ORIGINAL ARTICLE

Multiphase CTA Collateral Circulation is an Excellent CT Indicator than CT ASPECTS in Predicting Clinical Outcome in Acute Ischemic Stroke

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Objective: The prognosis of acute ischemic stroke patients is influenced by collateral vasculature. The present study aimed to evaluate the predictive value of the initial collateral circulation score (ICS) obtained from multiphase computed tomography angiography (mCTA) in determining clinical outcomes. The authors hypothesized that the initial mCTA collateral circulation score may serve as a superior predictor of clinical outcomes compared to the CT Alberta Stroke Program Early CT Score (ASPECTS). Additionally, the first phase CTA ASPECTS (f-CTA ASPECTS) derived from mCTA may offer enhanced predictive accuracy over the CT ASPECTS.

Materials and Methods: The authors conducted a retrospective analysis of 300 patients diagnosed with acute ischemic stroke between 2020 and 2021. Collateral scores were assessed using mCTA, and the first phase CTA ASPECTS score was also evaluated. Clinical outcomes were measured using the modified Rankin Scale (mRS) at hospital discharge, categorizing outcomes as good with mRS 0 to 2, or poor with mRS 3 to 6. Both univariate and multiple linear regression models were employed to predict patient outcomes.

Results: Univariate analysis demonstrated a significant association between both the collateral score and first phase CTA ASPECTS with clinical outcomes. However, in the multiple linear regression model, only the CTA ASPECTS emerged as a significant predictor of discharge mRS. The model accounted for 45.7% of the variance in mRS at discharge. A comparison of the reperfusion and non-reperfusion groups with good collateral scores revealed no significant difference in discharge mRS outcomes (p=0.954).

Conclusion: While both the collateral score and the first phase CTA ASPECTS were associated with clinical outcomes, only the first phase CTA ASPECTS was a statistically significant predictor of mRS at discharge. The absence of a difference in mRS outcomes between reperfusion and non-reperfusion groups among patients with initially good collateral scores on mCTA suggested that aggressive reperfusion procedures may not always be warranted.

Keywords: Multiphase CTA brain; CT brain; CT ASPECT score; Collateral score

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Cerebral ischemia is a prevalent condition that can result in fatalities or severe disability[1]. In 2010, the estimated number of ischemic and hemorrhagic strokes worldwide was 11.6 million and 5.3 million, respectively. By 2016, the number of new strokes had increased to 13.7 million. In the same year, 5.5 million deaths globally were attributed to stroke[2]. In Thailand, there are more than 250,000 new stroke cases each year. Stroke claims approximately 50,000 deaths annually[3].

Cerebral infarction arises from the blockage of brain blood vessels, resulting in tissue damage due to inadequate blood supply of less than 10 mL/100 g/minute, and leading to irreversible tissue damage. However, certain areas where blood supply can still reach constitute the penumbra area, which is reversible if the blood flow to the tissue increased[4]. In cases of acute blockage of brain blood vessels, if individuals retained collateral circulation to supply the brain tissue in the regions affected by the blockage, cell death in that brain area would be minimal. Consequently, patients with good collateral circulation have a better prognosis compared to those with limited or absent collateral circulation.

Collateral circulation consists of the opening of alternative vascular channels distal to an occluding intracranial artery resulting in a massive vasodilatation

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that improves blood flow in hypoperfused brain regions.

Previous studies have established a correlation between collateral circulation and clinical outcomes[5]. Patients with good collateral circulation often experience better clinical outcomes compared to those with poor collateral circulation, particularly among individuals who underwent thrombolysis or recanalization treatments[6-8]. Earlier research has revealed that multiphase computed tomography angiography (mCTA) is an effective tool for assessing collateral circulation[9].

The Alberta Stroke Program Early CT Score (ASPECTS) is a tool used to quantify early ischemic changes (EIC) in middle cerebral artery (MCA) strokes across ten distinct brain regions. It deducts one point from a maximum total score of ten for each region displaying EIC. This evaluation is conducted via computed tomography (CT) brain scans without the need for contrast injection. It interprets brain tissue swelling, or hypodensity, in the initial phase and subtracts points based on predefined areas of brain swelling due to ischemia. A higher remaining score suggests less blood-deprived dead brain tissue, leading to better prognosis. Therefore, ASPECTS demonstrates an inverse relationship with the National Institutes of Health Stroke Scale (NIHSS) and functional outcomes[10].

The objectives of the present study were 1) to apply the mCTA collateral score as a predictive tool for determining the clinical outcomes of acute stroke patients, and 2) to investigate whether the mCTA collateral circulation score and first phase CTA ASPECT are superior to the CT ASPECT in predicting the clinical outcomes of stroke patients, both those received reperfusion therapy and those who did not, at the time of discharge.

Materials and Methods

Study design and patient selection

The present study was a retrospective study, received approval from the Institutional Review Board, Certificate of Approval (Si 067/2023), and informed consent was not required. The authors examined the clinical and radiological data of 300 patients diagnosed with acute ischemic stroke at Siriraj Hospital, all of whom had undergone comprehensive radiological assessments, including native CT and mCTA, to identify the location of the ischemic stroke. Data collection spanned between November 2020 and December 2021, with an initial 597 patients. Exclusions were made due to incomplete data quality in 43 cases, and alternative diagnoses in 254 cases, resulting in a final analysis cohort of 300 patients (Figure 1). Demographic information of all patients, including age, gender, underlying diseases, treatment, and complications, were recorded. Clinical outcomes, measured by the modified Rankin Scale (mRS) and NIHSS at hospital discharge, were also documented.

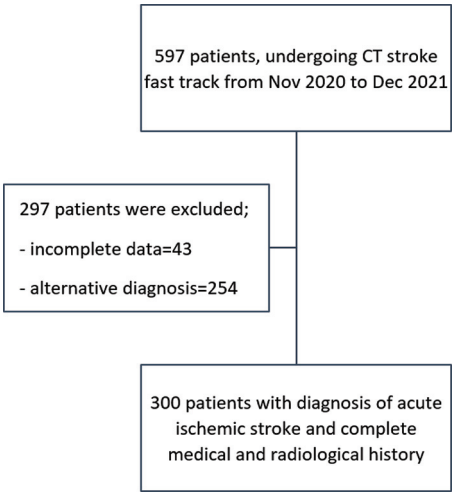

Figure 1. Flow chart shows patient selection.

Collateral scores and CT ASPECTS were evaluated by the staff neuroradiologists. The collateral score was categorized into three groups, good (score of 4 to 5), intermediate (2 to 3), and poor (0 to 1). The CTA ASPECTS were independently assessed by two neuroradiologists using first-phase CTA scans following contrast administration.

Imaging protocol and review

All imaging in the present study was conducted using 64-slice and 256-slice CT scanners (Discovery CT750 HD and Revolution Apex; GE Healthcare), with tube voltage set at 100 to 120 kV, tube current at 150 to 490 mA, and rotation speed between 0.5 and 0.7 seconds. The mCTA protocol was as follows:

- Contrast bolus: 60 to 80 mL administered at a rate of 4 to 5 mL/second, followed by a saline chaser.
- First phase, the peak arterial phase: Coverage extended from the aortic arch through the vertex. Image acquisition was triggered by bolus monitoring with a region of interest (ROI) in the proximal descending aorta at a trigger value of 100 HU.
- Second phase, the peak venous phase: Coverage extended from the skull base through the vertex, performed four seconds after the peak arterial phase scan.

• Third phase, the late venous phase: Coverage extended from the skull base through the vertex, performed four seconds after the second phase.

Collateral scores were assigned as 0 (no vessel was visible in any phase within the ischemic vascular territory), 1 (few vessels were visible in any phase within the occluded vascular territory), 2 (two-phase delay in peripheral vessel filling with decreased prominence and extent, or a one-phase delay with some ischemic regions devoid of vessels), 3 (two-phase delay in peripheral vessel filling, or a one-phase delay with significantly reduced vessel number in the ischemic territory), 4 (one-phase delay in peripheral vessel filling, with unchanged prominence and extent), and 5 (normal or increased prominence of pial vessels/normal extent within the ischemic territory in the symptomatic hemisphere)[9]. Scores were grouped into good (4 to 5), intermediate (2 to 3), and poor (0 to 1).

The ASPECTS score was derived from two standardized axial CT cuts from NCCT and first-phase CTA. A point was subtracted for each region showing EIC, such as focal swelling or parenchymal hypoattenuation. A normal CT scan received an ASPECTS of ten points[11].

Outcome

Clinical outcomes were evaluated using the mRS at discharge. Patients with mRS scores of 0 to 2 were classified as having good clinical outcomes, while those with scores of 3 to 6 were classified as having poor clinical outcomes[12].

Statistical analysis

Data analysis was performed using PASW Statistics, version 18.0 (SPSS Inc., Chicago, IL, USA). Normally distributed data was presented as means and standard deviations (SDs), while non-normal data was expressed as medians and interquartile ranges (IQRs). To evaluate the impact of risk factors, demographic variables, collateral status, and treatment on functional outcomes, univariate models were computed for each outcome variable with Cramers' V tests for nominal variables and Pearson's r for categorical data. Baseline predictors with a univariate model p-value of less than 0.2 were included in multiple linear regression analyses. A p-value of less than 0.05 was considered statistically significant.

Results

The demographic profile of the present study cohort was summarized in Table 1. Among the 300 participants, males constituted 55% and females 45%, with a mean age of 68.74 years (range of 29 to 89 years). At discharge, clinical outcomes were stratified as favorable, for mRS scores of 0 to 2, in 97 patients (32.3%) and unfavorable for mRS scores of 3 to 6, in 203 patients (67.7%). Patients with favorable outcomes had a median age of 63 years, contrasting with 73 years for those with unfavorable outcomes.

Non-reperfusion therapy was administered to 76 patients (25.3%), while the majority 224 patients (74.7%), underwent interventions such as intravenous (IV) thrombolysis, mechanical thrombectomy, or combined treatments. The median NIHSS score at admission was 11, which improved to 4 at discharge.

The vast majority of participants (80.7%) in the present study exhibited a favorable collateral score (Figure 2). Conversely, none of the patients with an unfavorable collateral score achieved a favorable outcome (Figure 3).

Comparison between the reperfusion and non-reperfusion groups regarding favorable collateral scores showed no statistically significant differences in discharge mRS outcomes or rates of hemorrhagic transformation (p=0.954, 0.101), respectively (Table 2, 3). Similarly, among patients with favorable collateral scores, the presence or absence of hemorrhagic transformation did not significantly impact clinical outcomes (p=0.146). Importantly, a significant disparity was noted between CT ASPECTS and CTA ASPECTS (p<0.001) (Figure 4), with first-phase CTA ASPECTS scoring lower in up to 60% of cases compared to non-contrast CT ASPECTS.

In the present study, univariate multiple linear regression analysis incorporated collateral score, age, gender, underlying diseases, treatment modalities, hemorrhagic transformation, old lesions, CT ASPECTS, CTA ASPECTS, smoking status, and discharge NIHSS as predictors mRS. This model accounted for 45.7% of the variance in discharge mRS outcomes (Table 4). Subsequently, predictors with a p-value less than 0.2, specifically age, gender, collateral score, CTA ASPECTS, and discharge NIHSS were integrated into a multiple linear regression model. This refined analysis identified younger age, male gender, higher CTA ASPECTS, and lower discharge NIHSS scores as statistically significant predictors of favorable clinical outcomes (Table 4).

Table 1. Baseline data of studied patients

	Total (n=300)	Poor outcome (n=203)	Good outcome (n=97)
Age (year); mean±SD or median (range)	68.74±13.42 (29 to 97)	73 (29 to 97)	63 (29 to 89)
Sex; n (%)			
Female	135 (45.0)	104 (51.2)	31 (32.0)
Male	165 (55.0)	99 (48.8)	66 (68.0)
U/D; n (%)	282 (94.0)	193 (95.1)	89 (91.8)
DM; n (%)	111 (37.0)	80 (39.4)	31 (32.0)
HT; n (%)	227 (75.7)	154 (75.9)	73 (75.3)
AF; n (%)	107 (35.7)	79 (38.9)	28 (28.9)
Smoking; n (%)	120 (40.0)	68 (33.5)	52 (53.6)
Treatment; n (%)			
IV thrombolysis	96 (32.0)	62 (30.5)	34 (35.1)
Mechanical thrombectomy	66 (22.0)	47 (23.2)	19 (19.6)
Combined	62 (20.7)	41 (20.2)	21 (21.6)
No intervention	76 (25.3)	53 (26.1)	23 (23.7)
Hemorrhagic transformation; n (%)	60 (20.0)	55 (27.1)	5 (5.2)
Old lesion; n (%)	183 (61.0)	136 (67.0)	47 (48.5)
Collateral score; n (%)			
Poor	15 (5.0)	15 (7.4)	0 (0.0)
Intermediate	43 (14.3)	38 (18.7)	5 (5.2)
Good	242 (80.7)	150 (73.9)	92 (94.8)
NIHSS admission; median (IQR)	11 (13)		
NIHSS discharge; median (IQR)	4 (10)		
mRS admission; median (IQR)	5 (1)		
mRS discharge; median (IQR)	4 (4)		
MCA territory only; n (%)	188 (62.7)		
Length of stay (days)	10.97		

U/D=underlying disease; DM=diabetes mellitus; HT=hypertension; AF=atrial fibrillation; IV=intravenous; NIHSS=National Institutes of Health Stroke Scale; mRS=modified Rankin Scale; MCA=middle cerebral artery; SD=standard deviation; IQR=interquartile range

Table 2. Comparison of reperfusion and non-reperfusion group within good collateral score associate with the clinical outcome

	mRS; n (%)		p-value
	Poor	Good	
Reperfusion	37 (24.7)	23 (25.0)	0.954
Non-reperfusion	113 (75.3)	69 (75.0)	

mRS=modified Rankin Scale

Table 3. Comparison of reperfusion and non-reperfusion group regarding good collateral score associate with hemorrhagic transformation

	Hemorrhagic transformation; n (%)		p-value
	No	Yes	
Reperfusion	151 (73.3)	31 (86.1)	0.101
Non-reperfusion	55 (26.7)	5 (13.9)	

Discussion

In patients with acute ischemic stroke, CTA has been the study of choice for the initial diagnosis of large-vessel occlusion and other important vascular pathologies such as dissection. The mCTA is a more recent variant of CTA that is time-resolved, acquiring an arterial phase and two venous phases. The mCTA offers advantages over the traditional single-phase CTA technique (sCTA), including improved detection of large-vessel occlusions[13], higher interrater reliability, and improved characterization of collateral status[9].

The present study explored the relationship between collateral scores assessed via mCTA and clinical outcomes in acute ischemic stroke patients.

Reperfusion and non-reperfusion groups regarding favorable collateral scores showed no statistically significant differences in discharge mRS outcomes or rates of hemorrhagic transformation.

The previous study from Menon et al.[9] found mCTA to be superior to first-phase CTA and CT perfusion in determining clinical outcome.

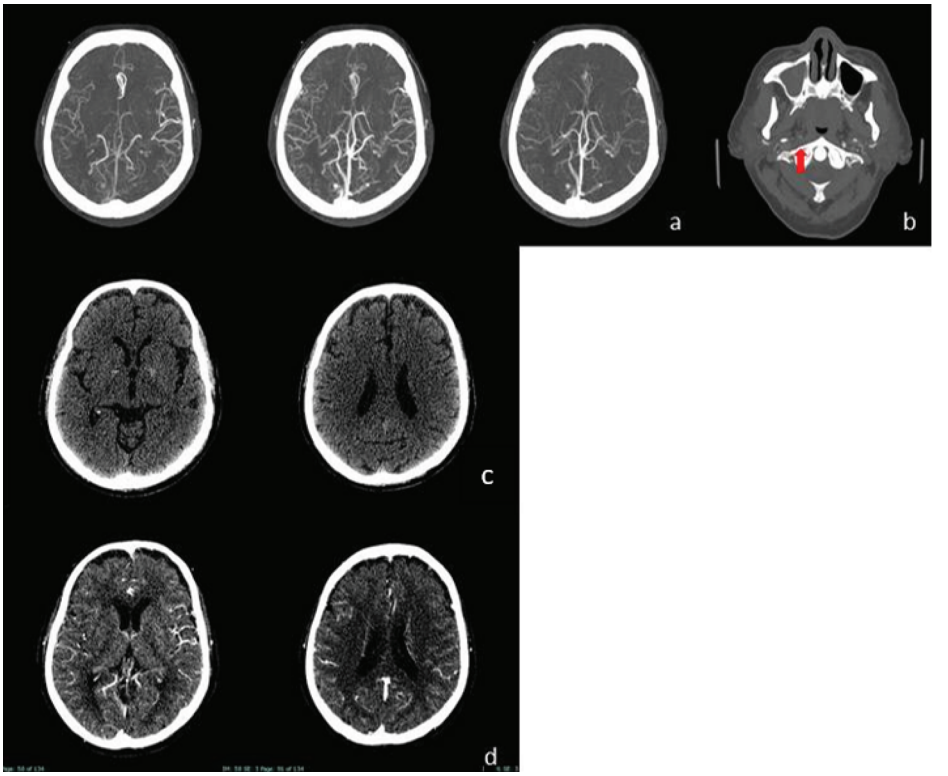

Figure 2. Demonstrative case of A 72-year-old male presented with left hemiparesis. (a) Multiphase CTA showed good collateral score (5/5), (b) MIP CTA showed total occlusion at right proximal ICA (arrow), (c) CT ASPECTS and (d) CTA ASPECTS showed ASPECTS=10/10.

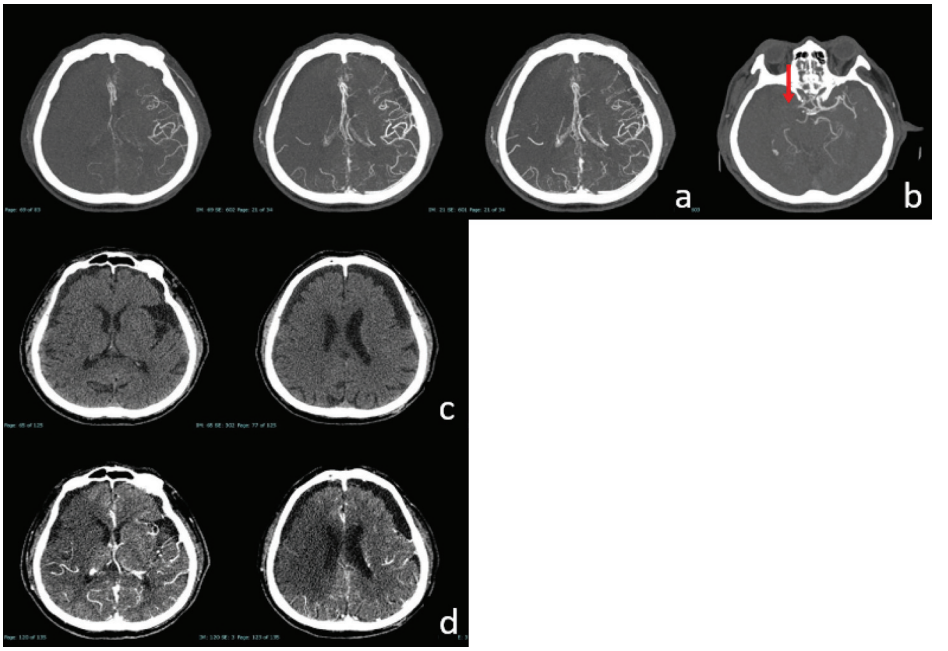

Figure 3. Demonstrative case of a 78-year-old male known case AF on warfarin presented with left hemiparesis (a) Multiphase CTA showed poor collateral score (1/5), (b) MIP CTA showed total occlusion at supraclinoid part of right ICA (arrow), (c) Noncontrast ASPECTS showed 5/10 and (d) 1st phase CTA ASPECTS showed 0/10.

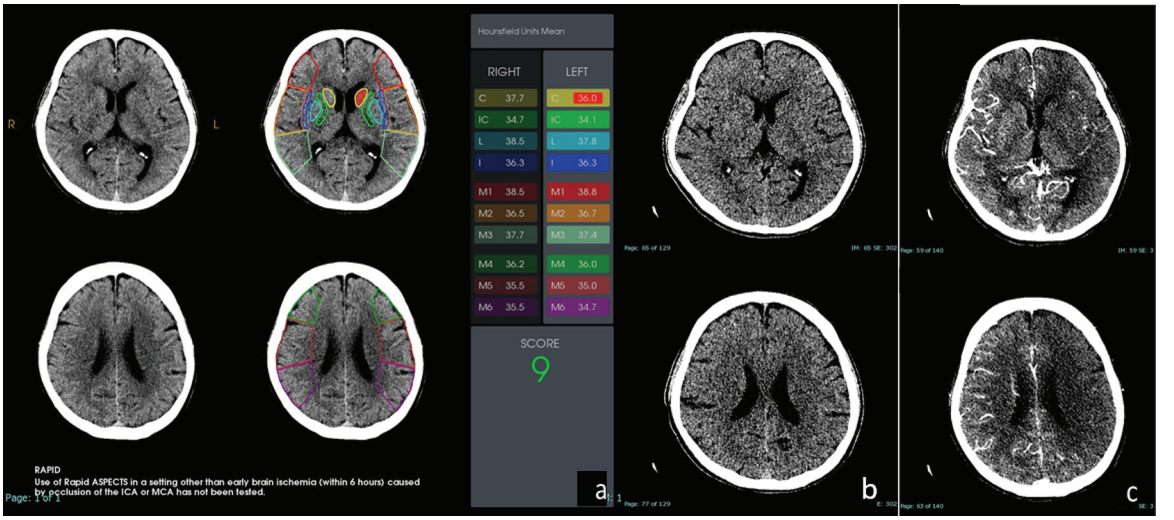

Figure 4. A 60-year-old male, presented with right hemiparesis 3 hours PTA, (a) RAPID ASPECTS=9/10, (b) CT ASPECTS=9/10, (c) 1st phase CT ASPECTS=0/10.

Table 4. Factors associated with mRS at discharge time

Factor	Univariate linear regression				Multivariate linear regression			
	β	SE	Std β	p-value	β	SE	Std β	p-value
Age (year)	0.032	0.008	0.224	<0.001*	0.019	0.006	0.137	0.004*
Sex	0.689	0.221	0.178	0.002*	0.413	0.171	0.115	0.017*
U/D	0.59	0.468	0.073	0.209	-	-	-	-
DM	0.14	0.231	0.035	0.545	-	-	-	-
DLP	–0.016	0.223	–0.004	0.944	-	-	-	-
HT	–0.016	0.223	–0.004	0.944	-	-	-	-
CKD	–0.267	0.335	–0.046	0.427	-	-	-	-
AF	0.284	0.232	0.071	0.222	-	-	-	-
Old CVA	–0.257	0.294	–0.051	0.383	-	-	-	-
Treatment	–0.007	0.104	–0.004	0.944	-	-	-	-
Hemorrhagic transformation	1.529	0.264	0.318	<0.001*	-	-	-	-
Old lesion	0.643	0.226	0.163	0.005*	-	-	-	-
Collateral score	–1.228	0.197	–0.34	<0.001*	-	-	-	-
CT ASPECTS	–0.284	0.043	–0.359	<0.001*	-	-	-	-
CT ASPECTS 1st	–0.172	0.030	–0.318	<0.001*	–0.053	0.024	–0.103	0.032*
Smoking	–0.739	0.224	–0.188	<0.001*	-	-	-	-
Discharge NIHSS	0.153	0.011	0.643	<0.001*	0.144	0.011	0.605	<0.001*

β=unstandardized coefficient; SE=standard error; Std β=standardized coefficient; U/D=underlying disease; DM=diabetes mellitus; DLP=dyslipidemia; HT=hypertension; CKD=chronic kidney disease; AF=atrial fibrillation; CVA=cerebrovascular accident; CT=computed tomography; ASPECTS=Alberta Stroke Program Early CT Score; NIHSS=National Institutes of Health Stroke Scale

Multivariate model: R^2=0.682, Adjusted R^2=0.457, p<0.0001*

* p<0.05 indicates statistical significance

- indicates variable not included in multivariate model

In contrast, secondary analysis of data from the DEFUSE 3 randomized clinical trial by de Havenon et al. showed no correlation between good collaterals assessed by CTA and improved clinical outcome[14].

At the univariate level, collateral score, age, gender, smoking status, discharge NIHSS, hemorrhagic transformation, old lesions, CT ASPECTS, and CTA ASPECTS exhibited correlations with clinical outcomes, consistent with previous literature[5,8,15]. However, multivariate multiple linear regression analysis revealed that collateral scores from mCTA did not consistently predict outcomes,

despite explaining 45.7% of the variance.

In contrast to prior studies focusing exclusively on large vessel occlusion and mechanical thrombectomy eligibility[10,12], the present investigation included a diverse spectrum of acute ischemic stroke patients with varied treatment modalities, mirroring real-world clinical scenarios[16]. Moreover, while previous research often assessed functional outcomes using mRS at 90 days post-treatment[17-19], the present study utilized discharge mRS, reporting favorable outcomes in 32.3% and unfavorable outcomes in 67.7% of cases. These findings underscore methodological variability and clinical outcome disparities across stroke research[20].

The inability to elucidate more than 50% of the variance in the present study models suggests the influence of unaccounted factors[21]. Furthermore, the authors observed no significant differences in clinical outcomes between treated and untreated patients with favorable collateral scores, consistent with findings in mild stroke populations[22]. Nevertheless, our study identified a higher incidence of hemorrhagic transformation among patients receiving IV thrombolysis, contrary to previous reports[23].

Visual assessments highlighted the first-phase CTA ASPECTS's superior ability to distinguish normal from abnormal tissues compared to NCCT ASPECTS, aligning with studies favoring CTA source image ASPECTS for predictive accuracy[24]. However, the authors' analysis indicated that NCCT ASPECTS alone did not independently predict favorable outcomes.

Study limitations warrant acknowledgment, including its retrospective design, lack of randomization, and modest sample size, which may restrict the detection of associations discernible in larger cohorts. Patients with different treatments and reperfusion statuses were included. Additionally, using discharge mRS as a proxy for clinical outcomes may overlook long-term recovery trajectories. Future investigations should expand sample sizes and incorporate randomized controlled trials to comprehensively evaluate predictors of clinical outcomes. Furthermore, exploring specific factors influencing outcomes among reperfusion and non-reperfusion groups with favorable collateral scores could yield valuable insights.

Conclusion

While collateral scores derived from multiphase CTA correlate with clinical outcomes, they did not emerge as significant predictors of discharge outcomes in the present study. The comparable mRS outcomes observed between reperfusion and non-reperfusion groups among patients with favorable collateral scores show no significant difference in mRS outcomes. This information will challenge the necessity of aggressive reperfusion strategies. Further research is needed to elucidate factors influencing clinical outcomes in acute ischemic stroke and to optimize treatment approaches accordingly.

What is already known about this topic?

CT ASPECTS is used worldwide to evaluate the area in an ischemic stroke and predict the outcome prognosis.

What does this study add?

Multiphase CTA brain provides not only information about the intracranial arteries status but also information about collateral circulation as well as CTA first phase ASPECTS scores. It is more accurate in predicting clinical outcomes. Its application is helpful to assist clinical decision in making acute stroke management.

Conflicts of interest

The authors declare no conflict of interest.

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