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The prognostic significance of hyperdense middle cerebral artery sign in cardioembolic stroke patients undergoing mechanical thrombectomy

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Abstract

Objective To investigate the association between the presence of the HMCAS on CT prior MT and the occurrence of poor functional outcomes and sHT in LVO patients attributed to CE and LAA etiology.

Methods We conducted a retrospective analysis using patient data from three comprehensive stroke centers. Patients were categorized into four groups: (1) LAA with HMCAS, (2) LAA with no HMCAS, (3) cardioembolic with HMCAS, (4) cardioembolic with no HMCAS based on the presence of HMCAS and the underlying stroke etiology. We compared the 90-day modified Rankin score (mRS) and the incidence of sHT between 1 vs. 2, and 3 vs. 4.

Results 295 patients were included, of which 93 (31.5%) exhibited HMCAS. Patients with HMCAS associated with cardioembolism (CE) had a less favorable outcome, and there was no significant difference in the rate of sHT between group 3 and 4. Conversely, there was no significant difference in prognosis and the rate of sHT between patients between group 3 and 4. In multivariate logistic regression analysis, the HMCAS independently predicted poor prognosis in patients who underwent MT due to CE (OR: 0.193, 95% CI: 0.040–0.937, $p = 0.041$).

Conclusion In patients with AIS-LVO attributed to cardioembolic etiology who underwent MT, the presence of HMCAS on initial NCCT scans was found to be associated with an unfavorable outcome.

Clinical trial registration ChiCTR 2,300,074,368.

Keywords Hyperdense middle cerebral artery sign, Outcome, Mechanical thrombectomy, Large artery atherosclerosis, Cardioembolism

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Introduction

Mechanical thrombectomy(MT) has become the established standard of care for individuals afflicted by AIS resulting from large vessel occlusion (LVO) despite different stroke etiology [1]. On non-contrast computed tomography (NCCT), hyperdense middle cerebral artery sign (HMCAS) is serves as one of the initial CT manifestations of the occlusion of MCA [2]. In the context of diagnosing MCA occlusion, HMCAS exhibits a sensitivity ranging from 27 to 54% and an impressively high specificity nearing 100% [3]. Previous investigations have established a correlation between the presence of HMCAS and unfavorable outcomes in AIS patients treated with intravenous thrombolysis [4, 5]. Recently, researchers have turned their attention toward evaluated the role of HMCAS as a predictive factor for outcomes in AIS patients undergoing mechanical thrombectomy (MT).

A study conducted in 2017 suggests that the prognostic implication of an HMCAS in predicting outcomes after endovascular therapy in patients with acute MCA occlusion may be low [6]. However, Kiddy et al. [7] have demonstrated that the absence of HMCAS is associated with worse functional outcome in patients presenting with M1 occlusions undergoing thrombectomy. Proximal HMCAS on initial NCCT was independently associated with aHT in patients who received MT for acute MCA occlusion and both aHT and sHT had a detrimental effect on clinical outcom [8]. The findings of these studies exhibit certain contradictions.

Prior studies have usually concentrated on assessing prognostic disparities between patients with positive and negative HMCAS. While, recent research findings have uncovered significant disparities in clinical outcomes when comparing patients with large artery atherosclerosis(LAA) to those with a cardioembolic(CE) etiology [9]. Sun et al. [10] have revealed that patients with stroke of LAA etiology had significantly higher rate of favorable functional outcome compared to patients with stroke of CE etiology. The relationship between HMCAS and prognosis under different stroke types has been overlooked, which may be a possible reason for the contradictory findings in previous studies.Therefore, we hypothesize that the relationship between HMCAS and the prognosis of thrombectomy varies among patients with different stroke etiologies.

Method

Patient selection

We conducted a comprehensive review of medical records and brain imaging data pertaining to patients who underwent MT treatment at three general hospitals in China: The Affiliated Ganzhou Hospital of Nanchang University, Nanfang Hospital of Southern Medical University, and People's Hospital of Huichang County. Our data collection spanned from January 2021 to December 2022. It is important to note that this study received ethical approval from the medical ethics committees of each respective research center.

We enrolled all consecutive patients with AIS, including those: (a) $\geq$ 18 years old; (b) who underwent MT within 24 h of symptom onset; (c) with the isolated middle cerebral artery (MCA) occlusion, or (d) MCA occlusion in a context of a tandem lesion with internal carotid artery (ICA) occlusion. We excluded patients such as those (a) pretreatment CT images were not available and (b) isolated ICA or arteria cerebri anterior(ACA) occlusion not involving of the MCA segment. Importantly, the assessment and management of acute stroke patients adhered to contemporary recommendations at these three general hospitals.

Data collection and clinical evaluation

We conducted a comprehensive assessment of each patient's clinical profile, encompassing factors such as age, gender, hypertension, diabetes, atrial fibrillation, prior stroke or transient ischemic attack (TIA), coronary heart disease, smoking history, and the administration of intravenous thrombolysis. To gauge the severity of stroke, we employed the National Institutes of Health Stroke Rating Scale (NIHSS) [11]. Additionally, we utilized the Alberta Stroke Project Early CT Score (ASPECTS) to estimate the extent of early ischemic damage in the MCA region [12]. Functional outcomes at admission and the three-month mark post-stroke were assessed using the modified Rankin score (mRS) [13]. Data about post-discharge mRS scores were acquired through either telephonic discussions with the patient or their primary caregiver or during the patient's regular clinical follow-up visits. We invited two stroke experts to independently evaluate the mTICI, ASPECT, and TOAST(FZ and WL).

Neuroimaging

HMCAS refers to a condition marked by heightened vascular lumen density in the MCA in comparison to adjacent or contralateral arteries. Two independent stroke doctors (BL and QF) examined the NCCT to determine whether HMCAS was present. (89.58% overall agreement, k = 0.80, 95% CI 0.70–0.91). When there was disagreement, images were examined and consensus was made (Fig. 1). All NCCT scans were performed using a 64-row scanner. The main NCCT technical parallel were the following: kV: 120 – mA: 350 – row thickness: 5 mm.

Stroke etiology

Stroke etiology was assessed according to the criteria of Trial of Org 10,172 in Acute Stroke Treatment (TOAST) [14], including large- artery atherosclerosis (LAA),

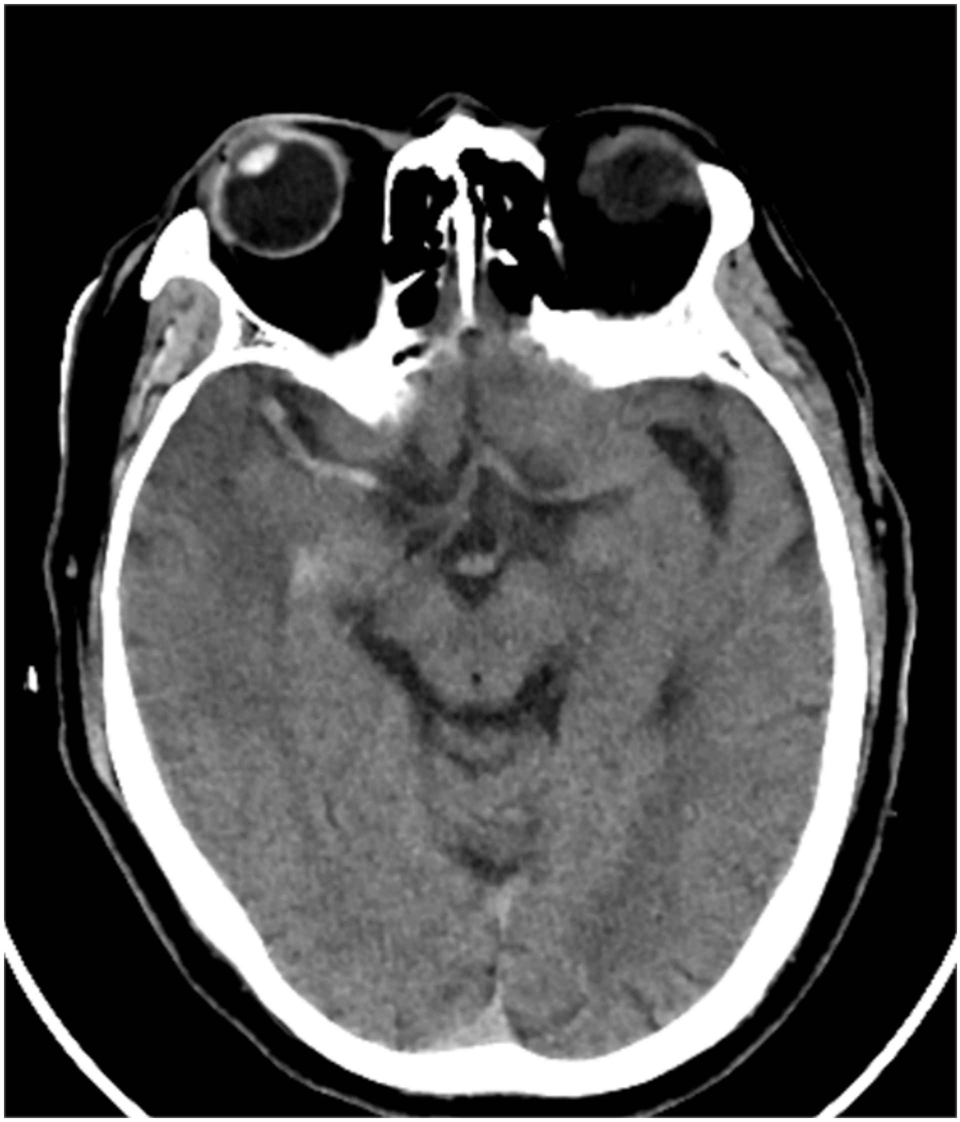

Fig. 1 A patient with positive hyperdense middle cerebral artery sign

cardioembolism (CE), and undetermined cause (UC) by two stroke experts(FZ and HZ) blinded to functional outcomes. If there was a disagreement on the presence or absence of HMCAS, a final decision was made by consensus between the two readers(k = 0.82). LAA stroke was defined as localized residual with more than 50% stenosis in the nonbifurcation location occlusion after thrombectomy from digital subtraction angiography (DSA), or tandem occlusions due to atherosclerosis of the ipsilateral extracranial internal carotid artery (ICA). Cardioembolic stroke (CE) was diagnosed in patients with clean non-atherosclerotic cerebral vasculature and harboring any of the following: valvular and nonvalvular atrial fibrillation, infective endocarditis, left atrial dilatation with in situ thrombosis, global hypokinesia with apical akinesia, mitral or aortic valve replacement, patent foramen ovale with an interatrial septum, and dilated cardiomyopathy. Patients with neither alleged high-risk cardioembolic source nor culprit stenotic lesion that could be set forth on the angiography were designated to have UC.

Thrombectomy

DSA was conducted on the occluded artery prior to MT to assess the thrombus location. The choice of thrombus extraction method, whether it involved stent retrieval, aspiration, or a combination thereof, the selection of device size or type, and the number of procedural iterations were all determined by the operator. In cases of severe stenosis, post-thrombectomy intervention involved balloon angioplasty, and in situations where angioplasty failed to maintain distal blood flow, consideration was given to stent implantation. For patients with AIS featuring tandem occlusion, the decision to undertake emergency intracranial and extracranial carotid artery stent implantation was at the discretion of the attending physician.

Several critical parameters were documented, including first-pass recanalization success, the number of attempts required, the onset-to-groin puncture time (OPT), the door-to-groin puncture time (DPT), and the groin puncture-to-recanalization time (PRT). Successful recanalization was defined as achieving a modified Thrombolysis in Cerebral Infarction (mTICI) score of 2b–3 [15]. Subsequent to the thrombectomy, patients were diligently managed and continuously monitored in the stroke unit. In cases of neurological deterioration or within the time frame of 12 to 36 h post-MT, an NCCT scan of the head was performed to assess the potential occurrence of symptomatic hemorrhagic transformation(sHT).

Clinical outcomes

We assessed the following key endpoints: (1) Primary Outcome: The primary outcome was defined as a favorable 90-day outcome, specifically, a mRS of 0–2 at the three-month mark. (2) The diagnosis of SICH: namely the National Institute of Neurological Diseases and Stroke definition or any ICH on follow-up CT or MRI 24–48 h after thrombolysis with an increase of >4 points on the NIHSS score from baseline [16]. (3) Hemorrhagic Transformation Rate: This was characterized by the presence of any hemorrhagic imaging findings observed in the initial NCCT scan conducted after MT. It encompassed various types of hemorrhagic transformations, including transformation of infarcted brain tissue, hemorrhage within and outside infarcted brain tissue, subdural hematoma, intraventricular hemorrhage, or remote parenchymal hematoma.

Statistical analysis

The data analysis was performed utilizing SPSS version 27.0. Continuous variables, expressed as either mean and standard deviation (mean ± SD) or median and interquartile range (median, IQR), were compared using either Student's t-test or the Mann-Whitney U test. Categorical variables were presented as numbers and percentages, and their comparisons were conducted through Chi-square tests or Fisher exact tests. To investigate the relationship between HMCAS and outcomes, a multivariate logistic regression model was employed. The odds ratio (OR) and its corresponding 95% confidence interval (CI) were subsequently computed for each variable. All reported p-values are based on two-tailed tests, with statistical significance set at $p < 0.05$.

Result

Between January 2021 and December 2022, a total of 621 individuals were subjected to MT for acute anterior circulation LVO across three general hospitals. After a meticulous screening process, 295 patients were ultimately included in the study. A visual representation of this selection process is provided in Fig. 2.

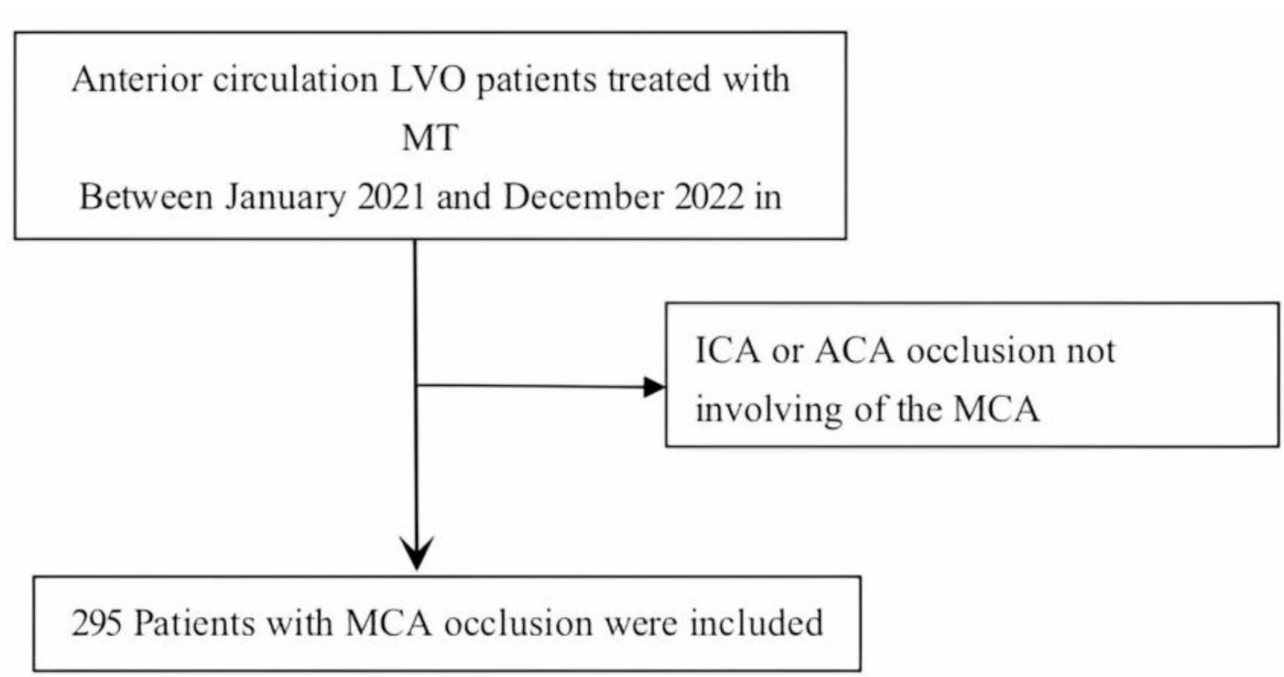

Fig. 2 Flowchart illustrating the selection and exclusion process of the study participants

HMCAS in patients with MCA occlusion

Out of the total sample of 295patients, 93 (31.5%) displayed HMCAS on their initial NCCT scans. The mean age in the cohort was 66.13 ± 12.86 years, with 177 (60.0%) being male. Among these patients, 24 (11.48%) exhibited sHT, 225 (76.27%) achieved successful recanalization, and 144 (41.81%) experienced a favorable prognosis. Participants were stratified into two distinct groups: the HMCAS group and the Non-HMCAS group. Notably, there were no discernible differences between the two groups in terms of hyperlipidemia, previous stroke/transient ischemic attack (TIA), or smoking history. In the HMCAS group, a higher proportion of males and a greater incidence of atrial fibrillation were observed (41.94% vs. 26.73%, $p = 0.009$ for males). Additionally, the HMCAS group exhibited a higher baseline NIHSS score and a lower ASPECTS (12.50 [7.00, 17.00] vs. 15.00 [11.00, 18.00], $p = 0.009$ for NIHSS; 9.00 [8.00, 10.00] vs. 8.00 [6.00, 10.00], $p < 0.001$ for ASPECT). In terms of recanalization efficacy, the Non-HMCAS group demonstrated a higher rate of first-pass recanalization and a reduced number of procedural passes compared to the HMCAS group (36.63% vs. 20.24%, $p = 0.005$ for first-pass recanalization; 2.00 [1.00, 3.00] vs. 2.00 [2.00, 4.00], $p < 0.001$ for the number of passes). There are no statistical significance was found in the rate of good clinical outcome and sHT among the HMCAS group and the Non-HMCAS group. (48.00% vs. 36.60%, $p = 0.066$ for good outcomes; 11.85 vs. 10.81%, $p = 0.821$ for sHT) (Table 1).

HMCAS in patients with LAA

The included cases were categorized into two groups, LAA, and CE, based on the TOAST criteria. Among the individuals with LAA, 116 patients were further stratified based on the presence or absence of HMCAS into Non-HMCAS-LAA ($n = 83$) and HMCAS-LAA ($n = 33$) subgroups. Comparing these subgroups, it was evident that HMCAS-LAA demonstrated a higher rate of first-pass recanalization and required fewer procedural passes than their HMCAS-LAA counterparts (32.53% vs. 12.12%, $p = 0.025$ for first-pass recanalization; 2.00 [1.00, 3.00] vs. 3.00 [2.00, 4.00], $p < 0.001$ for the number of passes). However, there were no statistically significant

Table 1 Clinical characteristics of enrolled patients

Variables	Total ($n = 295$)	Non-HMCAS($n = 202$)	HMCAS($n = 93$)	p value
Age (years), Mean ± SD	66.13 ± 12.86	66.36 ± 12.87	65.63 ± 12.87	0.653
Male sex, n(%)	177 (60.00)	124 (61.39)	53 (56.99)	0.474
Hypertension, n(%)	183 (62.03)	136 (67.33)	47 (50.54)	**0.006**
Diabetes mellitus, n(%)	71 (24.07)	58 (28.71)	13 (13.98)	**0.006**
Hyperlipidemia, n(%)	50 (16.95)	37 (18.32)	13 (13.98)	0.356
Previous stroke or TIA, n(%)	46 (15.59)	36 (17.82)	10 (10.75)	0.120
Atrial fbrillation, n(%)	93 (31.53)	54 (26.73)	39 (41.94)	**0.009**
Coronary heart disease, n(%)	44 (14.92)	29 (14.36)	15 (16.13)	0.691
Smoking, n(%)	83 (28.14)	63 (31.19)	20 (21.51)	0.086
Intravenous thrombolysis, n(%)	92 (31.19)	60 (29.70)	32 (34.41)	0.418
ASPECTS, M (Q_1, Q_3)	9.00 (7.00, 10.00)	9.00 (8.00, 10.00)	8.00 (6.00, 10.00)	**< 0.001**
Baseline NIHSS score, M (Q_1, Q_3)	13.00 (9.00, 17.00)	12.50 (7.00, 17.00)	15.00 (11.00, 18.00)	**0.009**
TOAS, n(%)				**0.004**
1	116 (39.32)	83 (41.09)	33 (35.48)	
2	93 (31.53)	52 (25.74)	41 (44.09)	
3	86 (29.15)	67 (33.17)	19 (20.43)	
PRT, M (Q_1, Q_3)	88.00 (65.00, 124.00)	90.00 (65.00, 125.00)	80.00 (55.00, 120.00)	0.130
OPT, M (Q_1, Q_3)	335.00 (245.00, 413.00)	318.00 (238.50, 391.50)	360.00 (260.00, 420.00)	**0.017**
DPT, M (Q_1, Q_3)	107.00 (87.50, 133.00)	107.00 (87.00, 132.50)	106.00 (89.00, 135.00)	0.839
first-pass recanalization, n(%)	93 (31.53)	74 (36.63)	19 (20.43)	**0.005**
Number of passes, M (Q_1, Q_3)	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	2.00 (2.00, 4.00)	**< 0.001**
Successful recanalization, n(%)	225 (76.27)	156 (77.23)	69 (74.19)	0.569
All HT, n(%)	104 (35.25)	64 (31.68)	40 (43.01)	0.058
sHT, n(%)	28 (9.49)	20 (9.90)	8 (8.60)	0.724
Good outcome, n(%)	131(44.41)	97 (48.00)	34 (36.60)	0.066

Bold p values indicate statistical significance

HMCAS: hyperdense middle cerebral artery sign

Non-HMCAS: None-hyperdense middle cerebral artery sign

TIA, transient ischemic attack; NIHSS, National Institute of Health Stroke Scale; ASPECTS, Alberta stroke program early CT score; OPT, onset-to-groin puncture time; DPT, door-to-recanalization time; PRT, groin puncture-to-recanalization time; HT, hemorrhagic transformation; sHT, symptomatic hemorrhagic transformation differences in the rates of successful reperfusion and favorable 90-day outcomes between patients in the Non-HMCAS-LAA group and those in the HMCAS-LAA group (81.93% vs. 84.85%, $p=0.707$ for successful reperfusion; 42.71% vs. 45.45%, $p=0.747$ for good outcomes) (Table 2).

HMCAS in patients with CE

A total of 116 patients diagnosed with cardiac embolism were included in this study and categorized into two groups: the Non HMCAS-CE group ($n=52$) and the HMCAS-CE group ($n=41$). Notably, the HMCAS-CE group exhibited lower scores in terms of the ASPECTS and a reduced rate of first-pass recanalization (9.00 [8.00, 10.00] vs. 8.00 [6.00, 10.00] $p=0.007$ for ASPECT; 50.00% vs. 26.83%, $p=0.023$ for first-pass recanalization). Furthermore, patients in the HMCAS-CE group required more procedural passes (1.00 (1.00, 3.00) vs. 2.00 (2.00, 3.00), $p=0.023$). There were no statistically significant differences in the rates of sHT between patients in the Non-HMCAS-CE group and those in the HMCAS-CE group (11.54% vs. 12.20%, $p>0.999$). In contrast, the Non-HMCAS-CE group displayed a higher percentage of favorable outcomes and a lower incidence of HT (51.92% vs. 21.30%, $p=0.028$ for good outcomes; 34.62% vs. 56.10%, $p=0.038$ for HT) (Table 4).

The comparison of results between patients with a good prognosis ($n=39$) and those with a poor prognosis ($n=54$) in the CE subgroup is outlined in Table 4. In patients with CE, variables including intravenous thrombolysis, baseline NIHSS, first-pass recanalization, the number of passes, HT, and the presence of HMCAS were all associated with the 90-day mRS. Multivariate logistic regression models were used for evaluating the association of HMCAS with the endpoints. These models were adjusted for gender, intravenous thrombolysis, baseline NIHSS, HCMAS, first-pass recanalization and smoking, and identified positive HMCAS as an independent risk factor for an unfavorable outcome (OR: 0.193, 95% CI: 0.040–0.937, $p=0.041$) (Table 5).

Discussion

This study presents suggested that patients with CE attributed to MCA occlusion, who exhibit HMCAS on their initial NCCT scans upon admission have poorer clinical outcomes and higher rate of HT following MT. Notably, the prognosis of CE patients is associated with several factors, including the baseline NIHSS, intravenous thrombolysis, first-pass recanalization.Additionally, our study indicates that HMCAS can serve as a valuable imaging marker to predict adverse outcomes in CE patients suffering from acute MCA occlusion post MT.

Table 2 Clinical characteristics of enrolled patients with LAA

Variables	Total ($n=116$)	Non-HMCAS in LAA ($n=83$)	HMCAS in LAA ($n=33$)	*p* value
Age (years), Mean ± **SD**	62.79 ± 11.85	62.63 ± 12.33	63.21 ± 10.73	0.811
Male sex, **n(%)**	59 (50.86)	45 (54.22)	14 (42.42)	0.252
Hypertension, **n(%)**	85 (73.28)	63 (75.90)	22 (66.67)	0.310
Diabetes mellitus, **n(%)**	30 (25.86)	25 (30.12)	5 (15.15)	0.097
Hyperlipidemia, **n(%)**	24 (20.69)	18 (21.69)	6 (18.18)	0.674
Previous stroke or TIA, **n(%)**	23 (19.83)	16 (19.28)	7 (21.21)	0.814
Atrial fbrillation, n(%)?	5 (4.31)	3 (3.61)	2 (6.06)	0.937
Coronary heart disease, **n(%)**	13 (11.21)	11 (13.25)	2 (6.06)	0.434
Smoking, **n(%)**	45 (38.79)	31 (37.35)	14 (42.42)	0.613
Intravenous thrombolysis, **n(%)**	32 (27.59)	19 (22.89)	13 (39.39)	0.073
ASPECTS, **M (Q_1, Q_3)**	9.00 (7.00, 10.00)	9.00 (7.00, 10.00)	9.00 (7.00, 9.00)	0.306
Baseline NIHSS score, M **(Q_1, Q_3)**	12.00 (7.00, 16.25)	10.00 (6.00, 17.00)	13.00 (10.00, 16.00)	0.142
PRT, M (Q_1, Q_3)	98.50 (75.00, 124.25)	107.00 (75.50, 126.00)	90.00 (71.00, 120.00)	0.344
OPT, M (Q_1, Q_3)	342.00 (260.00, 410.50)	300.00 (240.00, 375.50)	385.00 (356.00, 495.00)	**< 0.001**
DPT, M **(Q_1, Q_3)**	110.00 (90.00, 140.00)	108.00 (90.00, 132.00)	114.00 (86.00, 149.00)	0.723
first-pass recanalization, **n(%)**	31 (26.72)	27 (32.53)	4 (12.12)	**0.025**
Number of passes, **M (Q_1, Q_3)**	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	3.00 (2.00, 4.00)	**< 0.001**
Successful recanalization, n(%)	96 (82.76)	68 (81.93)	28 (84.85)	0.707
All HT, n(%)	35 (30.17)	23 (27.71)	12 (36.36)	0.360
S-ich, n(%)	13 (11.21)	10 (12.05)	3 (9.09)	0.897
Good outcome, n(%)	50 (43.10)	35 (42.17)	15 (45.45)	0.747

Bold *p* values indicate statistical significance

HMCAS: hyperdense middle cerebral artery sign

Non-HMCAS: None-hyperdense middle cerebral artery sign

TIA, transient ischemic attack; NIHSS, National Institute of Health Stroke Scale; ASPECTS, Alberta stroke program early CT score; OPT, onset-to-groin puncture time; DPT, door-to-recanalization time; PRT, groin puncture-to-recanalization time; HT, hemorrhagic transformation; sHT, symptomatic hemorrhagic transformation

Table 3 Clinical characteristics of enrolled patients with CE

Variables	Total ($n=93$)	Non-HMCAS in CE ($n=52$)	HMCAS in CE ($n=41$)	*p* value
Age (years), Mean ± **SD**	71.08 ± 12.60	74.33 ± 10.08	66.95 ± 14.30	**0.007**
Male sex, **n(%)**	61 (65.59)	33 (63.46)	28 (68.29)	0.626
Hypertension, **n(%)**	47 (50.54)	30 (57.69)	17 (41.46)	0.120
Diabetes mellitus, **n(%)**	20 (21.51)	14 (26.92)	6 (14.63)	0.152
Hyperlipidemia, **n(%)**	11 (11.83)	6 (11.54)	5 (12.20)	1.000
Previous stroke or TIA, **n(%)**	10 (10.75)	8 (15.38)	2 (4.88)	0.198
Atrial fbrillation, **n(%)**	61 (65.59)	36 (69.23)	25 (60.98)	0.405
Coronary heart disease, **n(%)**	17 (18.28)	8 (15.38)	9 (21.95)	0.416
Smoking, **n(%)**	15 (16.13)	10 (19.23)	5 (12.20)	0.360
Intravenous thrombolysis, **n(%)**	38 (40.86)	24 (46.15)	14 (34.15)	0.242
ASPECTS, M **(Q_1, Q_3)**	9.00 (7.00, 10.00)	9.00 (8.00, 10.00)	8.00 (6.00, 10.00)	**0.007**
Baseline NIHSS score, **M (Q_1, Q_3)**	15.00 (11.00, 18.00)	15.00 (10.00, 19.00)	15.00 (13.00, 18.00)	0.285
PRT, M **(Q_1, Q_3)**	70.00 (50.00, 110.00)	70.50 (50.00, 106.25)	70.00 (50.00, 124.00)	0.831
OPT, M **(Q_1, Q_3)**	284.00 (218.00, 363.00)	253.50 (198.00, 348.00)	308.00 (237.00, 370.00)	0.131
DPT, M **(Q_1, Q_3)**	103.00 (82.00, 135.00)	106.00 (80.00, 136.50)	100.00 (89.00, 120.00)	0.538
first-pass recanalization, **n(%)**	37 (39.78)	26 (50.00)	11 (26.83)	**0.023**
Number of passes, M (Q_1, Q_3)	2.00 (1.00, 3.00)	1.00 (1.00, 3.00)	2.00 (2.00, 3.00)	**0.023**
Successful recanalization, n(%)	65 (69.89)	35 (67.31)	30 (73.17)	0.541
All HT, **n(%)**	41 (44.09)	18 (34.62)	23 (56.10)	**0.038**
S-ich, **n(%)**	11 (11.83)	6 (11.54)	5 (12.20)	>0.999
Good outcome, **n(%)**	44 (47.31)	27 (51.92)	12 (29.30)	0.028

Bold *p* values indicate statistical significance

HMCAS: hyperdense middle cerebral artery sign

Non-HMCAS: None-hyperdense middle cerebral artery sign

TIA, transient ischemic attack; NIHSS, National Institute of Health Stroke Scale; ASPECTS, Alberta stroke program early CT score; OPT, onset-to-groin puncture time; DPT, door-to-recanalization time; PRT, groin puncture-to-recanalization time; HT, hemorrhagic transformation; sHT, symptomatic hemorrhagic transformation

Recent study has revealed that good clinical outcome will decreases with number of retrieval attempts in Stroke Thrombectomy [17]. Further explanation, studies have reported that clinical outcomes are most favorable in patients achieving a TICI score of 3 after the first retrieval attempt [18]. Our study highlights that patients in the HMCAS-CE group underwent a greater number of passes during the thrombectomy procedure, similar results have also been documented in prior studies [19]. Bai at al. [20] have demonstrated that patients subjected to more than three passes experienced inferior functional outcomes, longer treatment durations, and a reduced likelihood of successful recanalization. Previous research has established a link between an increased number of passes and endothelial injury [21], which can result in stenosis, re-occlusion of the artery post-recanalization, or embolization into distal arteries, thereby limiting lateral branch perfusion to potentially salvageable tissue [22, 23]. Patients may have a bad prognosis as a result of these mechanical thrombectomy consequences.

The results of our study show that patients in the HMCAS-CE group had significantly lower ASPECTS than those in the Non-HMCAS-CE group. Furthermore, the HMCAS-CE group exhibited a higher incidence of HT, however the sHT conversion rate was not significantly differ between the two groups. Although not reaching statistical significance, patients with HMCAS-positive status undergoing thrombectomy demonstrated a higher tendency toward sHT [6, 24]. An additional recent study categorized MCA occlusive patients into four groups based on MCA segment location and the presence or absence of HMCAS. The presence of proximal HMCAS was strongly associated with higher rates of HT, and proximal HMCAS patients exhibited significantly lower ASPECTS compared to their proximal HMCAS-negative counterparts [8]. This disparity in ASPECTS may account for the increased frequency of hemorrhagic transformation in patients with positive proximal HMCAS. Previous studies have consistently demonstrated that HMCAS is correlated with larger cerebral infarct volumes, measured using the "one-third middle cerebral artery area" principle or ASPECTS on initial NCCT scans [5, 25–27], which is a well-established risk factor for HT following MT [28–30].

Traditionally, it was believed that sHT with parenchymal hemorrhage represented the most common type of HT associated with poor clinical outcomes [28]. Nevertheless, recent research have shown a connection between poorer functional outcomes and asymptomatic hemorrhagic transformation (aHT) following MT [31, 32]. KANG et al. [8] similarly that individuals with HT, including aHT and sHT types, exhibited fewer positive

Table 4 Comparative analysis of outcomes in CE patients post-MT: good vs. poor

Variables	Total ($n=93$)	Good outcome in CE ($n=39$)	Poor outcome in CE ($n=54$)	*P*
Age (years), Mean ± **SD**	71.08 ± 12.60	70.10 ± 10.83	71.78 ± 13.79	0.530
Male sex, **n(%)**	32 (34.41)	14 (35.90)	18 (33.33)	0.797
Hypertension, **n(%)**	47 (50.54)	17 (43.59)	30 (55.56)	0.255
Diabetes mellitus, **n(%)**	20 (21.51)	8 (20.51)	12 (22.22)	0.843
Hyperlipidemia, **n(%)**	11 (11.83)	4 (10.26)	7 (12.96)	0.941
Previous stroke or TIA, **n(%)**	10 (10.75)	2 (5.13)	8 (14.81)	0.251
Atrial fbrillation, **n(%)**	61 (65.59)	24 (61.54)	37 (68.52)	0.484
Coronary heart disease, **n(%)**	17 (18.28)	4 (10.26)	13 (24.07)	0.089
Smoking, **n(%)**	15 (16.13)	11 (28.21)	4 (7.41)	**0.007**
Intravenous thrombolysis, **n(%)**	38 (40.86)	24 (61.54)	14 (25.93)	**< 0.001**
ASPECTS, M **(Q_1, Q_3)**	9.00 (7.00, 10.00)	9.00 (8.00, 10.00)	9.00 (7.00, 10.00)	0.216
Baseline NIHSS score, M **(Q_1, Q_3)**	15.00 (11.00, 18.00)	12.00 (8.50, 15.50)	16.50 (15.00, 19.00)	**< 0.001**
PRT, M **(Q_1, Q_3)**	70.00 (50.00, 110.00)	65.00 (46.50, 85.00)	95.00 (56.00, 130.00)	**0.007**
OPT, M **(Q_1, Q_3)**	284.00 (218.00, 363.00)	340.00 (184.50, 377.50)	260.00 (218.50, 330.00)	0.315
DPT, M (Q_1, Q_3)	103.00 (82.00, 135.00)	99.00 (81.00, 118.50)	109.50 (89.50, 137.50)	0.183
first-pass recanalization, **n(%)**	37 (39.78)	24 (61.54)	13 (24.07)	**< 0.001**
Number of passes, **M (Q_1, Q_3)**	2.00 (1.00, 3.00)	1.00 (1.00, 2.00)	3.00 (2.00, 3.00)	**< 0.001**
Successful recanalization, **n(%)**	65 (69.89)	35 (89.74)	30 (55.56)	**< 0.001**
All-HT, n(%)	41 (44.09)	7 (17.95)	34 (62.96)	**< 0.001**
sHT, n(%)	11 (11.83)	0 (0.00)	11 (20.37)	**0.007**
HMCAS, n(%)	41 (44.09)	12 (30.77)	29 (53.70)	**0.028**

Bold *p* values indicate statistical significance

HMCAS: hyperdense middle cerebral artery sign

Non-HMCAS: None-hyperdense middle cerebral artery sign

TIA, transient ischemic attack; NIHSS, National Institute of Health Stroke Scale; ASPECTS, Alberta stroke program early CT score; OPT, onset-to-groin puncture time; DPT, door-to-recanalization time; PRT, groin puncture-to-recanalization time; HT, hemorrhagic transformation; sHT, symptomatic hemorrhagic transformation

Table 5 Multivariate logistic regression models predicting poor outcome

	OR	95%CI	*p* value
Baseline NIHSS	1.018	0.975–1.063	**0.419**
Intravenous thrombolysis	0.551	0.216–1.409	**0.214**
first-pass recanalization	0.581	0.234–1.443	0.242
Male sex	1.058	0.316–3.542	0.927
HMCAS	0.193	0.040–0.937	**0.041**
smoking	1.647	0.685–3.963	0.265

Bold *p* values indicate statistical significance

HMCAS: hyperdense middle cerebral artery sign

NIHSS: National Institutes of Health Stroke Rating Scale; OPT, onset-to-groin puncture time; OR, odds ratio; CI, confidential interval

outcomes. Correspondingly, in our study, HT was linked to an unfavorable prognosis in CE patients. Consequently, we advocate for a more alarming approach to blood pressure management post-MT in patients with HMCAS attributed to CE, aiming to mitigate the risk of HT. Moreover, efforts should be directed towards minimizing the occurrence of HT in clinical practice.

The histology of thrombi can influence the effectiveness of thrombectomy [33]. Liebeskind et al. [34] discovered that in their investigation of thrombus composition analysis in patients receiving MT for acute MCA occlusion, the presence of HMCAS was linked to thrombi that were primarily made up of red blood cells (RBCs). Recent research has indicated that RBC-dominant thrombi are associated with shorter procedure times during MT [35, 36]. In contrast, our study identified that HMCAS is linked to an increased number of thrombectomy passes especially in CE-HMCAS group which can be attributed to differences in thrombus composition. Ahn et al. [37] discovered that thrombus composition in CE patients was predominantly fibrin-rich, which correlated with an increased number of thrombectomy passes and poorer prognosis [38]. Current research results suggest that thrombi with a high WBC fraction are related to more organized thrombi of cardioembolic origin associated with less favorable recanalization and clinical outcome in acute ischemic anterior circulation stroke [39].

In this study, we found that in the CE subgroup, HMCAS was significantly associated with poor clinical outcome and an increased incidence of HT, which suggests that more careful intraoperative manipulation and strict postoperative blood pressure control may be necessary for CE patients with positive HMCAS. To the best of our knowledge, this is the first study to investigate the relationship between HMCAS and the prognosis of AIS patients with different etiologies, and in this study, we made a rigorous distinction of the TOAST classification. Recently, an increasing number of studies have found that patients with different etiologies undergoing thrombectomy have different prognoses, which indicates that in future research, it is necessary to include stroke etiology, such as TOAST classification, as a variable for analysis.

Our study has several limitations. Firstly, as a registry study, system biases may be generated from the retrospectively collected data and potentially limiting researchers' control over confounding variables. Secendly, in patients with dysphagia or very poor clinical conditions, transthoracic echography was necessarily used as a substitute for transesophageal echography, consequently, the underestimate of CE became unavoidable. Moreover, no specialized biomarkers or histological analyses were performed for the retrieved thrombi to verify the etiological diagnosis. In our forthcoming research, we intend to delve deeper into exploring the correlations between HMCAS and the composition of thrombi based on the TOAST etiological classification.

Conclusion

Our study has illuminated the presence of HMCAS as a risk factor associated with unfavorable outcomes and HT in patients with LVO-AIS who underwent MT due to CE etiology. This discovery offers clinicians a valuable imaging marker to identify individuals at a heightened risk of poor prognosis. Furthermore, it appears that patients with HMCAS in the CE subgroup may require a greater number of thrombus passes during MT procedures, although the underlying mechanism remains unclear.

Abbreviations

HMCAS	Hyperdense middle cerebral artery sign
NCCT	Pre-treatment non-contrast CT
HT	Hemorrhagic transformation
AIS-LVO	Acute ischemic stroke due to large vessel occlusion
MT	Mechanical thrombectomy
mRS	Modified Rankin score
CE	Cardioembolism
LAA	Large artery atherosclerosis
MCA	Middle cerebral artery
AIS	Acute ischemic stroke
LVO	Large vessel occlusion
TOAST	Trial of Org 10172 in Acute Stroke Treatment
DSA	Digital subtraction angiography
TIA	Transient ischemic attack
NIHSS	National Institutes of Health Stroke Rating Scale
ASPECTS	Alberta Stroke Project Early CT Score
OPT	The onset-to-groin puncture time
DPT	Door-to-groin puncture time
RPT	Groin puncture-to-recanalization time
mTICI	Modified Thrombolysis in Cerebral Infarction
MRI	Magnetic resonance imaging
OR	Odds ratio
CI	Confidence interval
Non-HMCAS	None-hyperdense middle cerebral artery sign
sHT	Symptomatic hemorrhagic transformation
aSH	Asymptomatic hemorrhagic transformation
RBCs	Red blood cells

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Author contributions

XL, FZ, and WL drafted the manuscript. HZ, BL, JG, and CZ analyzed the data and then reviewed and revised the manuscript. ZJ and GZ revised the manuscript. All authors reviewed the manuscript and approved the final version of the manuscript.

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Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. It is with utmost pride and pleasure that I stand before you today to make this declaration. This declaration is a testimony to our collective commitment towards a common goal.

Declarations

Ethics approval and consent to participate

This study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Medical Ethics Committee of The Affiliated Ganzhou Hospital of Nanchang University (Approval number: TY-ZKY-2023-041-01).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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