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Original Research Article

Early identification of potential brain death organ donors based on prediction of spontaneous respiratory arrest

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ABSTRACT

Background: This study was designed to build a Nomogarm prediction model of spontaneous respiratory arrest (SRA) in nerocritical patients within 72 hours after brain injury for early identification of potential brain death organ donors.
Methods: From October 2017 to May 2019, the neurocritical patients admitted to the First Affiliated Hospital of Sun Yat-sen University, were enrolled. The occurrence of SRA within 72 hours after brain injury was regarded as the time interest point and grouping factor, factors associated with SRA were screened by univariate and multivariate analysis, and then the Nomogarm prediction model was developed. Finally, the Nomogarm prediction model was tested in the validation set.
Results: In training set, univariate and multivariate analysis showed that the midline shift (OR=4.56, 95% 1.87-19.21), absent of ambient cistern (OR=4.83, 95% 1.35-16.34), cough reflex absence (OR=3.82, 95% 1.15-12.42), intraventricular hemorrhage (OR=3.16, 95% 1.53-14.52) and serum Na+<125mmol/L (OR=3.06, 95% 1.53-13.44) were associated with SRA within 72 hours. In the training set and validation set, the predicted C index of SRA rate within 72 hours was 0.81 (95% CI 0.76-0.85) and 0.80 (95% CI 0.75-0.83), respectively. Further statistical analysis showed that 140 points, 160 points and 170 points were dangerous cut-off points, of which 140 points, 160 points and 170 points were 30.1%, 65.6% and 93.4% associated with SRA within 72 hours, respectively.
Conclusions: Nomogram prediction model based on brain injury assessment parameters can predict the time of SRA in neurocritical patients, and can be used for early identification of potential brain death organ donors.

Keywords: Brain death, Neurocritical patients, Nomogram, Prediction, Spontaneous respiration arrest

INTRODUCTION

The criteria and practical guidance for determination of brain death has been applied to clinical practice in China. It is a factual judgment on the state of brain death, and owned no predictive value of the occurrence of brain death.[1] There had been a few reports on the prediction of brain death, however, the low specificity of the selected parameters leads to poor applicability.[2] Neurocritical patients are the main source of potential brain death organ donors, and spontaneous respiratory arrest (SRA) is the most important early clinical manifestation of neurocritical patients progressing to brain death. Therefore, analyzing the related factors of SRA in neurocritical patients within 72 hours is important for early identification of brain death donors. Based on the clinical practice of organ donation after brain death, authorsinitially built a Nomogram for predicting SRA, which can be used for early identification of potential brain death organ donors.

Landmarks, the nearest distance of the same from sigmoid and transverse sinus and also the thickness at the center of the asterion that may be of importance to

anthropologists, anatomists, forensic pathologists and neurosurgeons.

METHODS

From October 2017 to May 2019, the neurocritical patients (mainly including traumatic brain injury and spontaneous cerebral haemorrhage) who were admitted to the First Affiliated Hospital of Sun Yat-sen University, were prospectively enrolled. The vital parameters, neurological examination and laboratory tests of patients were recorded dynamically until SRA.

Inclusion criteria

- Neurocritical patients: brain injury time less than 72 h and GCS less than 8.[3,4]
- Age more than 1 year
- No lesions of other parts of the body.

Spontaneous respiratory arrest criteria

- According to China criteria and practical guidance for determination of brain death, spontaneous respiratory arrest was confirmed by apnea test.[1,5]

Statistical analysis

The statistical analysis was completed by SPSS (23.0 version). In the training set, according to the grouping factors, the factors related to SRA were screened by univariate and multivariate analysis, and the Nomogram prediction model was built. Then, its performance was tested in the validation set.

RESULTS

According to the inclusion criteria, a total of 127 patients were included in the study; 65 patients entered the training set and 62 entered the validation set. The average age of the training set was 33.22±14.76y; 59 males and 6 females; 36 cases of traumatic brain injury, 23 cases of spontaneous cerebral haemorrhage, 6 cases of hypoxic-ischemic encephalopathy; the average age of the patients in the validation set was 33.24±15.83y; 54 males and 8 females; including 35 cases of traumatic brain injury, 18 cases of spontaneous cerebral haemorrhage, and 9 cases of hypoxic-ischemic encephalopathy (Table 1).

In the training set, univariate and multivariate analysis showed that the midline shift (OR=4.56, 95% 1.87-19.21), absent of ambient cistern(OR=4.83, 95% 1.35-16.34), cough reflex absence (OR=3.82, 95% 1.15-12.42), intraventricular hemorrhage (OR=3.16, 95% 1.53-14.52) and serum Na^+<125mmol/L (OR=3.06, 95% 1.53-13.44) were associated with SRA within 72 hours in neurocritical patients (Table 2). Then, a Nomogram prediction model was constructed with relevant factors (Figure 1). In the training set and validation set, the predictive C-index for spontaneous respiratory arrest in neurocritical patients was 0.81 (95% CI 0.76-0.85) and 0.80 (95% CI 0.75-0.83), respectively. Further statistical analysis showed that the scores of 140 points, 160 points and 170 points were dangerous cut-off points, of which 140 points, 160 points and 170 points were 30.1%, 65.6% and 93.4%, associated with spontaneous respiratory arrest within 72 hours, respectively.

Table 1: General information of patients included.

Factors	Training set	Validation set	p	
Age	33.22±14.76	33.24±15.83	0.91	0.74
Male	59	54		
Female	6	8	0.43	0.51
Diagnosis				
TBI	36	35		
SCH	23	18		
HIC	6	9	1.15	0.56

Table 2: The factors related to spontaneous respiratory arrest in training set.

Factors	OR (95% CI)	p
The midline shift	4.56(1.87-19.21)	0.007
Absent of ambient cistern	4.83(1.35-16.34)	0.001
Cough reflex absence	3.82(1.15-12.42)	0.012
Intraventricular hemorrhage	3.16(1.53-14.52)	0.021
Serum Na^+<125mmol/L	3.06(1.53-13.44)	0.035

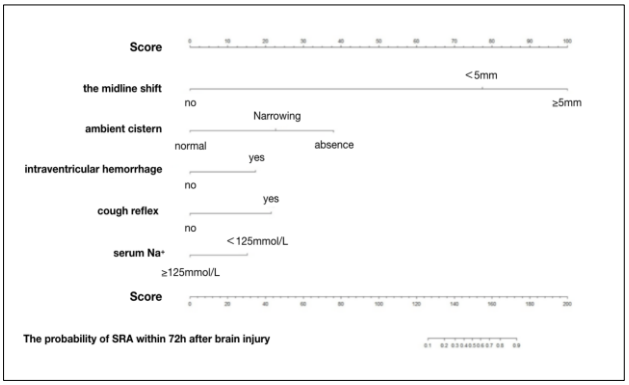

Figure 1: Nomogram prediction model with relevant factors.

DISCUSSION

Brain death is a gradual process based on the time axis, and spontaneous respiratory arrest (SRA) is the most important early manifestation of progression to brain death in neurocritical patients. The intracranial pressure increases rapidly and reached its peak 24-48 hours after traumatic brain injury, and the peak period will last for 4-6 days. The 72h after brain injury was the important time point for the respiratory center damage of the brain-stem,

which leaded to the irreversible spontaneous respiratory arrest.[6,7] The abnormal or arrest of spontaneous respiration in neurocritical patients is a visual manifestation of brain injury progression, which is closely related to the development of brain death along the time axis. Esteban et al, reported 40% neurocritical patients developed irreversible SRA and progress to brain death in the United States.[8] Therefore, the SRA can be used for the predictor of brain death.

At present, the early evaluation tools of prognosis in neurocritical patients are mainly GCS and FOUR score.[9] The GCS is an objective and easy-to-use scale for the initial assessment of the degree of brain injury in acute neurocritical patients. In the assessment of the prognosis of neurocritical patients (GCS < 8), as the score decreases, the accuracy of prediction increases. However, the GCS lacks assessment of brain stem reflex and spontaneous respiration, so the predictive value of brain death is low. The FOUR score has more application value in the prognosis evaluation of neurocritical patients.[10] The study of 138 acute neurocritical patients showed that the FOUR score was more useful than the GCS in predicting mortality, but similar in predicting poor prognosis with GCS.[11] However, the parameters included in these scores are all neurological examination parameters, although they are objective signs, but own subjectivity of the examiner.

The cough reflex centre is located in and around the solitary tract nucleus of the brainstem, adjacent to the respiratory center.[12] Studies have shown that breathing and cough have the same motor neurons, indicating that cough reflexes are closely related to spontaneous respiration in anatomical structures.[13] Sharshar et al, in a study of 72 neurocritical patients showed that early assessment of brain stem reflex was useful to predict the severity of brain injury, and confirmed that cough reflex absence is consistent with SRA; the result of this study is consistent with them.[14] Since the respiratory centre is located in the brainstem, introducing neuroimaging evaluation indicators for the brainstem is useful for the prognosis evaluation in neurocritical patients.[15] Current studies have shown that the narrowing or disappearance of ambient cistern in neurological patients may cause cerebrospinal fluid circulation disorder, which leads to the continuous increase of intracranial pressure, and directly determine the prognosis of patients.[16,17] In this study, the disappearance of ambient cistern was associated with SRA within 72 hours in neurocritical patients. In 75 neurocritical patients study of Quattrocchi et al, showed that the degree of midline shift can be used as an effective predictor of the prognosis of brain injury in neurocritical patients.[18] The study of Bartels et al, further showed that midline shift ≥4 mm predicted a poor prognosis, while midline shift ≥ 5 mm predicted mortality in neurocritical patients.[18] This study showed that midline structural displacement ≥5 mm was associated with SRA within 72 hours in neurocritical patients.

Nomogram is a statistical method that integrates multiple predictive factors to predict the probability of outcomes. It transforms complex regression equations into visual graphics, making the predictive results more readable and easy to use. At present, the Nomogram prediction model had been widely used, mainly in predicting the survival rate of cancer patients.[19,20] In this study, univariate and multivariate analysis showed that the midline shift, absent of ambient cistern, cough reflex absence, intraventricular haemorrhage and serum Na^+<125mmol/L were associated with SRA within 72 hours in neurocritical patients. In this study, the C-index of Nomogram predictive model in the training set and the validation set were 0.81 (95% CI 0.76-0.85) and 0.80 (95% CI 0.75-0.83) respectively, and own good applicability.

Although this study is a prospective study, it excludes basic diseases and injuries in other parts of the body when determining inclusion criteria, which inevitably affects the universality of Nomogram prediction model. At the same time, single-center research has selection bias, and needs further validation of external data.

In summary, the Nomogram predictive model of SRA based on brain injury assessment parameters can predict the occurrence of brain death, and can be used to identify potential brain death organ donors early.

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