Evaluation of the PRE-DELIRIC (PREdiction of DELIRium in ICu patients) delirium prediction model in intensive care units in Turkey

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Abstract

Purpose: This methodological study was aimed to the Turkish adaptation and validation of the “PRE-DELIRIC Score” delirium prediction model in patients hospitalized in the ICU. **Method:** The study was conducted with patients who were treated in the ICUs of a training and research hospital between October 2019 and April 2020. The data were collected with (1) the Data Collection Form for the Descriptive Characteristics of the Subjects, (2) the PRE-DELIRIC Score, and (3) the Confusion Assessment Method for the ICU (CAM-ICU). The ROC analysis and diagnosis screening tests were used to determine the cut-off point according to the groups. The sensitivity and specificity characteristic of the score were calculated. Significance was evaluated at the $p < 0.05$ level. **Results:** The study was completed with 172 patients. A statistically significant relationship was found between the cut-off point obtained for the PRE-DELIRIC Score ($[?]7.58\%$) and the groups ($p = 0.003$). The risk of being CAM-ICU positive was 7.404 times higher in patients with a PRE-DELIRIC Score of 7.58 or more (OR:7.404; 95% CI:1.638-33.469). **Conclusion:** The PRE-DELIRIC Score was evaluated in this study and the PRE-DELIRIC Score was found to be easy to administer with reliable results.

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1. Background

Delirium is a neuropsychiatric disorder characterized by impaired consciousness, distraction, and disorganized thinking.¹ It can be seen at rates of up to 80% in intensive care patients and causes increased morbidity and mortality, prolonged duration of mechanical ventilation and intensive care unit stay, and long-term cognitive impairment.^{2,3}

Although there are certain organic reasons that lead to delirium development, there is no laboratory test to confirm delirium presence. The condition can often be overlooked when an attempt is made to diagnose the patient with clinical data.⁴ The standard methods of obtaining a general medical, psychiatric and neurological history and conducting a physical examination are required for the diagnosis. The final diagnosis is made by evaluating the findings obtained through interviews. Many different scales have been developed for the screening, diagnosis and grading of symptoms. Making a proper diagnosis requires periodic evaluation of the diagnostic criteria and knowledge of the patient's initial mental state.⁵ The most common methods used for delirium evaluation are the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)⁶ and the Intensive Care Delirium Screening Checklist.⁷ Delirium has been detected at a rate of 30-70% in intensive care patients using these measurement methods.⁸

The appropriate interventions are extremely important in preventing delirium. According to the guidelines on pain, agitation and delirium management⁹, the application of non-pharmacological methods is highly recommended for the prevention of delirium but the evidence supporting pharmacological approaches is inadequate. In addition, the implementation of such interventions takes a long time with a significant increase in the workload. Various prediction models that can help identify high-risk patients have therefore been developed.⁴ The PREdiction of DELIRium in ICu patients (PRE-DELIRIC), which is one of these models, has been validated in various intensive care units (ICU) and reported to be useful.¹⁰ This model was developed based on the results of a systematic review where delirium risk factors were investigated.¹¹ The model estimates the development of delirium within 24 hours after the patient's admission to the ICU according to the result of the calculation made by considering 10 risk factors that can cause delirium development and that are objectively and precisely defined. This model for predicting delirium risk^{4,12,13} was also used in a recent study from our country but without evaluation of the model's predictive ability for this condition.¹⁴

The purpose of this methodological study was to evaluate the usability of the "PRE-DELIRIC Score" delirium prediction model in general ICU patients.

2. Methods

This methodological study was aimed to the Turkish adaptation and validation of the "PRE-DELIRIC Score" delirium prediction model in patients hospitalized in the ICU.

The study was conducted with patients who were treated in the ICUs of a training and research hospital between October 2019 and April 2020. Patients who were hospitalized and treated for more than 24 hours in the general ICU, aged 18 years or older; without a history of chronic alcoholism, dementia or delirium; who were not pregnant or breastfeeding, had no communication problems, had a Richmond Agitation Sedation Scale (RASS) value of +4 to -2, and whose relative accepted to participate were included in the study. There were a total of 189 cases in the study. However, the study was conducted with 172 patients in the end as 8 cases had dementia, 3 had a history of delirium, 1 had a history of alcoholism, and 5 were aged under 18.

The data were collected with (1) the Data Collection Form for the Descriptive Characteristics of the Subjects, (2) the PRE-DELIRIC Score, and (3) the Confusion Assessment Method for the ICU (CAM-ICU). Data collection took place during the relevant date range by a doctor and a nurse who took part as researchers. The general data were collected in the first 24 hours. Data on the diagnostic and clinical characteristics were obtained from the patients' relatives and patient charts. Data on the clinical course were also collected

within the first 24 hours. The Data Collection Form for the Descriptive Characteristics of the Subjects was created by the researchers after reviewing the relevant literature.^{9,15,16,17} The form includes a total of 19 questions regarding the patient socio-demographic data and clinical characteristics.

2.1 The PRE-DELIRIC Score

The PRE-DELIRIC Scoring System developed by van den Boogaard et al. (2012) considers the age, APACHE II score, blood urea level, amount of morphine used, sedation use, metabolic acidosis, coma state, infection, planned/emergency intensive care admission, and the reason for hospitalization to provide a score.¹⁰ A pre-delirium score ≥ 50 is reported to be associated with a high incidence of delirium. The scoring system is used within the first 24 hours after the patient is admitted to the ICU. The blood results were obtained from the patient's medical chart by the researchers and recorded in the questionnaire. The PRE-DELIRIC Score was determined within the first 24 hours after the patient's ICU admission in this study.

After the scale was independently translated into Turkish by three translators consisting of an English teacher, an English linguist, and a medical doctor proficient in English, the translators agreed on a common text in terms of the Turkish appropriateness and comprehensibility of the translations. The scale thus obtained was then backtranslated into English by three English teachers. There was no meaning change in the backtranslated scale when compared to the original English document and the form was finalized after preliminary administration to 5 intensive care nurses and 10 patients. The PRE-DELIRIC Scoring System does not include intercultural differences as it is based on objective criteria and not on patient statements or interpretation. The risk factors including these objective data have the same meaning in all languages and cultures. Determining content validity by obtaining an expert opinion was therefore not required for the PRE-DELIRIC Score.

2.2. CAM-ICU

This scale is in common use and is reported to provide the best compliance with DSM IV criteria [16]. It was developed by Ely et al. (2001)⁶ The Turkish reliability and validity study was performed by Akıncı et al. (2005) and the scale was found to have an acceptable level of sensitivity (65-69%), together with perfect specificity (97%) and reliability (Kappa=0.96)¹⁸ The scale consists of four subcategories consisting of changes in the patient's state of consciousness, attention disorder, impaired thought process, and the level of consciousness. Sub-categories are not taken into account and a conclusion is reached as the "presence" or "absence" of delirium according to the answers to the scale questions. All the first and second category answers must be negative, and one of the third and fourth categories must be present in order to talk of the "presence" of delirium. This scale can be applied to all intensive care patients aged over 18 who are not comatose and who can communicate. It is recommended to complete the scale within 24 hours after the patient's ICU admission. A repeat evaluation is performed during the day if there is any change in the patient's state. Otherwise evaluation once a day is appropriate. CAM-ICU was measured within 24 hours after the patient's admission to ICU in this study.

The NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) software program was used for the statistical analysis. The mean, standard deviation, median, frequency, ratio, minimum and maximum were used while evaluating the study data and the compliance of the data with a normal distribution were tested with the Shapiro-Wilk test and graphical evaluations. "Student's t-test" was used for comparisons of normally distributed variables between the two groups and the "Mann-Whitney U" test for comparisons of variables without a normal distribution. ROC analysis and diagnosis screening tests were used to determine the cut-off point according to the groups. The sensitivity and specificity characteristic of the score were calculated. Significance was evaluated at the $p < 0.05$ level.

Local ethics committee approval (Decision no: 2019-SBEK-08) was obtained from the institution where the study was conducted in addition to consent from the patients who were included in the study with the permission of the necessary institution. Written permission was obtained by e-mail from van den Boogaard to use the PRE-DELIRIC Score.

3. Results

The study was completed with 172 patients. The CAM-ICU measurement revealed that 90.1% (n= 155) of the patients were negative and 9.9% (n= 17) positive for delirium. The age range of the subjects was 35-94 years and the mean age was 72.94 ± 13.99 years. The mean age ($p= 0.036$) and the cerebrovascular event (CVE) incidence rate ($p= 0.036$) of the patients who were positive on CAM-ICU were statistically significantly higher than those who were negative. No statistically significant difference was found between the groups in terms of the other variables ($p>0.05$) (Table 1).

Patients who were positive on the CAM-ICU required statistically significantly more physical restriction ($p= 0.07$) and developed more pressure ulcers ($p= 0.001$) than the patients who were negative. Statistically significantly larger amounts of sedatives were required for patients who were negative on the CAM-ICU than those who were positive ($p= 0.017$). A statistically significant difference was found between the groups in terms of the form of discharge from intensive care ($p= 0.047$) and those who died were usually negative while those who were transferred were usually positive. No statistically significant difference was found between the groups in terms of the other variables ($p>0.05$) (Table 2).

The 1st PRE-DELIRIC Score of the patients who were negative on CAM-ICU was 3.9-11.9 with a mean value of 7.85 ± 1.91 . The 1st PRE-DELIRIC Score of the patients who were positive for CAM-ICU was 6.7-14.9 with a mean value of 9.04 ± 2.09 (Figure 1). A statistically significant difference was found between the 1st PRE-DELIRIC Scores of the CAM-ICU negative and positive groups ($p= 0.017$), and the scores of the positive patients were higher than the negative patients. An increase of one unit in the PRE-DELIRIC scores increased the risk of being CAM-ICU positive by 1.358 times (OR: 1.358; 95% CI: 1.047-1.761) (Table 3).

3.1. Determining the Cut-off Point for PRE-DELIRIC Scores Based on the CAM-ICU Status

A statistically significant difference was found between the 1st PRE-DELIRIC Score of the patients who were CAM-ICU negative and positive ($p= 0.017$), with the CAM-ICU positive patients having higher scores (Table 3). Based on this significance, the cut-off point for the PRE-DELIRIC Score was calculated. ROC analysis and diagnostic screening tests were used to determine this cut-off point by group. The cut-off point for the PRE-DELIRIC Score was 7.58. This PRE-DELIRIC Score cut-off value had a sensitivity of 88.24%, specificity of 49.68%, positive predictive value of 16.13%, negative predictive value of 97.47%, and accuracy of 53.49%. The area under the ROC curve was 64.9% (95% CI: 0.538-0.760) and the standard error was 5.6% ($p=0.044$) (Figure 2).

A statistically significant relationship was found between the cut-off point obtained for the PRE-DELIRIC Score ([?]7.58%) and the groups ($p= 0.003$). The risk of being CAM-ICU positive was 7.404 times higher in patients with a PRE-DELIRIC Score of 7.58 or more (OR:7.404; 95% CI:1.638-33.469). An increase of 5% or more in the PRE-DELIRIC Score had a sensitivity of 100%, a specificity of 6.45%, a positive predictive value of 10.49%, a negative predictive value of 100%, and an accuracy of 15.70%. An increase of 10% or more in the PRE-DELIRIC Score had a sensitivity of 29.41%, a specificity of 29.41%, a positive predictive value of 17.85%, a negative predictive value of 91.67%, and an accuracy of 79.65%.

4. Discussion

We investigated the usability of the PRE-DELIRIC model in intensive care, and the sensitivity of the model to predict delirium with certain physical and medical parameters when compared with the CAM-ICU, the current gold standard, in this study. The delirium development rate found (9.9%) was close to the lower limit specified in the literature. The reported delirium rate in intensive care units has quite a wide range at 10% to 80% and it is important to have a measurement that can easily detect delirium, as it is vital for the condition's follow-up, treatment and care.^{19,20,21} Delirium development is affected by many factors and its prediction and prevention will enable decreasing the rate of disorders that could lead to patient mortality and morbidity.¹⁴ Some evidence reports that delirium increases the length of the hospital stay, increases the risk of transmission of hospital infections, and puts the patient at risk of pressure ulcers and injuries.^{22,23,24}

The relevant factors in patients who develop delirium according to the CAM-ICU were found to be age,

previous CVE, being physically restrained, presence of a pressure ulcer, and the form of intensive care discharge in the current study. Delirium was found to develop more commonly in elderly patients, those under physical restraint, patients with a history of CVE, patients with pressure ulcers. (Table 1, Table 2). The predisposing factors reported to be related to delirium occurrence in the literature are similar to those found in this study.^{12,25,26} In addition, alcohol abuse, a history of dementia, hypertension, sedation, a high APACHE II score, mechanical ventilation, and metabolic acidosis have also been reported to be risk factors for the development of delirium in other studies.^{4,12,25,26} Since we only included intensive care patients with no history of chronic alcohol abuse, delirium or dementia, and no communication problems, and with a Richmond Agitation Sedation Scale (RASS) score of +4 to -2 in this study, we may have been unable to detect all predisposing factors. However, it is controversial as to whether the PRE-DELIRIC model should not be taken into accounts in patients with a history of dementia or alcohol abuse and those who may have significant risk factors for delirium. Van den Boogaard et al. (2012), excluded groups of patients with a history of alcohol abuse and dementia from their PRE-DELIRIC regression model due to the low prevalence rate and reported that preventive measures can be taken directly instead of predicting the delirium risk, as the present evidence shows that these patients are already at a high risk of delirium.¹⁰ This has been criticized as a deficiency of the PRE-DELIRIC model by many researchers in the literature.^{4,27,28}

This study cannot be generalized to the general population since it was conducted at a single center within a limited time frame. In addition, the inclusion of only conscious and communicating patients at the intensive care unit where a delirium evaluation was not routinely performed may have resulted in a lower incidence than usual in this study where we found an incidence rate at the lower limit of the range reported in the literature.

5. Conclusion

Routine use of the PRE-DELIRIC Score would enable safely and easily predicting the risk of delirium within the first 24 hours after the patients' admission to the ICU. Evidence-based literature support of whether the model provides a fully valid and reliable risk estimate will require its common use in intensive care patients in addition to further interventional and observational studies to decrease the risk of delirium. In addition, CAM-ICU can predict the presence of delirium and the PRE-DELIRIC model is beneficial when making a preliminary prediction and evaluation. The PRE-DELIRIC score is convenient for determining the risk of delirium development in patients hospitalized in the ICU and connected to a mechanical ventilator. There is currently no suitable screening test for delirium diagnosis, especially in disorientated patients. The present delirium screening tests require evaluation with a subjective method, in other words with the answers given to the questions directed to conscious and communicating patients. The PRE-DELIRIC Score is easily applied and uses objective data, without the need for the patient to be conscious. This score can also be used as an important screening tool in detecting the delirium incidence in patients who are unable to communicate. We recommend the use of the PRE-DELIRIC Score in determining the risk of developing delirium in intensive care patients as it is easy to use and calculate and can contribute to clinical practice.

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