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Prolonged hospitalization in intensive care unit; contributing factors and impact on mortality

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ABSTRACT

Aims: Prolonged stay in the intensive care unit (ICU) is a significant problem. It contributes to increased costs, scarcity of resources, morbidity, and mortality. This study aims to investigate the factors contributing to prolonged ICU stay and its association with mortality.

Methods: We retrospectively analysed 312 patients who stayed in the ICU between January 2020 and September 2023. Patients were divided into 2 groups according to the days of ICU stay: 14 days or more (Group 1) and 30 days or more (Group 2). The effects of APACHE II, SOFA, GCS, age, gender, duration and reason for hospitalization, mechanical ventilation type and duration, renal replacement therapy, tracheotomy, blood transfusion, procalcitonin and acute phase reactants on the length of stay in the ICU were analyzed.

Results: A total of 299 patients were enrolled in the study. There were 112 patients who stayed in ICU for longer than 14 days (Group 1) and 187 patients who stayed for longer than 30 days (Group 2). The mean age of Group 1 was 68.6 years and the mean age of Group 2 was 70.9 years. In Group 1, male gender predominated with 62.5%, and in Group 2, it was 56.7%. Among the patients, 29.4% were hospitalized in the ICU for surgical reasons and 70.6% for non-surgical reasons. There were statistically significant differences between the groups regarding GCS, SOFA scores and PaO_2, duration of mechanical ventilation, mechanical ventilation method, ICU mortality, renal-replacement therapy, tracheostomy status, and transfusion status ($p<0.05$). APACHE, expected mortality, lactate, procalcitonin, albumin, pH, $PaCO_2$, HCO_3^-, and GFR, the reasons for ICU admission, comorbidities, and the existence of any infection were not significantly different between the groups.

Conclusion: Age, MV duration, and SOFA score were found to be associated with both prolonged ICU stay and mortality. Regardless of mortality, there was a significant difference between the two groups in terms of GCS, tracheostomy, and the need for RRT.

Keywords: Intensive care unit, length of stay, mortality

INTRODUCTION

Intensive care units (ICU) are specialized and advanced medical care units for critically ill patients. Providing that patients receive care in these units as indicated and as long as necessary plays an essential role in the efficient utilization of the available inpatient bed potential. The length of hospitalization in the ICU has been extending in recent years with the increase in the elderly population and the use of advanced treatment modalities. Length of stay (LOS) in intensive care unit is used as a measurement benchmark to ensure efficient use of health resources and to reduce costs.[1]

The type of intensive care unit and the patient profile results in different definitions of prolonged stays. Therefore, there is no complete consensus on the LOS. Despite the differences in definitions, an intensive care stay longer than 14 days has been associated with an increased risk of infection and costs, the duration of hospitalization before intensive care, age, and severity of the disease in different studies.[2-6]

Various studies have indicated that as little as 4-11% of patients in the ICU are hospitalized for prolonged periods. Yet, this constitutes the majority of intensive care unit bed occupancy.[7,8]

Several studies have investigated the relationship between various factors and LOS in the ICU, most of which focused on specific populations or uniform ICUs.[9,10] In our study, 3rd level 4 ICU hospitalizations were analyzed.

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These were the Internal Medicine ICU, Neurology ICU, and General ICU where postoperative patients are followed up.

Identifying the associated factors of prolonged ICU stays has become a priority for clinicians, hospital administrations, and healthcare policy, as it allows early identification of these patients.

We believe that defining common criteria for different patient populations is important for standardisation. We hypothesised that ICU scoring systems, patients' comorbidities, renal function, inflammatory markers and blood gas parameters may predict prolonged hospital stay. Our primary aim was to investigate the role of these factors in predicting prolonged hospital stay. Our secondary aim was to evaluate the predictive factors on mortality during prolonged hospitalisation.

METHODS

Following the approval of the Giresun Training and Research Hospital Ethics Committee (Date: 27.12.2023, Decision No: 18.12.2023/19), patients who were hospitalized for more than 14 days for the last 3 years in a total of 48 beds of 4 3rd-Level ICU Units of a Giresun Training and Research Hospital were retrospectively screened. Data were mainly obtained from 2 ICUs with 24 beds where an attending anesthesiologist was available 24 hours a day and postoperative patients were admitted. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

We identified 312 patients who had been in intensive for more than 14 days from the hospital records. Patients were divided into 2 groups according to the days of ICU stay: 14 days or more (Group 1) and 30 days or more (Group 2). Age, gender, reasons for hospitalization (surgical, non-surgical), length of ICU stay, comorbidities, mechanical ventilator support (invasive, noninvasive), mechanical ventilation duration (21 days and more). Sequential Organ Failure Assessment (SOFA) score, Glasgow coma scale (GCS), Acute Physiology and Chronic Health Evaluation (APACHE) II score, expected mortality, glomerular filtration rate (GFR), CRP, procalcitonin, albumin, Renal Replacement Therapy (RRT) and blood gas parameters such as pH, PaO_2, $PaCO_2$, HCO_3^-, lactate, and culture positive current infections were retrospectively analyzed using electronic patient files and survival status of the patients were recorded.

The comorbidities of the patients at the time of admission were classified and recorded as cardiovascular system diseases (CVD), respiratory system diseases, neurological diseases, diabetes, and chronic renal failure (CRF).

Statistical Analysis

Statistical analyses were performed using IBM SPSS v23. Normality analyses of quantitative data were performed using the Kolmogorov-Smirnov test. Comparison of normally distributed data was performed using the independent samples t-test, and comparison of non-normally distributed data was performed using the Mann-Whitney U test. Comparison of qualitative data was performed using the Pearson chi-square test. Univariate and multivariate logistic regression analyses were performed to identify predictors of mortality. Data are presented as n (%) and mean (95% CI). Statistical significance was accepted as $p<0.05$.

RESULTS

The study was completed with 299 patients, 13 patients were excluded from the study due to inaccessibility of all data. Long stays accounted for 7.5% of total ICU admissions. Here were 112 patients hospitalized longer than 14 days (Group 1) and 187 patients hospitalized longer than 30 days (Group 2) (**Figure**). The mean age of Group 1 was 68.6 years and the mean age of Group 2 was 70.9 years. The male gender predominated in Group 1 with 62.5% and in Group 2 with 56.7% (**Table 1**). Mortality was 23.2% in Group 1 and 52.4% in Group 2, and there was a significant difference between the two groups ($p<0.001$) (**Table 1**) Statistically significant difference in SOFA scores between groups. SOFA score was 5 in Group 1 and 7 in Group 2 ($p<0.001$) (**Table 2**). In the regression analysis to evaluate the predictors of mortality, age ($p=0.001$), SOFA score ($p=0.002$), and MV duration ($p<0.001$) were found to be the most important predictors (**Table 3**).

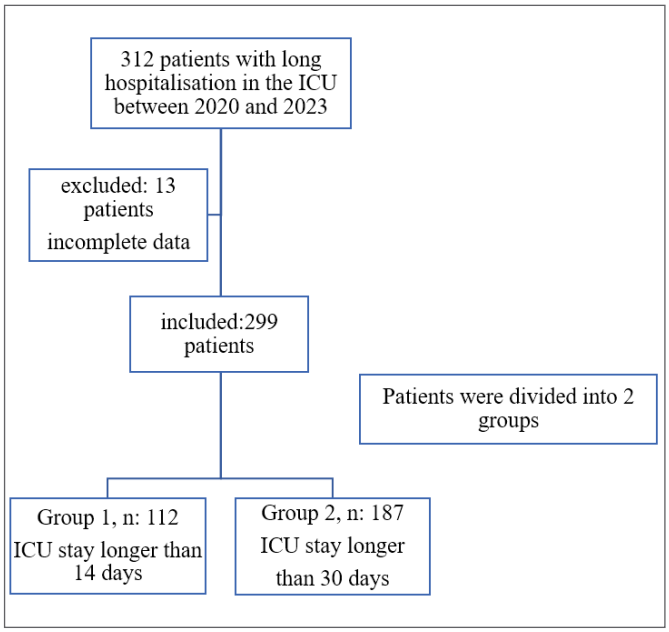

Figure. Flow chart
ICU: Intensive care unit

Table 1. Demographic data and clinical characteristics of the patients and groups

	Grup 1(n%)*	Grup 2(n%)*	p
Sex			0.323
Male	70 (62.5)	106 (56.7)	
Female	42 (37.5)	81 (43.3)	
Case of ICU admission			0.065
Surgical	40 (35.7)	48 (25.7)	
Non-surgical	72 (64.3)	139 (74.3)	
Comorbidity			0.433
-	11 (9.8)	24 (12.8)	
+	101 (90.2)	163 (87.2)	
Cardiovascular diseases			0.865
-	45 (40.2)	77 (41.2)	
+	67 (59.8)	110 (58.8)	
Neurological diseases			0.887
-	90 (80.4)	149 (79.7)	
+	22 (19.6)	38 (20.3)	
Respiratory system diseases			0.635
-	94 (83.9)	149 (79.7)	
+	18 (16.1)	38 (20.3)	
Diabetes mellitus			0.925
-	101 (90.2)	168 (89.8)	
+	11 (9.8)	19 (10.2)	
Chronic renal failure			0.060
-	109 (97.3)	172 (92)	
+	3 (2.7)	15 (8)	
MV duration			<0.001
>21	25 (22.3)	71 (38)	
<21	43(38.4)	95(50.8)	
MV requirement			<0.001
none	44 (39.3)	21 (11.2)	
NIMV	20 (17.9)	20 (10.7)	
IMV	48 (42.9)	146 (78.1)	
Mortality			<0.001
+	26 (23.2)	98 (52.4)	
-	86 (76.8)	89 (47.6)	
Tracheotomy			<0.001
+	11 (9.8)	51 (27.3)	
-	101 (90.2)	136 (72.7)	
RRT			0.031
+	7 (6.3)	27 (14.4)	
-	105 (93.8)	160 (85.6)	
Transfusion			<0.001
+	40 (35.7)	117 (62.6)	
-	72 (64.3)	70 (37.4)	
Infection			0.577
+	29 (25.9)	54 (28.9)	
-	83 (74.1)	133 (71.1)	

*n (%), ICU: Intensive care unit, MV: Mechanical ventilation, NIMV; Noninvasive mechanical ventilation, IMV; Invasive mechanical ventilation, RRT: Renal replacement therapy

The proportion of patients with more than 21 days of mechanical ventilation (MV) was 22.3% in Group 1 and 38% in Group 2. Patients with MV duration below 21 days were 38.4% in Group 1 and 50.8% in Group 2. There was a significant difference between the two groups. (p<0.001) (**Table 1**). Patients not receiving mechanical ventilator care was 39.3% in Group 1, which was significantly higher than in Group 2. (p<0.001) (**Table 1**). The need for tracheotomy, RRT, and blood transfusion was significantly different between the groups. The presence of tracheotomy in Group 2 was significantly higher at 27.3%. (p<0.001) (**Table 1**). The requirement for RRT was 14.4% significantly higher in Group 2 (p=0.03). The need for blood transfusion was significantly higher in Group 2 by 62.6%. (p<0.001) (**Table 1**).

Among the patients, 29.4% were hospitalized in the ICU for surgical reasons and 70.6% for non-surgical reasons. The number of non-surgical ICU admissions was higher in both groups (**Table 1**). 64.3% in Group 1 and 74.3% in Group 2. Statistically significant difference in GCS and PO_2 between groups (**Table 2**). GCS was 11 in Group 1 and 10 in Group 2 (p=0.007). PaO_2 was 81.9 in Group 1 and 117.2 in Group 2 (p=0.007).

APACHE, expected mortality, lactate, procalcitonin, albumin, pH, $PaCO_2$, HCO_3-, and GFR were not significantly different (**Table 2**).

Comorbidities were present in 88.3% of the patients. The most common associated comorbidity causing the longest hospitalization in the ICU was found to be cardiovascular disease. The rate was 59.8% in Group 1 and 58.8% in Group 2 and there was no statistically significant difference between the two groups (**Table 1**). There was no significant difference between the groups for reasons for ICU admission, comorbidities and presence of infection.

Table 2. Patients' findings on admission

	Grup 1 (n=112)*	Grup 2 (n=187)*	p
Age	68.5 (65.9-71)	70.9 (68.3-73.4)	0.026
CRP	107.71 (86.46- 128.96)	109.56 (94.51-124.61)	0.538
GKS	11 (10-12)	10 (9-11)	0.007
SOFA	5 (4-6)	7 (6-7)	<0.001
APACHE	15 (13-16)	16 (15-18)	0.280
PDR	25.24 (21.52-28.96)	29.4 (25.92-32.89)	0.309
Laktat	1.9 (1.7-2.2)	2.8 (1.4-4.1)	0.490
Procalcitonin	4.05 (1.63-6.47)	3.52 (1.93-5.11)	0.727
Albumin	29.76 (28.62-30.9)	29.98 (28.79-31.17)	0.927
pH	7.37 (7.35-7.39)	7.38 (7.37-7.4)	0.509
PO_2	81.9 (69.6-94.1)	117.2 (101.7-132.6)	0.007
PCO_2	43.8 (41.1-46.5)	44.5 (42.3-46.7)	0.875
HCO_3	25.2 (24.1-26.3)	26.1 (25.1-27.1)	0.166
GFR	63 (57-69)	65 (60-70)	0.601

*Mean (95% CI) CRP: C -reactive protein, GCS: Glasgow Coma Scale, SOFA: Sequential Organ Failure Assessment, APACHE: Acute Physiology and Chronic Health Evaluation, PDR: Predicted Death Rate, GFR: Glomerular Filtration Ratio p<0,05:

v 3. Univariant-multivariant regression analysis between independent variables with significant results

	Univariant regression		Multivariant regression*		Multivariant regression**	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age	1.028 (1.011-1.044)	0.001	1.041 (1.015-1.068)	0.002	1.033 (1.013-1.053)	0,001
GCS	0.935 (0.886-0.986)	0.012	1.160 (1.037-1.298)	0.009	1.168 (1.058-1.289)	0,002
SOFA	1.290 (1.185-1.405)	<0.001	1.420 (1.202-1.678)	<0.001	1.402 (1.211-1.623)	<0,001
APACHE	1.033 (1.006-1.060)	0.016	0.992 (0.952-1.034)	0.712		
Albumin	0.955 (0.921-0.991)	0.014	0.972 (0.934-1.011)	0.157		
GFR	0.992 (0.985-0.999)	0.025	1.007 (0.995-1.019)	0.236		
Case of ICU admission	0.416 (0.242-0.715)	0.002	0.838 (0.413-1.701)	0.625		
MV duration	5.340 (3.457-8.248)	<0.001	4.615 (2.601-8.189)	<0.001	5.341 (3.248-8.782)	<0,001
Tracheotomy	2.780 (1.563-4.943)	<0.001	0.924 (0.408-2.093)	0.850		
RTT	3.960 (1.818-8.625)	0.001	1.664 (0.602-4.597)	0.326		
Transfusion	2.934 (1.813-4.750)	<0.001	1.467 (0.775-2.777)	0.239		

*Enter method, ** Backward: Wald method GCS: Glasgow coma scale, SOFA: Sequential organ failure assessment, APACHE: Acute pysiology and chronic health evaluation, GFR: Glomerular filtration ratio, MV: Mecanic ventilation, RRT: Renal replacement therapy

DISCUSSION

This study evaluated a group of patients with long stays in the ICU. Hospitalizations over 14 days in the ICU were compared with very prolonged hospitalizations over 30 days. Studies do not contain sufficient information on the outcomes of very long hospitalizations in the ICU. As these studies focus on a specific group of patients, they enroll a smaller number of patients.[10-12] In this study, we wanted to determine the predictive factors and their relationship with mortality in patients with prolonged ICU stays.

Most patients were being followed up in the ICU for non-surgical reasons in our study. There was a statistically significant difference between the mean ages of the two groups. The prevalence of critical illnesses in elderly patients was found to be high and the LOS in the ICU before recovery was long. Moreover, it has also been reported that prolonged ICU stay is associated with increased mortality and morbidity.[2,4,5,13,14] Our results are similar to studies indicating that advanced age is associated with prolonged hospitalization in the ICU.

The APACHE II score is an ICU scoring system used to indicate the degree of physiologic impairment. It is used to estimate mortality. However, there are different opinions that it can be used in the prediction of conditions such as ICU LOS and separation from MV. Martini et al.[4] have associated the APACHE II score with prolonged hospitalization in their studies. Conversely Suistomaa et al.[15] demonstrated that the predictive value of scoring systems such as APACHE and SOFA diminished in hospitalizations over 7 days. Schönhofer et al.[16] indicated that APACHE II did not predict mortality in prolonged hospitalizations. Several studies have argued that the APACHE II score is an indicator of success or failure in the separation of the patient from the ventilator.[17,18] There was no difference in APACHE II scores between Group 1 and Group 2 in our study. It is toughted that the predictive value of the APACHE II score decreases as the LOS ICU increases.

SOFA is a system for scoring organ failure and dysfunction. There is evidence that the SOFA score in the ICU is a good predictor of patient's separation from mechanical ventilation, LOS, and mortality. Antonelli et al.[19] reported that it may also be useful in identifying patients with a poor prognosis as well as patients who are likely to stay in the ICU for a long time. In our study, we found SOFA scores significantly different between the two long hospitalization groups. In ICU over 30 days, the SOFA score was higher than the other group. We suggest that the SOFA score is predictive for prolonged hospitalizations and remains predictive as the length of hospitalization increases.

The GCS used to assess the level of consciousness, has been reported to predict the LOS in the ICU and mortality in studies conducted on specific groups.[20-24] Despite the heterogeneous group in our study, GCS was significantly lower in very longstay group.

Previous studies have shown that prolonged MV duration leads to prolonged ICU hospitalisation.[2,5,13] Higgins et al.[2] associated prolonged MV duration with infection and poor prognosis. In our study, there was a significant difference between the two groups in terms of the number of patients not on MV. In group 2, the number of patients not on MV was significantly lower with 11.2%. In addition, the number of patients followed up in MV for more than 21 days was 38% and the number of patients followed up in MV for less than 21 days was 50.8% in Group 2, which was significantly higher than in Group 1.

When we examined the method of MV, the number of patients followed up with invasive mechanical ventilation was higher in both groups. The number of patients who did not receive invasive or noninvasive MV treatment was 39.3% in the group of patients hospitalized longer than 14 days. In the group hospitalized longer than 30 days, it was 11.2%. Regarding the MV method, there was

a significant difference between the two groups. From a clinical point of view, it is not surprising that the LOS of patients undergoing invasive MV is prolonged as this period is prolonged.

In our study, the number of tracheotomies was significantly higher in patients who stayed longer than 30 days, similar to other studies.[6,25]

Several studies have associated the prevalence of infection with prolonged hospitalization in the ICU.[3,26] In this study, we found no difference in the prevalence of infection, procalcitonin, and CRP values between the groups. We believe that this is because of the comparison of the two long hospitalization groups. The predictive value of the prevalence of infection may be decreasing beyond 14 days. We suggest that this finding should be supported by more studies.

The need for RRT has been associated with LOS in the ICU in several studies.[4,5,13] We recorded both the need for RRT and the GFR of the patients during our study. We did not find any difference between the GFR of the patients on the day of admission to the ICU. However, we determined that the need for RRT increased with the number of days. In a multinational study of the development of AKI in critically ill patients, sepsis, medication use and MV were found to be predictors of the development of AKI.27 In our study, the need for RRT during prolonged hospitalisation may be related to prolonged mechanical ventilation, sepsis and antibiotherapy.

Nozawa et al.[28] reported that cardiac dysfunction, low ejection fraction, left ventricular dysfunction, cardiogenic shock and cardiac surgery were among the factors that had a negative impact on removing patients from MV. Several studies have shown that CVS diseases increase the risk of long hospitalization in the ICU.[29,30] Similarly, in our study, we also observed a high number of patients with additional CVS diseases other than the reason for ICU admission. Those with CVS disease constituted 59.8% of Group 1 and 58.8% of Group 2 second place followed those with neurological diseases and third place was taken by those with respiratory system diseases.

The mortality rate was 52.4% in Group 2 and was significantly higher than in Group 1. Friedric et al.[13] reported a mortality rate of 42% in patients with very long hospitalization in the ICU. This rate varies between 40-53% in studies investigating hospitalizations in the ICU over 28-30 days.[4,5] The mortality rate is similar in our study.

When multivariate logistic regression analysis was used, age, SOFA score, and MV duration were identified as predictors of mortality. There are studies in which age and MV duration were identified as predictors of mortality. Friedrich et al.[13] found age, ventilation for more than 90 days, dialysis, and inotrope support for more than a minimum of 3 days as predictors of mortality. In contrast, Laupland et al.[7] found advanced age and previous comorbidities as predictors of mortality. In our study, SOFA score was found to be a predictor for both prolonged ICU hospitalisation and mortality. We believe that this should be supported by multicentre studies with larger patient samples.

Multivariate regression analysis revealed an inverse association between GCS and mortality. Mortality increased as the GCS increased. We think that this result is because trauma patients were also monitored in a mixed ICU and early mortality of patients with very low GCS.

Limitations

This study is single-centre. Although it includes ICUs with different patient populations, it only reflects our results. The reasons for long ICU stays may vary in different regions due to many factors, such as the number of beds, lack of palliative care centres, management of non-resuscitated patients. Multicentre studies are needed to understand the reasons for long ICU stays.

CONCLUSION

Age, MV duration and SOFA score were associated with both prolonged ICU stay and mortality. Independent of mortality, GCS, need for tracheotomy and RRT were significantly different between the two groups. Patients who stayed in the ICU for more than 30 days had higher mortality rates. Despite the differences in opinion regarding the SOFA score, we concluded that the SOFA score may be predictive of prolonged ICU stays. We think that more studies are needed to better define the clinical outcomes.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study protocol was approved by the Giresun Training and Research Hospital Ethics Committee (Date: 27.12.2023, Decision No: 18.12.2023/19).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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