

## The relationship between the PRE-DELIRIC score and the prognosis in COVID-19 ICU patients

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### Ethics Committee Approval

The study was approved by Afyonkarahisar  
University Medical Faculty Clinical Research  
Ethics Committee (Decree no: 510, date: 2021).  
All procedures in this study involving human  
participants were performed in accordance with  
the 1964 Helsinki Declaration and its later  
amendments.

### Conflict of Interest

No conflict of interest was declared by the  
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### Abstract

**Background/Aim:** The PRE-DELIRIC score is a test to detect delirium in the intensive care unit (ICU). Delirium has been studied as a factor associated with the clinical course of patients in COVID-19 intensive care. Our study aimed to investigate the relationship between the PRE-DELIRIC score and prognosis in patients followed in the COVID-19 ICU.

**Methods:** Patients hospitalized in the COVID-19 ICU between March 2020 and May 2021 were retrospectively analyzed, and 461 patients were included in the study. The PRE-DELIRIC scores of the patients were calculated using data obtained from the hospital information system. Patients with a PRE-DELIRIC score  $\geq 50$  were considered Group 1, and those with a score  $< 50$  were considered Group 2. The groups were compared in terms of gender, Glasgow Coma Scale (GCS), Acute Physiology and Chronic Health Evaluation (APACHE II) score, Sequential Organ Failure Evaluation Score (SOFA), length of hospital stay, and mortality rates.

**Results:** Of the 461 patients included in the study, 153 were female, and 308 were male. A high PRE-DELIRIC score was determined in 157 (34.1%) patients (Group 1), while 304 patients (65.9%) had lower scores (Group 2). The hospitalization duration was 9.6 (6.7) days, and the mortality rate was 87.2% in Group 1, compared to 8.2 (6.03) days and 38.1% in Group 2, respectively. A significant difference was observed in the length of hospital stay and mortality between the groups ( $P < 0.001$ ). The rate of patients who were intubated and followed up on an invasive mechanical ventilator (MV) was 81.5% in Group 1, whereas it was 16.4% in Group 2 ( $P < 0.001$ ).

**Conclusion:** Our study found that patients with a high PRE-DELIRIC score indicating delirium had higher mortality rates and longer hospital and MV stays. Delirium is one of the factors affecting mortality in COVID-19 disease. We believe that the PRE-DELIRIC score, as one of these factors, can serve as an important prognostic test in COVID-19 ICU patients.

**Keywords:** delirium, critical care, COVID-19, mortality, PRE-DELIRIC score

## Introduction

Delirium is defined as the impairment of attention, awareness, and consciousness that develops within hours or days due to a critical illness [1]. Despite affecting over 20% of hospitalized patients, delirium is frequently overlooked [2,3].

Critically ill patients receiving treatment in the intensive care unit (ICU) are exposed to an unfavorable environment characterized by uncontrolled lighting and noise. Additionally, pain can cause agitation, sleep disruption, and delirium in these patients. Delirium is linked to detrimental clinical outcomes, including prolonged ICU stays, increased mechanical ventilation duration, and higher mortality rates [4,5]. Consequently, early identification and management of delirium are crucial. Patients who are promptly diagnosed with delirium and receive prompt treatment exhibit similar prognoses to those who do not develop delirium [6].

A study conducted in an ICU demonstrated that individuals who experienced delirium during hospitalization had an elevated risk of developing cognitive impairment or psychiatric issues after discharge [7]. This condition, known as post-intensive care syndrome, adversely affects patients' quality of life [8]. To mitigate this situation, early mobilization, minimizing sedation, and providing emotional and psychiatric support are crucial [9].

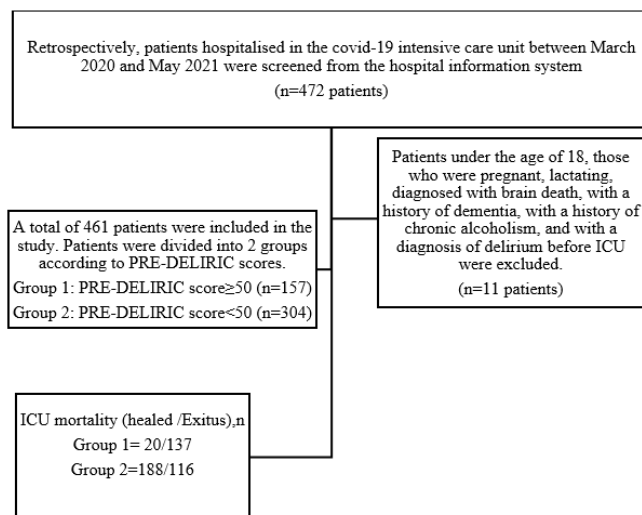
SARS-CoV-2 infection can potentially invade the central nervous system, leading to delirium and neurological symptoms, thereby increasing the risk of delirium in patients. Factors such as sedation, immobilization, social isolation, mechanical ventilation, and organ failure significantly worsen the prognosis [10]. Furthermore, patients who experience delirium in the ICU may continue to experience neuropsychological disorders even after discharge [11].

The PRE-DELIRIC score, introduced in 2012, serves as a predictive test for delirium in ICU patients [12]. Our study aimed to examine the prognostic impact of the PRE-DELIRIC score, specifically in COVID-19 ICU patients, where it is utilized as a delirium prediction tool.

## Materials and methods

This study was retrospectively conducted in the COVID-19 ICU between March 2020 and May 2021. Approval for the study was obtained from the Clinical Research Ethics Committee of the Afyon Health Sciences University Medical Faculty, in accordance with the Ministry of Health (Decree no: 510, date: 2021). Patients under the age of 18, pregnant or lactating individuals, those diagnosed with brain death, individuals with a history of dementia or chronic alcoholism, and those already diagnosed with delirium before ICU admission were excluded from the study. Figure 1 shows the flow chart that includes patients in the study. The following data were recorded for all patients: age, gender, duration of hospitalization, Glasgow Coma Scale (GCS) score, Sequential Organ Failure Evaluation (SOFA) score, and Acute Physiology and Chronic Health Evaluation (APACHE II) score on the first day of ICU admission, pre-delirium score, and prognosis.

Figure 1: Flow chart shows the patient selection process



The study enrolled patients with severe pneumonia associated with COVID-19, confirmed by a positive RT-PCR test for SARS-CoV-2. Additionally, patients with a negative RT-PCR test who were classified as suspected COVID-19 cases according to the diagnosis, treatment, and follow-up guidelines of the Ministry of Health of the Republic of Turkey were also included.

The PRE-DELIRIC scoring system evaluates various factors, including age, APACHE II score, blood urea level, morphine usage, sedation, metabolic acidosis, coma status, infection, planned/emergency ICU admission, and reason for hospitalization. A score is obtained based on these criteria, as shown in Table 1. The PRE-DELIRIC score has been validated, and it has been reported that a score of  $\geq 50$  is associated with a high incidence of delirium [12]. For this study, we adopted the same cut-off value. Patients with a PRE-DELIRIC score of  $\geq 50$  were classified as the high delirium risk group (Group 1), while those with a score of  $< 50$  were classified as the low delirium risk group (Group 2). The study compared gender, GCS score, Sequential Organ Failure Assessment (SOFA) score, duration of hospital stay, and mortality rates between the two groups.

Table 1: PRE-DELIRIC scoring system [12]

Parameters
+ 0.04 x age
+ 0.06 x APACHE II score
+ 0 no coma or 0.55 drug-associated coma or 2.70 different comas or 2.84 coma combinations
+ 0 for surgical patients or 0.31 for medical patients 1.13 for trauma patients or 1.38 for neurology/neurosurgery patients
+ 1.05 for infection
+ 0.29 for metabolic acidosis
+ 0 no morphine use or 0.41 0.01-7.1 mg/24 h for morphine or 0.13 7.2-18.6 mg/24 h for morphine or 0.51 > 8.6 mg/24 h for morphine use
+ 1.39 for use of sedatives
+ 0.03 x urea concentration (mmol/L)
+ 0.40 for urgent admission

APACHE II: Acute Physiology and Chronic Health Assessment

### Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 20. The data were presented as percentages, median with interquartile range (IQR), and mean, standard deviation (SD) values. The normal distribution of variables was assessed through visual examination (histogram) and analytical methods (Kolmogorov-Smirnov test). Continuous variables were compared using either Student's t-test or the Mann-Whitney U test, while categorical variables were compared using the chi-

square test. Statistical significance was defined as *P*-values less than 0.05.

## Results

Four-hundred-sixty-one patients who were followed up in the COVID-19 ICU between March 2020 and May 2021 were included in the study. Among them, 157 patients (31.2%) were in Group 1, while 304 patients (60.8%) were in Group 2. There was no statistically significant difference between the groups regarding gender (*P*=0.817). The median age of Group 1 was significantly higher than that of Group 2 (*P*=0.011). The hospitalization duration was 9.6 (6.7) days in Group 1 and 8.2 (6.03) days in Group 2. The duration of hospital stay in the ICU was significantly higher in Group 1 than in Group 2 (*P*<0.001). When examining intensive care mortality, the mortality rate was 87.2% in Group 1 and 38.1% in Group 2 (*P*<0.001). In Group 1, 81.5% of the patients were intubated and followed up on an invasive mechanical ventilator (MV), whereas, in Group 2, this rate was 16.4% (*P*<0.001) (Table 2).

Table 2: Demographic data, intensive care mortality and distribution of intensive care unit length of stay according to PRE-DELIRIC scores of the patients

	Group 1 (n=157)	Group 2 (n=304)	P-value
Gender (Female/Male), n	51/106	102/202	0.817*
Age (Year), median;IQR	70;14	67;15	0.011#
ICU mortality (healed /Exitus),n	20/137	188/116	<0.001*
ICU length of stay (days), median;IQR	9;9	7;7	<0.001#
Invasive MV,yes/no, n	128/29	50/204	<0.001*

Group 1: PRE-DELIRIC score ≥50, Group 2: PRE-DELIRIC score <50, ICU: Intensive care, MV: mechanical ventilation, \* Chi-Square, #Mann-Whitney U, Values are given as number, median; IQR (interquartile range)

The distribution of comorbidities was analyzed in relation to the groups, and it was observed that the incidence of hypertension (HT) in Group 1 was higher than in Group 2 (*P*=0.004) (Table 3).

Table 3: Distribution of additional diseases of patients according to groups

	Group 1 (n=157)	Group 2 (n=304)	P-value*
Hypertension, yes/no, n	88/69	128/176	0.004
DM, yes/no, n	59/98	89/215	0.070
CAD, yes/no, n	46/111	67/237	0.086
Lung disease, yes/no, n	30/127	69/235	0.374
CRF, yes/no, n	10/147	28/276	0.293
Liver disease, yes/no, n	5/152	5/299	0.282
Malignancy, yes/no, n	16/141	41/263	0.308

Group 1: PRE-DELIRIC score ≥50, Group 2: PRE-DELIRIC score <50, DM: Diabetes Mellitus, CAD: Coronary Artery Disease, CRF: Chronic renal failure, \* Chi-Square

The SOFA and APACHE II scores were higher in Group 1 compared to Group 2 (*P*<0.001) (Table 4). The median GCS was 12 in Group 1 and 14 in Group 2, with a statistically significant difference between them (*P*<0.001) (Table 4). Analyzing all the patients who survived and died, it was observed that the PRE-DELIRIC score was lower in the patients who survived (*P*<0.001).

Table 4. Distribution of patients' GCS, SOFA and APACHE II scores according to groups

	Group 1 (n=157)	Group 2 (n=304)	P-value#
GCS	12;4	14;3	<0.001
SOFA	4;2	3;2	<0.001
APACHE II	22;7	20;6	<0.001

Group 1: PRE-DELIRIC score ≥50, Group 2: PRE-DELIRIC score <50, GCS: Glasgow Coma Scale, SOFA: Sequential Organ Failure Evaluation Score, APACHE II: Acute Physiology and Chronic Health Evaluation, # Mann-Whitney U, Values are given as number, median; IQR (Interquartile range).

## Discussion

Our study found that the PRE-DELIRIC score of patients monitored in the ICU was significantly associated with

mortality, duration of ICU stay, and the need for mechanical ventilation (MV).

The PRE-DELIRIC score was initially developed in 2012 by van der Boogaard et al. [12]. This scoring system incorporates various factors, including age, APACHE II score, blood urea level, morphine usage, sedation, metabolic acidosis, coma status, infection, planned/emergency ICU admission, and reason for hospitalization to calculate a score. The researchers found that this assessment tool is valuable for the early prediction of delirium, particularly when the PRE-DELIRIC score exceeds 50. In a subsequent study conducted by van der Boogaard et al. [13] in 2014, they further examined the PRE-DELIRIC score using a sample of 1,824 patients from ICUs in different countries. The findings indicated that the score remained effective despite variations between countries and patient groups.

Linkaitė et al. [14] conducted a study in the ICU. Their findings demonstrated that the PRE-DELIRIC score exhibited reliable predictive capability for the occurrence of delirium within 24 h of ICU admission.

Likewise, a comprehensive review of 33 studies revealed a strong association between delirium and several factors, including age, history of dementia, hypertension (HT), pre-intensive care trauma or emergency surgery, high APACHE II score, mechanical ventilation, metabolic acidosis, and coma [15]. Importantly, these very parameters are incorporated into the PRE-DELIRIC scoring system.

A study conducted in South Korea explored the risk factors associated with the occurrence of delirium. The analysis revealed several significant correlations, including age, mechanical ventilation, APACHE II score, presence of comorbidities, patient restraint applications, and the education level of the patients [16]. These factors were found to be closely linked to the likelihood of developing delirium.

Delirium affects approximately one-third of patients admitted to the ICU. According to a recent meta-analysis, the prevalence of delirium among ICU patients was found to be 31% [17]. Studies have shown that delirium occurs in 60% to 80% of mechanically ventilated patients and in 20% to 50% of non-ventilated patients [18]. In the context of COVID-19, the incidence of delirium in ICU patients ranges from 65% to 80% [19]. It is worth noting that the risk of delirium may be amplified by the restrictions imposed due to COVID-19. The reduced number of nurses in the ICU and the increased workload can limit access to patient rooms, resulting in decreased screening for delirium. Additionally, the greater need for sedation and the occasional use of muscle relaxants due to the frequent application of the prone position may contribute to the occurrence of delirium.

A point prevalence survey conducted in COVID-19 ICUs revealed a low level of implementation of the ABCDEF bundle, which includes regular delirium assessment, in COVID-19 patients [20]. The ABCDEF package is an integral part of multidisciplinary care in the ICU and comprises the assessment of pain (A), spontaneous breathing trials (B), choice of sedation (C), delirium assessment (D), early mobilization (E), and family participation (F). However, several factors hindered the utilization of bundles, including changes in the ICU team

structure due to COVID-19, insufficient availability of personal protective equipment, physical constraints, heightened sedation requirements, and limited respirator supplies [21].

A meta-analysis revealed that delirium in elderly patients is associated with poor outcomes, irrespective of major confounding factors such as age, gender, comorbidities, disease severity, and baseline dementia [22]. Furthermore, Peterson et al. [23] found a significant increase in the incidence of delirium among intensive care patients aged 65 and above. In our study, patients in group 1, who had higher PRE-DELIRIC scores, also exhibited a higher average age. However, it is important to note that our study had limitations, as we did not specifically investigate the relationship between PRE-DELIRIC scores and mortality in patients over 65 years of age.

While our study did not find a relationship between PRE-DELIRIC scores and gender, a study by Ragheb reported that 70% of patients with delirium were women [19]. It is worth noting that in certain studies, being male has been identified as a risk factor for delirium [24, 25].

Delirium is a frequent occurrence in mechanically ventilated adults and has been linked to extended durations of mechanical ventilation and hospital stays [26]. In our study, we observed that the number of patients who required invasive mechanical ventilation (MV) and the duration of their stay in the ICU were higher in Group 1, consisting of individuals with a PRE-DELIRIC score of  $\geq 50$ .

In a study examining psychiatry consultations in a hospital during the COVID-19 pandemic, it was determined that 50.68% of intensive care patients were diagnosed with delirium. Additionally, delirium was identified as a strong predictor of mortality in the same study [27]. Similarly, in the study conducted by İnal et al. [28] in the ICU, patients with high PRE-DELIRIC scores exhibited higher mortality rates. Consistent with these findings, we also observed a high mortality rate among our COVID-19 ICU patients with elevated PRE-DELIRIC scores.

Previous studies have shown an increased incidence of delirium in patients with comorbid conditions [25]. While our study did not establish a relationship with other comorbidities, we did find that patients with hypertension (HT) had significantly higher PRE-DELIRIC scores.

### Limitation

Our study has several limitations. First, delirium screening was not conducted for the patients included in the study. Additionally, the PRE-DELIRIC score was calculated retrospectively, and its impact on prognosis was investigated. It is important to note that numerous factors can influence mortality in COVID-19 cases, and our study did not account for certain variables such as ferritin levels, CRP level, and Pao<sub>2</sub>/Fio<sub>2</sub> ratio in the relationship between PRE-DELIRIC score and mortality. This omission represents another limitation of our study. Future prospective studies could be conducted to address these limitations, encompassing these additional factors, for a more comprehensive analysis.

### Conclusion

Identifying parameters that can predict the clinical trajectory of COVID-19 patients is crucial for guiding appropriate treatment decisions and optimizing the utilization of

limited resources. Early recognition and management of delirium play a pivotal role in the prognosis of ICU patients. We believe that the PRE-DELIRIC score holds the potential as a valuable prognostic tool for COVID-19 patients receiving intensive care.

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