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Relationship Between Collateral Status, Infarct Growth and Outcome in Patients with Middle Cerebral Artery Occlusion by CT Angiography and CT Perfusion Imaging

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ABSTRACT

Introduction: Unveiling the dynamic penumbra region represents another crucial stage in treating individuals with ischemic strokes. Our objective was to explore how collateral blood flow assessments using multiphasic (triphasic) CT angiography (mpCTA) and CT perfusion (CTP) examinations correlate with the expansion of infarcted areas and disability levels in patients with middle cerebral artery (MCA) M1 and M2 occlusion.

Methods: The research was carried out as a prospective, descriptive, case series study. mpCTA and CTP were performed while patients were referred to the emergency department. Baseline National Institutes of Health Stroke Scale (NIHSS), Modified Rankin Scale (mRS) and the Barthel Index for Activities of Daily Living at 3 months were calculated. The connection between perfusion parameters that represent penumbral information derived from CTP and collateral flow information obtained from mpCTA with infarct expansion and outcome was investigated.

Results: Thirty-six patients were included in the study. The mean age of the participants in the research was found 73.47±10.67. 52.8% of the individuals were male. 72.3% of the patients exhibited an unfavorable functional outcome according to mRS at 3 months. Based on the Menon collateral score from the mpCTA, the infarct expansion showed a statistically significant difference between the groups (p=0.037). The mRS scores at 3 months did not show a statistically significant difference between the groups according to the mpCTA Menon collateral score (p=0.073). Penumbra volume information obtained by using Tmax/CBV and CBF/CBV thresholds on CTP showed statistically significant differences among good and poor clinical outcome groups based on mRS at 3 months (respectively p=0.010, 0.029). The average MTT value within the penumbra obtained from the MTT/CBV map exhibited a statistically significant difference among the groups based on the mRS at 3 months (p=0.011). There was a weak but statistically significant relationship between the volume of the penumbra obtained from CTP maps created by selecting Tmax=6 sec and the infarct growth (p=0.028).

Conclusion: Final infarct volume and infarct growth can be predicted using collateral circulation data acquired through mpCTA. The patient's disability can be assessed by analyzing the penumbral MTT value and the penumbral volume data obtained from CTP maps generated using various threshold values. Moreover, penumbra volume obtained from CTP maps created by selecting Tmax as a threshold can give information about infarct growth.

Keywords: Angiography, collateral, outcome, perfusion, pial, stroke

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INTRODUCTION

Acute ischemic stroke (AIS) due to large vessel occlusion (LVO) is a serious condition that causes mortality and morbidity. Collateral circulation in patients with acute middle cerebral artery (MCA) occlusion has the potential to preserve perfusion and extend the duration of penumbral viability. Leptomeningeal anastomoses represent one of the key fundamental anatomical characteristics responsible for collateral blood flow to the brain. The leptomeningeal collaterals are the small arteriolar connections that bridge distant segments of the major cerebral arteries. Middle cerebral artery is connected to both the anterior cerebral artery (ACA) and posterior cerebral artery (PCA) through these arteriolar anastomoses (1,2). The revealing of the dynamic penumbra area by using appropriate imaging methods is one of the leading steps for the treatment and prognosis of acute MCA occlusion.

Conventional cerebral angiography is considered to be the gold standard for evaluating leptomeningeal collaterals (3). However, this approach is invasive and cannot be carried out upon admission for the majority of acute ischemic stroke patients. As a result, in the context of the diagnosis, treatment, and prediction of infarct growth and prognosis, collateral status should be examined noninvasively.

Highlights

- **Pial collateral score obtained from mpCTA may give information about infarct growth.**
- **Patients with increased MTT are at a higher risk of poor clinical outcome.**
- **CTP maps using Tmax as a threshold give information about infarct growth and outcome.**

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Multiphase (Triphasic) CT angiography (mpCTA) has been developed as an imaging technique that provides real-time information about the degree and extent of pial arterial filling across the entire brain. Moreover, it is easy and rapid to perform and reveals images that are easy to obtain and comment. mpCTA was found to be superior to single-phase CTA in evaluating collaterals (4). Likewise, a study demonstrated that time-invariant CTA outperformed single-phase CTA when it came to predicting clinical outcomes based on the collateral score (5).

Although CT perfusion (CTP) does not provide direct information about the number and extent of pial collaterals, it provides data on blood flow and perfusion, which are directly related to the durability of these collaterals (6). The assessment of collateral vessels within the Sylvian fissure through CTP, by measuring the maximum cerebral blood flow (cCBFmax), has been demonstrated to be a viable method for quantifying collaterals. This measurement was found to be linked to the clinical outcome in patients with acute ischemic stroke (7).

In this study, we used mpCTA and CTP to evaluate leptomeningeal collaterals in patients who had acute occlusions in the M1 or M2 segments of the MCA and assessed the relationship between pial collaterals with clinical outcome and infarct growth.

METHODS

This was a prospective cohort study conducted between February 2020 and October 2020. The research protocol received approval from the Ankara City Hospital Clinical Research Ethics Committee (Date: 30.01.2020, Number: E.Kurul-E1-20-272). Written informed consent was acquired from either all patients or their designated proxy.

Patients

Patients who applied to our center with a clinical and preliminary diagnosis of stroke with the onset of symptoms within 0 and 24 hours, were included in the study. All acute stroke patients underwent non-contrast brain CT. mpCTA was performed on patients who had no evidence of intracranial bleeding. CT perfusion imaging was performed on patients who had occlusions in the M1 or M2 segments of the MCA with or without internal carotid artery, for whom recanalization therapies such as mechanical thrombectomy and/or IV tPA have not yet been decided. CT perfusion imaging was not performed in patients who were planned to be given IV tPA, in order not to delay the administration of the drug.

Demographic data and previous medical history of patients were collected. Stroke symptoms onset time or patients' last-seen-well time, baseline National Institutes of Health Stroke Scale (NIHSS) score, vital signs and time of cranial imaging were recorded.

Patients underwent control brain CT or MRI 1 week later. It was checked whether there was an infarct growth. mRS and Barthel Index for Activities of Daily Living (ADL) were calculated at 3 months. NIHSS was categorized as mild (0–7), moderate (8-16), or severe (>16). mRS was dichotomized as good clinical outcome (0–2) and poor clinical outcome (3–6). Barthel Index was classified as total dependency (0–20), severe dependency (21–61), moderate dependency (62–90), slight dependency (91–99), independent (100) and exitus. If the patient was discharged, the patient or his/her relative was contacted via phone.

Imaging Protocol

All patients underwent mpCTA and CTP imaging at admission. All scans were performed on a 64 or 128 detector-row scanner (Revolution CT, GE Healthcare, Illinois, U. S. A). For mpCTA, 35 mL of iohexol (Omnipaque 350 mg I/mL 100 mL, GE Healthcare, Marlborough, MA, U. S. A) was injected at a flow rate of 4 mL/sec into the antecubital vein. The scanner was initialized after the administration of contrast material; but image acquisition started at approximately 13–14 seconds when the scanner captured the contrast material. The aortic arch to vertex CTA made up the first phase. The subsequent two phases, one in the early venous phase and one in the late venous phase, covered the area from the skull base to the vertex. Images were acquired with a section thickness of 0.625 mm. The initial phase of the CTA, spanning from the aortic arch to the vertex, was captured within a 4-second timeframe. The second phase was obtained following an 8-second delay, which permitted the repositioning of the table to the skull base. The time taken for each subsequent phase of scanning was 2.3 seconds. Consequently, there was an 8-second gap between each of the three phases. An important feature of this imaging protocol was that the two extra phases of mpCTA were performed without requiring any additional contrast material.

For CTP, 45 mL of iohexol was injected into the antecubital vein at a flow rate of 4 mL/sec. The scanner was initialized after the administration of contrast material; but image acquisition started at approximately 8 seconds later. After the first acquisition, which lasted 44.5 seconds, the second shooting was done for 2 seconds after waiting for 10 seconds. After the second wait of 10 seconds, the last shooting was done again for 2 seconds, and the imaging acquisition process was completed.

Assessment of Collateral Status

A neuroradiologist (K. E., with 28 years of experience) assessed collateral circulation on both mpCTA and CTP. The filling of pial arteries within the ischemic region was measured on mpCTA by assessing the extent of arterial filling and delay in that filling compared with the similar arteries in the unaffected hemisphere within and between the regions of ACA–MCA and PCA–MCA by using a six-point scale for both areas as Menon et al described before (Table 1). The highest score was calculated 10. Then it was trichotomized into three clinically relevant categories 8–10 points correspond to good, 6–7 points equivalent to intermediate, and 0–5 points mean poor pial arterial filling (8).

CTP images were processed using the CT Brain Stroke protocol from CT Perfusion 4D (GE Medical Systems SCS, France) software on the AW VolumeShare 7 (GE Medical Systems SCS, France) Workstation. Arterial input function and venous outflow function were selected from the basilar artery and the confluens sinuum, respectively. Tissue classification was performed to visualize segmented tissues based on user-defined Cerebral Blood Volume (CBV) and Cerebral Blood Flow (CBF); CBV and Mean Transit Time (MTT); CBV and Time-to-Maximum (Tmax) thresholds. Maps were created by selecting Tmax=6 seconds, Blood Volume (BV)=1.0 mL/100 g brain tissue, Blood Flow (BF)=10 mL/100 g/min, Mean Transit Time=10 seconds. These maps were automatically generated by using deconvolution algorithms. Penumbral volume information and other perfusion parameters were created by collecting the data obtained from each section according to the determined threshold value. Moreover, mirror image of the penumbral area was created on the unaffected hemisphere. The reason for taking symmetrical ROI from the unaffected hemisphere in our research was to compare the data obtained from the penumbra area proportionally to the opposite side.

Infarct volumes were also calculated manually by using the Free hand ROI tool on the AW VolumeShare 7 Workstation at the admission to the hospital and 1 week later. Each section included the infarct area was obtained and then multiplied by the section thickness of 2.5 mm on CT or section thickness of 5 mm by the sum of the interslice gap of 1 mm (6 mm) on diffusion MRI to create volume information.

Statistical Analysis

Descriptive statistical analyses were determined as frequency,

Table 1. Pial arterial filling score within the symptomatic ischemic territory using mpCTA

Pial arterial filling score using mpCTA (Menon et al.)	
Score	Multiphase CT angiography
5	When compared with the asymptomatic contralateral hemisphere, there is no delay and normal or increased prominence of pial vessels/normal extent within the ischemic territory in the symptomatic hemisphere
4	When compared with the asymptomatic contralateral hemisphere, there is a delay of one phase in filling in of peripheral vessels, but prominence and extent is the same
3	When compared with the asymptomatic contralateral hemisphere, there is a delay of two phases in filling in of peripheral vessels or there is a one-phase delay and significantly reduced number of vessels in the ischemic territory
2	When compared with the asymptomatic contralateral hemisphere, there is a delay of two phases in filling in of peripheral vessels and decreased prominence and extent or a one-phase delay and some ischemic regions with no vessels
1	When compared with the asymptomatic contralateral hemisphere, there are just a few vessels visible in any phase within the occluded vascular territory
0	When compared with the asymptomatic contralateral hemisphere, there are no vessels visible in any phase within the ischemic vascular territory

mpCTA: multiphasic CT angiography.

percentage, mean, standard deviation, minimum and maximum. Frequency analyses of the patient's medical history and clinical follow-up information (such as mpCTA collateral score, Barthel Index at 3 months, baseline NIHSS) were also applied and number and percentage values were calculated.

Before comparing the infarct volume values of patients based on mpCTA collateral score, variables were tested with Shapiro-Wilk Test for Normality. Since the infarct volume values did not show a normal distribution based on mpCTA collateral score, Kruskal-Wallis H Test (Non-parametric Test) was applied. Bonferroni post-hoc test was also applied to determine the difference between the groups that showed statistically significant results.

χ^2 test was used to compare differences between mRS and Barthel Index at 3 months with mpCTA collateral score.

Before comparing the infarct volume values of patients based on mRS at 3 months, variables were tested with Shapiro-Wilk Test for Normality. Since the infarct volume values did not show a normal distribution based on mRS, Mann-Whitney U Test (Non-parametric Test) was applied.

One Way ANOVA, independent sample t test, Mann Whitney U Test and Kruskal-Wallis H Test were used to compare differences between the perfusion parameters (Penumbra volume, CBV, CBF, MTT, Tmax) with Barthel Index and mRS at 3 months.

The relationship between the above-mentioned perfusion parameters of the individuals and the infarct volume difference was examined by correlation analysis. Pearson Correlation Coefficient and Spearman's rho (ρ) correlation coefficient were calculated.

Statistical analyses were conducted using IBM Statistical Package for Social Sciences (SPSS) program version Statistics 21.0 (IBM Corp. Released 2012. Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). P value of <0.05 was used to determine statistical significance.

RESULTS

Patient Characteristics

A total of 39 patients met the inclusion criteria. Of these patients, 3 were excluded. One of these patients died in the first week. A patient's perfusion data could not be processed on the workstation. Lastly, the perfusion imaging of a patient could not be performed in accordance with the protocol, so the maps obtained from the data were not optimal. The mean age of the total group (*n*=36) was 73.47±10.67, and 19 (52.8%) patients were men. These patients had occlusions in the M1 (*n*=32), and M2 (*n*=4). Mechanical thrombectomy was administered in 14 patients. Three patients were given IV tPA. Patient characteristics are listed in Table 2.

Baseline NIHSS score ranged from 5 to 24 (median, 19; interquartile range [IQR], 13–21). A median time from stroke symptom onset to baseline imaging at the emergency department was 188 minutes (IQR, 105–315). Clinical follow-up information is listed in Table 3.

Relationship Between Menon mpCTA Collateral Score with Infarct Growth and Clinical Outcome

There was no difference in baseline infarct volumes among poor, intermediate, and good collateral status groups. The infarct volume calculated in the control imaging and infarct growth showed differences between the groups (Table 4). Control infarct volume and infarct growth were higher at the poor collateral group (p=0.011; p=0.037). It was determined that the groups that made the difference were good collateral and poor collateral groups.

Good clinical outcome was observed in the majority of those with good collaterals (*n*=7, 53.8%) The majority of individuals with poor clinical outcome (*n*=13, 54.2%) had poor collateral scores. But it didn't show any statistical difference (p=0.073). The majority of patients in the total dependent group based on Barthel Index were found to have poor collaterals. The majority of individuals in the independent group were in the good collateral group in Menon collateral score. Due to a shortage of individuals in the groups, a test statistic could not be provided when comparing the Barthel Index at 3 months between Menon collateral score groups.

Relationship Between CT Perfusion Parameters with Infarct Growth and Clinical Outcome

Penumbra volume obtained from CTP maps which were created by selecting Tmax=6 sec and BV=1.0 mL/100 g, was lower in patients with good clinical outcomes than in those with poor clinical outcomes and there was a statistical difference in groups (median, 109.98 cm³ [SD,

Table 2. Patient characteristics

Characteristics	n (%) x̄±SD
Age, mean±SD	73.47±10.67
Sex	
Female Male	17 (47.2) 19 (52.8)
Prior stroke history	8 (22.2)
Prior antiplatelet/anticoagulant use	
None Antiplatelet Anticoagulant	9 (25.0) 18 (50.0) 9 (25.0)
Hypertension	26 (72.2)
Diabetes mellitus	9 (25.0)
Coronary artery disease	25 (69.4)
Hyperlipidemia	10 (27.8)
Prior atrial fibrillation	11 (30.6)
Smoking	12 (34.3)
Imaging findings	
Affected hemisphere (Right)	19 (52.8)
Occlusion site of MCA on mpCTA	
M1 M2	32 (88.9) 4 (11.1)
Reperfusion therapy	17 (47.2)
IV rTPA Mechanical thrombectomy	3 (8.3) 14 (38.9)

IV rTPA: intravenous recombinant tissue plasminogen activator; MCA: middle cerebral artery; SD: standard deviation; x̄: mean.

Table 3. Clinical follow-up information in patients

Clinical Follow-up	n (%)
Baseline NIHSS	
Mild (0–7) Moderate (8–16) Severe (>16)	1 (2.8) 11 (30.6) 24 (66.6)
mRS at 3 months	
Good clinical outcome (0–2) Poor clinical outcome (3–6)	10 (27.7) 26 (72.3)
Barthel index at 3 months	
Total dependency (0–20) Severe dependency (21–61) Moderate dependency (62–90) Slight dependency (91–99) Independent (100) Exitus	10 (27.7) 1 (2.8) 3 (8.3) 2 (5.6) 7 (19.4) 13 (36.2)

mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale.

Table 4. Comparison of infarct volumes based on mpCTA collateral score

	Menon mpCTA collateral score			Test statistic	
	Poor Collateral (0–5) Median (IQR) Min; Max	Intermediate Collateral (6–7) Median (IQR) Min; Max	Good Collateral (8–10) Median (IQR) Min; Max	χ^2	p
Baseline infarct volume	25.62 (122.54) 0; 233.96	24.70 (47.87) 0; 111.01	10.78 (13.97) 0; 29.24	2.518	0.284
Control infarct volume	209.27 (178.38) 19.21; 470.66	95.53 (139.46) 15.14; 437.68	27.95 (93.37) 2.85; 417.91	9.073	0.011*
Infarct growth	118.82 (141.10) 12.29; 470.66	79.86 (124.40) 15.14; 417.79	13.55 (93.79) -2.56; 403.27	6.585	0.037*

p: Kruskal-Wallis non parametrical test; *: p≤0.05.

Table 5. Comparison of CTP parameters by selecting Tmax/CBV and MTT/CBV with clinical outcome at 3 months

	mRS at 3 months		Test statistic	
	Good clinical outcome x̄±SD	Poor clinical outcome x̄±SD	t	p
Tmax=6 Sec				
Penumbra volume	109.98±62.56	165.83±55.68	2.724	0.010*
CBV average	3.31±0.62	3.33±0.70	0.087	0.931
CBV mirror ratio (rCBV)	109.97±7.49	100.50±15.91	1.947	0.060
CBF average	23.15±8.67	25.69±12.17	0.645	0.523
CBF mirror ratio (rCBF)	53.02±13.03	55.30±18.66	0.378	0.708
MTT average	13.64±2.91	13.49±2.75	0.148	0.883
MTT mirror ratio (rMTT)	243.35±54.01	236.78±72.47	0.277	0.784
Tmax average	9.81±1.37	10.42±1.01	1.507	0.141
Tmax mirror ratio (rTmax)	391.67±131.31	364.18±144.70	0.553	0.584
MTT=10 sec				
Penumbra volume	97.83±69.83	119.38±59.23	0.969	0.339
CBV average	3.78±0.82	3.90±0.94	0.392	0.698
CBV mirror ratio (rCBV)	118.10±7.45	112.54±16.24	1.121	0.270
CBF average	16.50±4.12	16.33±4.53	0.107	0.916
CBF mirror ratio (rCBF)	37.58±7.45	36.22±8.93	0.451	0.655
MTT average	16.16±1.50	17.68±1.63	2.701	0.011*
MTT mirror ratio (rMTT)	299.10±73.14	304.67±71.08	0.220	0.828
Tmax average	8.55±2.20	9.69±1.31	1.966	0.058
Tmax mirror ratio (rTmax)	367.63±116.84	353.72±121.18	0.328	0.745

CBF: Cerebral Blood Flow; CBV: Cerebral Blood Volume; CTP: CT Perfusion; MTT: Mean Transit Time; p: Independent sample t test; SD: standard deviation; Tmax: Time-to-Maximum; x̄: mean; *: p≤0.05.

Table 6. Comparison of CTP parameters by selecting Tmax=6 sec with infarct growth

	Infarct volume growth	
Perfusion parameters	**Pearson correlation coefficient**	**p**
Penumbra volume	0.366	0.028*
CBV average	-0.066	0.700
CBV mirror ratio (rCBV)	-0.239	0.160
CBF average	0.099	0.567
CBF mirror ratio (rCBF)	0.064	0.713
MTT average	-0.133	0.440
MTT mirror ratio (rMTT)	-0.112	0.517
Tmax average	0.143	0.407
Tmax mirror ratio (rTmax)	0.069	0.689

CBF: Cerebral Blood Flow; CBV: Cerebral Blood Volume; CTP: CT Perfusion; MTT: Mean Transit Time; p: Spearman rho correlation coefficient; Tmax: Time-to-Maximum; *: p≤0.05.

62.56] vs 165.83 cm³ [SD, 55.68]; p=0.010). The mean values of CBV, CBF, MTT and Tmax in the penumbra and their relative values (their mirror in the asymptomatic hemisphere) didn't show a statistical difference between the groups (p>0.05). Similarly, penumbra volume obtained from CTP maps which were created by selecting BF=10 mL/100 g/min and BV=1.0 mL/100 g, was lower in patients with good clinical outcomes than in those with poor clinical outcomes and there was a statistical difference in groups (median, 16.55 cm³ [IQR, 18.31] vs 28.55 cm³ [IQR, 29.30]; p=0.029). The mean MTT value obtained from CTP maps which were created by selecting MTT=10 sec and BV=1.0 mL/100 g, was lower in patients with good clinical outcomes than in those with poor clinical outcomes and there was a statistical difference in groups (mean, 16.16 sec [SD, 1.50] vs 17.68 sec [SD, 1.63]; p=0.011). Other variables didn't show a statistical difference between the groups (Table 5).

A linear, positive, weak and statistically significant relationship was found between the volume of the penumbra information obtained from CTP imaging created by selecting Tmax=6 sec and the infarct growth. Thus, as the penumbra volume of patients increases, the infarct growth increases. No significant relationship was shown between other variables and infarct growth (p>0.05) (Table 6). In addition, there was no significant relationship between perfusion parameters obtained from CTP imaging created by selecting BF=10 mL/100 g/min and BV=1.0 mL/100 g or MTT=10 sec and BV=1.0 mL/100 g and infarct growth.

DISCUSSION

It has been shown that good collateral status as determined by collateral flow assessment from CTA using a scoring system based on Menon et al, had a low correlation with baseline ASPECTS but a strong correlation with follow-up ASPECTS score (9). Another study found that the pial collateral score created by Menon is independently correlated with the hyperacute increase in infarction size in patients experiencing an LVO stroke of the anterior circulation (10). Another study conducted by Wintermark

et al. revealed a relation between collateral flow information and infarct growth (11). Interventional Management of Stroke (IMS) III trial manifested that good collateral circulation information obtained from CTA was associated with small ischemic core information obtained from CTP (12). In our study, despite no statistically significant difference observed between the baseline infarct volume and Menon collateral score, it was observed that patients with good collaterals had small infarct volumes and patients with poor collaterals had big infarcted tissue. This statistical insignificance may be explained by the small number of patients in our study. Also, it can be related to the difference about the method to calculate the baseline infarct volume. In the IMS III trial, infarct core volume information was obtained from CTP; but we used brain diffusion MRI to get the baseline infarct volume information. Menon et al defined areas with Tmax >6 sec as penumbra; and accepted areas with CBF <10 mL/100 g/min in gray matter and areas with CBF <7 mL/100 g/min in white matter as core. We created CTP maps by selecting Tmax=6 sec and BV=1.0 mL/100 g; BF=10 mL/100 g/min and BV=1.0 mL/100 g; MTT=10 sec and BV=1.0 mL/100 g as default values determined by the manufacturer. Furthermore, similarly to how good collateral status was found to have a strong correlation with the follow-up ASPECTS score, we discovered that the final infarct volume and infarct growth had a significant relationship with the collateral scores.

Collateral assessment is predictive in terms of clinical outcome as well as radiological results as mentioned before. This situation was revealed in the study conducted by Tan et al (13). In our study, while there was no statistically significant difference observed between clinical outcome (mRS at 3 months) and mpCTA collateral score; it was observed that patients with good collaterals have good functional results, and patients with poor collaterals have poor functional outcomes. This is probably due to the insufficient number of patients in the groups. Likewise, when Barthel Index at 3 months was compared on the basis of mpCTA collateral score, test statistics could not be given due to the lack of subjects in the groups. This may be since we tried to obtain functional results by dividing the Barthel Index into 5 categories, as in the original. In our study, the reason why we did not classify the Barthel Index into 2 subgroups as good and poor functional outcomes like mRS, is that there are a few studies on establishing a threshold value for the Barthel Index at an acute stroke. Additionally, it is not preferred due to different threshold values used in the literature (14).

Some studies are showing that there is a complementary relationship between the ischemic penumbra defined by CTP and the collateral situation on CTA (15). In our study, there are statistically significant differences in penumbra volume obtained from the CTP maps calculated by selecting Tmax=6 sec and BV=1.0 mL/100 g and BF=10 mL/100 g/min and BV=1.0 mL/100 g threshold values among good and poor clinical outcome groups based on mRS at 3 months. According to our results, penumbra volumes of patients were found to be higher with poor functional results. Several studies with similar results are available in the literature. There may be various reasons for this. Some studies in which interventional procedures were performed, had some criteria in patient selection such as a maximum baseline infarct volume of 70 or 80 cm^3 and a target mismatch ratio of at least 1.7 or 1.8. All of these patients had reperfusion therapy. However we didn't establish criteria like infarct volume, penumbra volume or mismatch ratio for the patients to be a candidate for reperfusion therapies. This situation may have caused poor clinical outcomes after reperfusion. Besides, reperfusion treatment could not be performed to all patients due to age, onset of symptom time or additional contraindications. When we consider about the relationship between collateral scores and good functional outcome; it is an unexpected result that the penumbra, which is directly related to the durability of collaterals, was not associated with good functional outcomes in our study. A possible explanation for this finding was made by Wintermark et al that poor collaterals bring about early infarct and good collaterals to benign oligemia, decreasing the critical hypoperfused (penumbra) region that lies between these two thresholds (16).

Previous research has demonstrated that patients with increased MTT delay have a higher risk of developing infarct in the future (17). In our study, although the average value of MTT calculated in the penumbra area obtained from CTP maps created by selecting MTT=10 sec and BV=1.0 mL/100 g threshold was not directly related to the infarct growth, this value showed statistically significant difference among good and poor clinical outcome groups based on mRS at 3 months. Mean MTT value was lower (16.16 sec) in patients with good clinical outcomes than in those with poor clinical outcomes (17.68 sec). This may be due to the relationship between infarct growth and poor functional outcome, as increased MTT value which is the average transit time of the contrast agent through the brain parenchyma within the specified voxel, leads to new infarct areas, which leads to poor clinical results.

We found a weak but statistically significant relationship between the volume of the penumbra obtained from CTP imaging created by selecting Tmax=6 sec and the infarct growth. Thus, as the penumbra volume of patients increases, the infarct growth increases. Again, these findings may be a result of the fact that reperfusion therapy was not performed in all patients or that the patients who received reperfusion did not have the same success rate. Infarct growth due to lack of reperfusional intervention to save the large penumbra area is a normal result, and as we mentioned above, this will additionally affect the functional results of the patients. A similar finding that we obtained in our study was shown in patients without reperfusion therapy in the SWIFT PRIME study, where Tmax=6 sec was used as a threshold (18).

Several limitations of this study deserve mention. First, there are a small number of patients. As previously mentioned, it was not feasible to establish a correlation between the pial collateral score and clinical outcome due to a lack of available clinical data. Second, CT scans were performed on 2 different CT scanners that contained either 64 or 128 detectors. So, this could affect the numeral results of CTP perfusion variables. Third, the study involved patients that had not only MCA M1 occlusion, but also M2 occlusion even though a large proportion of them were M1. Besides, not all patients had reperfusion therapies. This caused differences in outcome. Furthermore we did not examine imaging indicators, such as the thrombus length, and this could have had an impact on the results. Finally, regarding the radiological protocol, we used 3 different thresholds to obtain CTP images. There are no international guidelines addressing the CTP threshold levels to create CTP maps. In addition, recent research has demonstrated that the appropriate threshold values may differ depending on the length of time after the beginning of symptoms (19).

In conclusion, the Menon collateral score obtained from mpCTA may give information about the baseline infarct volume. Moreover, the pial collateral score includes information about the final infarct volume and infarct growth. Besides, collaterals may include valuable data about clinical outcomes. Different penumbra variables including penumbra volume and MTT revealed by using various thresholds on CTP provide information about functional outcome and infarct growth. Imaging of the pial collateral flow is challenging, but multimodal CT techniques appear to be the most promising methods for the regular evaluation and measurement of this important phenomenon.

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REFERENCES

1. Krishnaswamy A, Klein JP, Kapadia SR. Clinical cerebrovascular anatomy. Catheter Cardiovasc Interv. 2010;75(4):530–539. [Crossref]
2. Brozici M, van der Zwan A, Hillen B. Anatomy and Functionality of Leptomeningeal Anastomoses. Stroke. 2003;34(11):2750–2762. [Crossref]
3. Menon BK, O'Brien B, Bivard A, Spratt NJ, Demchuk AM, Miteff F, et al. Assessment of Leptomeningeal Collaterals Using Dynamic CT Angiography in Patients with Acute Ischemic Stroke. J Cereb Blood Flow Metab. 2012;33(3):365–371. [Crossref]
4. Kim EY, Shin DH, Noh Y, Goh BH, Lee Y-B. Comparison of Imaging Selection Criteria for Intra-Arterial Thrombectomy in Acute Ischemic Stroke with Advanced CT. Eur Radiol. 2016;26(9):2974–2981. [Crossref]
5. Smit EJ, Vonken E, van Seeters T, Dankbaar JW, van der Schaaf IC, Kappelle LJ, et al. Timing-Invariant Imaging of Collateral Vessels in Acute Ischemic Stroke. Stroke. 2013;44(8):2194–2199. [Crossref]
6. Heit JJ, Zaharchuk G, Wintermark M. Advanced Neuroimaging of Acute Ischemic Stroke: Penumbra and Collateral Assessment. Neuroimaging Clin N Am. 2018;28(4):585–597. [Crossref]
7. Shi F, Gong X, Liu C, Zeng Q, Zhang M, Chen Z, et al. Acute Stroke: Prognostic Value of Quantitative Collateral Assessment at Perfusion CT. Radiology. 2019;290(3):760–768. [Crossref]
8. Menon BK, d'Esterre CD, Qazi EM, Almekhlafi M, Hahn L, Demchuk AM, et al. Multiphase CT Angiography: A New Tool for the Imaging Triage of Patients with Acute Ischemic Stroke. Radiology. 2015;275(2):510–520. [Crossref]
9. Menon BK, Smith EE, Modi J, Patel SK, Bhatia R, Watson TWJ, et al. Regional Leptomeningeal Score on CT Angiography Predicts Clinical and Imaging Outcomes in Patients with Acute Anterior Circulation Occlusions. AJNR Am J Neuroradiol. 2011;32(9):1640. [Crossref]
10. Puhr-Westerheide D, Tiedt S, Rotkopf LT, Herzberg M, Reidler P, Fabritius MP, et al. Clinical and Imaging Parameters Associated With Hyperacute Infarction Growth in Large Vessel Occlusion Stroke. Stroke. 2019;50(10):2799–2804. [Crossref]
11. Jiang B, Ball RL, Michel P, Li Y, Zhu G, Ding V, et al. Factors influencing infarct growth including collateral status assessed using computed tomography in acute stroke patients with large artery occlusion. Int J Stroke. 2019;14(6):603–612. [Crossref]
12. Vagal A, Menon BK, Foster LD, Livorine A, Yeatts SD, Qazi E, et al. Association Between CT Angiogram Collaterals and CT Perfusion in the Interventional Management of Stroke III Trial. Stroke. 2016;47(2):535–538. [Crossref]
13. Tan IYL, Demchuk AM, Hopyan J, Zhang L, Gladstone D, Wong K, et al. CT Angiography Clot Burden Score and Collateral Score: Correlation with Clinical and Radiologic Outcomes in Acute Middle Cerebral Artery Infarct. AJNR Am J Neuroradiol. 2009;30(3):525. [Crossref]
14. Uyttenboogaart M, Stewart RE, Vroomen PCAJ, De Keyser J, Luijckx G-J. Optimizing Cutoff Scores for the Barthel Index and the Modified Rankin Scale for Defining Outcome in Acute Stroke Trials. Stroke. 2005;36(9):1984–1987. [Crossref]
15. Miteff F, Levi CR, Bateman GA, Spratt N, McElduff P, Parsons MW. The independent predictive utility of computed tomography angiographic collateral status in acute ischaemic stroke. Brain. 2009;132(8):2231–2238. [Crossref]
16. Nannoni S, Cereda CW, Sirimarco G, Lambrou D, Strambo D, Eskandari A, et al. Collaterals are a major determinant of the core but not the penumbra volume in acute ischemic stroke. Neuroradiology. 2019;61(9):971–978. [Crossref]
17. Keedy AW, Fischette WS, Soares BP, Arora S, Lau BC, Magge R, et al. Contrast Delay on Perfusion CT as a Predictor of New, Incident Infarct. Stroke. 2012;43(5):1295–1301. [Crossref]
18. Albers GW, Goyal M, Jahan R, Bonafe A, Diener H-C, Levy EI, et al. Ischemic core and hypoperfusion volumes predict infarct size in SWIFT PRIME. Ann Neurol. 2016;79(1):76–89. [Crossref]
19. Qiu W, Kuang H, Lee TY, Boers AM, Brown S, Muir K, et al. Confirmatory Study of Time-Dependent Computed Tomographic Perfusion Thresholds for Use in Acute Ischemic Stroke. Stroke. 2019;50(11):3269–3273. [Crossref]