# The CHA<sub>2</sub>DS<sub>2</sub>-VASc risk score predicts futile recanalization after endovascular treatment in patients with acute ischemic stroke

<sup>1</sup>Mehmet Bülent Vatan *MD*, <sup>2</sup>Bilgehan Atılgan Acar *MD*, <sup>2</sup>Türkan Acar *MD*, <sup>2</sup>Yeşim Güzey Aras *MD*, <sup>3</sup>Perihan Varım *MD*, <sup>4</sup>Sena Boncuk Ulaş *MD*, <sup>5</sup>Halil Alper Eryılmaz *MD*, <sup>5</sup>Şule Dalkılıç *MD*, <sup>5</sup>Ayşe Polat Zafer *MD*, <sup>5</sup>Oğuzhan Turhan *MD*, <sup>3</sup>Ahmet Can Çakmak *MD*, <sup>1</sup>Mustafa Tarık Ağaç *MD*, <sup>1</sup>Ersan Tatlı *MD* 

<sup>1</sup>Department of Cardiology, Sakarya University Faculty of Medicine, Sakarya; <sup>2</sup>Department of Neurology, Sakarya University Faculty of Medicine, Sakarya; <sup>3</sup>Department of Cardiology, Sakarya University Training and Research Hospital, Sakarya; <sup>4</sup>Department of Neurology, Keşan State Hospital Keşan, Edirne; <sup>5</sup>Department of Neurology, Sakarya University Training and Research Hospital, Sakarya, Turkey

### Abstract

Objective: This study aimed to evaluate the utility of the CHA, DS,-VASc score for predicting futile recanalization among patients with acute ischemic stroke (AIS) who underwent endovascular treatment (EVT). Methods: A total of 97 AIS patients who achieved complete or near-complete recanalization after EVT were included in our study. Clinical, angiographic, and laboratory data were analyzed retrospectively. Using the modified Rankin Scale (mRS) at 90 days after the intervention, the patients were divided into two groups, the futile recanalization group (mRS  $\geq$ 3) and the favorable recanalization group (mRS  $\leq$ 2). The receiver-operating characteristics (ROC) curve was used to determine the cut-off value of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score for predicting futile recanalization.Multivariate stepwise logistic regression analysis analyzed the association between the CHA<sub>3</sub>DS<sub>3</sub>-VASc score and futile recanalization risk after EVT. Results: The CHA<sub>2</sub>DS<sub>2</sub>-VASc score was significantly higher in patients with futile recanalization compared to patients with favorable recanalization [4 (3-6) vs. 3 (1-4), p=0.002]. A ROC curve analysis revealed that the cut-off value of CHA,DS,-VASc score for predicting futile recanalization was >3, with sensitivity and specificity of 65% and 72%, respectively (Area under curve (AUC), 0.697; 95% Confidence interval (CI):0.580-0.814). In multivariate analysis; the CHA, DS,-VASc score (Odds ratio (OR)=1.637, 95% CI:1.181-2.334, p=0.004) and baseline National Institutes of Health Stroke Scale score (OR=1.217, 95% CI:0.985-1.503, p=0.039) were found independent predictors for futile recanalization after EVT.

*Conclusion:* The  $CHA_2DS_2$ -VASc score can be used as a simple and effective tool to predict futile recanalization in patients with AIS.

Keywords: CHA<sub>2</sub>DS<sub>2</sub>-VASc score, endovascular treatment, stroke

## INTRODUCTION

Acute ischemic stroke (AIS) is a leading cause of mortality and morbidity worldwide and brings heavy economic and social consequences.<sup>1</sup> The primary therapeutic goal for patients with AIS is the earliest restoration of cerebral blood flow. Timely endovascular treatment (EVT) has become the optimal strategy for managing eligible patients with AIS as it significantly improves clinical outcomes.<sup>2.3</sup> Nevertheless, successful recanalization does not always translate into good clinical outcomes. Recent studies reported that successful recanalization of the occluded artery is reached in more than three-quarters of patients with AIS undergoing EVT. However, over 50% of these patients do not achieve an excellent clinical outcome.<sup>4,5</sup> The term 'futile recanalization phenomenon' is widely used to describe poor clinical outcomes after successful recanalization of the infarct-related artery.<sup>4</sup> Early and individualized risk stratification to predict this phenomenon after EVT can improve clinical

Address correspondence to: Mehmet Bülent Vatan, MD, Department of Cardiology, Sakarya University Training and Research Hospital, Adnan Menderes Street, 54000, Sakarya, TURKEY. Tel: +90 532 6064117, E-mail: bvatan@sakarya.edu.tr

Date of Submission: 4 November 2022; Date of Acceptance: 27 January 2023 https://doi.org/10.54029/2023kep outcomes by allowing physicians to make more precise decisions regarding appropriate patient selection for EVT, allocation of clinical resources, and triage among alternative levels of intensive care.<sup>5</sup>

The CHA<sub>2</sub>DS<sub>2</sub>-VASc score is widely used to predict thromboembolic risk in nonvalvular atrial fibrillation (AF) patients.<sup>6</sup> It is associated with adverse clinical outcomes in patients with AIS.<sup>7,8</sup> Recently, this score has been useful in predicting procedural success in patients with AIS undergoing EVT.<sup>9</sup> However, the relationship between the CHA<sub>2</sub>DS<sub>2</sub>-VASc score and futile recanalization in patients with AIS remains unclear.

In the present study, we evaluated the  $CHA_2DS_2$ -VASc score as a simple tool for predicting the futile recanalization among patients with AIS who underwent EVT.

#### **METHODS**

#### Study population

We retrospectively evaluated the data of 123 patients with AIS who underwent EVT within 6h from symptom onset.

Patients who met the following criteria were eligible for the study: AIS patients who underwent EVT for large vessel occlusion and achieved nearcomplete or complete recanalization (defined as the Modified Thrombolysis in Cerebral Infarction (mTICI) grade 2c or 3); age  $\geq$  18 years; a National Institutes of Health Stroke Scale (NIHSS) score  $\geq$ 6 at admission; an Alberta Stroke Program Early CT Score (ASPECTS)  $\geq$  6 based on non-contrast computerized cranial tomography (CT) or diffusion-weight magnetic resonance imaging (DWI); and a CT ruling out intracranial hemorrhagia.

The exclusion criteria were as follows: Patients with a significant pre-stroke disability (pre-stroke modified Rankin Scale (mRS) score >2); history of major surgery or trauma within four weeks before the hospital admission, and had a diagnosis of an intracranial tumor or arteriovenous malformation.

All patients were managed according to the guidelines for the early management of patients with AIS from the American Heart Association/ American Stroke Association.<sup>2</sup> A non-contrast CT scan was performed to rule out the possibility of a hemorrhagic stroke on admission to the emergency department. Intravenous thrombolysis with alteplase at a maximum dose of 0.9 mg/ kg was administered in eligible patients within 4.5 hours after stroke onset. As identified by cervical and cranial CT-angiogram (CT-A) or DWI, EVT was performed in patients with AIS caused by occlusion of the middle cerebral artery with or without the internal carotid artery or basilar artery. Digital subtraction angiography (DSA) was performed to determine the definite location of the occluded vessels. The two most common EVT techniques for reperfusion were used: Direct aspiration alone or a combination of direct aspiration and mechanical thrombectomy with a stent retriever. The first line technique was manual aspiration with a SOFIA distal access catheter (MicroVention Europe, Saint-Germainen-Laye-France). If it did not achieve adequate recanalization, a combination of direct aspiration and a stent retriever was used with the NeVa thrombectomy device (Vesalio LLC, Lake Forest, CA). Regarding EVT procedures, the choice of the particular device or intervention modality was left to the discretion of the interventionist. A routine cranial CT scan was performed 24 h after the therapy or earlier in cases of changed or worsening neurological symptoms.

The clinical outcome was evaluated with the mRS score at 90 days. Futile recanalization was defined as an unfavorable functional outcome (mRS score  $\geq$ 3) at 90 days despite successful recanalization of the occluded vessel (mTICI grade 2c or 3), while favorable recanalization was defined as functional independence (mRS score; 0-2). Consequently, the patients were divided into the futile recanalization and favorable recanalization groups.

This study is retrospective and observational. The local ethics committee approved the study in accordance with the declaration of Helsinki (Approval number: 71522473-050.01.04-136929-146). Each patient or his/her family member had signed written informed consent.

# Clinical, angiographic, and laboratory data collection

The following data of baseline demographic and clinical characteristics were obtained from the hospital database: age and sex, history of hypertension, diabetes mellitus, coronary artery disease, heart failure, peripheral vascular disease, prior stroke, atrial fibrillation, dyslipidemia, smoking, prior use of antiplatelet or anticoagulant drugs, AIS characteristics including stroke etiology based on Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria<sup>10</sup>, baseline NIHSS, and symptom to puncture time.

Severe stroke was defined as a baseline NIHSS score  $\geq 10$ . The following digital subtraction angiography (DSA) data were also reviewed: arterial occlusion site, cerebral reperfusion status, and presence of first-pass reperfusion. The cerebral reperfusion status was analyzed by two interventional specialists (an expert interventional neurologist and an interventional cardiologist) blinded to patients' clinical data based on the Modified Thrombolysis in Cerebral Infarction (mTICI) grades.<sup>11</sup> In case of disagreement, the final result was reviewed by consensus or by a third interventional neurologist. Definition of the mTICI grades was as follows: Grade 0 refers to no/minimal reperfusion; grade 1 refers to partial filling <%50 of territory; grade 2b refers to  $\ge50\%$ of territory; grade 2c refers to near-complete perfusion except slow flow or few distal cortical emboli, and grade 3 refers to complete perfusion. The successful recanalization was identified in patients with antegrade mTICI grade 2c or 3.12 First-pass complete reperfusion was defined as achieving complete reperfusion (TICI  $\geq 2c$ ) with a single thrombus aspiration without rescue treatment with intra-arterial thrombolytics or stent retriever. Collateral arterial supply was assessed based on CT-A using the TAN grading system, which ranges from 0 to 3 (0 for absent collateral circulation, 1 for collateral supply filling >0% and  $\leq$ 50% of the occluded territory, 2 for collateral supply filling >50% and <100% of the occluded territory, and 3 for collateral supply filling 100% of the occluded territory).<sup>13</sup> A poor collateral score refers to grades 0 to 1. Safety outcomes included symptomatic intracerebral hemorrhage (ICH) and hemorrhagic transformation (HT) of the infarct. The symptomatic ICH was defined as any intracranial hemorrhage with an increase of  $\geq$ 4 points on the total NIHSS score.

Laboratory analysis included the results of complete blood counts, creatinine, serum lipids, glucose, and CRP. Venous blood samples were collected from all patients at admission to the emergency department.

Clinical follow-up data were obtained through the out-patient visits performed by specialist neuro-interventionist.

The CHA<sub>2</sub>DS<sub>2</sub>-VASc score was calculated by scoring specific diseases and conditions: congestive heart failure (1 point), hypertension (1 point), age  $\geq$ 75 (2 points), diabetes mellitus (1 point), previous stroke or transient ischemic attack (2 points), vascular disease (1 point), age 65–75 years (1 point), and female sex (1 point). The maximum calculated CHA<sub>2</sub>DS<sub>2</sub>-VASc score was nine points.

#### Statistical analysis

Statistical analysis was performed using SPSS for Windows (version 21.0; SPSS Inc, Chicago, Illinois). Continuous variables were expressed as mean±standard deviation or median (interquartile range) depending on normality, assessed using the Kolmogorov-Smirnov test.

According to normality, group means for continuous variables were compared using the independent samples t-test or the Mann-Whitney U test. The categorical variables were presented as counts (n) and percentages and compared with the chi-square test. Spearman's correlation coefficients were used to determine the correlations between the CHA<sub>2</sub>DS<sub>2</sub>-VASc score and the futile recanalization. Receiver operating characteristic (ROC) curve analysis was performed to define thresholds for the CHA<sub>2</sub>DS<sub>2</sub>-VASc score for predicting the futile recanalization with corresponding specificity and sensitivity. Multivariate stepwise logistic regression was used to identify independent predictors of futile recanalization after EVT, and odds ratios (ORs) with 95% confidence intervals (CI) were calculated. Covariates with p < 0.20 in univariate analysis were entered into a backward multivariate model. A two-tailed p-value of <0.05 was considered statistically significant.

#### RESULTS

Among the study population, 97 AIS patients who were successfully recanalized after EVT were included in the analyses. The mean age of the patients was  $66.5\pm12$  years, and 49 (50.1%) were females. 23 patients (%23.9) have a history of prior stroke. Among them, only four patients in the favorable recanalization group and two in the futile recanalization group have premorbid mRs of 1. All of the other participants have premorbid mRs of 0 (p=0.941). According to the mRS score at 3 months, the patients were divided into futile recanalization group (mRS score: 3-6, n=31, 32%) and favorable recanalization group (mRS score: 0-2, n= 66, 68%), respectively. The median value of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was significantly higher in the futile recanalization group compared to the favorable recanalization group [4 (3-6) vs.3(1-4), p=0.002]. The futile recanalization group had a higher baseline NIHSS score [19 (17-21) vs 17 (14-18), p=0.001], had a higher prevalence of hypertension [28 (90.3%) vs. 45 (68.2), p=0.023], and had a higher prevalence of diabetes mellitus [11 (35.5%) vs. 9 (13.6%), p=0.017] compared with the favorable recanalization group. Patients

in the futile recanalization group also had significantly higher mortality at three months (p<0.001). Demographics, laboratory, and clinical

data of the patients are summarized in Table 1. All patients underwent EVT by direct aspiration, with the clot aspirated with a large-diameter distal

	Favorable	Futile	<i>p</i> -value	
Characteristics	recanalization	recanalization		
	n=66	n=31		
Age, years	66±12	66±13	0.929	
Female sex, % (n)	34 (51.5)	15 (48.3)	0.830	
Hypertension, % (n)	45 (68.2)	28 (90.3)	0.023	
Dyslipidemia, % (n)	48 (72.7)	23 (74.2)	1.000	
Coronary artery disease, % (n)	22 (33.3)	12 (38.7)	0.652	
Diabetes mellitus, % (n)	9 (13.6)	11 (35.5)	0.017	
History of heart failure, % (n)	7 (10.6)	3 (9.6)	0.823	
Obesity, % (n)	11 (16.7)	8 (25.8)	0.411	
Smoking, % (n)	23 (34.8)	9 (29.1)	0.648	
Prior stroke, % (n)	19 (28.8)	4 (12.9)	0.168	
CHA,DS,-VASc score, median (IQR)*	3 (1-4)	4 (3-6)	0.002	
Prior use of antiplatelets, % (n)	20 (30.3)	9 (29.1)	1.000	
Prior use of anticoagulants, % (n)	24 (36.3)	11 (35.5)	1.000	
Baseline NIHSS score, median (IQR)*	17 (14-18)	19 (17-21)	0.001	
Systolic blood pressure, mmHg, median (IQR)*	150 (130-170)	155 (140-185)	0.290	
Baseline ASPECTS, median (IQR)*	10 (9-10)	9(9-10)	0.783	
Stroke etiology				
Atherosclerosis, % (n)	8 (12.1)	6 (19.3)		
Cardioembolic, % (n)	38 (57.6)	17 (54.8)	0.625	
Other or undetermined, % (n)	20 (30.3)	8 (25.8)		
Atrial fibrillation, % (n)	33 (50.0)	13 (41.9)	0.517	
Laboratory findings				
LDL-C, mg/dl	125±37	123±37	0.815	
HDL-C, mg/dl	43±10	38±12	0.060	
Triglyceride, mg/dl, median (IQR)*	85 (62-117)	98 (68-177)	0.256	
Total cholesterol, mg/dl	178±49	175±49	0.739	
hs-CRP, mg/dl, median (IQR)*	6.8 (3.7-16.5)	9.3 (4.8-44.4)	0.142	
Admission glucose, mg/dl, median (IQR)*	122 (103-149)	157 (97-225)	0.148	
Creatinine, mg/dl, median (IQR)*	0.8 (0.6-1.0)	0.8 (0.7-1.0)	0.429	
GFR, µL, median (IQR)*	87 (72-97)	82 (61-99)	0.496	
Hemoglobin, g/dl	12.8±1,9	12.9±2.2	0.897	
Clinical outcomes				
3-month mortality, % (n)	0 (0)	17 (54.8)	<0.001	
Hemorrhagic transformation, % (n)	6 (9.1)	7 (22.6)	0.107	
Symptomatic ICH, % (n)	1(1.5)	4 (12.9)	0.143	

Table 1: Demographic, laboratory, and clinical characteristics of the study population

Data were shown as mean ±standard deviation and number (%). \*Data are presented as median (IQR: interquartile range) ASPECTS, Alberta Stroke Program Early CT Score; NIHSS, National Institutes of Health Stroke Scale; ICH, intracerebral hemorrhage; hs-CRP, high-sensitivity C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; GFR, glomerular filtration rate.

access catheter. In 15 patients, primary suction failed, and a rescue treatment was performed with a stent retriever coaxially introduced through the same distal access catheter. There was no significant difference between the two groups regarding the use of stent retrievers [5 (16%) vs. 10 (15%), p=1.00). The DSA results showed 61.9% MCA occlusion, 23.7% ICA-MCA tandem occlusion, and 8.2% basilar artery occlusion. There was no difference between the two groups regarding the arterial occlusion site. As shown in Table 2, there were no significant differences in other angiographic and procedural characteristics. To identify the risk factors for futile recanalization in patients with AIS who underwent EVT, we conducted univariate logistic regression analysis. We found that baseline NIHSS score (OR=0.810, 95% CI: 0.703-0.934, p=0.004), the CHA<sub>2</sub>DS<sub>2</sub>-VASc score (OR=0.681, 95% CI: 0.535-0.866, p=0.002), hypertension (OR=0.230, 95% CI: 0.063-0.841, p=0.026), diabetes mellitus (OR=0.287, 95% CI: 0.104-0.794, p=0.016), and admission glucose levels (OR=0.991, 95% CI: 0.984-0.998, p=0.009) were risk factors for futile recanalization. We also established a multivariate logistic regression model using futile racanalization as the dependent variable with adjustments for significant variables (as identified from the univariate regression analysis). Multivariate analysis showed that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score (OR=1.637, 95% CI:1.181-2.334, p=0.004) and baseline NIHSS score (OR=1.217, 95% CI:0.985-1.503, p=0.039) were independent predictors of futile recanalization after EVT in patients with AIS (Table 3).

Using The ROC curve analysis, we evaluated the predictive efficacy of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score and baseline NIHSS score. We showed that the area under curve (AUC) for the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was 0.697 (95% CI: 0.580-0.814), and the best cut-off value was > 3, with sensitivity and specificity of 65% and 72%, respectively. The AUC for baseline NIHSS was 0.708 (95% CI: 0.595-0.822), and the cut-off value was ≥17, with sensitivity and specificity of 65% and 61%, respectively (Figure 1).

#### DISCUSSION

To the best of our knowledge, this is the first study in the literature demonstrating the association between the  $CHA_2DS_2$ -VASc score and futile recanalization in patients with AIS undergoing EVT. The common findings of this study were as follows: patients with AIS who developed futile recanalization following EVT have significantly higher  $CHA_2DS_2$ -VASc scores, and the  $CHA_2DS_2$ -VASc score is independently associated with the futile recanalization in these patients.

Futile recanalization is encountered in a remarkable proportion of patients with AIS who underwent EVT, which leads to impaired

Table 2: Angiographic and procedural characteristics of the study population

Characteristics	Favorable recanalization n=66	Futile recanalization n=31	<i>p</i> -value
Symptom to recanalization time, minute, median (IQR)*	222 (171-308)	260 (210-332)	0.266
General anesthesia, % (n)	2 (3.0)	4 (12.9)	0.132
Arterial occlusion site			
Middle cerebral artery, % (n)	40 (61.5)	20 (64.5)	0.825
Internal carotid artery and middle cerebral artery tandem lesion, % (n)	18 (27.2)	5 (16.1)	0.308
Posterior circulation, % (n)	3 (4.5)	5 (16.1)	0.106
Poor collateral supply, % (n)	8 (12.1)	3 (9.7)	0.754
Bovine arch, % (n)	8 (12.1)	6 (19.3)	0.365
First pass recanalization, % (n)	37 (56.1)	21 (67.7)	0.276
Procedure technique			
Direct aspiration, % (n)	66 (100)	31 (100)	-
Direct aspiration and stent retriever, % (n)	10 (15.2)	5 (16.1)	1.000
IVT and EVT, % (n)	17 (25.8)	4 (12.9)	0.192

Data were shown as mean ±standard deviation and number (%). \*Data are presented as median (IQR: interquartile range). IVT, intravenous thrombolysis; EVT, endovascular treatment

#### Neurology Asia

Variables	Univariate analysis		Multivariate analysis			
	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Age	0.996	0.964-1.034	0.928	-	-	-
Female sex	0.887	0.376-2.073	0.774	-	-	-
Diabetes mellitus	0.287	0.104-0.794	0.016*	-	-	-
Smoking	1.307	0.518-3.301	0.570	-	-	-
Prior stroke	0.437	0.156-1.219	0.114	-	-	-
Dyslipidemia	0.982	0.370-2.607	0.970	-	-	-
Hypertension	0.230	0.063-0.841	0.026*	-	-	-
Obesity	1.739	0.619-4.884	0.294	-	-	-
Atrial fibrillation	1.385	0.585-3.276	0.459	-	-	-
SBP on admission	0.991	0.984-1.006	0.219	-	-	-
<b>Baseline NIHSS score</b>	0.810	0.703-0.934	0.004*	1.217	0.985-1.503	0.039*
CHA2DS2-VASc score	0.681	0.535-0.866	0.002*	1.637	1.181-2.334	0.004*
<b>Baseline ASPECTS</b>	1.058	0.677-1.652	0.805	1.170	0.512-2.672	0.710
General anesthesia	1.399	0.918-2.323	0.118	0.674	0.379-2.301	0.172
Symptom to recanalization time	0.999	0.995-1.003	0.606	0.997	0.989-1.005	0.452
First pass recanalization	0.608	0.248-1.489	0.276	1.210	0.314-4.663	0.782
Use of stent retriever	0.928	0.288-2.992	0.929	-	-	-
Poor collateral status	1.255	0.306-5.155	0.753	2.610	0.419-16.26	0.304
ICA occlussion	1.950	0.649-5.857	0.234	0.282	0.058-1.366	0.116
Posterior circulation occlusion	0.250	0.055-1.127	0.071	0.210	0.062-0.735	0.383
Prior use of antiplatelets	1.063	0.417-2.711	0.899	-	-	-
IVT	2.342	0.715-7.668	0.160	0.524	0.108-2.559	0.425
Admission glucose	0.991	0.984-0.998	0.009*	1.007	0.999-1.016	0.096
GFR	1.006	0.987-1.026	0.525	-	-	-
LDL	1.001	0.990-1.013	0.812	-	-	-
HDL	1.038	0.998-1.081	0.063	0.939	0.888-0.993	0.069
hs-CRP	0.995	0.987-1.003	0.225	-	-	-

Table 3: Predictors of futile recanalization in univariate and multivariate logistic regression analyses

OR, odds ratio; CI, confidence interval; SBP, systolic blood pressure; NIHSS, National Institutes of Health Stroke Scale; ASPECT, Alberta Stroke Program Early CT Score; ICA, internal carotid artery; IVT, intravenous thrombolysis; GFR, glomerular filtration rate; LDL, low-density cholesterol; HDL, high-density cholesterol, hs- CRP, high sensitive C-reactive protein

Covariates with p<0.20 in univariate analysis were entered into a backward multivariate model \*Statistically significant

patients' autonomy and severe health care costs.<sup>4</sup> In line with current developments in intervention techniques, the indications for EVT are constantly expanded –for example, the time window of thrombectomy can be extended up to 24 hours after symptom onset, which may increase the rate of futile recanalization.<sup>14</sup> A recent meta-analysis comprising five EVT trials reported that the

successful recanalization rate was 71%, while the favorable outcome rate was 46%.<sup>15</sup> Although the underlying mechanisms of futile recanalization are still not fully elucidated, there is accumulating evidence that poor collateral circulation, subacute reocclusion, large hypoperfusion volumes, microvascular compromise, and impaired cerebral auto-regulation play an essential role in



Figure 1. Receiver operating characteristic (ROC) curve analysis for the CHA<sub>2</sub>DS<sub>2</sub>-VASc and National Institutes of Health Stroke Scale (NIHSS) scores regarding the futile recanalization

this condition.<sup>16</sup> Identifying predictors of futile recanalization in patients with AIS candidates for EVT may enable physicians to select the best treatment strategy. Therefore, a reliable predictor of futile recanalization is essential to identify patients who would most likely not benefit from EVT even in case of successful recanalization.

Various neural function evaluation methods, clinical features, and imaging parameters to predict this condition in AIS patients have been evaluated. In a multicenter study, it has been observed that high baseline NIHSS score (NIHSS score >10), older age (age >70 years), and delayed intervention have been identified as possible predictors of unfavorable outcomes after successful recanalization.<sup>17</sup> Subsequent studies have also supported these findings.<sup>4,18</sup>

A previous study using non-contrast CT scan to identify the risk factors in AIS patients who underwent EVT has revealed that moderate-severe leukoaraiosis and brain atrophy is independently associated with poor outcome in successfully recanalized patients.<sup>19</sup> Furthermore, another study employing preintervention DWI to predict futile recanalization has shown that large ischemic lesions in the deep white matter might be a probable predictor for futile recanalization, and the patients with large preintervention DWI lesions might be poor candidates for EVT.<sup>20</sup>

However, using the parameters mentioned in assisting EVT decision-making may be an overly assertive approach. The reliability of these approaches remains unclear due to various issues among studies, including a small number of patients enrolled and apparent heterogeneity in clinical characteristics and techniques of endovascular treatment. In addition, it may not be feasible to adapt the imaging approaches to clinical practice, as they cause delays in workflow timepoints (admission to imaging time, imaging to puncture time). In this regard, a more simple and time-saving index for risk stratification of futile recanalization needs to be established.

A CHA<sub>2</sub>DS<sub>2</sub>-VASc score is a well-validated tool for predicting clinical outcomes in patients with stroke.<sup>7,8</sup> Ntaios *et al.*<sup>7</sup> reported pre-stroke CHA<sub>2</sub>DS<sub>2</sub>-VASc score is associated with 5-year mortality, stroke recurrences, and cardiovascular events in AIS patients without AF. Tu *et al.*<sup>8</sup> found that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is associated with the 90-day poor clinical outcomes in AIS patients with AF. However, the role of the CHA2DS2-VASc score in predicting the therapeutic benefits of EVT has not been previously evaluated. Our novel finding revealed that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is independently associated with futile recanalization in AIS patients treated with EVT.

Why is the  $CHA_2DS_2$ -VASc associated with futile recanalization in patients with AIS? We will highlight possible explanations in the following text.

The CHA<sub>2</sub>DS<sub>2</sub>-VASc score is a composite indicator integrating clinical and demographic constituents. Most of the individual components

of the  $CHA_2DS_2$ -VASc score have previously been shown to be related to futile recanalization. However, whether a high  $CHA_2DS_2$ -VASc score has an additional independent effect beyond its components remains controversial. This study revealed that combining the separate components of the  $CHA_2DS_2$ -VASc score might increase the complementary value to predict futile recanalization.

Previous studies have shown that elderly patients with AIS who undergo EVT achieve equally remarkable recanalization rates to those of younger patients.<sup>21,22</sup> Despite comparable recanalization rates, elderly patients may experience worse clinical outcomes after EVT than younger patients.<sup>23</sup> Presence of more comorbidities, impaired collateral circulation, more frequent microvascular pathology, and reduced neurological reserve secondary to agerelated neuronal loss may explain poorer clinical outcomes in elderly patients after EVT.

Hypertension (HT) is the most prevalent risk factor for stroke. HT promotes endothelial cell dysfunction, increased shear stress, and significant artery stiffness, contributing to stroke. HT is also associated with poor functional outcomes, mortality, and hemorrhagic transformation in AIS receiving reperfusion therapy.<sup>24</sup> A pooled analysis of 2138 patients with AIS demonstrated that HT is significantly associated with futile recanalization.<sup>25</sup> However, recent studies have revealed conflicting results regarding the relationship between HT and futile recanalization.<sup>4,17,18</sup>

Diabetes mellitus is also a well-established risk factor for stroke. Pathological changes in the diabetic microvasculature can alter organ perfusion and lead to stroke if cerebral vessels are directly affected. Additionally, hyperglycemia confers a greater risk of mortality and poststroke poor functional outcome.<sup>26</sup> Observational studies have reported a positive correlation between diabetes mellitus and the risk of futile recanalization.<sup>4,25</sup> However, these studies have not consistently shown that diabetes mellitus independently predicts futile recanalization.

The female gender is the other component of the  $CHA_2DS_2$ -VASc score. Hussein *et al.*<sup>4</sup> reported that the female gender is independently associated with futile recanalization. However, there are conflicting results in the literature on this subject.<sup>26</sup>

Our study showed that age and female gender were not significantly associated with the futile recanalization. In contrast, a significant association was found between hypertension and diabetes mellitus and futile recanalization. We revealed that none of these individual parameters of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score independently predicted futile recanalization. However, combining the different weights of these risk factors (CHA<sub>2</sub>DS<sub>2</sub>-VASc score) showed significantly improved risk prediction over the individual parameters. Thus, the overlap of these individual risk factors and shared pathophysiological pathways can explain why the CHA<sub>2</sub>DS<sub>2</sub>-VASc score may independently predict futile recanalization.

There are several limitations to consider in this study. First, this study is a single-center, retrospective design with a limited sample size, which may lead to selection bias. Second, the absence of a core laboratory for image interpretation might affect the accuracy of the results. Therefore, prospective studies in larger sample sizes must verify our results.

In conclusion, the CHA<sub>2</sub>DS<sub>2</sub>-VASc score can be a simple and comprehensive risk assessment tool that provides additional risk stratification beyond individual risk factors in predicting futile recanalization in AIS patients undergoing EVT. Thus, we tentatively propose that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score may represent a promising index for predicting futile recanalization after EVT.

#### DISCLOSURE

Financial support: None

Conflict of interest: None

#### REFERENCES

- GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019; 18:439-58. Doi:10.1016/ s1474-4422(19)30034-1.
- Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2019; 50:344-418. Doi:10.1161/ str.000000000000211.
- Turc G, Bhogal P, Fischer U, et al. European Stroke Organisation(ESO)-European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischaemic stroke endorsed by Stroke Alliance for Europe (SAFE). Eur Stroke J 2019; 4:6-12. Doi:10.1177/2396987319832140.
- 4. Hussein HM, Saleem MA, Qureshi AI. Rates and predictors of futile recanalization in patients undergoing endovascular treatment in a multicenter

clinical trial. *Neuroradiology* 2018; 60:557-63. Doi:10.1007/s00234-018-2016-2.

- Molina CA. Futile recanalization in mechanical embolectomy trials: a call to improve the selection of patients for revascularization. *Stroke* 2010; 41:842-3. Doi:10.1161/strokeaha.110.580266.
- 6. Hindricks G, Potpara T, Dagres N, *et al.* ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the Diagnosis and Management of Atrial Fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021; 42:373-498. Doi:10.1093/eurheartj/ehaa612.
- Ntaios G, Lip GY, Makaritsis K, *et al.* CHADS<sub>2</sub>, CHA<sub>2</sub> S<sub>2</sub> DS<sub>2</sub>-VASc, and long-term stroke outcome in patients without atrial fibrillation. *Neurology* 2013; 80:1009-17. Doi:10.1212/wnl.0b013e318287281b.
- Tu HTH, Campbell BCV, Meretoja A, *et al*. Pre-stroke CHADS2 and CHA2DS2-VASc scores are useful in stratifying three-month outcomes in patients with and without atrial fibrillation. *Cerebrovasc Dis* 2013; 36:273-80. Doi:10.1159/000353670.
- Yaşar E, Akalın Y, Aktaş İ, Çakmak T, Karakuş Y, Bayramoğlu A. The CHA2DS2-VASc risk score predicts successful endovascular treatment in patients with acute ischemic stroke. *Acta Neurol Scand* 2022; 145:407-13. Doi:10.1111/ane.13564.
- Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 1993; 24:35-41. Doi:10.1161/01. str.24.1.35.
- Goyal M, Fargen KM, Turk AS, *et al.* 2C or not 2C: defining an improved revascularization grading scale and the need for standardization of angiography outcomes in stroke trials. *J Neurointerv Surg* 2014; 6:83-6. Doi:10.1136/neurintsurg-2013-010665.
- Kleine JF, Wunderlich S, Zimmer C, Kaesmacher J. Time to redefine success? TICI 3 versus TICI 2b recanalization in middle cerebral artery occlusion treated with thrombectomy. *J Neurointerv Surg* 2017; 9:117-21. Doi:10.1136/neurintsurg-2015-012218.
- Tan IY, Demchuk AM, Hopyan J, et al. CT angiography clot burden score and collateral score: correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct. Am J Neuroradiol 2009; 30:525-31. Doi:10.3174/ajnr.a1408.
- Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med 2018; 378:11-21. Doi:10.1056/nejmoa1706442.
- Goyal M, Menon BK, van Zwam WH, et al. HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016; 387:1723-31. Doi:10.1016/s0140-6736(16)00163-x.

- Nie X, Pu Y, Zhang Z, Liu X, Duan W, Liu L. Futile recanalization after endovascular therapy in acute ischemic stroke. *Biomed Res Int* 2018; 2018:5879548. Doi:10.1155/2018/5879548.
- Xu H, Jia B, Huo X, et al. Predictors of futile recanalization after endovascular treatment in patients with acute ischemic stroke in a multicenter registry study. J Stroke Cerebrovasc Dis 2020; 29:105067. Doi:10.1016/j.jstrokecerebrovasdis.2020.105067.
- Pan H, Lin C, Chen L, et al. Multiple-factor analyses of futile recanalization in acute ischemic stroke patients treated with mechanical thrombectomy. *Front Neurol* 2021; 12:704088. Doi:10.3389/ fneur.2021.704088.
- Kaginele P, Beer-Furlan A, Joshi KC, et al. Brain atrophy and leukoaraiosis correlate with futile stroke thrombectomy. J Stroke Cerebrovasc Dis 2021; 30:105871. Doi:10.1016/j. jstrokecerebrovasdis.2021.105871.
- Tateishi Y, Wisco D, Aoki J, *et al*. Large deep white matter lesions may predict futile recanalization in endovascular therapy for acute ischemic stroke. *Interv Neurol* 2015; 3:48-55. Doi:10.1159/000369835.
- 21. Parrilla G, Carreón E, Zamarro J, *et al*. Recanalization and mortality rates of thrombectomy with stentretrievers in octogenarian patients with acute ischemic stroke. *Cardiovasc Intervent Radiol* 2015; 38:288-94. Doi:10.1007/s00270-014-0920-3.
- Kawabata Y, Nakajima N, Miyake H, Fukuda S, Tsukahara T. Endovascular treatment of acute ischaemic stroke in octogenarians and nonagenarians compared with younger patients. *Neuroradiol J* 2019; 32:303-8. Doi:10.1177/1971400919840847.
- Rezai MK, Advani R, Dalen I, Fjetland L, Kurz KD, Kurz MW. Endovascular thrombectomy in the elderly: Do radiological and clinical outcomes differ from those in younger patients? A prospective singlecenter experience. *Cerebrovasc Dis* 2019; 47:65-71. Doi:10.1159/000497315.
- Shah QA, Patel S, Qureshi AI. Induced hypertension in patients with partial recanalization after intraarterial thrombolysis for acute ischemic stroke. J Neurosurg Anesthesiol 2008; 20:154-5. Doi:10.1097/ ana.0b013e3181616c4d.
- Deng G, Xiao J, Yu H, et al. Predictors of futile recanalization after endovascular treatment in acute ischemic stroke: a meta-analysis. J Neurointerv Surg 2022; 14:881-5.Doi:10.1136/ neurintsurg-2021-017963.
- Chen R, Ovbiagele B, Feng W. Diabetes and stroke: Epidemiology, pathophysiology, pharmaceuticals and outcomes. *Am J Med Sci* 2016;351:380-6. Doi:10.1016/j.amjms.2016.01.011.
- Rexrode KM, Madsen TE, Yu AYX, Carcel C, Lichtman JH, Miller EC. The impact of sex and gender on stroke. *Circ Res* 2022; 130:512-28. Doi:10.1161/ circresaha.121.319915.