Relationship of Core Growth Rate, Collateral Circulation Status and Clinical Outcome in Patients with Acute Ischemic Stroke from Anterior Circulation Occlusion

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Abstract

Introduction: Collateral circulation status demonstrated the strong relationship with core growth rate and clinical outcome in patient with acute cerebral infarction receiving thrombolysis treatment.

Objectives: To evaluate relationship of core growth rate, collateral circulation status, and clinical outcome, in patients with anterior circulation occlusion (known and unknown time of symptom onset.)

Materials and Methods: A retrospective chart review was conducted. 47 patients with anterior circulation occlusion (known and unknown time of symptom onset). Core growth rate defined as baseline core volume divided by time of symptom onset or last seen well to CTP. Collateral circulation status was scoring 0 to 5. Spearman correlation coefficients was performed to evaluate the correlation and simple linear regressions were performed the predictive power.

Results: The median core growth rate was 1.24 ml/h with IQR 0.55-0.44 ml/h. This study demonstrated the inversely relationship of core growth rate and collateral status (Rho = -0.284, P-value = 0.026). The relationship of core growth rate and clinical outcomes showed correlation (Rho = 0.043, P-value = 0.386), especially in unknown time of onset group (Rho = 0.62, P-value = 0.021). For relationship of treatment, core growth rate and clinical outcomes, IVT plus EVT or EVT only group, core growth rate showed inverse correlation with 3-month mRS (Rho = -0.049, P-value = 0.396).

Conclusion: The core growth rate has a relationship with collateral status and clinical outcome, in overall and uncertain onset cases.

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Introduction

Acute large vessel occlusion accounted for one out of three in patients with acute cerebral infarction who arrive within first 24 hours of symptom onset and associated with the worst clinical outcomes and high mortality rates. Thrombolysis treatment, intravenous (IVT) and endovascular thrombolysis treatment (EVT), in the eligible patients showed the benefit on clinical outcomes.[1-7]

Collateral circulation status demonstrated the strong relationship with core growth rate[8] and clinical outcomes in patient with acute cerebral infarction receiving thrombolysis treatment.[5, 6, 9-11] A previous prospective cohort study showed that collateral status was a major determinant of ischemic core growth.[12] However, the relationship of core growth rate, collateral circulations status and clinical outcomes in patients with uncertain onset of symptom has not been established.

Recently, multimodal computed tomography, including Non-contrasted Computer tomography CT (NCCT), multiphase CT Angiography (CTA) and perfusion CT (CTP) were applied to evaluate collateral circulation status and infarct core growth rate which implied the benefit of revascularization and clinical decision for the appropriate choice of treatment.[13-17]

This study aimed to evaluate the relationship of core growth rate, collateral circulation status, and clinical outcomes, in patients had anterior circulation large vessel occlusion with known and unknown time of symptom onset.

Methods

Study design and Patients

This retrospective chart review, enrolled patients who had anterior circulation large vessel occlusion with known and unknown time of symptom onset and admitted to Stroke Unit at Thammasat University Hospital between December 2019 to September 2022. All patients underwent complete baseline NCCT, CTP, and multiphase CTA within 24 hours of symptom onset. Ethical approval was obtained by Thammasat University Hospital ethics committee in October 2022 and inform consent was obtained by each patient.

Imaging processing

Baseline multimodal CT included NCCT, CTP, and multiphase CTA was obtained with various CT scanners (Philips, Siemens). Collateral circulation status was scoring 0 to 5.[8] Data from CTP were processed by commercial software (Philips, Siemens). Three parameters (cerebral blood flow, cerebral blood volume and mean transit time) were generated. Penumbra volume defined as the volume of total ischemic lesion minus with acute core volume. Acute core volume was measured on acute CTP. Final core volume was measured by the ABC/2 rule.[18] Hemorrhagic transformation was detected by 24 to 72 hours control NCCT.

Calculation of core growth rate

Core growth rate defined as baseline core volume divided by time from symptom onset or last seen well to CTP. The definition of core growth rate was described and validated a method of estimating core growth rate by core volume and time of stroke onset and was assumed a near linear pattern of core growth in first 24 hours of symptom onset. Patients with wake-up stroke or unknown time of symptom onset were excluded.[12] In this study, we established a new definition of core growth rate by including patients with unknown time of symptom onset.

Outcomes

The primary outcome was the relationship of core growth rate, collateral circulation status, and clinical outcome, in patients with anterior circulation large vessel occlusion with known and unknown time of symptom onset. The secondary outcomes were the relationship of treatment (no thrombolysis, IVT alone and IVT with EVT or EVT alone), core growth rate and clinical outcome.

The clinical outcome was the modified Rankin scale (mRS) at 3 months after discharge. Good clinical outcome was defined by mRS score of 0-2 and poor clinical outcome was defined by mRS of 3-6.

Statistical analysis

Continuous data were summarized by median and interquartile range. Categorical variables were described as proportion. Core growth rate was summarized as median and interquartile range. Relationship of core growth rate and collateral circulation status was assessed by Spearman correlation coefficient; same analyses were applied to assess relationship of core growth rate and patient outcomes, and relationship of treatment, core growth rate and patient outcomes.

Predictive power of collateral circulation status on core growth rate was assessed by simple linear regression models, same as the predictive power of patient outcome on core growth rate.

All statistical analysis was done using SPSS Software version 27.

Results

Patients

This study included 70 patients who had anterior circulation large vessel occlusion with CTP Performed within 24 hours of stroke onset or last seen well in case of unknown time of stroke onset. Of the 70 patients, 21 patients were excluded due to no final core volume, and 2 patients were excluded due to no baseline collateral circulation status. Thus 47 patients were selected. All core growth rate, collateral circulation status, and 3-month mRS were recorded. Patient characteristics are summarized in Table 1.

Table 1 Baseline characteristics of 47 patients

Characteristics	N	%
Sex		
Female	22	46.8
Male	25	53.2
Age		
< 70 years	27	57.4
≥ 70 years	20	42.6
Clinical presentation		
Alteration of consciousness	1	2.1
Aphasia	2	4.3
Hemiparesis	44	93.6

Table 1 Baseline characteristics of 47 patients (cont.)

Characteristics	N	%
Risk		
HTN	30	63.8
DM	13	27.7
DLP	20	42.6
CAD	1	2.1
Old ischemic stroke	4	8.5
TIA	0	0
AF	14	29.8
Smoking	8	17
Valvular heart disease	0	0
Alcohol	3	6.4
Other		
Amphetamine	2	2.2
CKD	3	6.4
Stroke subtypes		
Cardioembolism	24	51.1
Large-artery atherosclerosis	14	29.8
Stroke of other determined etiology	2	4.3
Stroke of undetermined etiology	7	14.9
NIHSS at onset, median (QR)	16 (11, 19)	
Acute treatment		
No thrombolysis	13	27.7
IVT alone	3	6.4
IVT plus EVT or EVT alone	31	66
TICI		
0	3	6.4
2a	2	4.3
2b	13	27.7
2c	3	6.4
3	9	19.1
Onset to door (in recanalization case), median (QR)	567 (411.25, 827.25)	
Door to recanalization (except TICI 0), median (QR)	128 (96, 188.75)	
Lesion		
M1 occlusion	23	48.9
Intracranial ICA occlusion	17	36.2
M2 occlusion	3	6.4
Severe stenosis M1	2	4.3
Severe stenosis ICA	1	2.1
CT ASPECT, median (QR)	7 (5, 9)	
Collateral score, median (QR)	4 (3, 4)	
Poor	17	36.2
Good	30	63.8

Table 1 Baseline characteristics of 47 patients (cont.)

Characteristics	N	%
Onset to CTP time (min), median (QR)		
Overall case	525 (423, 776)	
Unknown onset case (n=36)	557 (423.25, 795.75)	
Time known onset case (n=11)	465 (371, 712)	
Penumbra volume (ml), median (QR)		
Overall case	140 (89, 190.8)	
Unknown onset case (n=36)	160.5 (89.3, 202.65)	
Time known onset case (n=11)	137.5 (86.7, 184.5)	
Core infarct volume (ml)), median (QR)		
Overall case	29.06 (5.6, 45.1)	
Unknown onset case (n=36)	11.35 (6.03, 41)	
Time known onset case (n=11)	27.9 (4.2, 85)	
Final infarct core (ml), median (QR)	21.5 (9, 83.9)	
Core growth rate (ml/h), median (QR)		
Overall case	1.24 (0.55, 4.4)	
Unknown onset case (n=36)	1.18 (0.58, 3.56)	
Time known onset case (n=11)	3.6 (0.47, 11.54)	
NIHSS at 24 hr, median (QR)	14 (10, 17)	
mRS at 3 months	4 (1, 5)	
Poor	31	66
Good	16	34
Length of stay (days), median (QR)	7 (5, 13)	
Hemorrhagic transformation		
No	26	55.3
Yes	21	44.7

Relationship of core growth rate, collateral circulation status and clinical outcomes

Core growth rate and collateral circulation status

The median core growth rate in this study was 1.24 ml/h with IQR 0.55-0.44 ml/h. For patients with known time of onset, mean core growth rate was 3.6 (0.47-11.54). The mean core growth rate in unknown time of onset was 1.18 (0.58-3.56).

Increase in core growth rate inversely correlated with baseline collateral circulation status (Rho = -0.284, P-value = 0.026) (Table 2). Higher core growth rate associated with poorer collateral circulation status. The correlation showed higher in patients with known time of onset groups (Rho = -0.24, P-value = 0.079). Comparing to unknown time of onset group, increase in core growth rate also showed inverse correlation (Rho = 0.505, P-value = 0.057).

The predictive power of collateral circulation status for core growth rate revealed an increment in collateral circulation status by 1 resulted in the decrease of core growth rate by 2 ml/h (Coefficient -2.004, 95% CI: -4.24 to 0.23, R^2 0.047).

Table 2 Correlation of CGR and Collateral divided by onset case

Variable	Median	IQR	N	Correlation coefficeint*	P-value
Overall case					
Core growth rate (ml/h)	1.24	0.55, 4.4	47	-0.284	0.026
Collateral score	4	3, 4	47		
Unknown onset case					
Core growth rate (ml/h)	1.18	0.58, 3.56	36	-0.24	0.079
Collateral score	4	3, 4	36		
Time known onset case					
Core growth rate (ml/h)	3.6	0.47,11.54	11	-0.505	0.057
Collateral score	4	3, 4	11		

Core growth rate and clinical outcome

Regarding to 3-month mRS, increment of core growth rate relatively correlated with clinical outcome (Rho = 0.043, P-value = 0.386) (Table 3). Especially, core growth rate in patient with unknown time of onset group, the correlation was strongly relative with clinical outcome at 3 months (Rho = 0.62, P-value = 0.021). For known time of onset group, correlation was dissimilar to overall results (Rho = -0.186, P-value = 0.139); however, small populations might interfere this result.

Increase core growth rate showed predictive power of increasing mRS score. (Coefficient 0.046, 95% CI: -0.07 to 0.16, R^2 0.015).

Table 3 Correlation of CGR and mRS at 3 month divided by onset case

Variable	Median	IQR	N	Correlation coefficeint*	P-value
Overall case					
Core growth rate (ml/h)	1.24	0.55, 4.4	47	0.043	0.386
mRS at 3 month	4	1, 5	47		
Unknown onset case					
Core growth rate (ml/h)	3.6	0.47,11.54	36	0.62	0.021
mRS at 3 month	4	2, 5	36		

Table 4 Correlation of CGR and mRS at 3 month divied by treatment group

Variable	Median	IQR	N	Correlation coefficeint*	P-value
No thrombolysis					
Core growth rate (ml/h)	1.07	0.62, 4.58	13	0.258	0.198
mRS at 3 month	5	2.5, 5	13		
IVT plus EVT or EVT alone					
Core growth rate (ml/h)	1.24	0.49, 3.71	31	-0.049	0.396
mRS at 3 month	4	1, 5	31		

Relationship of treatment, core growth rate, and clinical outcome

The IVT plus EVT or EVT alone group, core growth rate showed inverse correlation with 3-month mRS (Rho = -0.049, P-value = 0.396). For no thrombolysis group, core growth rate was relative with 3-month mRS (Rho = 0.258, P-value = 0.198). The correlation in IVT alone group was different

(Rho = 0.5, P-value = 0.333); however, this result might relate to small populations in this group (n=3). (Table 4)

Discussion

This study demonstrates that the core growth rate shows the relationship with baseline collateral circulation status and has the predictive value of clinical 3-month outcomes. Treatment with IVT plus EVT or EVT alone associates with a lower core growth rate and a better clinical outcome.

The core growth rate in this study shows inversely associates with baseline core growth rate from multiphase CT angiography which is importance to support estimating baseline collateral status by CTA and predicting the inclination of the core growth rate. Previous study, similarly, demonstrated the relationship of CTA collateral status and core growth rate.[10, 18] Another study evaluated the collateral status by CTP collateral index also showed the relationship.[12]

Regarding to unknown time of onset group, the median core growth rate is less then known time onset group. The equation of core growth rate that bases on baseline core volume divided by time from symptom onset or last seen well to CTP. The time from symptom onset to CTP is shorter in known time of onset group, that might explain this finding.

This study also adds to the evidence of relationship of core growth rate and collateral status among uncertain onset patients. In previous studies, the definition of core growth rate was core volume divided by time of symptom onset to CTP, which was different from this study.[12] Clinicians might estimate the inclination of core growth rate by the baseline collateral status even uncertain onset of symptom; however, due to uncertain time of onset, the core growth rate might not correspond to the near linear pattern within 24 hours of onset, as we could not estimate the true onset of symptom.

For the predictive power of core growth rate, the increment of collateral status by 1, shows increasing in core growth rate by 2 ml/h which is applicable for clinician to evaluate the inclination of the core growth rate after evaluating the baseline collateral status.

According to 3-months mRS, the core growth rate also shows the trend of relative association to clinical outcome. Higher core growth rate associates to higher 3-month mRS, which is poor outcome. This study adds to the evidence that uncertain onset group also has the similar relationship to clinical outcome. Predicting the clinical outcome by core growth rate might challenge clinicians to decide for treatment. On the other hand, core growth rate in known time of onset group is not relative to clinical outcome. This finding might explain by small populations and effect of the treatment.

As relationship of core growth rate and clinical outcome, this study implies that IVT plus EVT or EVT alone likely relate to better clinical outcome. In addition, no thrombolysis group also supports the relationship that higher core growth rate relates to higher 3-month mRS. Clinician might imply this finding to decide for treatment, especially in higher core growth rate.

There are limitations in this study. First, this is a retrospective study using data from Thammasat University Hospital database. Second, the small populations might disturb the results of this study as seeing the non-correspondence of results. Third, the final infarct volume was measured by ABC/2 rules, and NCCT in all cases was performed on 24 t0 72 hours which might lead to an overestimation. Fourth, in uncertain onset cases, the core growth rate is not same definition as previous studies, validating of core growth rate is suggested.

Conclusion

The core growth rate has a relationship with collateral status and clinical outcome, in overall and uncertain onset cases.

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