Original Article A nomogram predictive model for factors influencing prognosis of acute ischemic stroke patients after intravenous thrombolysis

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Received January 22, 2025; Accepted March 19, 2025; Epub April 15, 2025; Published April 30, 2025

Abstract: Aims: This study aimed to develop and validate a nomogram for the early prediction of prognosis in patients with acute ischemic stroke (AIS) following intravenous thrombolysis (IVT), to facilitate clinical decision-making. Methods: This retrospective study included 393 consecutive AIS patients who underwent IVT between January 2021 to December 2023. Patients were classified into either a good or a poor prognosis group. Logistic regression analysis was performed to identify prognostic factors associated with clinical outcome, including medical records, laboratory findings, and independent risk factors. The independent factors were then used to construct a prognostic nomogram. Results: Among the 393 AIS patients treated with IVT, 142 had a poor prognosis. Six independent predictors were identified: baseline National Institutes of Health Stroke Scale (NIHSS) score (95% Cl: 1.133-1.229, P<0.001), B-type natriuretic peptide (95% Cl: 1.044-1.532, P=0.036), age group (Group 1: 95% Cl: 0.004-0.086, P<0.001; Group 2: 95% CI: 0.034-0.063, P=0.004), time from onset to thrombolysis (95% CI: 1.004-1.067, P=0.014), diabetes (95% CI: 0.315-0.887, P=0.016), and pre-thrombolysis prothrombin time (PT) (95% CI: 1.050-1.553, P=0.015). These factors were incorporated into a nomogram, which achieved an under the receiver operating characteristic curve (AUC-ROC) of 0.8075882, 95% CI (0.664-0.962). Conclusion: We identified six independent prognostic factors for AIS patients after IVT, including NIHSS score, B-type natriuretic peptide, pre-thrombolysis PT, age, diabetes, and time from onset to thrombolysis. The developed nomogram demonstrated strong predictive performance and may aid clinicians in prognosis assessment for AIS patients receiving IVT.

Keywords: Acute ischemic stroke, intravenous thrombolysis, clinical prognosis, influencing factors, nomogram, predictive model

Introduction

Acute ischemic stroke (AIS) is caused by the sudden occlusion of cerebral blood flow, leading to ischemic and hypoxic injury in the affected brain regions and subsequent neurologic deficits [1]. According to the latest epidemiological data, approximately 15 million people worldwide suffer from stroke each year, with over 6 million dying and another 5 million experiencing permanent disability [2]. Stroke remains a major global health threat [3, 4]. Given the aging population and demographic shifts in China, the incidence of stroke is expected to rise. Ischemic stroke, the most prevalent stroke subtype, accounts for approximately 71% of all cases [5]. Therefore, early and effective prevention and treatment strategies for AIS are of paramount importance. Currently, various guidelines recommend intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA) as the most effective treatment for AIS [6]. When administered within 3-4.5 hours of symptom onset, rt-PA has been shown to effectively restore cerebral perfusion, preserve neurological function, and improve clinical prognosis [7]. However, patient responses to thrombolytic therapy vary significantly.

Previous studies have identified several factors influencing the prognosis of AIS patients following intravenous thrombolysis. Key determinants include the time to treatment, stroke severity, comorbidities, and demographic factors such as age and gender [8-11]. For example, evidence suggests that earlier intervention within the therapeutic window of 3-4.5 hours is associated with better recovery, whereas patients with severe strokes or multiple comorbidities tend to have poorer outcomes [12, 13]. Additionally, age and gender play a role in prognosis, with older patients generally experiencing worse outcomes [14]. These findings highlight the necessity of evaluating these prognostic factors to improve outcome in AIS patients undergoing thrombolysis.

As such, a comprehensive evaluation of these prognostic factors before initiating thrombolytic therapy is critical for optimizing patient selection, minimizing complications, and enhancing both the efficacy and safety of treatment. Building upon prior research, this study aims to further investigate the key predictors of clinical prognosis in AIS patients treated with IVT and to develop a predictive model using a nomogram. This model will provide clinicians with an evidence-based tool to guide clinical decision-making.

Materials and methods

Study population

AlS patients who underwent IVT were consecutively enrolled at our hospital from January 2021 to December 2023. A total of 393 patients met the inclusion criteria. Among them, 251 patients with a modified Rankin Scale (mRS) score of 0-1 were classified into the good prognosis group, while the remaining 142 patients with an mRS score of 2-6 were categorized into the poor prognosis group. This study was approved by the Ethics Review Board of Suizhou Hospital. Given its retrospective design, the requirement for informed consent was waived.

Inclusion and exclusion criteria

Inclusion criteria: (1) Neurological deficits attributable to ischemic stroke. (2) Symptom onset within 3-4.5 hours. (3) Age \geq 18 years. (4) Completion of a 3-month follow-up. (5) Availability of complete clinical data.

Exclusion criteria: (1) History of significant head trauma or stroke within the past 3 months. (2) Suspected subarachnoid hemorrhage. (3) Arterial puncture in a non-compressible site

within the past week. (4) History of intracranial hemorrhage. (5) Presence of intracranial tumor, arteriovenous malformation, or aneurysm. (6) Recent intracranial or intraspinal surgery. (7) Uncontrolled blood pressure, defined as systolic blood pressure \geq 180 mmHg or diastolic blood pressure \geq 100 mmHg. (8) Active internal bleeding. (9) Acute bleeding tendency, including a platelet count < 100×10⁹/L or other coagulopathies. (10) Use of low-molecularweight heparin within the past 24 hours. (11) Use of oral anticoagulants with an international normalized ratio (INR) > 1.7 or prothrombin time (PT) > 15 seconds. (12) Use of thrombin inhibitors or factor Xa inhibitors within 48 hours, or abnormal coagulation parameters [e.g., activated partial thromboplastin time (APTT), international normalized ratio (INR), platelet count, external carotid thrombosis (ECT), thrombin time (TT), or factor Xa activity]. (13) Blood glucose levels < 2.8 mmol/L or > 22.22 mmol/L. (14) Computed Tomography (CT) scan indicating extensive cerebral infarction (low-density area involving > 1/3 of the middle cerebral artery territory). (15) Insufficient imaging or laboratory data, inadequate blood pressure monitoring, or patients undergoing additional endovascular interventions (e.g., mechanical thrombectomy, intra-arterial thrombolysis, bridging therapy).

Data collection

Demographic data, National Institutes of Health Stroke Scale (NIHSS) scores before and 24 hours after IVT, 90-day mRS scores, and infarction location were collected. Case report forms (CRFs) were reviewed for comorbidities, including hypertension, atrial fibrillation, coronary artery disease, heart failure, diabetes, hyperlipidemia, and history of stroke, as well as lifestyle factors such as smoking and alcohol consumption. An electrocardiogram and cranial CT were performed before IVT, along with laboratory tests assessing relevant biomarkers. The 90-day mRS scores were obtained by telephone follow-up, outpatient records, or hospital readmission data.

Treatment protocol

All patients received intravenous alteplase at a dose of 0.9 mg/kg. After dilution, the initial 10% of the total dose was administered intra-

venously over 1 minute, followed by continuous intravenous infusion of the remaining 90% over 60 minutes. Vital signs and neurological status were closely monitored throughout the thrombolytic procedure. A follow-up cranial CT was performed 24 hours post-thrombolysis to evaluate for hemorrhagic transformation. Subsequently, all patients received secondary stroke prevention therapy, symptomatic management, and neurorehabilitation training.

Evaluation criteria and grouping methods

For all AIS patients who received IVT with rt-PA, the NIHSS score was assessed by professional neurologists upon admission and 24 hours after treatment [15]. Neurological functional prognosis was evaluated at 90-day follow-up using the mRS score [16]. A favorable prognosis was defined as an mRS score of 0-1, whereas a poor prognosis was defined as an mRS score of 2-6. Based on these criteria, patients were classified into a good or a poor prognosis group.

Statistical analysis

All statistical analyses were performed using SPSS 26.0. The required sample size was determined through power analysis, applying the formula: corrected sample size = sample size/(1-[% attrition/100]). Based on this estimation, a final sample size of 393 was selected. The Kolmogorov-Smirnov test was used to assess the normality of continuous variables. Normally distributed data were presented as mean ± standard deviation (SD) and compared using the independent samples t-test. Nonnormally distributed continuous variables were reported as median and interguartile range and analyzed using the Mann-Whitney U test. Categorical variables were presented as frequencies (percentages) and compared using the chi-square test or Fisher's exact test. Initially, univariate analysis was conducted to compare baseline characteristics between the good and the poor prognosis groups. Variables that reached statistical significance in the univariate analysis were subsequently included in a multivariate binary logistic regression model to identify independent prognostic factors. To enhance the robustness of the results, a bootstrap resampling procedure with 1,000 iterations was applied. A predictive nomogram model was developed using R software (version 3.6.3) with the rms package to estimate clinical prognosis in AIS patients after intravenous thrombolysis. Internal validation of the model was constructed using bootstrap resampling, and its accuracy was evaluated using calibration curves and the Hosmer-Lemeshow goodness-of-fit test. The discriminative ability of the nomogram was evaluated using receiver operating characteristic (ROC) curve analysis. A *p*-value of less than 0.05 was considered significant.

Results

Comparison of clinical characteristics

Among the 393 AIS patients who underwent IVT, 251 achieved a favorable prognosis (mRS score 0-1), while the remaining 142 experienced a poor prognosis (mRS score 2-6). As shown in **Table 1**, significant differences were observed between the two groups in terms of age, presence of coronary heart disease, CRF stratification, diabetes, and baseline NIHSS score (P < 0.05).

Comparison of biochemical markers

Statistically significant differences were identified between the two groups across multiple biochemical indicators (Table 2). Median white blood cell (WBC) count was 7.17 (2, 20.2) in the good prognosis group, compared to 7.8 (2.8, 34.7) in the poor prognosis group (P=0.04). Median urea level was 5.63 (2.08, 15.52) mmol/L in the good prognosis group, significantly lower than 6.57 (2.51, 36.9) mmol/L in the poor prognosis group (P=0.001). Median B-type natriuretic peptide (BNP) level was 493.93 (10, 7290) pg/mL in the good prognosis group, whereas the poor prognosis group had a higher median of 1019.38 (10, 35000) pg/mL (P=0.019). Additionally, median free thyroxine (FT4) levels were 8.3 (0.3, 37.93) pmol/L in the good prognosis group, significantly higher than 6.41 (0.79, 22.19) pmol/L in the poor prognosis group (P=0.016). The good prognosis group had a median prothrombin time (PT) of 11.89 (11.46, 12.89) seconds, while the poor prognosis group had a longer median PT of 12.06 (11.98, 12.06) seconds (P=0.014).

Multivariate logistic regression analysis

Variables identified as significant (P < 0.05) by the univariate analysis, including age, diabetes,

Factor	Good prognosis group (n=251)	Poor prognosis group (n=142)	Statistic	р
Gender (% male)	158 (62.9%)	91 (64.08%)	0.050	0.822
Age (years, range)	64.3 (37-88)	69.9 (26-89)	4.997	0.000
Age grouping			11.775	0.003
31-50	26 (10.36%)	5 (3.5%)		
51-70	136 (54.18%)	65 (45.77%)		
71-90	89 (35.46%)	72 (50.70%)		
Hypertension	151 (60.16%)	88 (61.97%)	0.125	0.724
Diabetes	29 (11.55%)	35 (24.65%)	11.406	0.001
Hyperlipidemia	5 (2.00%)	3 (2.11%)	0.007	0.935
Atrial fibrillation	20 (8.00%)	10 (7.04%)	0.110	0.740
Coronary heart disease	37 (14.74%)	35 (24.65%)	5.948	0.015
History of cardiac insufficiency	3 (1.20%)	5 (3.5%)	2.460	0.117
History of stroke	56 (22.31%)	35 (24.65%)	0.278	0.598
Smoking history	71 (28.29%)	30 (21.13%)	2.435	0.119
Alcohol consumption history	63 (25.10%)	35 (24.65%)	0.010	0.921
CRF stratification			11.406	0.001
≤ 2	222 (88.45%)	107 (75.35%)		
> 3	29 (11.55%)	35 (24.65%)		
Baseline NIHSS score	5.11 (0, 31)	13.11 (2, 39)	10.209	0.000

Table 1. Clinical characteristics of patients

Note: CRF: Case Report Forms; NIHSS: National Institutes of Health Stroke Scale.

Factor	Good prognosis group (n=251)	Poor prognosis group (n=142)	t	р
White blood cell count (*10 ⁹ /L)	7.17 (2, 20.2)	7.8 (2.8, 34.7)	-2.054	0.041
Platelet count (*10 ⁹ /L)	187.69 (102, 555)	181.96 (106, 428)	0.928	0.340
Total cholesterol (mmol/L)	4.52 (1.78, 11.51)	4.3 (1.96, 7.9)	1.872	0.062
Low density lipoprotein (mmol/L)	2.92 (0.81, 5.93)	2.75 (0.55, 5.69)	1.847	0.066
Apolipoprotein B (g/L)	0.95 (0.27, 4.92)	0.9 (0.27, 1.8)	1.750	0.081
Apolipoprotein A1 (g/L)	1.39 (0.59, 2.43)	1.36 (0.91, 2.63)	0.783	0.434
Albumin (g/L)	35.79 (26.5, 60)	38.82 (29.7, 48.4)	0.069	0.945
Indirect bilirubin (µmol/L)	9.89 (2.8, 43.5)	10.73 (2.4, 29.9)	1.621	0.106
Creatinine (µmol/L)	74.17 (22.1, 270.3)	80.16 (36, 502)	1.569	0.117
Urea (µmol/L)	5.63 (2.08, 15.52)	6.57 (2.51, 36.9)	3.427	0.001
Uric acid (µmol/L)	329.16 (118, 708)	340.55 (183, 888)	0.806	0.330
BNP (pg/mL)	493.93 (10, 7290)	1019.38 (10, 35000)	2.346	0.019
Homocysteine (µmol/L)	17.81 (5, 90)	19.4 (7, 234)	1.147	0.252
α-HBDH (U/L)	190.75 (22.8, 780)	193.5 (73, 745)	1.198	0.224
Total serum calcium (mmol/L)	2.29 (1.66, 3.1)	2.28 (1.51, 2.76)	0.797	0.426
HbA1c (%)	5.99 (4.1, 13.3)	6.21 (4.8, 13.3)	1.699	0.090
FT3 (pmol/L)	2.68 (0.78, 16.11)	3.47 (1.86, 9.04)	1.707	0.089
FT4 (pmol/L)	8.3 (0.3, 37.93)	6.41 (0.79, 22.19)	2.409	0.016
TSH (mIU/L)	2.08 (0.01, 19.93)	1.70 (0.11, 19.11)	0.674	0.501
PT (s)	11.89 (11.46, 12.89)	12.06 (11.98, 12.06)	-2.481	0.014

Table 2. Comparison of biochemical indicators

Note: HbA1c: Hemoglobin A1c; FT3: Free Triiodothyronine; FT4: Free Thyroxine; TSH: Thyroid Stimulating Hormone; PT: Prothrombin Time; BNP: B-type natriuretic peptide.

Table 3. Multivariate binary logistic regression analysis of neuro
logical function prognosis 90 d after IVT

Variable	В	OR	Р	95% CI
Divided into three age groups			0.000	
Divided into three age groups (1)	-3.973	0.776	0.000	0.004-0.086
Divided into three age groups (2)	0.462	0.325	0.004	0.034-0.063
Divided into three age groups (3)	0.223	0.300	0.457	1.250-2.650
PT	0.244	0.100	0.015	1.050-1.553
BNP	0.000	0.998	0.036	1.044-1.532
Time from onset to thrombolysis	0.034	1.008	0.014	1.004-1.067
Baseline NIHSS score	0.165	0.021	0.000	1.133-1.229
Diabetes	0.638	0.264	0.016	0.315-0.887

Note: PT: Prothrombin Time; NIHSS: National Institutes of Health Stroke Scale.



Figure 1. Nomogram for predicting poor outcome in patients with acute ischemic stroke after intravenous thrombolysis. Note: BNP: B-type natriuretic peptide; PT: Prothrombin Time; NIHSS: National Institutes of Health Stroke Scale.

coronary heart disease, CRF stratification, baseline NIHSS score, WBC count, urea, BNP, FT4, and PT, were further analyzed using multivariate logistic regression. The analysis revealed the following factors as independent predictors of poor prognosis at 90 days after IVT (**Table 3**): baseline NIHSS score (95% CI: 1.133-1.229, P<0.001), BNP levels (95% CI: 1.044-1.532, P=0.036), age stratification (Group 1: 95% CI: 0.004-0.086, P<0.001; Group 2: 95% CI: 0.034-0.063, P=0.004), onset-to-thrombolysis time (95% CI: 1.004-1.067, P=0.014), diabetes (95% CI: 0.315-0.887, P=0.016), and pre-thrombolysis PT (95% CI: 1.050-1.553, P=0.015).

Nomogram development and validation

A nomogram was developed based on the logistic regression model, incorporating the six identified prognostic factors (**Figure 1**).

Model performance was evaluated using multiple validation methods: Calibration curve analysis (Figure 2) demonstrated a close agreement between the predicted and observed probabilities of poor prognosis in AIS patients following IVT, indicating excellent model calibration. ROC curve analysis (Figure 3) assessed the model's discriminative power. The area under the curve (AUC) was 0.808 (95% CI: 0.664 to 0.962), suggesting a high degree of predictive accuracy. An AUC > 0.8 suggests strong differentiation between high- and low-risk patients, supporting the clinical applicability of the nomogram in risk stratification for this patient population.

Clinical utility

The decision curve analysis (DCA) curve (**Figure 4**) demonstrated that the nomogram provided a net clinical benefit

across a broad range of threshold probabilities. The highest net benefit was observed within a specific threshold range (20%-75%). Within this range, the nomogram effectively identified patients at high risk for poor prognosis. Even beyond this range, the model maintained reasonable predictive utility. These findings underscore the clinical value of our nomogram in guiding therapeutic intervention and prognosis estimation for AIS patients undergoing IVT.

Discussion

Among the 393 AIS patients who underwent IVT, 142 experienced a poor outcome. This study identified six independent predictors of



Figure 2. Calibration curve of the nomogram.



Figure 3. ROC curve area. Note: ROC: Receiver Operating Characteristic.

clinical prognosis (**Table 3**). A nomogram incorporating these factors was developed to facilitate individualized prognosis prediction for AIS patients after -IVT, providing a valuable tool for clinical decision-making.

Our study found that baseline NIHSS score was an independent predictor of clinical prognosis. The NIHSS is a widely used tool for assessing neurological deficits in patients with acute stroke, with scores ranging from 0 to 42, and higher values indicating more severe neurological deficits [17]. A strong correlation between baseline NIHSS score and 90day prognosis post-IVT was observed, with lower baseline scores associated with favorable prognosis. This finding aligns with previous studies [18-20]. In 2012, a retrospective multicenter study in Japan involving 566 AIS patients demonstrated that a lower baseline NIHSS score was independently predictive of early clinical efficacy post-IVT [21]. Given its prognostic significance, early and accurate NIHSS assessment upon admission is essential for guiding treatment strategies and optimizing patient management.

Compared to younger individuals, elderly patients often present with multiple underlying diseases, such as cerebral aneurysms and heart failure, which significantly increase the incidence of AIS. Additionally, age-related vascular degeneration and other physiologic changes may reduce the responsiveness to thrombolytic therapy, diminishing the efficacy of intravenous thrombolysis (IVT) and leading to higher rates of mortality and recurrence [22]. Consistent with prior research [23-25], our study

identified age as an independent predictor of poor prognosis. A one-year follow-up study in India showed that middle-aged patients (< 60



Figure 4. Decision curve analysis of the nomogram model.

years) had better outcomes, with lower risks of death and recurrence compared to older patients [26, 27]. However, other studies suggest that IVT remains effective and safe in elderly AIS patients, without an increased risk of intracranial hemorrhage, mortality, or adverse outcome [28-30]. Thus, no definitive consensus has been reached regarding whether thrombolytic efficacy and safety differ significantly between elderly and younger patients. The discrepancies among studies may stem from variations in individual patient characteristics, sample size, age stratification cutoffs used, and evaluation criteria. Future research should focus on expanding sample sizes, refining inclusion criteria, minimizing confounding biases, and conducting multicenter studies to enhance the robustness of findings. Moreover, IVT administration should not be determined solely by patient age but should also be guided by a comprehensive, individualized evaluation of both the potential benefits and risks of thrombolysis to optimize treatment decisions. The safety and efficacy of IVT in middle-aged AIS patients are well established [31].

Diabetes mellitus was another independent risk factor for clinical prognosis in AIS patients post-IVT. Poor glycemic control and insulin dysfunction in diabetic patients can disrupt anticoagulation and fibrinolysis, impair vascular recanalization, and compromise the blood-brain barrier, increasing the risk of post-perfusion hemorrhage and reperfusion injury [32]. Therefore, strict blood glucose monitoring and optimal glycemic control are crucial in mitigating AIS-related complications and improving patient outcome.

The time from symptom onset to thrombolysis was also an independent risk factor for AIS patients post-IVT. Studies have shown that prolonged onsetto-thrombolysis time leads to a larger cerebral infarct core, a diminished ischemic penumbra, and extensive neuronal apoptosis, thereby exacerbating neurological impairment

[33]. Conversely, reducing the time to thrombolysis has been shown to salvage the ischemic penumbra, promote cerebral vascular recanalization, lower the risk of hemorrhagic transformation, and improve overall patient prognosis [34]. Therefore, minimizing the delay between AIS onset and thrombolysis is essential to optimize prognosis.

Prothrombin time (PT) is a key measurement in clinical anticoagulant therapy, determined by adding calcium ions and tissue factors to plasma [35]. In this study, multivariate analysis identified pre-thrombolysis PT as an independent prognostic factor. Among patients with PT values within the normal range, those in the good prognosis group exhibited slightly higher pre-thrombolysis PT values than those in the poor prognosis group. However, the precise mechanism linking PT to thrombolysis outcomes remains unclear due to limited existing literature. One possible explanation is that an increased pre-thrombolysis PT may indicate greater thrombolytic responsiveness, leading to more effective thrombolysis. Nonetheless, excessively high PT values can predispose patients to hemorrhagic complications [36]. PT also reflects fibrinogen (coagulation factor I) concentration and activity, with significantly

elevated PT values suggesting reduced fibrinogen levels or activity. Research has shown that fibrinogen concentration directly influences factor XIII (FXIII) activity, with a 1 g/L increase in fibrinogen concentration corresponding to a 5.7% rise in FXIII activity [37]. As a fibrin-stabilizing factor, FXIII plays a crucial role in hemostasis [38]. Recent studies have reported that FXIII is significantly associated with AIS prognosis, serving as an independent predictor of post-thrombolysis hemorrhage and short-term mortality [39]. Given these findings, a thorough pre-thrombolysis coagulation assessment is essential for clinical practice. Adhering strictly to thrombolysis indications, dynamically monitoring coagulation data, and performing followup cranial CT scans within 24 hours after thrombolysis are critical for mitigating bleeding risk and improving outcome.

Our study identified BNP as another independent prognostic factor in AIS patients receiving IVT. BNP, a cardiac hormone secreted in response to ventricular stress, plays a key role in regulating blood pressure and fluid homeostasis. Elevated BNP levels are frequently observed in patients with heart failure and various cardiovascular disorders. Previous studies have reported that BNP levels rise in AIS patients following IVT, likely due to cardiovascular strain and the systemic response to brain injury [40, 41]. The underlying pathophysiologic mechanisms of BNP elevation in AIS patients post-IVT may involve heightened sympathetic nervous system activity and activation of the renin-angiotensin-aldosterone system, resulting in increased blood pressure, fluid retention, and myocardial stress, all of which contribute to BNP release [42-44]. Elevated BNP levels have been associated with worse clinical outcomes, including an increased risk of complications such as heart failure and death. Therefore, monitoring BNP levels in AIS patients undergoing IVT may guide treatment strategy.

This study has several limitations. First, as a single-center, retrospective study with a relatively small sample size, selection bias could not be ruled out, and the findings require further validation. Second, our follow-up period was limited to 90 days, precluding an assessment of long-term prognostic outcomes in AIS patients after IVT. Lastly, due to constraints in study duration and data availability, only inter-

nal validation of our predictive model was performed. External validation is necessary to confirm its generalizability and clinical use.

Conclusion

We established a prognostic model incorporating NIHSS score, BNP, pre-thrombolysis PT, age, diabetes, and onset-to-thrombolysis time to predict clinical outcome in AIS patients after IVT. The proposed nomogram offers a practical tool for clinicians to assess prognosis and facilitate informed discussions with patients and their families. Future research should focus on refining and externally validating this predictive model, as well as exploring potential pharmacological interventions to improve outcome in this patient population.

Disclosure of conflict of interest

None.

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