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Original Article

Predictive Modeling of Symptomatic Intracranial Hemorrhage Following Endovascular Thrombectomy: Insights From the Nationwide TREAT-AIS Registry

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Background and Purpose Symptomatic intracranial hemorrhage (sICH) following endovascular thrombectomy (EVT) is a severe complication associated with adverse functional outcomes and increased mortality rates. Currently, a reliable predictive model for sICH risk after EVT is lacking.

Methods This study used data from patients aged ≥20 years who underwent EVT for anterior circulation stroke from the nationwide Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke (TREAT-AIS). A predictive model including factors associated with an increased risk of sICH after EVT was developed to differentiate between patients with and without sICH. This model was compared existing predictive models using nationwide registry data to evaluate its relative performance.

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Results Of the 2,507 identified patients, 158 developed sICH after EVT. Factors such as diastolic blood pressure, Alberta Stroke Program Early CT Score, platelet count, glucose level, collateral score, and successful reperfusion were associated with the risk of sICH after EVT. The TREAT-AIS score demonstrated acceptable predictive accuracy (area under the curve [AUC]=0.694), with higher scores being associated with an increased risk of sICH (odds ratio=2.01 per score increase, 95% confidence interval=1.64–2.45, *P*<0.001). The discriminatory capacity of the score was similar in patients with symptom onset beyond 6 hours (AUC=0.705). Compared to existing models, the TREAT-AIS score consistently exhibited superior predictive accuracy, although this difference was marginal.

Conclusions The TREAT-AIS score outperformed existing models, and demonstrated an acceptable discriminatory capacity for distinguishing patients according to sICH risk levels. However, the differences between models were only marginal. Further research incorporating periprocedural and postprocedural factors is required to improve the predictive accuracy.

Keywords Symptomatic intracranial hemorrhage; Endovascular thrombectomy; Prediction

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Introduction

Symptomatic intracranial hemorrhage (sICH) after endovascular thrombectomy (EVT) is a critical complication in the management of acute ischemic stroke (AIS) with large vessel occlusion (LVO). Pooled data from five randomized controlled trials (RCTs) within the HERMES (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials) collaboration indicated an incidence of sICH in EVT-treated patients of approximately 4.4%.[1] Other large cohort studies have consistently reported sICH rates ranging from 4% to 7%, with variations attributed to patient demographics and diagnostic criteria.[2-4] Patients experiencing sICH after EVT typically exhibit poorer functional outcomes and higher mortality rates compared with those who do not develop sICH. Studies have demonstrated substantially lower rates of favorable functional outcomes, defined as a modified Rankin Scale (mRS) score of 0–2 at 90 days (6.5% vs. 43.3%), and higher mortality rates (54.8% vs. 25.4%).[5,6]

Several models can be used to predict the risk of sICH following EVT, such as the IER-SICH (Italian Registry of Endovascular Stroke Treatment in Acute Stroke–symptomatic intracerebral hemorrhage) nomogram, TAG (TICI-ASPECTS-glucose) score, and ASIAN (ASPECTS, baseline glucose, poor collateral circulation, passes with retriever, and onset-to-groin puncture time) score models; these models are based on various factors, including age, National Institutes of Health Stroke Scale (NIHSS) score, glucose levels, Alberta Stroke Program Early CT Score (ASPECTS), collateral status, time from stroke onset to treatment, and reperfusion success.[7-9] Although studies have claimed that these models have a high prediction accuracy, with area under the curve (AUC) values ranging from 0.685 to 0.79, each has its own inherent limitations. External validation of existing models for predicting sICH after EVT using data from the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) registry revealed a low predictive ability of existing models, with concordance (C) statistics ranging from 0.51 to 0.61, indicating that these models have limited discriminative ability for the accurate prediction of sICH.[10] These models barely outperform random chance (C statistic=0.50), highlighting the need for improved predictive models.

This study investigated the risk of sICH after EVT using data from the published Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke (TREAT-AIS).[11] By analyzing the latest TREAT-AIS data and conducting comparative analyses with previous research, we developed a novel predictive model to identify patients at a high risk of sICH following EVT. The study findings offer insights into the factors contributing to post-EVT hemorrhage, potentially leading to improved patient outcomes through more precise risk stratification, and enabling the development of proactive management strategies.

Methods

Study design and participants

TREAT-AIS is a comprehensive, prospective cohort study initiated in 2019 by the Taiwan Stroke Society to investigate the outcomes of EVT among patients with AIS and LVO. This multicenter registry encompasses 19 comprehensive stroke centers across Taiwan, enrolling patients aged ≥20 years who underwent EVT according to the guidelines of the American Heart Association/

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American Stroke Association and Taiwan Stroke Society. To assess the risk of sICH after EVT, a retrospective analysis was conducted on participants enrolled in the TREAT-AIS study who experienced an anterior circulation stroke involving the internal carotid artery (ICA) and middle cerebral artery (M1 and M2 segments). The study protocol was approved by the Joint Institutional Review Board of Taipei Medical University (N202005013) and the institutional review boards of all participating hospitals. A comprehensive list of TREAT-AIS investigators and personnel is presented in Supplementary Table 1.

Data collection

Data collection for the TREAT-AIS was a collaborative effort between project investigators, subproject investigators, stroke case managers, research assistants, and study nurses. Baseline patient demographics including age, sex, medical history (hypertension, diabetes mellitus [DM], dyslipidemia, heart disease, and prior stroke), medication profile (antiplatelets and anticoagulants), stroke severity (NIHSS score), stroke etiology (Trial of ORG 10172 in Acute Stroke Treatment [TOAST] classification), laboratory results, time metrics (stroke onset, arrival, initial imaging, arterial puncture, and first and final recanalization times), image information (pre-EVT ASPECTS, collateral scores for computed tomography angiography [CTA], and occluded vessels), procedural details (type of sedation, type of aortic arch, stenotic degree, technique employed, device used for EVT, number of passes, and modified Thrombolysis in Cerebral Infarction [mTICI] score), and functional outcomes (mRS score at discharge and 90 days).

Outcome assessment

The outcome measures included functional status, sICH, successful reperfusion, and mortality. Functional status was assessed at discharge and 90 days using the mRS score, which ranged from 0 (no symptoms) to 6 (death), with higher scores indicating worse functional deficits. sICH was defined as type 2 parenchymal hemorrhage on follow-up imaging (computed tomography or magnetic resonance imaging) approximately 24 to 36 hours following EVT, accompanied by a ≥4-point increase in NIHSS score within 36 hours posttreatment. Successful reperfusion was defined as an mTICI score of 2b to 3. All outcome assessments were independently reviewed and confirmed by the principal investigators at each site.

Statistical analysis

Categorical variables are presented as frequencies and percentages, while continuous variables are reported as means with standard deviations or medians with interquartile ranges (IQR). Categorical variables were compared using the chi-square test or Fisher's exact test, and continuous variables were analyzed using Student's t-test or the Mann–Whitney U test, as appropriate. Subsequently, least absolute shrinkage and selection operator (LASSO) regression was applied to identify independent predictors of sICH, using 1,000 iterations of bootstrap resampling.[12] This analysis yielded four significant predictors: ASPECTS, platelet count, glucose level, and collateral score. The TREAT-AIS score was subsequently developed using the regression coefficients of these four predictors to assign corresponding points within the scoring system. Patients with missing data were excluded from the analysis. Receiver operating characteristic (ROC) curve analysis was applied to assess the discriminatory ability of the TREAT-AIS score in predicting sICH. The performance of the TREAT-AIS score was compared with that of the IER-SICH nomogram, TAG, ASIAN, and STBA (systolic blood pressure, time from acute ischemic stroke until groin puncture, blood glucose, and ASPECTS) scores. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), with a P value of <0.05 considered statistically significant.

Results

Participant characteristics

A total of 3,069 patients were enrolled in the TREAT-AIS registry between January 2019 and February 2024. Of these, 205 were excluded because of ongoing follow-up, leaving 2,864 patients for analysis. Of these, 2,507 patients presented with anterior circulation stroke (ICA+M1+M2), of whom 158 developed sICH (Supplementary Figure 1). The baseline characteristics of the study participants are presented in Table 1. No significant differences were observed in age (mean, 71.4 vs. 72.1, P=0.546) or sex (female, 45.3% vs. 44.3%, P=0.800) between the two groups. Compared with patients without sICH, a higher proportion of patients with sICH had DM (42.4% vs. 33.1%, P=0.016), while a lower proportion of patients with sICH had dyslipidemia (43.7% vs. 52.3%, P=0.004). The incidence of other medical comorbidities, including hypertension, prior stroke, atrial fibrillation, ischemic heart disease, chronic kidney disease, and cancer, did not differ between the groups. Additionally, no significant differences were observed in prior antiplatelet or anticoagulant use.

In terms of clinical presentation, patients with sICH exhibited higher diastolic blood pressure (DBP; mean, 91.9 vs. 87.4 mm Hg, P=0.005), higher NIHSS score (median, 19 vs. 17, P=0.003), and lower ASPECTS score (median [IQR], 8 [6–9] vs. 8 [7–10], P=0.001) compared with those without sICH. The percentage of participants who received intravenous thrombolysis (IVT) did not differ between the two groups. Laboratory findings revealed lower platelet counts (mean, 186.5×10^3/μL vs. 211.3×10^3/μL, P<0.001),

Table 1. Baseline characteristics of the study participants

	Without sICH (n=2,349)	With sICH (n=158)	*P*
Demographic characteristics			
Age (yr)	71.4±13.3	72.1±12.0	0.546
Female sex	1,065 (45.3)	70 (44.3)	0.800
Past medical history			
Hypertension	1,726 (73.5)	122 (77.2)	0.302
Diabetes mellitus	777 (33.1)	67 (42.4)	0.016
Dyslipidemia	1,229 (52.3)	69 (43.7)	0.004
Prior stroke	452 (19.2)	27 (17.1)	0.505
Atrial fibrillation	1,290 (54.9)	96 (60.8)	0.153
Ischemic heart disease	351 (14.9)	16 (10.1)	0.097
Chronic kidney disease	170 (7.2)	9 (5.7)	0.467
Cancer	323 (13.8)	18 (11.4)	0.403
Prior medication			
Antiplatelets	425 (18.1)	28 (17.7)	0.907
Anticoagulants	374 (15.9)	32 (20.3)	0.153
Clinical presentation			
Systolic blood pressure (mm Hg)	152.8±29.5	153.6±28.0	0.747
Diastolic blood pressure (mm Hg)	87.4±19.8	91.9±20.3	0.005
NIHSS	17 [13–23]	19 [16–23]	0.003
ASPECTS	8 [7–10]	8 [6–9]	0.001
IVT (n=2,379)	919 (41.2)	66 (45.2)	0.346
Laboratory data			
White blood count (×10^3/μL)	8.9±4.2	9.5±5.0	0.158
Platelet count (×10^3/μL)	211.3±76.7	186.5±58.2	<0.001
INR	1 [1.0–1.1]	1 [1.0–1.1]	0.959
Creatinine (mg/dL)	1.2±1.1	1.2±1.0	0.707
Glucose (mg/dL)	143.9±55.8	160.8±60.1	<0.001
HbA1c (%)	6.3±1.3	6.4±1.4	0.142
Triglyceride (mg/dL)	111.5±99.2	112.1±105.0	0.940
LDL cholesterol (mg/dL)	94.6±35.5	88.3±32.5	0.043
Time metrics (min)			
Onset to needle	110 [86–152]	125.5 [94–153.5]	0.270
Onset to puncture	250 [185–359]	275 [194–358]	0.184
Puncture to recanalization	48 [27–80]	55 [32–102]	0.038
Onset to recanalization	315 [237–432]	325 [259–428]	0.570
Collateral score (n=1,672)			<0.001
mCTA score 0–2	423 (27.0)	51 (48.1)	
mCTA score 3–5	1,143 (73.0)	55 (51.9)	
Cause of stroke			0.365
Large-artery atherosclerosis	769 (32.7)	42 (26.6)	
Cardioembolic	1,134 (48.3)	87 (55.1)	
Others	446 (19.0)	29 (18.3)	
Occluded vessels			
ICA (cervical ICA+carotid terminus)	684 (29.1)	59 (37.3)	0.029
M1	1,553 (66.1)	110 (69.6)	0.367
M2	599 (25.5)	33 (20.9)	0.196
Others	123 (5.2)	10 (6.3)	0.553
Outcome			
Successful reperfusion	1,971 (83.9)	119 (75.3)	0.005
90-day mRS 0–2 (n=2,278)	661 (31.0)	4 (2.8)	<0.001
Death	363 (15.5)	76 (48.1)	<0.001

Values are presented as mean±standard deviation, n (%), or median [interquartile range].
sICH, symptomatic intracranial hemorrhage; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; IVT, intravenous thrombolysis; INR, international normalized ratio; HbA1c, hemoglobin A1c; LDL, low-density lipoprotein; mCTA, multiphase computed tomography angiography; ICA, internal carotid artery; M1, middle cerebral artery first segment; M2, middle cerebral artery second segment; mRS, modified Rankin Scale.

higher glucose levels (mean, 160.8 mg/dL vs. 143.9 mg/dL, *P*< 0.001), and lower low-density lipoprotein (LDL) cholesterol levels (mean, 94.6 mg/dL vs. 88.3 mg/dL, *P*=0.043) in the sICH group compared with the non-sICH group.

Regarding time metrics, no significant differences were observed between the two groups in the onset-to-needle or onset-to-puncture times. However, the puncture-to-recanalization time was longer in the sICH group (median, 55 min vs. 48 min, *P*= 0.038). A higher prevalence of patients in the sICH group further demonstrated low collateral scores (multiphase CTA [mCTA] collateral score 0–2: 48.1% vs. 27.0%, *P*<0.001) and ICA occlusion (37.3% vs. 29.1%, *P*=0.029), the EVT procedures did not differ between the two groups (Supplementary Table 2). Successful reperfusion rates were lower in the sICH group (75.3% vs. 83.9%, *P*=0.005) than the non-sICH group. Notably, patients in the sICH group had worse outcomes, including higher mortality rates, and a significantly lower proportion of favorable outcomes (mRS 0–2) at 90 days.

Predictors of sICH development

Multivariate logistic regression analysis, with variables selected using the LASSO method, identified several independent predictors of sICH after EVT, including DBP (odds ratio [OR]=1.02, 95% confidence interval [CI]=1.01–1.03), ASPECTS (OR=0.85, 95% CI=0.76–0.96), platelet count (OR=0.99, 95% CI=0.99–1.00), glucose level (OR=1.01, 95% CI=1.00–1.01), collateral score (OR=0.56, 95% CI=0.34–0.90), and successful reperfusion (OR=

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Table 2. Results of the univariate and multivariate logistic regression analyses

Variable	Univariate analysis		Multivariate analysis		
	OR (95% CI)	*P*	Beta coefficient	OR (95% CI)	*P*
Age	1.01 (0.99–1.02)	0.379			
Systolic blood pressure	1.00 (0.99–1.01)	0.897			
Diastolic blood pressure	1.01 (1.00–1.02)	0.065	0.019	1.02 (1.01–1.03)	0.006
NIHSS	1.02 (0.99–1.06)	0.167			
ASPECTS	0.81 (0.73–0.89)	<0.001	-0.162	0.85 (0.76–0.96)	0.007
White blood count	1.03 (0.99–1.08)	0.111			
Platelet count	0.99 (0.99–1.00)	<0.001	-0.007	0.99 (0.99–1.00)	<0.001
Glucose level	1.01 (1.00–1.01)	0.003	0.006	1.01 (1.00–1.01)	<0.001
Triglyceride	1.00 (0.99–1.00)	0.316			
Low-density lipoprotein cholesterol	0.99 (0.99–1.00)	0.051			
Puncture to recanalization	1.00 (1.00–1.01)	0.252			
mCTA score 3–5	0.44 (0.29–0.66)	<0.001	-0.586	0.56 (0.34–0.90)	0.017
mTICI 2b-3	0.56 (0.35–0.90)	0.016	-0.560	0.57 (0.33–0.99)	0.047

NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; mCTA, multiphase computed tomography angiography; mTICI, modified Thrombolysis in Cerebral Infarction; OR, odds ratio; CI, confidence interval.

Table 3. Components of the TREAT-AIS score

Variable	Range	Score
ASPECTS	≤7	1
	>7	0
Platelet count	<100,000/μL	2
	≥100,000/μL	0
Glucose level	>150 mg/dL	1
	≤150 mg/dL	0
mCTA score	0–2	1
	3–5	0

TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; ASPECTS, Alberta Stroke Program Early CT Score; mCTA, multiphase computed tomography angiography.

0.57, 95% CI=0.33–0.99) (Table 2). After bootstrapping with 1,000 iterations, only the ASPECTS, platelet count, glucose level, and collateral score were retained as independent predictors of sICH after EVT.

TREAT-AIS score

To predict sICH after EVT, a TREAT-AIS score was developed based on the four predictors identified in multivariate logistic regression analysis (Supplementary Table 3). The score components are listed in Table 3. The cutoff value for the ASPECTS was based on the Interventional Management of Stroke (IMS)-III trial, which categorized patients into two groups: scores of 8–10 and scores of 0–7.[13] For glucose level, a cutoff of 150 mg/dL was applied, in accordance with the Stroke Hyperglycemia Insulin Network Effort (SHINE) trial.[14] The TREAT-AIS score includes points for ASPECTS ≤7 (1 point), platelet count <100,000/μL (2 points), glucose level >150 mg/dL (1 point), and mCTA score 0–2 (1 point). The sICH rates according to TREAT-AIS scores are shown in Supplementary Table 4. Higher TREAT-AIS scores were correlated with increased sICH risk (OR=2.01 per score increase, 95% CI=1.64–2.45, *P*<0.001) (Supplementary Table 5), demonstrating an acceptable predictive accuracy (AUC=0.694) (Figure 1). Additionally, considering the extended EVT treatment window of 6–24 hours post-stroke onset, an analysis of patients with symptom onset beyond 6 hours further revealed an acceptable predictive accuracy for the TREAT-AIS score (AUC=0.705) (Figure 2). However, the calibration of the total score using the Hosmer-Lemeshow test was not satisfactory (Supplementary Figure 2).

Comparison with existing predictive models

The predictive accuracy of the TREAT-AIS score was compared with that of previously published models (IER-SICH nomogram and the TAG, ASIAN, and STBA scores) using the same TREAT-AIS data. Table 4 presents a summary of the performance of current predictive models for predicting the risk of sICH in patients who have undergone EVT.[7-9,15-19] These models, predominantly developed in China, enrolled patients from 2011 to 2021. Among the eight relevant studies assessed, four employed clinical predictors, and four used a combination of clinical and imaging predictors. The results revealed varying predictive abilities across the models, with AUC values ranging from 0.571 to 0.668, which were below the accuracy value of the TREAT-AIS score (Figure 1 and Table 4). Pairwise comparisons of the AUCs between the TREAT-AIS and the other predictive models indicated that both the

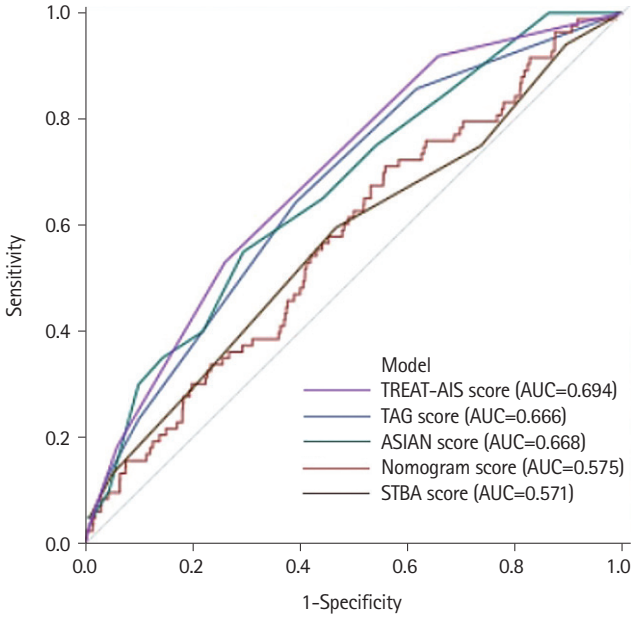

Figure 1. Receiver operating characteristic (ROC) curve for the prediction of symptomatic intracranial hemorrhage after endovascular thrombectomy. The ROC curve showed that the TREAT-AIS score had a higher predictive accuracy than the TAG, ASIAN, IER-SICH nomogram, and STBA scores. TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; AUC, area under the curve. TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; TAG, TICI-ASPECTS-glucose; ASIAN, ASPECTS, baseline glucose, poor collateral circulation, passes with retriever, and onset-to-groin puncture time; IER-SICH, Italian Registry of Endovascular Stroke Treatment in Acute Stroke–symptomatic intracerebral hemorrhage; STBA, systolic blood pressure, time from acute ischemic stroke until groin puncture, blood glucose, and ASPECTS.

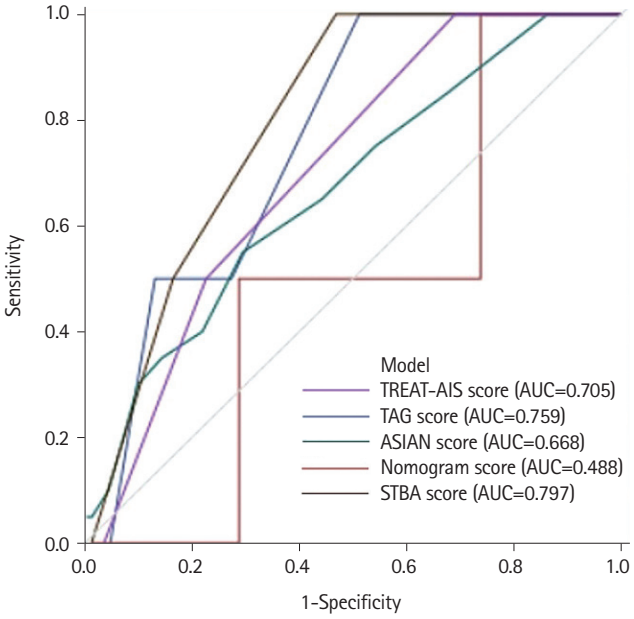

Figure 2. Receiver operating characteristic curve for the prediction of symptomatic intracranial hemorrhage after endovascular thrombectomy in patients with symptom onset beyond 6 hours. In patients who underwent endovascular thrombectomy with symptom onset beyond 6 hours, most scores demonstrated improved predictive accuracy, except for the IER-SICH nomogram. AUC, area under the curve; TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; TAG, TICI-ASPECTS-glucose; ASIAN, ASPECTS, baseline glucose, poor collateral circulation, passes with retriever, and onset-to-groin puncture time; IER-SICH, Italian Registry of Endovascular Stroke Treatment in Acute Stroke–symptomatic intracerebral hemorrhage; STBA, systolic blood pressure, time from acute ischemic stroke until groin puncture, blood glucose, and ASPECTS.

TREAT-AIS and TAG scores outperformed the STBA score; however, no significant differences were observed between the remaining models (Supplementary Table 6). In addition, these models exhibited poor calibration (Supplementary Table 5 and Supplementary Figure 3). When validated using data from the MR CLEAN registry, all models demonstrated limited predictive ability (C-statistic=0.51 to 0.61) (Table 4).[10] However, most models, with the exception of the IER-SICH nomogram, exhibited improved predictive accuracy in patients with symptom onset beyond 6 hours (Figure 2).

Discussion

In the present study, the TREAT-AIS score was developed to predict sICH following EVT, incorporating the ASPECTS, platelet count, glucose level, and collateral scores as predictive factors. The model demonstrated acceptable overall prediction accuracy in patients receiving EVT within and beyond 6 hours of symptom onset. Although the TREAT-AIS score showed better predictive accuracy than existing models, none of the models achieved excellent predictive performance. Nevertheless, the TREAT-AIS score still represents a valuable tool for clinicians to assess the risk of sICH in patients undergoing EVT, thereby supporting informed decision-making and potentially improving patient outcomes.

The TREAT-AIS registry was the result of a large-scale prospective cohort study that examined patient outcomes following EVT for AIS and LVO. Of the 2,507 patients included in this study, 158 (6.3%) developed sICH after EVT, which aligns with the results of previous large-scale clinical trials and RCTs.[1-4] Despite advancements in EVT techniques and improved overall outcomes, sICH remains a critical complication. Among the patients who developed sICH in the TREAT-AIS study, only 2.8% achieved favorable functional outcomes 90 days posttreatment. Additionally, nearly half of these patients died within three months. These findings underscore the severe impact of sICH on patient prognosis after EVT for patients with AIS and LVO.

Consistent with previous research, our study demonstrated a strong correlation between lower ASPECTS and an increased risk of sICH. Studies have reported poorer outcomes and higher sICH rates following EVT in patients with ASPECTS <6.[20] Our findings extend these observations, indicating that patients with ASPECTS ≤7 are at an increased risk of sICH. This aligns with the results

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Table 4. Summary of the performances of existing models in predicting sICH after EVT

Study	Country	Enrollment year	Patient with and without sICH	Definition of sICH*	Variables	AUC	MR CLEAN (C statistic)	TREAT-AIS (AUC)
Cappellari et al.[7] (IER-SICH)	Italy	2011–2016	110/878	ECASS II definition	Careggi collateral score, successful recanalization, onset-to-procedure time, age, NIHSS score	0.778	0.60	0.575
Montalvo et al.[8] (TAG)	USA	2014–2017	19/559	ECASS III definition	mTICI, ASPECTS, glucose levels	0.79	0.54	0.666
Zhang et al.[9] (ASIAN)	China	2014–2016	87/542	Heidelberg Bleeding Classification	ASPECTS, glucose levels, poor collateral circulation, passes with retriever, onset-to-groin puncture time >270 min	0.771	0.58	0.668
Qian et al.[15]	China	2015–2019	21/106	Heidelberg Bleeding Classification	Sex, age, infarction region, thrombectomy maneuvers, NIHSS score, DM, glucose levels	0.82	0.54	NA
Kang et al.[16]	China	2018–2021	23/220	ECASS III definition	Glucose levels, ASPECTS, rLMC score	0.856	NA	NA
Janvier et al.[17] (TAGE)	France	2015–2020	40/362	ECASS II definition	Time to successful reperfusion, ASPECTS, glucose levels, early venous filling	0.832	NA	NA
Lei et al.[18] (STBA)	China	2017–2020	30/238	Hemorrhagic transformation with an increase in NIHSS score ≥4	SBP, onset-to-groin puncture time ≥300 min, glucose levels, ASPECTS	0.858	NA	0.571
Chang et al.[19] (CAGA)	China	2016–2021	17/92	ECASS II definition	Age ≥70 yr, AF, glucose levels ≥11.1 mmol/L, CE-ASPECTS <5, CE locations	0.85	NA	NA

IER-SICH, Italian Registry of Endovascular Stroke Treatment in Acute Stroke–symptomatic intracerebral hemorrhage; TAG, TICI-ASPECTS-glucose; ASIAN, ASPECTS, baseline glucose, poor collateral circulation, passes with retriever, and onset-to-groin puncture time; TAGE, time–Alberta Stroke Program Early CT–glycemia–early venous filling; STBA, systolic blood pressure, time from acute ischemic stroke until groin puncture, blood glucose, and ASPECTS; CAGA, contrast enhancement–age–glucose–atrial fibrillation; sICH, symptomatic intracranial hemorrhage; EVT, endovascular thrombectomy; AUC, area under the curve; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; ECASS, European Cooperative Acute Stroke Study; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified Thrombolysis in Cerebral Infarction; ASPECTS, Alberta Stroke Program Early CT Score; DM, diabetes mellitus; rLMC, regional leptomeningeal score; SBP, systolic blood pressure; AF, atrial fibrillation; CE, contrast-enhanced; CT, computed tomography; MRI, magnetic resonance imaging.
*ECASS II definition: any intracranial hemorrhage on imaging control performed 24 h after mechanical thrombectomy, associated with neurological deterioration (a ≥4-point increase in NIHSS scores from baseline); ECASS III definition: any hemorrhage on follow-up brain image (CT or MRI) that caused neurologic deterioration, indicated by an NIHSS score ≥4 points compared with baseline or the lowest value within 24 h, or any hemorrhage leading to death; Heidelberg Bleeding Classification: new intracranial hemorrhage detected on brain imaging associated with any of the following items: (1) total NIHSS score ≥4 points at the time of diagnosis compared with immediately before worsening, (2) ≥2 points in one NIHSS category, or (3) leading to intubation/hemicraniectomy/external ventricular drain placement or other major medical/surgical intervention.

of other predictive models, including the TAG, ASIAN, STBA, and TAGE (time–Alberta Stroke Program Early CT–glycemia–early venous filling) scores, further emphasizing the prognostic importance of ASPECTS, particularly scores ≤7, in predicting sICH risk following EVT. These findings underscore the clinical utility of the ASPECTS for risk stratification.

In contrast to previous predictive models, the platelet count was identified as a novel predictor of sICH following EVT in the present study. Platelet counts <100,000/μL are contraindicated in IVT due to increased bleeding risk and uncertain safety and efficacy.[21,22] Previous EVT trials, such as SWIFT PRIME (Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment) and EXTEND IA (Extending the Time for Thrombolysis in Emergency Neurological Deficits — Intra-Arterial), also excluded patients with a platelet count <100,000/μL.[23,24] Our study represents the first attempt to use the platelet count as a predictor to predict sICH after EVT, particularly in patients with platelet count <100,000/μL. This result contrasts with the previous MERCI (Mechanical Embolus Removal in Cerebral Ischemia) and Multi MERCI trials, which indicated no association between abnormal hemostasis and sICH risk following EVT.[25] However, although the platelet count was identified as a risk factor, no significant differences were observed in other coagulation parameters such as international normalized ratio, partial thromboplastin time, and activated partial thromboplastin time between the two groups.

The glucose level is another predictor commonly used in most scoring systems to predict sICH risk following EVT which plays a crucial role in our scoring system. Hyperglycemia was demon-

strated to exacerbate endothelial apoptosis, leading to increased hemorrhagic transformation in the ischemic brain tissue.[26] Our study substantiated this finding, indicating that patients with hyperglycemia exhibited a higher risk of sICH following EVT. This aligns with our previously published study, which demonstrated that DM, admission glucose level, and glucose-to-HbA1C ratio were associated with poor functional outcomes and sICH.[27] These findings are further consistent with those from the MR CLEAN registry, and underscore the importance of glucose levels in the development of sICH among patients who have undergone EVT.[28]

Finally, consistent with prior research, our study demonstrated a strong association between poor collateral blood flow and an increased risk of sICH. Previous studies have emphasized the role of collateral circulation in mitigating hemorrhagic transformation following EVT.[29] Patients with a more developed collateral circulation may further experience a reduced infarct volume and subsequent reperfusion injury after EVT, which is believed to be associated with hemorrhage risk.[30,31] In the present study, patients with an mCTA score of 0–2 had a significantly higher risk of developing sICH, highlighting the importance of collateral circulation in influencing patient outcomes. This finding further supports the value of assessing collateral blood flow as part of the risk stratification process in patients undergoing EVT.

In addition to the TREAT-AIS score, we observed that elevated DBP was associated with an increased risk of sICH following EVT. This finding is inconsistent with the finding of the STBA score, which identified elevated systolic blood pressure (SBP) as a significant risk factor.[17] However, our study included a substantially larger number of patients than the STBA registry (2,507 vs. 268), and also demonstrated better predictive accuracy, thereby providing stronger evidence. Furthermore, a recent meta-analysis of four RCTs, namely the BEST-II (Blood Pressure After Endovascular Stroke Therapy-II), BP-TARGET (Blood Pressure Target in Acute Stroke to Reduce Hemorrhage After Endovascular Therapy), ENCHANTED2/MT (Second Enhanced Control of Hypertension and Thrombectomy Stroke Study), and OPTIMAL-BP (Outcome in Patients Treated With Intra-Arterial Thrombectomy–Optimal Blood Pressure Control) studies, suggested that intensive SBP control was associated with a higher incidence of sICH, further challenging the finding of elevated SBP as a predictor of sICH.[32] The possible explanation for our finding is that elevated DBP reflects a higher pressure in the arteries even when the heart is at rest, which may contribute to hemorrhage by increasing strain on the vascular walls.

Additionally, consistent with the findings from the IER-SICH nomogram and TAG score, patients in the TREAT-AIS cohort who developed sICH after EVT exhibited lower rates of successful reperfusion. Prolonged ischemia associated with unsuccessful reperfusion may weaken the integrity of blood vessels, predisposing them to rupture, and leading to subsequent hemorrhage when blood flow is eventually restored, even partially.[33,34] However, in contrast to other established models (IER-SICH nomogram and the ASIAN, TAGE, and STBA scores), no significant differences in onset-to-groin puncture time or procedural maneuvers (number of passes) were observed between the sICH and non-sICH groups. The absence of image-based predictors in the TREAT-AIS score further limited direct comparisons with other models such as the TAGE and CAGA (contrast enhancement–age–glucose–atrial fibrillation) scores.

Overall, the TREAT-AIS score revealed a marginally better predictive performance than the other models, especially when compared to the ASIAN and TAG scores. However, all the models exhibited only limited predictive accuracy. This finding aligns with the results of external validation using the MR CLEAN registry, which indicated that current predictive models may lack sufficient clinical utility.[10] The limited accuracy of these models may be attributed to other factors that are difficult to quantify, such as procedural technique, blood pressure management during and after thrombectomy, and postoperative care. These factors are likely to significantly contribute to sICH development. Despite these uncontrolled variables, our new model outperformed the existing models and provided additional evidence to validate the current risk factors associated with sICH.

A notable strength of the present study is the large sample size used to develop a predictive model for sICH after EVT. To the best of our knowledge, this study enrolled the largest cohort to date, benefiting from a period of refined EVT criteria from 2019. Furthermore, the incorporation of the platelet count as a predictor enhanced the model's predictive power, as it has not been used in prior models. However, this study has some limitations that should be considered. First, the observational nature of the study may have introduced a selection bias and limitations in establishing causality. Secondly, despite the large sample size, missing data related to certain registry variables may have influenced the outcomes. Third, the generalizability of our findings to diverse healthcare settings and populations warrants further investigation. Differences in healthcare systems, patient demographics, and clinical practices can further affect the applicability of predictive models in other contexts. Furthermore, as this study utilized data from a nationwide registry limited to the Taiwanese population, the predictive score should be tested using clinical datasets from multiple nations and ethnic groups. Finally, although the TREAT-AIS score incorporates platelet count as a predictor, which has not been previously included in other models, external validation in independent cohorts is essential to confirm its robustness and utility in diverse clinical environments.

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Conclusions

The findings of this study provide critical insights into the predictive factors for sICH following EVT, with particular emphasis on the importance of the ASPECTS, platelet count, glucose level, and collateral score. The inclusion of these variables in the predictive model enhances its accuracy and utility in clinical practice, thereby enabling healthcare providers to identify patients at an elevated risk for sICH and tailor management strategies accordingly. However, the marginal superiority of our model compared to existing models indicates that improving predictive accuracy remains an unmet need. In conclusion, the demonstration of the efficacy of the TREAT-AIS score represents a notable advancement in the prediction of sICH after EVT. Future research should focus on refining the model by validating its applicability across diverse populations, exploring additional predictors, and incorporating periprocedural and postprocedural factors to enhance its predictive accuracy.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2024.04119.

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Conflicts of interest

The authors have no financial conflicts of interest.

Author contribution

Conceptualization: LC. Study design: JHC. Methodology: YCH. Data collection: ICS, YHL, CHC, CJL, YWC, KHL, PSS, CWT, HJC, CHF, CLC, CYW, SYY, PLC, HLY, SFS, HML, CHL, ML, IHL. Investigation: SCT. Statistical analysis: YCH, HYC. Writing—original draft: JHC. Writing—review & editing: LC. Funding acquisition: LML, JTL, JSJ. Approval of final manuscript: all authors.

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Supplementary Table 1. Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke (TREAT-AIS) investigators

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Chang Bing Show Chwan Memorial Hospital	Cheng-Yu Wei (principal investigator), Chih- Lin Chen, Pei-han Wu, Yi-Ching Tsai
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Taichung Veterans General Hospital	Po-Lin Chen (principal investigator), Yuang-Seng Tsuei, Wen-Hsien Chen, Nien-Chen Liao, Yeng-Fung Liaw
Shin Kong WHS Memorial Hospital	Hsu-Ling Yeh (principal investigator), Li-Ming Lien, Chen-Yu Hsiao, Kuan-Yu Lin, Tsui-Hua Yang
Taipei Medical University Shuang-Ho Hospital	Lung Chan (principal investigator), Jia-Hung Chen, Shun-Fan Yu, I-Chang Su, Yueh-Hsun Lu
Ditmanson Medical Foundation Chia-Yi Christian Hospital	Sheng-Feng Sung (principal investigator), Tzu-Hsien Yang, Yung-Chu Hsu, Yu-Hsiang Su, Ling-Chien Hung, Mao-Hsun Lin, Chien-Yu Su
Fu Jen Catholic University Hospital	Hon-Man Liu (principal investigator), Yung-Chuan Huang, Chih-Cheng Wan
Kaohsiung Veterans General Hospital	Ching-Huang Lin (principal investigator), Cheng- Chang Yen, Ching-Sen Shih
Chiayi Chang Gung Memorial Hospital	Meng Lee (principal investigator), Yuan-Hsiung Tsai, Yen-Chu Huang, Wei-Tse Hung, Jiann-Der Lee

Supplementary Table 2. Procedures of endovascular thrombectomy

Procedures of EVT	Without sICH (n=2,349)	With sICH (n=158)	*P*
General anesthesia	1,332 (56.7)	94 (59.5)	0.493
Aspiration only	1,305 (55.6)	84 (53.2)	0.558
Stentriever+aspiration	202 (8.6)	17 (10.8)	0.352
Stentriever pass	2 [1–2]	2 [1–3]	0.240
Intra-arterial thrombolysis	63 (2.7)	2 (1.3)	0.278
Balloon angioplasty	181 (7.7)	8 (5.1)	0.223
Permanent stenting	101 (4.3)	4 (2.5)	0.283

Values are presented as n (%) or median [interquartile range].
EVT, endovascular thrombectomy; sICH, symptomatic intracranial hemorrhage.

Supplementary Table 3. Final model for the prediction of symptomatic intracranial hemorrhage

Variables	Beta coefficient	OR	95% CI	*P*	Score
ASPECTS ≤7 (ref: >7)	0.717	2.048	1.334–3.145	0.001	1
Platelet <100,000/μL (ref: ≥100,000/μL)	1.189	3.282	1.525–7.064	0.002	2
Glucose >150 mg/dL (ref: ≤150 mg/dL)	0.824	2.280	1.499–3.467	<0.001	1
mCTA score 0–2 (ref: 3–5)	0.670	1.954	1.273–2.998	0.002	1

ASPECTS, Alberta Stroke Program Early CT Score; mCTA, multiphase computed tomography angiography; OR, odds ratio; CI, confidence interval.

Supplementary Table 4. The sICH rates according to TREAT-AIS scores

TREAT-AIS scores	Patients (n)	sICH (n)	sICH rate (95% CI) (%)
0	507	8	1.58 (0.49–2.66)
1	615	38	6.18 (4.28–8.08)
2	326	34	10.43 (7.11–13.75)
3	93	15	16.13 (8.65–23.60)
4–5	12	3	25.00 (0.50–49.50)

TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; sICH, symptomatic intracranial hemorrhage; CI, confidence interval.

Supplementary Table 5. Calibration results of TREAT-AIS and other predictive models

Variable	Beta coefficient	OR (95% CI)	*P*
TAG score	0.360	1.43 (1.27–1.62)	<0.001
IER-SICH nomogram score	-0.130	0.88 (0.80–0.97)	0.009
ASIAN score	0.206	1.23 (1.06–1.43)	0.008
STBA score	0.214	1.24 (1.05–1.46)	0.010
TREAT-AIS score	0.696	2.01 (1.64–2.45)	<0.001

TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; TAG, TICI-ASPECTS-glucose; IER-SICH, Italian Registry of Endovascular Stroke Treatment in Acute Stroke–symptomatic intracerebral hemorrhage; ASIAN, ASPECTS, baseline glucose, poor collateral circulation, passes with retriever, and onset-to-groin puncture time; STBA, systolic blood pressure, time from acute ischemic stroke until groin puncture, blood glucose, and ASPECTS; OR, odds ratio; CI, confidence interval.

Supplementary Table 6. Pairwise comparisons of AUCs between TREAT-AIS and other predictive models

	TAG score	IER-SICH nomogram	ASIAN score	STBA score	TREAT-AIS score
TAG score	-	0.335	0.814	0.044	0.983
IER-SICH nomogram	-	-	0.798	0.257	0.553
ASIAN score	-	-	-	0.170	0.696
STBA score	-	-	-	-	0.049
TREAT-AIS score	-	-	-	-	-

AUC, area under the curve; TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; TAG, TICI-ASPECTS-glucose; IER-SICH, Italian Registry of Endovascular Stroke Treatment in Acute Stroke–symptomatic intracerebral hemorrhage; ASIAN, ASPECTS, baseline glucose, poor collateral circulation, passes with retriever, and onset-to-groin puncture time; STBA, systolic blood pressure, time from acute ischemic stroke until groin puncture, blood glucose, and ASPECTS.

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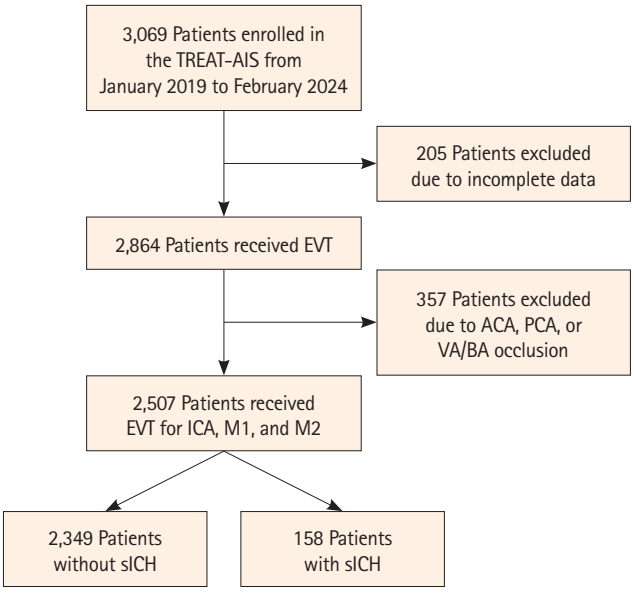
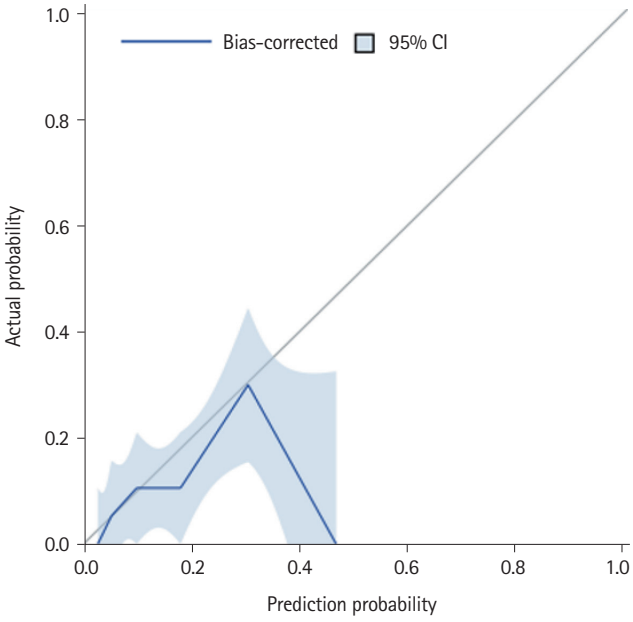
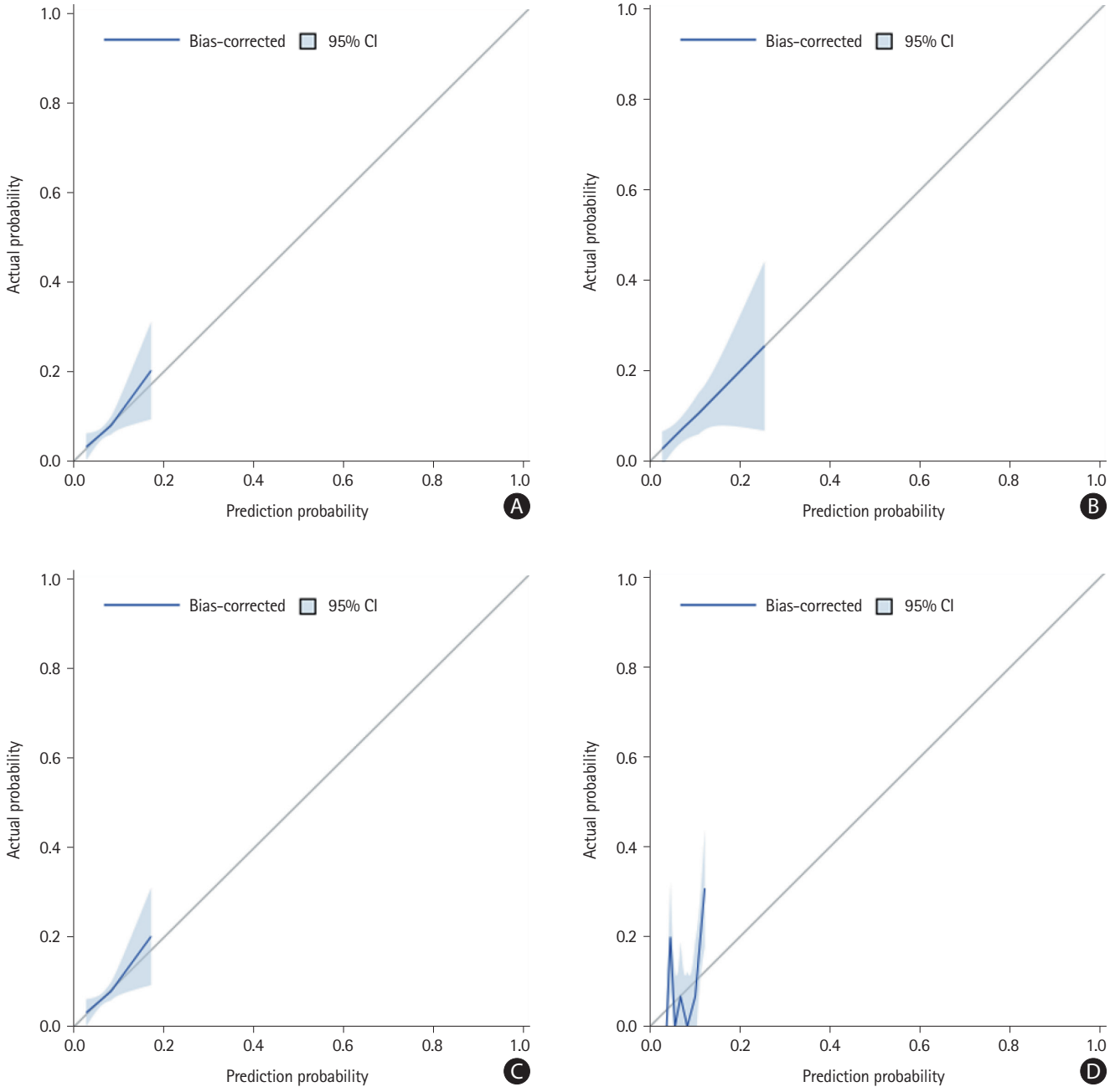


Supplementary Figure 1. Patient selection flowchart. TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; EVT, endovascular thrombectomy; ACA, anterior cerebral artery; PCA, posterior cerebral artery; VA, vertebral artery; BA, basilar artery; ICA, internal carotid artery; M1, middle cerebral artery first segment; M2, middle cerebral artery second segment; sICH, symptomatic intracranial hemorrhage.



Supplementary Figure 2. Calibration plot of the TREAT-AIS score using Hosmer-Lemeshow test. TREAT-AIS, Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; CI, confidence interval.



Supplementary Figure 3. Calibration plot of the (A) TAG score, (B) ASIAN score, (C) IER-SICH nomogram, and (D) STBA score using Hosmer-Lemeshow test. TAG, TICI-ASPECTS-glucose; ASIAN, ASPECTS, baseline glucose, poor collateral circulation, passes with retriever, and onset-to-groin puncture time; IER-SICH, Italian Registry of Endovascular Stroke Treatment in Acute Stroke–symptomatic intracerebral hemorrhage; STBA, systolic blood pressure, time from acute ischemic stroke until groin puncture, blood glucose, and ASPECTS; CI, confidence interval.

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