Association of Cardioembolism and Intracranial Arterial Stenosis with Outcomes of Mechanical Thrombectomy in Acute Ischemic Stroke

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■ OBJECTIVE: **To estimate the association of different etiologies of cardioembolism (CE), intracranial arterial stenosis (ICAS), or the combination of these conditions with outcomes of mechanical thrombectomy in acute ischemic stroke.**

■ METHODS: **Data from the intervention group of the Endovascular therapy for Acute ischemic Stroke Trial (EAST) were analyzed. In 140 patients, the presence of CE, ICAS, neither CE nor ICAS, or both conditions was assessed. The primary outcome was a favorable outcome at 90 days (modified Rankin Scale score 0–2); secondary outcomes included successful reperfusion (modified Thrombolysis In Cerebral Infarction grade 2b–3), symptomatic intracerebral hemorrhage, and 90-day mortality.**

■ RESULTS: **Of 140 patients, 47 had neither CE nor ICAS, 35 had ICAS but not CE, 46 had CE but not ICAS, and 12 had both CE and ICAS. The rate of favorable outcome was 67.1% in the no CE and no ICAS group, 74.3% in the ICAS without CE group, 41.3% in the CE without ICAS group, and 33.3% in the CE and ICAS group. The CE and ICAS group had poor outcomes (odds ratio = 0.20 after adjusting for age, sex, and National Institutes of Health Stroke Scale score; 95% confidence interval, 0.04–0.95; *P* = 0.043). No significant differences were observed in secondary outcomes.**

■ CONCLUSIONS: **The presence of both CE and ICAS was associated with poor outcome in patients with anterior circulation large-vessel occlusion treated with endovascular thrombectomy. Future studies are warranted to further explore this association.**

INTRODUCTION

Previous studies have indicated different outcomes in patients with acute ischemic stroke (AIS) who receive thrombolytic treatment based on the various etiologic

Key words
- Acute ischemic stroke
- Cardioembolism
- Intracranial arterial stenosis
- Mechanical thrombectomy

Abbreviations and Acronyms
AIS: Acute ischemic stroke
CE: Cardioembolism
EAST: Endovascular therapy for Acute ischemic Stroke Trial
ICAS: Intracranial arterial stenosis
MT: Mechanical thrombectomy
NIHSS: National Institutes of Health Stroke Scale
ODT: Onset-to-door time
sICH: Symptomatic intracerebral hemorrhage

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Table 1. Comparison of Baseline and Procedural Characteristics and Outcome Between Groups

Characteristics	No CE and No ICAS (n = 47)	ICAS without CE (n = 35)	CE without ICAS (n = 46)	CE and ICAS (n = 12)	P Value
Age, years, mean ± SD	62.06 ± 13.39	56.69 ± 11.41*	66.30 ± 10.14†	67.83 ± 8.00†	0.001
Male sex	30 (63.8)	27 (77.1)	21 (45.7)	8 (66.7)	0.033
Hypertension	27 (57.4)	21 (60.0)	23 (50.0)†	8 (66.7)	0.685
Diabetes mellitus	5 (10.6)	5 (14.3)	3 (6.5)	1 (8.3)	0.708
Hyperlipidemia	3 (6.4)	1 (2.9)	2 (4.3)	1 (8.3)	0.757
Smoker	23 (48.9)	17 (48.6)	15 (32.6)	5 (41.7)	0.368
ASPECTS	9 (8–10)	10 (8–11)	9 (9–10)	8 (8–11)	0.609
NIHSS score	17 (14–21)	14 (12–17)*	17 (13–22)†	18 (13–20)†	0.030
Location of occlusion site					0.228
ICA	15 (31.9)	9 (25.7)	13 (28.3)	6 (58.3)	
M1	22 (46.8)	23 (65.7)	25 (54.3)	5 (33.3)	
M2	10 (21.3)	3 (8.6)	8 (17.4)	1 (8.3)	
IV-tPA	8 (17.0)	6 (17.1)	10 (21.7)	0 (0.0)	0.367
General anesthesia	33 (70.2)	21 (60.0)	36 (78.3)	7 (58.3)	0.278
Number of stent retriever passes	2 (1–3)	2 (1–2)	2 (1–3)	2.5 (1–3)	0.216
Balloon expansion	0 (0.0)	11 (31.4)*	0 (0.0)†	6 (50.0)*‡	0.000
Stent retriever detachment	1 (2.1)	7 (20.0)*	1 (2.2)†	4 (33.3)*‡	0.000
Other stent	0 (0.0)	9 (25.7)*	0 (0.0)†	0 (0.0)	0.000
Proximal stenosis/occlusion	13 (27.7)	3 (8.6)	7 (15.2)	2 (16.7)	0.147
Onset-to-door time	160 (87–286)	145 (72–221)	96 (49–150)*†	165 (107–353)‡	0.011
Door-to-puncture time	114 (77–160)	120 (65–173)	90 (58–159)	109 (76–139)	0.556
Puncture-to-recanalization time	60 (40–107)	65 (42–88)	44 (34–66)*†	114 (49–217)*†‡	0.003
Onset-to-recanalization time	345 (274–469)	365 (263–472)	255 (193–318)*†	373 (283–687)‡	0.000
mTICI grade 2b–3	45 (95.7)	34 (97.1)	45 (97.8)	11 (91.7)	0.643
mRS score 0–2	29 (67.1)	26 (74.3)	19 (41.3)*†	4 (33.3)*†‡	0.008
sICH	3 (6.4)	1 (2.9)	1 (2.2)	1 (8.3)	0.519
Death	8 (17.0)	4 (11.4)	4 (8.7)	2 (16.7)	0.646

Values are reported as median (interquartile range) or number (%) except for age.
CE, cardioembolism; ICAS, intracranial arterial stenosis; ASPECTS, Alberta Stroke Program Early CT Score; NIHSS, National Institutes of Health Stroke Scale; ICA, internal carotid artery; M1, first segment of middle cerebral artery; M2, second segment of middle cerebral artery; IV-tPA, intravenous tissue plasminogen activator; mTICI, modified Thrombolysis In Cerebral Infarction; sICH, symptomatic intracerebral hemorrhage.
*Compared with no CE and no ICAS group $P < 0.05$.
†Compared ICAS without CE group $P < 0.05$.
‡Compared with CE without ICAS group $P < 0.05$.

subtypes.[1,2] However, the impact of etiology on the outcomes of patients with AIS who underwent mechanical thrombectomy (MT) with stent retrievers is unclear. The aim of this study was to estimate the association of different stroke etiologies, particularly cardioembolism (CE) and intracranial arterial stenosis (ICAS), with MT outcomes in patients with AIS.

MATERIALS AND METHODS

Patient Selection

This study is a post hoc analysis using data from the intervention group of the Endovascular therapy for Acute ischemic Stroke Trial (EAST), which was a multicenter prospective nonrandomized

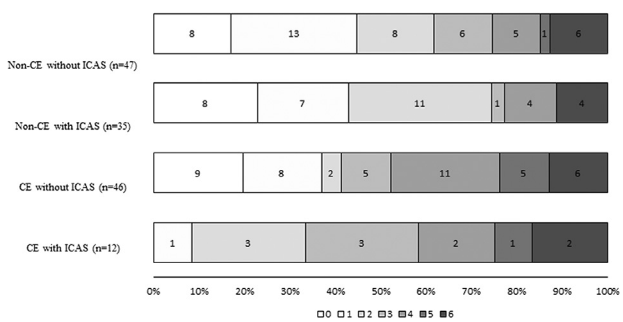

Figure 1. Distribution of 90-day modified Rankin Scale scores according to cardioembolism and intracranial arterial stenosis status. CE, cardioembolism; ICAS, intracranial arterial stenosis.

controlled trial involving 17 stroke centers in China to analyze the use of the Solitaire stent retriever (Medtronic, Minneapolis, Minnesota, USA) in patients with AIS with anterior circulation large-vessel occlusion. Details of this protocol have been published previously.[3] A diagnosis of CE was made based on evidence of atrial fibrillation, cardiac conditions that predispose to emboli formation (e.g., postinfarction akinetic left cardiac ventricular wall), and dilated cardiomyopathy. ICAS was defined as a fixed focal stenosis at the occlusion site after retrieval. Two experienced neurologists (B.X.J. and X.C.H.) blinded to each other assessed whether CE and ICAS were present according to clinical data and angiograms of all the patients after the trial was completed.

Outcome Measures

The primary outcome measure was a favorable outcome, which was defined as a 90-day modified Rankin Scale score between 0 and 2. Secondary outcomes included successful reperfusion (modified Thrombolysis In Cerebral Infarction grades of 2b–3), symptomatic intracerebral hemorrhage (sICH), and 90-day mortality.

Statistical Analysis

Continuous variables are expressed as mean ± SD or median and quartile. Comparisons of the baseline characteristics and outcomes among the 4 groups (no CE and no ICAS, ICAS without CE, CE without ICAS, and CE and ICAS) were made using one-way analysis of variance test or Kruskal-Wallis H test. If the P value was <0.05, comparisons between 2 groups were made using the least significant difference test or Mann-Whitney U test. Categorical data were expressed as number (%) and compared using either χ^2 test or Fisher exact test. Multiple regression analysis was performed with the no CE and no ICAS group as a reference, and the primary and secondary outcomes were compared after adjusting for age, sex, and National Institutes of Health Stroke Scale (NIHSS) score. Outcomes were compared between patients with ICAS and patients without ICAS using the multiple logistic regression analysis.

RESULTS

Of the 149 screened patients, 5 patients were excluded because they did not receive a Solitaire stent, and 4 were excluded because the presence of underlying ICAS could not be determined. Among the remaining 140 patients, 47 had neither CE nor ICAS, 35 had ICAS but not CE, 46 had CE but not ICAS, and 12 had both CE and ICAS. The rate of favorable outcome was 67.1% in the no CE and no ICAS group, 74.3% in the ICAS without CE group, 41.3% in the CE without ICAS group, and 33.3% in the CE and ICAS group. The average age in the ICAS without CE group was younger than in the no CE and no ICAS group, and the average age in the CE and ICAS and CE without ICAS groups was older than in the ICAS without CE group. The NIHSS score in the ICAS without CE group was lower than in the no CE and no ICAS group, and the NIHSS score in the CE and ICAS and CE without ICAS groups was higher than in the ICAS without CE group. The onset-to-door time (ODT) and puncture-to-recanalization time were both shorter in the CE without ICAS group than in the no CE and no ICAS and ICAS without CE groups. Both the CE and ICAS and ICAS without CE groups required more rescue treatments, such as balloon angioplasty, stent retriever detachment, and other stents (Table 1).

Figure 1 summarizes the 90-day clinical outcomes according to the 4 groups. The no CE and no ICAS group was established as the reference group as shown in Table 2, and patients with both CE and ICAS had a worse favorable outcome rate, with an odds ratio of 0.20 (95% confidence interval, 0.04–0.95) after adjusting for age, sex, and NIHSS score. However, there was no

Table 2. Outcome Comparison According to Pathogenesis

		ICAS without CE		CE without ICAS		CE and ICAS	
Outcomes	No CE and No ICAS	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
mRS score 0–2	Reference	0.97 (0.28–3.30)	0.954	0.32 (0.10–1.08)	0.059	0.20 (0.04–0.95)	0.043
mTICI grade 2b–3	Reference	0.35 (0.02–5.72)	0.461	2.66 (0.17–41.28)	0.485	0.54 (0.03–9.71)	0.674
sICH	Reference	0.83 (0.03–22.17)	0.911	0.65 (0.04–10.73)	0.764	2.47 (0.12–52.65)	0.562
Death	Reference	2.35 (0.37–20.59)	0.363	0.27 (0.06–1.31)	0.104	0.43 (0.06–3.36)	0.423

Results adjusted for age, sex, and National Institutes of Health Stroke Scale score.
CE, cardioembolism; ICAS, intracranial arterial stenosis; OR, odds ratio; CI, confidence interval; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; sICH, symptomatic intracerebral hemorrhage.

Table 3. Outcome Comparison of Intracranial Arterial Stenosis Versus No Intracranial Arterial Stenosis

Outcomes	β	Wald	*P*	OR	95% CI
mRS score 0–2	0.248	0.327	0.568	1.282	0.547–3.003
mTICI grade 2b–3	−0.524	0.283	0.595	0.592	0.086–4.081
sICH	−0.508	0.207	0.649	0.602	0.068–5.348
Death	0.733	1.106	0.293	2.081	0.531–8.151

Results were adjusted for age, sex, and National Institutes of Health Stroke Scale score. OR, odds ratio; CI, confidence interval; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; sICH, symptomatic intracerebral hemorrhage.

difference in secondary outcomes modified Thrombolysis In Cerebral Infarction grade, sICH, and 90-day mortality among the 4 groups after additional adjustments. Multiple logistic regression analysis found no significant difference in modified Rankin Scale score, modified Thrombolysis In Cerebral Infarction grade, sICH, and 90-day mortality between patients with ICAS and patients without ICAS (**Table 3**).

DISCUSSION

Research on the association of different etiologies with outcomes of MT in AIS is limited. One previous study showed that there was no significant difference between patients with AIS with intracranial atherosclerotic disease and embolism for MT therapy.[4] Among patients treated with MT for anterior circulation large-vessel occlusion, the patients with both CE and ICAS had a worse outcome.

There may be several explanations why patients with AIS with both CE and ICAS had poorer outcomes. The first is that patients with AIS with CE have poor collateral circulation. One previous study showed that patients with cardioembolic stroke had poorer collateral circulation than patients with atheroembolic stroke.[5] However, good collaterals are the most important factor for a favorable clinical outcome.[6] The second explanation is the large clot burden in patients with cardioembolic stroke.[7] These patients had greater rates of carotid terminal occlusions (58.3%) in our study and may have extensive thrombus that causes more resistant clots for MT.[8] Acute occlusion of the internal carotid artery is associated with poor clinical outcomes and severe neurologic deficits.[9] Furthermore, the CE and ICAS group had longer ODT and puncture-to-recanalization time. Patients in the CE without ICAS group had a shorter ODT because of the poor collaterals. The initial patient status was poorer in cases of CE than in cases of ICAS.[9] In other words, ICAS may improve the collateral circulation and then mask the effects of sudden vessel occlusion to some extent. Therefore, patients with both CE and ICAS took longer to be transferred to a hospital. In addition, these patients had a longer puncture-to-recanalization time owing to the difficulty in the procedure and higher rates of required rescue therapy. As is commonly known, time is essential for patients with AIS to achieve a good outcome.[10] A longer duration from symptom onset to recanalization is strongly associated with poor outcome in patients with stroke who undergo endovascular therapy.[11] Finally, patients with CE and ICAS may experience more difficulty during MT. The thrombectomy maneuver count was higher than in other groups (2.5 vs. 2), which indicated decreasing probability of both good outcome and recanalization.[12] Thus, more aggressive techniques may be required to reduce puncture-to-recanalization time and optimize processes to reduce the ODT and door-to-puncture time within this subset of patients.

In our study, similar rates of successful reperfusion were observed in different etiologies.[13] No differences were observed in safety outcomes, such as sICH and death rate. The CE and ICAS and ICAS without CE groups had more chances to undergo rescue therapy.[14] All rescue therapies, such as balloon angioplasty, stent retriever detachment, or other stent (which abruptly increases cerebral perfusion pressure and subsequent antiplatelet therapy), may increase hemorrhagic risk. In our study, 20 of 37 patients (54%) with ICAS underwent stent retriever detachment or other stent placement in the stenosis lesion. This therapeutic approach showed no significant differences regarding the safety outcomes.[15]

This study had several limitations. The primary limitations were that the diagnosis of underlying ICAS after thrombectomy depended on imaging characteristics of the local lesion during the procedure and that there was no evaluation of the collateral status. The association of the collaterals and the presence of ICAS as well as the outcomes should be investigated in future studies. Finally, the sample size was insufficient, which may have caused false-negative results. Large prospective controlled trials are needed to confirm our observations.

CONCLUSIONS

The presence of both CE and ICAS was associated with a worse outcome of patients with anterior circulation large-vessel occlusion that was treated with endovascular thrombectomy. Further studies are warranted to support our results.

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