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Predictors and Dynamic Nomogram to Determine the Individual Risk of Malignant Brain Edema After Endovascular Thrombectomy in Acute Ischemic Stroke

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Background and Purpose This study aimed to construct an optimal dynamic nomogram for predicting malignant brain edema (MBE) in acute ischemic stroke (AIS) patients after endovascular thrombectomy (ET).

Methods We enrolled AIS patients after ET from May 2017 to April 2021. MBE was defined as a midline shift of >5 mm at the septum pellucidum or pineal gland based on follow-up computed tomography within 5 days after ET. Multivariate logistic regression and LASSO (least absolute shrinkage and selection operator) regression were used to construct the nomogram. The area under the receiver operating characteristic curve (AUC) and decision-curve analysis were used to compare our nomogram with two previous risk models for predicting brain edema after ET.

Results MBE developed in 72 (21.9%) of the 329 eligible patients. Our dynamic web-based nomogram (https://successful.shinyapps.io/DynNomapp/) consisted of five parameters: basal cistern effacement, postoperative National Institutes of Health Stroke Scale (NIHSS) score, brain atrophy, hypoattenuation area, and stroke etiology. The nomogram showed good discrimination ability, with a C-index (Harrell's concordance index) of 0.925 (95% confidence interval=0.890−0.961), and good calibration (Hosmer-Lemeshow test, p=0.386). All variables had variance inflation factors of <1.5 and tolerances of >0.7, suggesting no significant collinearity among them. The AUC of our nomogram (0.925) was superior to those of Xiang-liang Chen and colleagues (0.843) and Ming-yang Du and colleagues (0.728).

Conclusions Our web-based dynamic nomogram reliably predicted the risk of MBE in AIS patients after ET, and hence is worthy of further evaluation.

Keywords brain edema; ischemic stroke; thrombectomy; nomograms.

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INTRODUCTION

Brain edema is a common and life-threatening complication of acute ischemic stroke (AIS). There are different definitions of cerebral edema, with reportedly 10%−78% of AIS patients developing malignant brain edema (MBE), and the risk of subsequent neurological deterioration and death ranging from 40% to 80%.[1,2] MBE has become a major stumbling block for the development of endovascular thrombectomy (ET), and is strongly associated with a poor postoperative prognosis.[3] The rapid and accurate identification of potential patients with MBE is imperative for both early neurosurgical intervention and specialized neurointensive care. Timely intervention and triaging to tertiary-care centers before the occurrence of MBE could significantly reduce the associated mortality.[4]

Predictive factors for brain edema have been widely discussed. A recent meta-analysis[1]

identified 44 potential predictors and 4 models from 38 studies, suggesting that higher National Institutes of Health Stroke Scale (NIHSS) score, larger parenchymal hypoattenuation, and younger age are reliable early indicators for malignant edema. Those authors also pointed out that four current models have the risk of overfitting because of the small-sample effect, and none of them has been validated externally. In addition, some previous well-known prediction tools, such as the TURN Score,[5] MBE score,[6] and modified EDEMA score,[7] were not specifically designed for mechanical thrombectomy patients. The Endovascular Stroke Treatment's Impact on Malignant Type of Edema (ESTIMATE) collaboration[8] that included 2,161 patients over 9 years found that patients after ET had an odds ratio (OR) for malignant edema of 0.80, whereas the ORs after intravenous (IV) thrombolysis and after no therapy were 0.88 and 1.57, respectively. Accordingly, those authors concluded that ET significantly reduced the incidence of MBE.

We have only found two existing risk models for predicting brain edema after ET, which were constructed by Chen et al.[9] in 2019 and by Du et al.[10] in 2020. Chen et al.[9] included the Alberta Stroke Program Early Computed Tomography Score (ASPECTS), hypertension, cisternal effacement, and recanalization in their nomogram for predicting patients with midline shift (MLS). Du et al.[10] included age, glucose, collateral circulation, baseline NIHSS score, and modified Thrombolysis in Cerebral Ischemia (mTICI) score in their nomogram for predicting patients with an MLS of >5 mm. The main shortcoming of these two models was that the baseline predictors gathered before constructing the nomograms were inadequate. Certain vital MBE risk factors such as consciousness status and brain atrophy were not mentioned in their studies, while the definitions of brain edema were not consistent with each other, and moreover both of them were only validated internally.

Therefore, the present study externally validated the performance of the two nomograms developed by Chen et al.[9] and Du et al.[10] Furthermore, a novel optimal dynamic nomogram was constructed to evaluate MBE after ET utilizing a larger number of potential predictors. The three tools were compared to determine whether the clinical utility and discrimination ability were better for our web-based model than for the previous two models.

METHODS

Study design and participants

This study continuously enrolled AIS patients after ET who had been admitted to the department of neurology and neurointensive care unit of the Second Affiliated Hospital of Soochow University between May 2017 and April 2021. The inclusion criteria for our study were as follows: 1) age ≥18 years, 2) large-artery occlusion in the anterior circulation confirmed by preoperative imaging, 3) time from stroke onset to puncture ≤24 hours, 4) baseline NIHSS score ≥6, and 5) no primary intracranial hemorrhage detected in admission computed tomography (CT). Cases were defined as patients who suffered from MBE, while controls were defined as AIS patients without MBE after ET. MBE was defined as an MLS of >5 mm at the septum pellucidum or pineal gland based on follow-up CT within 5 days after ET, which was consistent with the MLS criterion used in previous studies.[7,10-12] We routinely selected patients for ET and decompressive hemicraniectomy (DHC) at our institution according to the 2019 American Heart Association/American Stroke Association (ASA/AHA) guidelines[13] and previously published trials.[14,15] The exclusion criteria for our study were as follows: 1) comorbidity such as malignant tumor, severe organ failure, or other life-threatening disease; or 2) incomplete hospital records or follow-up imaging examinations.

All data involving human participants were approved by Institutional Review Board of the Second Affiliated Hospital of Soochow University (number: JD-HG-2021-035), and we were in accordance with the 1975 Helsinki declaration and its later amendments. The written informed consent was waived due to the retrospective nature of this study. The results obtained in this study were reported according to the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement.[16]

Data collection and definitions

The potential predictors of MBE selected in previous studies have been reported. The baseline data in our study included demographics, previous history, clinical features, laboratory data, ET procedures, and imaging findings. Demographics and previous history were obtained from medical records. Clinical features such as early nausea or vomiting, pupil size/reactivity, gaze, and consciousness status were extracted from the initial emergency department or admission notes. The stroke etiology was classified according to the Trial of Org 10712 in Acute Stroke (TOAST) etiology. Laboratory data were collected on admission before applying ET. The ET procedure at our institution followed the 2019 ASA/AHA guidelines.[13] Imaging information was collected from preoperative noncontrast computed tomography (NCCT), postoperative NCCT, and intraoperative digital subtraction angiography (DSA). The collateral status was assessed using the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) scale,[17] and successful recanalization was defined as an mTICI score of 2b or 3 based on DSA.[18] All CT scans were contiguous and

acquired at a slice thickness of 10 mm. Basal cistern effacement and hypoattenuation were assessed by postoperative CT after 24 hours. Additionally, the Global Cortical Atrophy (GCA) scale and the Van Swieten scale were employed to evaluate brain atrophy and white-matter disease in NCCT, respectively; these scales have been widely applied to AIS patients after thrombectomy.[19-21] Finally, a favorable functional outcome was regarded as a modified Rankin Scale (mRS) score of 0−2.

Two trained neurologists (Q.M.J. and S.Y.) blind to clinical information reviewed the MLS and the signs of MBE independently, and any disagreement was resolved by discussion and by consulting a third neurologist (G.D.X.). Supplementary Table 1 (in the online-only Data Supplement) provides a detailed explanation of each indicator collected in this study.

Statistical analysis

Continuous variables were summarized as mean±standard-deviation or median [interquartile range] values, while categorical variables were calculated as number (percentage) values. The *t*-test or Mann-Whitney U-test was employed to compare continuous variables, while the chi-square test or Fisher's exact test was used to analyze categorical variables. Least absolute shrinkage and selection operator (LASSO) regression was applied to reduce the dimensionality of the data obtained for all the clinical features.[22,23] According to LASSO regression outcomes and clinical significance, we selected significant predictors to perform multivariate logistic regression analysis and develop the nomogram. Variance inflation factors (VIFs) and tolerances were calculated to assess the collinearity assumption, with VIF <5 and tolerance >0.1 considered to indicate no significant collinearity.

The performance of the nomogram was evaluated by its discrimination ability, calibration, and clinical utility. First, the areas under the receiver operating characteristic curves (AUCs) and Harrell's concordance indexes (C-indexes) were measured to determine the discrimination abilities of the three models. Second, the calibration plot and Hosmer-Lemeshow goodness-of-fit test were used to explore the agreement between the actual MBE risk and the probability predicted using the nomogram. Third, the clinical utility was assessed using decision-curve analysis (DCA) to determine the net benefits at various threshold probabilities. We used 1,000 bootstrap resamples to internally validate our nomogram and reduce overfit bias. Fourth, we compared the clinical utility and discrimination ability of our new nomogram with those of the two models developed by Chen et al.[9] and Du et al.,[10] which were also designed to predict brain edema especially after ET in AIS.

All statistical analyses were performed using IBM SPSS Statistics (version 26.0; IBM Corp., Armonk, NY, USA), R software (version 4.1.1, R Development Core Team, Vienna, Austria), and the PROCESS Model (version 4; www.process-macro.org). The criterion for statistical significance was a two-sided p value of <0.05.

RESULTS

Patient characteristics

This study included 329 AIS patients who were treated with ET from May 2017 to April 2021, among whom MBE was detected in 21.9% (n=72) by follow-up NCCT. The demographics and clinical characteristics are compared between patients with and without MBE in Table 1.

Compared with the patients without MBE, those with MBE were more likely to have accompanying hypertension, atrial fibrillation, and nausea or vomiting (all p<0.05) (Table 1). There were also significant differences between the two groups with regard to occlusion site and stroke etiology. Patients with MBE exhibited higher initial NIHSS score, postoperative NIHSS score, diastolic blood pressure, glucose level, and numbers of stent retrievals and aspirations (all p<0.05) (Table 1). With respect to imaging findings, the ASPECTS and ASITN/SIR score were lower in the MBE group than in the no-MBE group. There were also significant intergroup differences in the hyperdense middle cerebral artery (HMCA) sign, basal cistern effacement, and postinterventional cerebral hyperdensity (PCHD) (all p<0.05) (Table 1).

The distributions of the 90-day mRS scores in the two groups are compared in Supplementary Fig. 1 (in the online-only Data Supplement). The patients without MBE were more likely to have favorable functional independence based on the 90-day mRS score (41.2% vs 15.3%, p<0.001). Supplementary Fig. 2 (in the online-only Data Supplement) illustrates that those who received DHC were more likely to have a 90-day mRS score of 3−6 (88.9% vs. 63.0%, p=0.026), but there was no significant difference in the death rate (22.2% vs. 21.9%, p>0.999). We also measured the moderating effects of DHC on the mRS score (Supplementary Fig. 3 in the online-only Data Supplement). The simple slope test showed that the two-way interaction effect of MBE and DHC was negative and significant (B=-2.55, t=-2.68, p=0.008) (Supplementary Fig. 3A in the online-only Data Supplement), as was the interaction effect of MLS and DHC (B=-0.24, t=-2.60, p=0.010) (Supplementary Fig. 3B in the online-only Data Supplement). However, no significant differences between two groups were found in other variables such as age, diabetes, cardiovascular diseases, smoking, alcohol consumption, baseline systolic blood pressure, creatinine, or calcium (all p>0.05) (Table 1).

Table 1. Comparison of demographics and clinical characteristics between patients with and without MBE

Characteristic*	With MBE (*n*=72)	Without MBE (*n*=257)	*p*
Demographics			
Age (yr)	67.0±13.0	66.0±13.7	0.665
Sex, male	30 (41.7)	146 (56.8)	0.023
Previous history			
Hypertension	55 (76.4)	160 (62.3)	0.026
Diabetes mellitus	15 (20.8)	47 (18.3)	0.625
Atrial fibrillation	44 (61.1)	114 (44.4)	0.012
Prior stroke	17 (23.6)	38 (14.8)	0.076
Cardiovascular diseases	18 (25.0)	57 (22.2)	0.614
Smoking	22 (30.6)	97 (37.7)	0.262
Alcohol consumption	17 (23.6)	67 (26.1)	0.672
Clinical features			
Nausea or vomiting on admission	17 (23.6)	28 (10.9)	0.006
Consciousness status on admission			<0.001
Drowsiness	31 (43.1)	125 (48.6)	
Lethargy	17 (23.6)	35 (13.6)	
Coma	17 (23.6)	20 (7.8)	
Gaze palsy on admission	56 (77.8)	169 (65.8)	0.053
Abnormal pupil size/reactivity on admission	22 (30.6)	29 (11.3)	<0.001
Left hemisphere stroke	33 (45.8)	129 (50.2)	0.513
Occlusion site			0.035
ICA	27 (37.5)	58 (22.6)	
MCA	40 (55.6)	181 (70.4)	
Other	5 (6.9)	18 (7.0)	
Intravenous thrombolysis	7 (9.7)	45 (17.5)	0.109
Stroke etiology			0.020
Large-artery atherosclerosis	21 (29.2)	117 (45.5)	
Cardioembolism	47 (65.3)	120 (46.7)	
Other	4 (5.6)	20 (7.8)	
Postoperative nausea or vomiting	14 (19.4)	17 (6.6)	0.001
Postoperative consciousness decline	45 (62.5)	33 (12.8)	<0.001
Postoperative gaze or abnormal pupil	63 (87.5)	124 (48.2)	<0.001
Initial NIHSS score	18 [14.0–22.8]	15 [12–18]	<0.001
Postoperative NIHSS score	22 [16.3–35.8]	13 [9–17]	<0.001
Baseline SBP (mmHg)	147.0±28.5	146.0±24.0	0.801
Baseline DBP (mmHg)	91.0±20.6	85.0±14.7	0.022
Laboratory data			
Creatinine (μmol/L)	67 [52.0–81.8]	67 [55–79]	0.908
Calcium (mmol/L)	2.2 [2.1–2.3]	2.2 [2.1–2.3]	0.792
Sodium (mmol/L)	140.0±4.0	140.0±9.2	0.882
Chloride (mmol/L)	102.2±4.7	103.2±7.3	0.258
Glucose (mmol/L)	8.3 [7.2–9.9]	7.4 [6.5–9.0]	0.005
TC (mmol/L)	4.6±1.0	4.3±1.0	0.046
TG (mmol/L)	0.9 [0.7–1.2]	1.0 [0.7–1.3]	0.739
ET			
Stent retrievals	2 [1–3]	1 [1–2]	0.010
Aspirations	1 [0–2]	0 [0–1]	0.014
Balloon dilatations	0 [0–0]	0 [0–0]	0.179
Stenting	4 (5.6)	44 (17.1)	0.014

Table 1. Comparison of demographics and clinical characteristics between patients with and without MBE (continued)

Characteristic*	With MBE (*n*=72)	Without MBE (*n*=257)	*p*
Intra-arterial thrombolysis	7 (9.7)	23 (8.9)	0.840
Postoperative mTICI score 2b/3	58 (80.6)	218 (84.8)	0.384
Duration of procedure (min)	90 [75.0–107.5]	90 [70–110]	0.957
OPT (min)	284.5 [229–343.8]	272 [208.5–370.0]	0.854
Imaging			
ASPECTS	7 [6–7]	7 [7–8]	<0.001
HMCA	41 (56.9)	101 (39.3)	0.008
Effacement of cortical sulci	45 (62.5)	128 (49.8)	0.057
ASITN/SIR score			<0.001
0, 1	69 (95.8)	188 (73.2)	
2	2 (2.8)	35 (13.6)	
3, 4	1 (1.4)	34 (13.2)	
Parenchymal hypoattenuation area			<0.001
<30%	2 (2.8)	128 (49.8)	
30–50%	2 (2.8)	35 (13.6)	
>50%	68 (94.4)	94 (36.6)	
Basal cistern effacement	53 (73.6)	35 (13.6)	<0.001
Brain atrophy	1 [0–2]	2 [1–3]	0.001
Severity of LA	3 [3–4]	3 [2.5–4.0]	0.216
Lacunar infarction	61 (84.7)	231 (89.9)	0.221
PCHD	64 (88.9)	160 (62.3)	<0.001
Symptomatic HT	14 (19.4)	70 (27.2)	0.180
Midline shift (mm)	9.4 [6.5–14.1]	0.0 [0.0–1.3]	<0.001
Decompressive hemicraniectomy	12 (16.7)	6 (2.3)	<0.001

Data are mean±SD, *n* (%), or median [IQR] values.
*A detailed explanation of each indicator is provided in Supplementary Table 1.
ASITN/SIR, American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; DBP, diastolic blood pressure; ET, endovascular thrombectomy; HMCA, hyperdense middle cerebral artery; HT, hemorrhage transformation; ICA, internal carotid artery; IQR, interquartile range; LA, leukoaraiosis; MBE, malignant brain edema; MCA, middle cerebral artery; mTICI, modified Thrombolysis in Cerebral Ischemia; NIHSS, National Institutes of Health Stroke Scale; OPT, onset to puncture time; PCHD, postinterventional cerebral hyperdensity; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglycerides.

Risk factors and nomogram for predicting MBE

LASSO regression and tenfold cross-validation identified the optimal λ (lambda.min=0.025). The 49 candidate characteristics were reduced to the following 13 features with nonzero coefficients: hypertension, previous stroke, consciousness status on admission, calcium, glucose, IV thrombolysis, postoperative NIHSS score, stenting, brain atrophy, HMCA, basal cistern effacement, hypoattenuation area, and postoperative consciousness (Fig. 1). Considering both the nonzero coefficients selected by LASSO regression and clinical significance, the dynamic nomogram was constructed using the following five features: basal cistern effacement, postoperative NIHSS score, brain atrophy, hypoattenuation area, and stroke etiology (Supplementary Fig. 4 in the online-only Data Supplement); this is also available at https://successful.shinyapps.io/DynNomapp/. The interface of this webpage is shown in Fig. 2. Items on the left side of the interface can be adjusted by the user, while the five colored lines on the right side represent the MBE probabilities and 95% confidence interval (CIs) of five individual patients as examples. Table 2 presents significant risk factors for MBE in AIS patients after ET identified in the multivariate logistic regression analysis. The statistical collinearity of the predictors included in our nomogram is presented in Supplementary Table 2 (in the online-only Data Supplement). All of the variables had VIFs of <1.5 and tolerances of >0.7, suggesting that there was no significant collinearity among them. Supplementary Table 3 (in the online-only Data Supplement) presents the scoring assignment for the nomogram in predicting MBE. For this logistic regression model, the C-index was 0.925 (95% CI=0.890–0.961) for predicting MBE, and it maintained a value of 0.915 after internal validation by 1,000 bootstrap samples. Additionally, the calibration plot (Fig. 3) and the Hosmer-Lemeshow test produced χ^2 and *p* values of 8.504 and 0.386, respectively, demonstrating good agreement between the observed and predicted probabilities of MBE and no evidence of a poor

model fit.

Comparison of nomograms

We externally validated the clinical utilities and discrimination abilities of the two nomograms developed by Chen et al.[9] and Du et al.,[10] and compared them with our nomogram using DCA plots and receiver operating characteristic curves. These two nomograms have previously been found to be useful for predicting brain edema, especially in patients who have undergone ET. Fig. 4 is a DCA plot comparing the clinical usefulness of the three nomograms, which demonstrates that our modified nomogram produced higher net benefits than the other two nomograms for all threshold probabilities. Our model exhibited a sensitivity of 69.4%, a specificity of 93.0%, a positive predictive value of 73.5%, and a negative predictive value of 91.6%. As Fig. 5 shows, the AUC of our nomogram

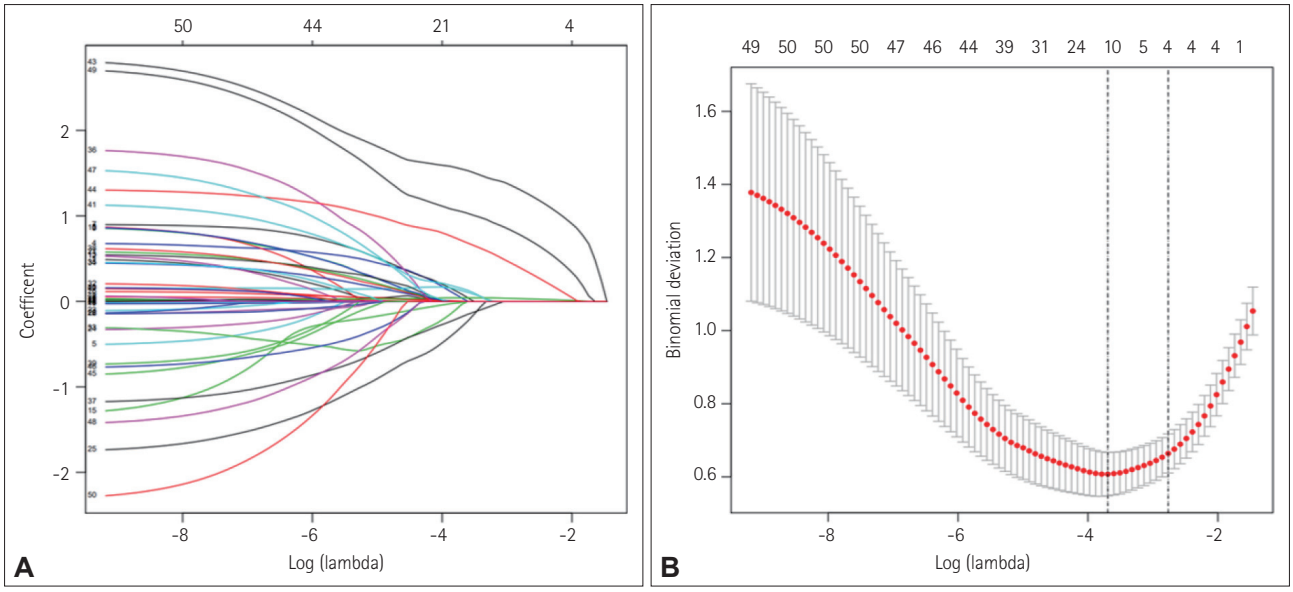

Fig. 1. Selection of predictors using the least absolute shrinkage and selection operator (LASSO) binary logistic regression model. A: Tuning parameter (λ) selection in the LASSO model used tenfold cross-validation. B: LASSO coefficient profiles of the 49 predictors. The lambda.min (0.025) resulted in 13 nonzero coefficients.

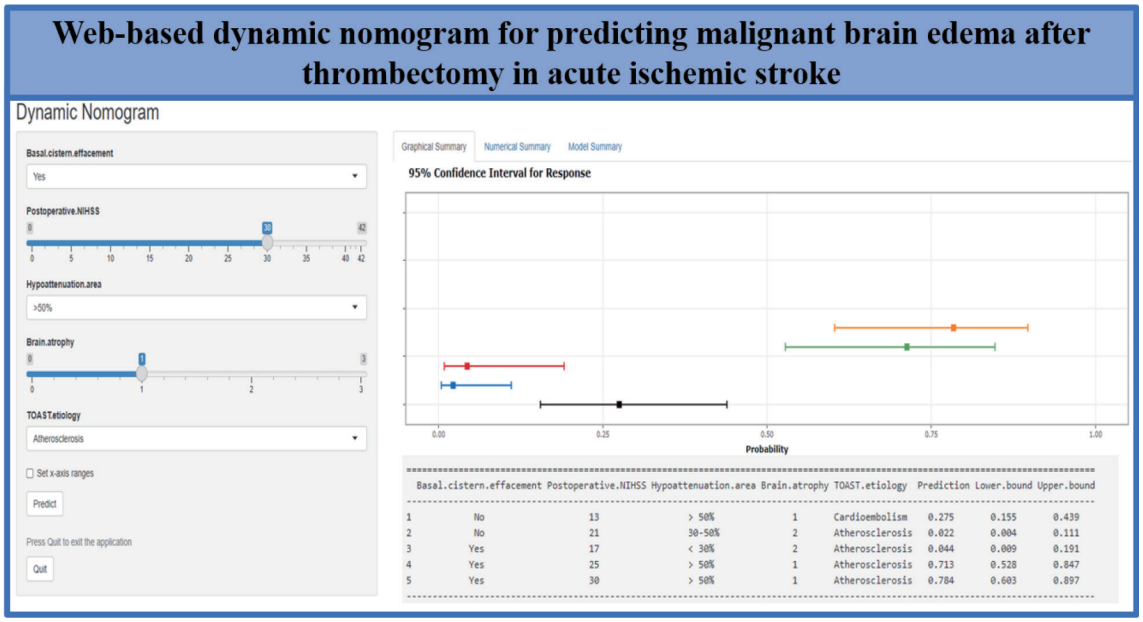

Fig. 2. Interface of the webpage for predicting malignant brain edema (MBE). Items on the left side of the interface can be adjusted by the user, while the five colored lines on the right side represent the MBE probabilities and 95% confidence intervals (CIs) for five individual patients as examples.

(0.925 [95% CI=0.890–0.961]) was superior to those of the other two prediction models: 0.843 (95% CI=0.784–0.901) for Chen et al.[9] and 0.728 (95% CI=0.664–0.792) for Du et al.[10] Our nomogram exhibited better clinical utility and discrimination ability than the previously reported nomograms.

DISCUSSION

This study established a dynamic web-based nomogram for predicting the risk of MBE especially after ET in acute anterior circulation stroke. This simple nomogram, consisting of basal cistern effacement, postoperative NIHSS score, brain atrophy, hypoattenuation area, and TOAST etiology, is a more practical and effective clinical decision-making tool than two previous nomograms.

Brain edema is a common complication that mediates a major part of the poor prognosis after thrombectomy in AIS patients.[24] The term "malignant brain edema" is sometimes referred to as "malignant cerebral edema" or "malignant middle cerebral artery infarctions," and its definitions have often been

Table 2. Significant predictors of MBE in acute ischemic stroke patients after ET from multivariate logistic regression analysis

Variable	Value	*p*
Postoperative NIHSS score	1.08 (1.03–1.13)	0.001
Stroke etiology		0.013
Large-artery atherosclerosis	Reference	
Cardioembolism	2.85 (1.17–6.94)	0.021
Other	0.41 (0.09–1.96)	0.266
Brain atrophy	0.53 (0.37–0.77)	0.001
Basal cistern effacement	7.45 (3.43–16.16)	<0.001
Parenchymal hypoattenuation area		<0.001
<30%	Reference	
30%–50%	2.72 (0.33–22.77)	0.356
>50%	15.78 (3.49–71.24)	<0.001

Data are odds ratio (confidence interval) values.
ET, endovascular thrombectomy; MBE, malignant brain edema; NIHSS, National Institutes of Health Stroke Scale.

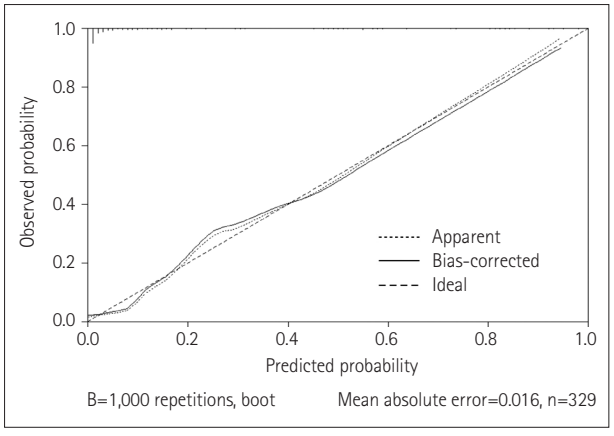

Fig. 3. Calibration plot for the nomogram. Dashed line is the reference line of an ideal nomogram. Dotted line is the performance of the new nomogram, and the solid line is the performance when bias in the nomogram is corrected.

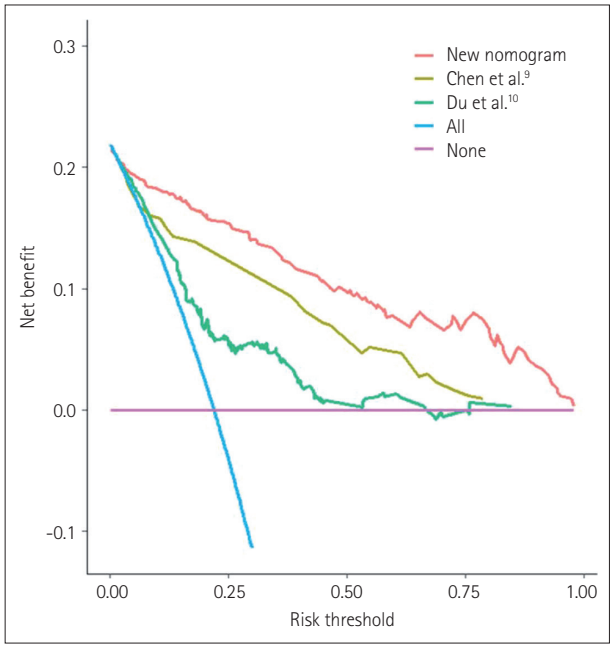

Fig. 4. Decision-curve analysis (DCA) plots comparing the clinical usefulness of the three nomograms. DCA plot demonstrating the positive net benefits of the three nomograms in predicting malignant brain edema. The net benefit is higher for our modified nomogram than for the other nomograms for all threshold probabilities.

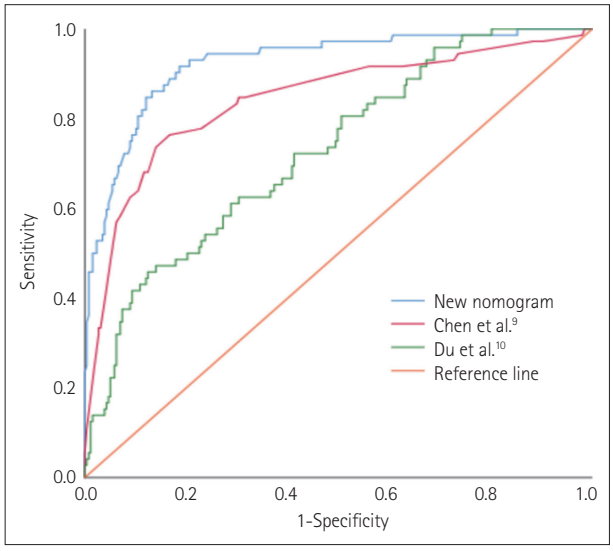

Fig. 5. Receiver operating characteristic (ROC) curves comparing the discrimination abilities of the three nomograms. ROC curves for the 2019 model of Chen et al.,[9] the 2020 model of Du et al.,[10] and our nomogram in predicting malignant brain edema. The area under the ROC curve of our nomogram (0.925 [95% CI=0.890–0.961]) was superior to those of the Chen et al.[9] model (0.843 [95% CI=0.784–0.901]) and the Du et al.[10] model (0.728 [95% CI=0.664–0.792]).

inconsistent in previous edema prediction models.[6,25] For example, most prediction models[7,10] defined malignant edema as MLS of >5 mm, whereas Chen et al.[9] distinguished brain edema by the presence or absence of MLS. Moreover, some models[5,26] differentiated it based only on clinical symptoms and outcomes. Given that such models are mainly utilized to identify when aggressive interventions are required, we defined malignant edema as an MLS of >5 mm. Malignant edema is a devastating complication for which currently therapeutic approaches are inadequate. DHC is the only treatment clearly recommended by the guideline,[2] and it was rarely performed over an 8-year period: applied to 112 (5.2%) patients in total at a rate of 2−28 operations/year, corresponding to a relative frequency of 0.00%−0.01%.[8] The present findings could be utilized as reference data for use in emergency triage, neurosurgical interventions, and postoperative stroke clinical care.

Previous studies[1,27] have evaluated numerous predictors of malignant edema. Wu et al.[1] concluded from a recent meta-analysis that younger age, higher NIHSS score, and larger parenchymal hypoattenuation on CT are reliable early predictors for malignant edema. Our findings were similar to theirs and expanded on them, with MBE being associated with the NIHSS score and parenchymal hypoattenuation but not age. We collected both the initial and postoperative NIHSS scores, and included only the latter in our final nomogram based on the outcome of LASSO regression. Moreover, we excluded age due to its broad multicollinearity and no statistical significance in our data, and added brain atrophy calculated using the GCA scale in our models, the predictive significance of which for MBE has also been demonstrated by previous studies.[28,29] Though TOAST etiology was not identified by LASSO regression, it was statistically significant in both the univariate and multivariate analyses, being highly representative of the clinical history. The basal cistern effacement, which is frequently included in published models,[9,11] also showed strong and independent associations with MBE in the present study. Moreover, in terms of radiographic predictors, we found that PCHD may be a risk factor for MBE, which has not been reported previously.[1,9,10] However, since PCHD has not being widely validated by other studies, we did not include it in our final nomogram. Radiographic or clinical variables collected immediately after thrombectomy might be more useful than their baseline characteristics, making it desirable to explore more-immediate postoperative imaging signs when attempting to predict MBE.

A few risk-assessment tools for brain edema have been reported. Among them, the TURN score[5] was used specifically for patients with IV thrombolysis, and two models[6,26] were designed for massive hemispheric ischemic stroke, accompanied by several grading scales[11,12,30] specifically for conventional AIS patients. Ultimately however, as mentioned above, only two previous studies[9,10] gathered predictors to establish models for predicting brain edema specially after ET, and these predictors were inadequate. In contrast, we identified 5 independent and easily available factors from 49 predictors in our nomogram, 3 of which were consistent with those used in previous studies: basal cistern effacement, NIHSS score, and hypoattenuation area. Although our model showed better clinical utility and discrimination ability than previous models, the comparisons were restricted to the circumstances of our data, and so external validation of our model is still required.

Our study was innovative in the following aspects: First, we have developed the first web-based dynamic nomogram for predicting MBE after thrombectomy, which can be conveniently applied in clinical practice with good clinical utility and discrimination ability. Second, we analyzed many more potential edema predictors than in previous studies to establish our nomogram. Collecting rich and abundant predictors before performing the analysis made our outcomes more scientific and meticulous. Specially designed for patients with thrombectomy, we also gathered detailed ET procedures in our studies, which contrasts with previous models. Third, we considered both preoperative and immediate postoperative predictors (e.g., pre- and postoperative NIHSS scores, and PCHD), and we newly discovered that PCHD may be a risk factor for MBE.

Despite these strengths, some limitations of this study must be acknowledged. Its retrospective design restricted the reliability of the outcomes. Furthermore, the two comparison nomograms were externally validated, but this still needs to be done for our model. To maintain the generalizability of the results and a suitable sample size, some advanced predictors based on magnetic resonance imaging or CT angiography such as venous outflow,[31] net water uptake,[32] and hypoperfusion intensity ratio[33] were not included in our study.

In summary, our web-based nomogram can be easily applied to predict the individual risk of MBE and provide vital treatment recommendations in clinical practice. We hope that future randomized case−control studies will cast further light on MBE predictors after ET, especially for predictors collected after the operation. A unified definition of MBE needs to be agreed upon so that a reliable diagnosis method can be identified.

In conclusion, this study is the first to construct a dynamic web-based nomogram from rich and abundant clinical, laboratory, and imaging parameters, which allows individual predictions of the risk of MBE specifically for patients after ET. More prospective studies are needed that focus on MBE predictors, especially those collected after the operation.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2022.18.3.298.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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