

## MiniReview

# Research Progress in the Construction of Delirium Risk Warning Model for ICU Patients Based on Decision Tree: A Review of the Literature

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## Abstract

Intensive Care Unit (ICU) delirium is a cerebral syndrome characterized by acute disturbance of consciousness, with an incidence of 38%-87%. The occurrence of delirium can lead to prolonged hospital stay, accidental extubation rate, mortality and other adverse consequences. Therefore, early identification of delirium and active correction of reversible causes appear to be particularly important. At present, the risk prediction models for delirium in ICU constructed at home and abroad mainly use logistic regression to build delirium risk prediction models for patients admitted to ICU $\geq$ 24h. However, studies have found that as many as 25% of critically ill patients will develop delirium within 24h of admission to ICU. Therefore, it is particularly important to construct a delirium early warning model for patients entering ICU24h. Logistic regression model has low processing efficiency for non-linear and interactive data, and can not intuitively show the importance of each variable in the predicted result. As a non-parametric statistical method, decision tree can overcome the disadvantages of Logistic regression model and build a better prediction model. Therefore, this study used 24h after admission to ICU as the segmentation point to build a decision tree model for predicting early and late delirium in ICU patients, forming a corresponding risk level system, and compared it with similar delirium models to verify the predictive value of the decision tree model for early and late delirium in ICU patients, providing a basis for the formulation of further intervention and nursing plans. Thereby reducing the incidence of ICU delirium.

**Keywords:** ICU, delirium, risk early warning model, decision tree, intervention strategy

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## 1 INTRODUCTION

When facing environmental changes, fear of death,

passive compliance, and potential permanent functional loss, Intensive Care Unit (ICU) patients may experience

a series of psychological and psychiatric syndromes, such as depression, anxiety, and post-traumatic stress disorder. Among them, ICU delirium is of higher risk. ICU delirium is an acute cognitive impairment characterized by acute fluctuations in consciousness and thought disorder, often presenting symptoms such as visual hallucinations, thought disorder, disorientation, and memory impairment<sup>[1]</sup>. Studies have shown that the incidence of ICU delirium in patients ranges from 38% to 87%. Once delirium occurs<sup>[2]</sup>, it significantly affects the prognosis of the disease, leading to prolonged mechanical ventilation time, increased complications and mortality rates, prolonged hospital stays and increased costs, as well as impaired cognitive function<sup>[3]</sup>. Considering the many adverse consequences associated with delirium, clinical practice guidelines emphasize the importance of early monitoring and assessment of delirium risk factors, prevention of delirium occurrence, thereby mitigating the adverse effects caused by ICU delirium<sup>[3]</sup>.

### 1.1 Foreign Research Status

Disease risk prediction models were first applied in the field of cardiovascular disease research. These models, based on multiple risk factors of the disease, allocate scores according to the magnitude of influence and utilize mathematical formulas to calculate the probability of a future event for an individual, providing a statistical assessment method<sup>[4]</sup>. They can be stratified by the magnitude of probability, such as extremely low risk, low risk, moderate risk, and high risk, to enable assessors to provide targeted treatment and care for different risk probability groups in clinical practice. The ICU delirium prediction model began with the model developed by Pisani in 2007, applied to elderly patients in medical ICUs<sup>[5]</sup>, and subsequently, more than ten delirium prediction models for assessing the risk of delirium occurrence in various populations emerged<sup>[6]</sup>. In 2012, Dutch scholars Boogaard first established the prediction model for delirium in ICU patients (PRE-DELIRIC) delirium prediction model for adult ICU patients, assessing ten risk factors within 24h of admission: age, maximum urea nitrogen concentration, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, diagnosis category, morphine use, coma status, emergency admission, infection, sedative use, and metabolic acidosis<sup>[7]</sup>. Risk values were calculated by plugging the regression coefficients, variable types, and assignment methods of each factor into the model formula. The research team used data from 3056 critically ill patients to draw receiver operator characteristic (ROC) curves, with an area under the ROC curve (AUC) of 0.85, indicating good discriminatory ability of the model. Hanison used PRE-DELIRIC for delirium risk stratification assessment of ICU patients and implemented targeted preventive measures for the intermediate- and high-risk groups, reducing the incidence of delirium by 13%<sup>[8]</sup>. The PRE-DELIRIC model is simple and easy to use, requiring only

input of the corresponding data into Excel or mobile app model software for assessment, and its predictive efficiency exceeds that of doctor and nurse prediction methods. However, its limitations include the inability to reflect the impact of changes in patient health status on delirium and the inability to assess the risk of delirium occurrence within 24h of admission. Moreover, it is primarily based on European and American ICU patient populations, with differences in race and treatment modalities, and predictive factors such as “morphine dose within 24h” may not be applicable to ICU patients globally. To enable delirium risk assessment upon ICU admission, Wassenaar conducted a prospective analysis of information from 2914 ICU patients across seven countries, ultimately incorporating nine risk factors: age, history of cognitive impairment, history of alcohol abuse, diagnosis category, emergency admission, use of steroids, blood urea nitrogen concentration, mean arterial pressure, and respiratory failure, to construct the Early prediction model for delirium in ICU patients (E-PRE-DELIRIC) prediction model<sup>[9]</sup>. Based on the time of first delirium occurrence after ICU admission, patients were divided into four groups: 0-1 day, 2 days, 3-6 days, and >6 days, with the AUC increasing from 0.71 to 0.81, indicating a significant improvement in the predictive efficiency of the model over time. The E-PRE-DELIRIC model enables risk assessment upon ICU admission and facilitates easier data acquisition, thus enabling early identification of high-risk patients for delirium within 24h of ICU admission<sup>[10]</sup>. Therefore, the E-PRE-DELIRIC model has unique advantages for patients with short ICU stays and high turnover rates in the intensive care unit. Currently, there is limited research on the predictive validity of E-PRE-DELIRIC for delirium risk in ICU patients, and its predictive effects in different environments remain to be explored.

### 1.2 Domestic Research Status

Domestic research mainly focuses on the analysis of risk factors for delirium in critically ill patients, with a relative lack of construction of risk scoring systems or prediction models. In 2017, Zhu Xiaoying constructed an ICU delirium risk prediction model through a prospective cohort study<sup>[11]</sup>. A total of 210 patients with ICU stays of  $\geq 24$ h were selected as the research subjects and randomly divided into modeling queue (70% of all patients) and validation queue (30% of all patients). The author selected 22 eligible factors through literature review and current situation investigation, including patient-related factors, disease-related factors, treatment-related factors, laboratory indicators, and admission status. Multivariate stepwise regression analysis was then used to determine infection, elevated blood urea nitrogen, and consciousness disorders as independent predictors of ICU delirium. Finally, risk values were calculated by plugging the regression coefficients and assignment methods of each factor into the formula based on the logistic model. The author divided the

risk into three levels based on the probability distribution pattern and optimal threshold points:  $\leq 20\%$  for low risk,  $20\%-40\%$  for moderate risk, and  $\geq 40\%$  for high risk. The area under the ROC curve of this model was 0.75, with the optimal prediction threshold being 19.24%. Its sensitivity and specificity were 83% and 60%, respectively, indicating a reasonable discriminative ability of the model. Although the specificity was not ideal, the sensitivity was relatively good, which has reference value for excluding low-risk patients for ICU delirium. In 2017, Chen Yu conducted a prospective, observational study, selecting 620 patients with ICU stays of  $\geq 24\text{h}$  as study subjects<sup>[12]</sup>. The first half of the patients were allocated to the training set for model development, while the latter half were assigned to the validation set for model confirmation. This model comprised 11 predictive factors: age, coma, APACHE II score, mechanical ventilation, emergency surgery, multiple injuries, metabolic acidosis, history of delirium, history of hypertension, history of dementia, and administration of dexmedetomidine injection. Delirium assessment was conducted twice daily using the Confusion Assessment Method for the ICU (CAM-ICU) scale as the diagnostic criterion for delirium. Linear regression and multivariate logistic regression were utilized to establish regression equations for delirium occurrence, and the risk was stratified into three levels:  $0\%-20\%$  for low risk,  $>20\%-40\%$  for moderate risk, and  $>40\%$  for high risk. The area under the ROC curve of this model was 0.78, indicating good discriminative ability. However, Green in their comparative study of the PRE-DELIRIC model, the E-PRE-DELIRIC model, and the Lanzhou model, highlighted that compared to the other two models, the Lanzhou model imposes higher data collection requirements<sup>[13]</sup>. Collectors/medical electronic records need to thoroughly and clearly comprehend/record patients' past medical history, which to some extent hampers the model's dissemination and adoption.

Currently, both domestically and internationally, most studies constructing ICU delirium risk prediction models typically exclude patients who have been in the ICU for  $<24\text{h}$  from their research. However, patients in the ICU for  $<24\text{h}$  are also a high-risk population for delirium occurrence. Therefore, exploring early and late-stage delirium risk prediction models suitable for the clinical environment in China is of significant importance for assisting healthcare professionals in screening and identifying high-risk populations for delirium occurrence.

## 2 RISK FACTORS FOR ICU DELIRIUM

The pathological and physiological mechanisms of ICU delirium remain unclear, with hypotheses including stress response theory, cholinergic theory, and inflammatory response theory<sup>[14]</sup>. However, it is typically the result of the combined effects of multiple risk factors, which can be categorized into patient-related factors, disease-related

factors, ICU environmental factors, and treatment-related factors. Understanding the related risk factors for ICU delirium occurrence and their controllable characteristics assists healthcare professionals in early identification of high-risk populations, enabling the implementation of corresponding preventive measures.

### 2.1 Patient-Related Factors

Ouimet in a prospective study, demonstrated that a history of hypertension and alcohol abuse increased the risk of ICU delirium by 1.88 and 2.03 times, respectively<sup>[15]</sup>. Critically ill patients with pre-existing cognitive impairments (such as dementia, depression, etc.) are highly sensitive to various triggers due to cerebral hypoperfusion and neural damage caused by brain lesions, showing a close positive correlation with the occurrence of ICU delirium<sup>[3]</sup>. Among these individual factors, only discontinuation of psychoactive substances (alcohol) can be modified. In ICU-admitted patients with chronic alcoholism, cessation of alcohol intake leads to decreased gamma-aminobutyric acid activity and increased dopamine activity, resulting in alcohol withdrawal syndrome with delirium as a clinical manifestation, a process that can be controlled. For non-critically ill patients, advanced age is one of the most important risk factors for delirium. However, its impact on ICU patients remains uncertain<sup>[16]</sup>. This uncertainty is related to variations in the age groups of the study population, as some studies only include postoperative or elderly patients, and the effect of age on delirium occurrence in critically ill patients is not clearly demonstrated.

### 2.2 Disease-Related Factors

Several domestic studies have shown that delirium is closely related to the duration of mechanical ventilation and the severity of illness<sup>[17,18]</sup>, with illness severity assessed using the APACHE II score. Additionally, correlation analysis and meta-analysis have identified hypocalcemia, liver dysfunction, and infection as independent risk factors for ICU delirium. Patients with multiple traumas and metabolic acidosis are considered a high-risk population for delirium occurrence<sup>[16,19,20]</sup>.

### 2.3 Treatment-Related Factors

Most ICU patients require mechanical ventilation, sedation and analgesia therapy, and physical restraints. Shehabi in a multicenter cohort study of 259 patients receiving invasive mechanical ventilation and sedation therapy for  $\geq 24\text{h}$  in 11 medical and surgical ICUs in Malaysia, found that early excessive sedation (within 48h) significantly increased the duration of coma and delirium within 28 days of ICU admission<sup>[21]</sup>. Benzodiazepines (such as midazolam, diazepam, lorazepam, etc.) have a mechanism of action similar to alcohol and repeated accumulation can induce neuro-psychiatric symptoms such as delirium. Results from a randomized controlled trial comparing the efficacy and safety of midazolam and

dexmedetomidine showed a 20% reduction in delirium occurrence with the latter<sup>[22]</sup>. Additionally, mobilization therapy can increase the release of neurotransmitters and neurotrophic factors, promote neurogenesis and angiogenesis, improve neuromuscular function, while restricted mobility increases the risk of delirium occurrence<sup>[23]</sup>.

### **3 METHODOLOGY FOR CONSTRUCTING AN EARLY AND LATE STAGE DELIRIUM RISK PREDICTION AND ASSESSMENT SYSTEM FOR ICU PATIENTS BASED ON DECISION TREE MODELS**

The decision tree method classifies large amounts of data according to specific objectives, representing the learned function from a set of training data as a decision tree, thus extracting useful and latent information. Commonly used in algorithmic prediction, decision tree methods offer features such as fast processing, high accuracy, and simplistic pattern generation, making them widely applicable in data mining. Decision trees are relatively comprehensive techniques in data mining, presenting classification results in a tree-like structure with two types of nodes: internal nodes, which make judgments based on classification attributes, and leaf nodes, representing the final categories. Functionally, decision trees primarily consist of two types: classification trees, which assign labels to training data and accurately categorize them, often providing class probabilities to indicate the accuracy of record classification. Regression trees, on the other hand, estimate continuous variables rather than categorical ones, making predictions about the target variable. Different decision tree algorithms, such as CHAID, C4.5/C5.0, and CART, generate distinct decision trees, differing mainly in three aspects: the number of split points allowed at each tree level, criteria for selecting split points during tree construction, and methods for limiting tree growth to prevent overfitting.

### **4 SIGNIFICANCE OF CONSTRUCTING AN EARLY AND LATE STAGE DELIRIUM RISK PREDICTION ASSESSMENT SYSTEM FOR ICU PATIENTS BASED ON DECISION TREE MODELS**

Due to differences in age, severity of illness, baseline health status, treatment and nursing methods, among other factors, the risk of delirium occurrence varies among ICU patients. Currently, clinical healthcare professionals often assess the risk of delirium based on experience, that is, they consider various risk factors and clinical manifestations from the specific context of the patient, drawing on their own experience and clinical knowledge to judge the degree of risk of delirium occurrence in the ICU. This assessment method has a certain degree of flexibility, but it is subjective and may be subject to significant assessor bias. If healthcare professionals lack knowledge about delirium, combined with limited experience, their ability to predict risks may be insufficient, thus reducing the accuracy of the assessment results<sup>[24]</sup>.

Research has shown that only 41% of delirious patients are identified by healthcare professionals in clinical settings, indicating a high rate of underdiagnosis<sup>[25]</sup>. Delirium risk prediction models can stratify ICU patients according to the probability of delirium onset, such as extremely low risk, low risk, moderate risk, and high risk, to enable assessors to provide targeted treatment and care for patients with different risk probabilities. Hanison applied PRE-DELIRIC to conduct delirium risk stratification assessment of ICU patients and implemented targeted preventive measures for moderate and high-risk groups, resulting in a 13% reduction in the incidence of delirium<sup>[8]</sup>. While this statistical assessment method provides more accurate results compared to empirical assessments by healthcare professionals, it still has some limitations, such as limited inclusion of risk factors and failure to consider factors, social and psychological factors, and potential risk factors, which may impact the occurrence of delirium in patients and lack flexibility. Therefore, it is necessary to combine empirical assessment and statistical assessment methods to form structured clinical judgments to collectively predict the risk of delirium occurrence in critically ill patients. Assessors analyze specific situations based on the risk factors listed in the risk assessment tool, making professional judgments on the impact of each factor on the occurrence of delirium in patients.

Currently, the commonly seen delirium risk prediction scoring systems in clinical practice are primarily constructed using logistic regression models. Indicators included in the model are assigned values according to certain rules, forming the corresponding scoring system. However, logistic regression models have limited efficacy in handling non-linear and interactive data, and they cannot intuitively display the importance of each variable in predicting the outcome. Decision trees, as a non-parametric statistical method, can overcome data collinearity issues and construct predictive models based on available data. The results are displayed as tree diagrams, and the importance of included indicators can be ranked to determine the main predictive factors, facilitating the construction of scoring systems. Moreover, many domestic and international studies exclude patients admitted to the ICU <24h when constructing delirium risk prediction models, but these patients are also at high risk of delirium occurrence. Furthermore, in clinical practice, healthcare professionals cannot accurately predict the length of stay in the ICU for patients upon admission. Instead, they use a unified delirium model to predict the likelihood of delirium occurrence. Therefore, it is necessary to establish early and late-stage delirium prediction models for ICU patients. It's worth exploring whether there are differences in the predictive performance of the model for patients admitted to the ICU <24h compared to those admitted >24h. In China, for critically ill patients, there are no specific guidelines recommended for the recognition, prevention, and treatment of delirium, nor has it received



sufficient clinical attention. Therefore, exploring and establishing a predictive model for the occurrence of early and late-stage delirium in critically ill patients is particularly important.

Currently, there are no effective treatments for ICU delirium. Studies have shown that early screening and prevention are the first steps in improving delirium outcomes<sup>[4]</sup>. Upon admission to the ICU, patients should undergo identification of risk factors, and intervention for high-risk groups can reduce the incidence, severity, and duration of delirium<sup>[26,27]</sup>. Risk prediction models, based on the multifactorial nature of the disease, utilize statistical models to predict the probability of future occurrence of a certain disease in specific populations<sup>[28]</sup>. By constructing ICU patient delirium risk prediction models, healthcare professionals can effectively detect and identify high-risk individuals for delirium early<sup>[6]</sup>. Targeted preventive measures can then be implemented to reduce the incidence of ICU delirium. Furthermore, patients can gain a clear understanding of the risk of delirium occurrence, enhancing awareness of delirium risk factors and increasing treatment compliance<sup>[29]</sup>. Currently, the ICU delirium risk prediction models constructed both domestically and internationally are primarily used to assess the risk of delirium occurrence after 24h of ICU admission<sup>[11,12,27]</sup>. These models often focus on the development of delirium prediction models using logistic regression, while neglecting model validation. However, patients admitted to the ICU <24h are also at high risk of delirium occurrence. Studies have shown that as many as 25% of critically ill adults develop delirium within 24h of ICU admission<sup>[22,30]</sup>, indicating the need for preventive measures to be initiated as early as possible. Therefore, it is necessary to include patients admitted to the ICU <24h; however, different models have different requirements for the variables included, and the algorithms used to generate branches during the model-building process vary<sup>[31]</sup>. Among them, logistic regression models have low efficiency in handling non-linear and interactive data and cannot intuitively display the importance of each variable in predicting the outcome. Decision trees, as a non-parametric statistical method, can overcome data collinearity issues and construct predictive models based on available data. The results are displayed as tree diagrams, and the importance of included indicators can be ranked to determine the main predictive factors, facilitating the construction of scoring systems. Therefore, constructing decision tree models to predict early and late-stage delirium in ICU patients, forming corresponding decision tree scoring systems, and conducting prospective validation are particularly important.

## 5 CONCLUSION

For critically ill patients, there are no specific recommended guidelines for recognising, preventing and treating insanity, and they have not received sufficient

clinical attention. Therefore, it is particularly important to explore and establish a prediction model to predict the occurrence of early and late psychosis in critically ill patients. Current studies, mainly focused on assessing the risk of developing psychosis after 24h of admission, however, patients admitted to the ICU for <24h are also at high risk of developing psychosis, and therefore, it is necessary to include patients admitted to the ICU for <24h in the observation as well. Decision trees, as a non-parametric statistical method, can overcome the problem of data covariance and construct predictive models based on the available data. The results are displayed in the form of a dendrogram, and the importance of the included indicators can be ranked to identify the main predictors and facilitate the construction of the scoring system. Therefore, in future studies, we can construct decision tree models to predict early and late psychosis in ICU patients, form corresponding decision tree scoring systems, and perform prospective validation.

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## Conflicts of Interest

The authors declared no conflict of interest.

## Author Contribution

Yan P and Zhang Y administrated this project and supervised by Zhang Y. Shu K and Chen X was responsible for conceptualisation, methodology and data curation, then validated by Zhang Y. Original draft was done by Yan P and Huo X. Following review and editing were completed by Zhang Y. All authors have read and agreed to this published version of the manuscript.

## Abbreviation List

APACHE II: Acute Physiology and Chronic Health Evaluation II

AUC, Area under the ROC curve

CAM-ICU: Confusion Assessment Method for the ICU

E-PRE-DELIRIC: Early prediction model for delirium in ICU patients

ICU: Intensive Care Unit

PRE-DELIRIC: Prediction model for delirium in ICU patients

ROC: Receiver operator characteristic

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