved varying degrees of success, with contradictory results in most cases.[3-5]

Several studies have been done in order to identify the factors that increase death and discharge among the patients admitted to ICUs. Based on the results, requiring ventilator or Central Venous Catheters (CVC) for more than 14 days, age over 65 years, septic shock, and kidney problems contributed to increased mortality in ICUs.[6] A study also revealed that age alone was an important factor in increasing mortality and that every five years of age led to a significant increase in mortality.[7]

The most common causes of hospitalization in ICUs include trauma, respiratory problems, and follow-up and post-operative care. Besides, the highest rate of mortality has been reported in the 40-60 age group. Another study showed that the highest percentage of ICU deaths was related to trauma admissions, while the lowest death rate was related to operating room admissions or admissions from the recovery room (surgery).[6-8] The risk factors for death and discharge that occur after clinical outcomes have been evaluated in numerous studies, revealing contradictory results.[4] However, some studies have overlooked the possibility that there are other factors that can compete with the desirable outcome, i.e. death in ICUs.[9, 10]

The competing risks method can effectively contribute to understanding the factors that increase mortality and reduce discharge due to various risk factors.[11] Competing risks occur when a person experiences more than one type of event, and the occurrence of the event (in-ICU death) prevents the occurrence of the other event (discharge from ICU). When there are competing risks, Kaplan-Meier estimates cannot be interpreted as probability and, consequently, a specific approach is needed based on cumulative incidence function. Competing risk regression models allow us to identify independent risk factors for the two outcomes (death and discharge) and create two different algorithms.[12, 13] The present study aimed to determine the risk factors associated with ICU death and discharge in patients admitted to an ICU in Shiraz, southern Iran using a competing risk method. Identification of the risk factors for ICU death and discharge may help improve healthcare services and reduce the length of stay and hospital costs.

Methods

This historical cohort study was conducted to evaluate the factors associated with the occurrence of ICU death/discharge in 2019. All 712 patients admitted in the ICU of Namazi hospital, Shiraz between January 2013 and December 2015 were enrolled in this study. The required data were extracted from the patients' medical records using a researcher-made questionnaire. The study variables included age, gender, reason for admission, use of mechanical ventilation and CVC, and type of ICU admission (surgical or trauma). The follow-up of patients' death or discharge until 2015, as the failure time, was also performed using their medical records. It should be noted that the patients who were lost to follow-up were considered as right-censored.

Descriptive statistics were presented as mean±Standard Deviation (SD) for continuous variables and frequency (percentage) for categorical ones. All quantitative variables were tested for normal distribution by Kolmogorov-Smirnov test and statistical graphs (i.e., histogram and box-plot).

The competing risks regression model was fitted for the factors associated with ICU death and discharge. ICU admission was considered as the starting point of follow-up, while ICU death/discharge was regarded as the competing risk. The cumulative incidence function is an important value that attracts the physicians' attention in conducting the competing risks method. This value calculates the probability of the occurrence of a particular cause. Nevertheless, the specific-cause hazard function calculates the proportion of the concurrence of events. The required data were collected by reviewing the medical records of the patients admitted to the ICU by a trained nurse. The competing risks regression model was used to evaluate the factors related to ICU discharge and death. Sub-distribution Hazard Ratio (SHR) refers to the instantaneous increase in the rate of the occurrence of the event of interest.[8] For modeling, variables with $P<0.2$ were entered into the multiple competing risks regression model. Data analysis was performed b using STATA, version 13.0. In addition, plot.predict.crr function was applied to plot the predicted cumulative incidence function curve on R project. The significance level was set at 0.05.

All the experimental procedures and study protocol of the study were approved by the local ethics committee of Shiraz University of Medical Sciences (protocol no. 94-7436), which were in complete accordance with the ethical standards and regulations of human studies of the Declaration of Helsinki (2014).

Results

The mean age of the participants was 53.3±20.7 years. Out of the 712 participants, 436 (61.2%) were male. Among the patients admitted to the ICU, 557 (82.2%) survived and 121 (17.8%) died. Besides, 565 participants (79.4%) were admitted to the ICU for surgical reasons and the rest were admitted due to medical reasons. The patients were followed up for 7884 days. The median and the 25th and 75th percentiles (first and third quartiles) of these days were 6.[4, 11] The majority of the patients stayed in the ICU for four days (mode=4). The baseline characteristics of the patients are presented in Table 1. Indeed, the cumulative incidence of the two outcomes has been depicted in Figure 1. According to the function, the length of ICU stay increased rapidly in the first few days of ICU stay, but decreased gradually over the next days. The results of univariate competing risks regression showed that when death was the event of interest, age (SHR=1.02; 95% CI: 1.01-1.03), total days of CVC (SHR=1.03; 95% CI: 1.02-1.04) and mechanical ventilation use (SHR=1.03; 95% CI: 1.02-1.04), and type of ICU (medical-surgical compared to trauma) (SHR=0.51; 95% CI: 0.35-0.74) decreased the risk of ICU death. As such, increased age and duration of CVC and mechanical ventilation use significantly increased the risk of death. This implied that trauma patients were

Table 1: Baseline characteristics of the patients (n=712)

Variables	Mean±SE	n (%)
Mechanical ventilation days	4.8±0.3	-
Central venous catheter days	5.9±0.3	-
Urinary catheter days	10.0±0.4	-
Sex		
Male	-	436 (61.2)
Female		276 (38.8)
Type of ICU admission		
Medical-surgical	-	642 (90.0)
Surgical		70 (10.0)

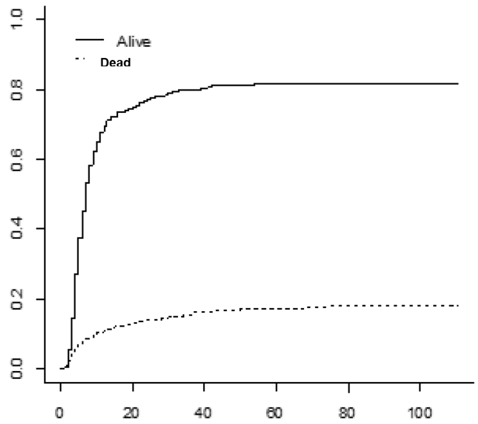

Figure 1: The cumulative incidence of the two outcomes using the Kaplan–Meier estimate (1-KM)

less likely than medical/surgical ones to be discharged from ICU, resulting in a longer ICU stay. Considering the type of ICU (SHR=1.40; 95% CI: 1.14-1.71), the patients admitted to the ICU due to surgical reasons were more likely to be discharged from this unit in comparison to those hospitalized for non-surgical or any other medical reasons (Table 2).

In the multiple competing risks model, when death was considered as the event of interest, age (SHR=1.02; 95% CI: 1.01-1.03; P=0.001), total days of CVC (SHR=1.03; 95% CI: 1.01-1.05; P=0.002) and mechanical ventilation use (SHR=1.26; 95% CI: 1.09-1.44; P=0.001) increased the risk of ICU death and decreased the length of ICU stay, especially among female patients (SHR=1.52; 95% CI: 1.06-2.18; P=0.020). However, admission type (medical compared to surgical) (SHR=0.61; 95% CI: 0.40-0.94; p=0.025) was displayed to reduce the risk of death and increase the likelihood of remission and discharge.

When discharge was considered as the event of interest in the multiple competing risks model, age (SHR=0.99; 95% CI: 0.98-0.99; P=0.001), total days of CVC (SHR=0.96; 95% CI: 0.95-0.98; P=0.001) and mechanical ventilation use (SHR=0.92; 95% CI: 0.89-0.94; P=0.001) reduced the risk of discharge through increasing the length of ICU stay. Moreover, the risk of ICU discharge was lower in females than in males (SHR=0.84; 95% CI: 0.71-0.99; P=0.045) as well as among the patients who were hospitalized due to trauma (medical-surgical compared to trauma; SHR=0.41; 95% CI: 0.29-0.57; P=0.001) in comparison to those admitted due to surgical reasons (medical compared to surgical; SHR=1.46; 95% CI: 1.18-1.81; P=0.001) (Table 3 and Figure 2).

Discussion

The present study aimed to identify the factors associated with death and discharge in ICU patients using a specific statistical analysis. In the competing risks model, when death was the event of interest, age and total days of CVC and mechanical ventilation use were shown to increase the risk of ICU death, especially among female patients. However, the type of ICU (medical or surgical) was shown to reduce the risk of ICU death. In other words, the risk of death was lower in the patients admitted to

Table 2: Univariate analysis of the relationship between the study factors and death/discharge

Variables	Competing risks	
	Discharge SHR (95%CI)	Death SHR (95% CI)
Age (years)	0.99 (0.98-0.99)**	1.02 (1.01-1.03)**
Sex (male to female)	0.88 (0.75-1.04)	1.35 (0.95-1.93)
ICU (medical-surgical compared to trauma)	0.63 (0.47-0.84)*	0.46 (0.20-1.05)
Admission type (medical compared to surgical)	1.40 (1.14-1.71)**	0.51 (0.35-0.74)**
Number of beds	0.99 (0.96-1.01)	0.99 (0.94-1.05)
Mechanical ventilation days	0.91 (0.89-0.93)**	1.03 (1.02-1.04)**
Central venous catheter days	0.95 (0.93-0.96)**	1.03 (1.02-1.04)**

**P<0.01, *P<0.05. SHR, sub-distribution hazard ratio

Table 3: Multivariate analysis of the relationship between the study factors and death/discharge

Variables	Competing risks	
	Discharge SHR (95%CI)	Death SHR (95% CI)
Age (years)	1.02 (1.01-1.03)**	0.99 (0.98-0.99)**
Sex (male to female)	1.52 (1.06-2.18)*	0.84 (0.71-0.99) *
ICU (medical-surgical compared to trauma)	0.41 (0.29-0.57)**	-
Admission type (medical-surgical)	1.46 (1.18-1.81)**	0.61 (0.40-0.94)*
Mechanical ventilation days	0.92 (0.89-0.94)**	1.26 (1.09-1.44)**
Central venous catheter days	0.96 (0.95-0.98)**	1.03 (1.01-1.05)**

**P<0.01, *P<0.05. SHR, sub-distribution hazard ratio

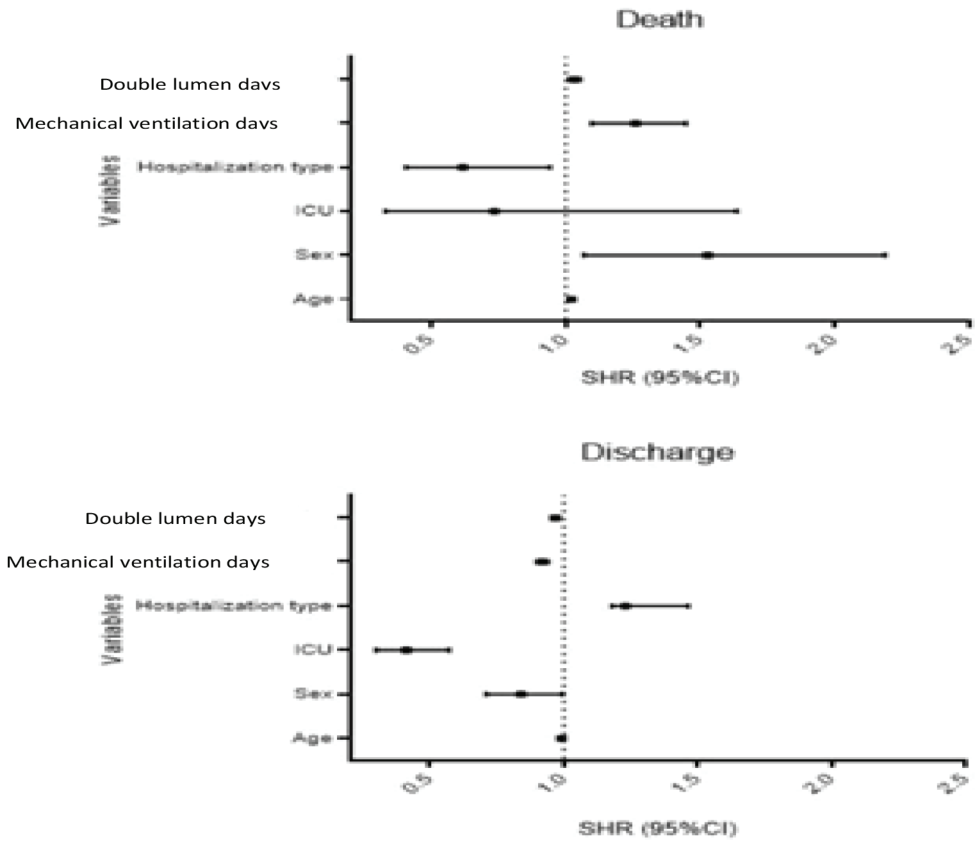

Figure 2: Sub-distribution hazard ratios (95% CI); death and discharge were the events of interest.

ICU due to surgical reasons. This was in accordance with the results of the study conducted by Wolkewitz et al., which demonstrated that nasogastric tube and mechanical ventilation use increased the risk of death, especially among females.[14] These findings were also supported by those of the studies conducted by Deslandes et al. (2010) and Wolkewitz et al. (2008).[11, 15] In the same vein, Safdar et al. carried out a systematic review on the clinical and economic outcomes of ventilator-associated pneumonia and revealed that the patients who were on mechanical ventilation for more than 48 hours were two times more likely to develop pneumonia compared to those who had not received mechanical ventilation.[16] The use of ventilation may lead to an increase in the incidence of pneumonia and infections, ultimately increasing the death rate among the patients admitted to ICU. The use of ventilation was also identified as one of the risk factors for increase in ICU death in the present study. Wong et al. used logistic regression analysis and proposed that older age and female gender were the independent risk factors for the length of ICU stay. These results were not consistent with those of the present investigation, which might be due to the utilization of different statistical methods.[17] Yet, it can be concluded that increased age was associated with the increased risk of ICU death.[18]

When discharge was considered as the event of interest in the competing risks model, age and total days of double-lumen and mechanical ventilation use reduced the risk of ICU discharge, leading to an elevated length of ICU stay. The risk of ICU discharge was lower in females than in male patients as well as among the patients who were hospitalized for trauma in comparison to those admitted due to surgical reasons. These findings were in compliance with the clinical evidence indicating that aging is associated with lower physical performance and development of many diseases, especially chronic disorders. Overall, it can be concluded that older age was associated with increased length of ICU stay.[18] Furthermore, the use of CVC and mechanical ventilation was shown to increase the length of stay and reduce the discharge rate through increasing the infection transmission inside the body organs. Sousa et al. evaluated the factors associated with ICU death and concluded that mechanical ventilation increased the rate of death due to nosocomial infections, which was in agreement with the current study findings.[19]

According to the cumulative incidence of the two outcomes (i.e. death and discharge), the rapid elevation of the patients' survival rates was due to the high rate of ICU discharge during the first days of ICU stay and that a few patients experienced prolonged ICU stay leading to death. However, time-to-discharge and time-to-death displayed different patterns, which was inconsistent with the results obtained by Ghorbani et al. They found that death rate followed a rapidly increasing trend during the first days of ICU stay and that a few patients were finally discharged from ICU.[20]

Strengths and Limitations

The relatively large sample size and long study period were some strong points of the current study. In addition, making use of a specific statistical analysis and competing risks method contributed to more precise identification of the factors related to ICU death and discharge. Nonetheless, the casual relationships could not be measured due to the retrospective nature of the study. Besides, this study was exclusively conducted on ICU patients. Thus, the results cannot be generalized to the entire hospitalized patients. Finally, since repeated measures analysis was not used in this study, time-dependent variables could not be measured.

Conclusion

According to the study results, the factors associated with ICU death and discharge were age, CVC use, and mechanical ventilation use. These factors were shown to reduce the risk of ICU discharge and increase the risk of ICU death. Furthermore, our findings indicated that the competing risk model was appropriate in evaluating the predictive factors associated with the occurrence of death and discharge in patients hospitalized in ICUs. Hence, this model could play an important role in managers' and clinicians' decision-making and improvement of the standard of care in ICUs.

Recommendations

The variables in future research are suggested to be investigated over time in a prospective cohort. The results also suggested that clinical and demographic factors were good predictors of ICU death and discharge.

Author contributions

Z. M gathering data, analysis and retained. H. G developed the idea and contributed to data analysis and critically reviewed the manuscript. M. G contributed to data analysis and critically reviewed the manuscript. F. Z helped to critically review the manuscript. All authors of this paper have read and approved the final version submitted.

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