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Capillary Index Score Derived from Computed Tomography Angiography as An Indicator of Collateral Flow after Acute Ischemic Stroke

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Abstract

Background The capillary index score (CIS) determined from DSA is used to evaluate cerebral collateral flow in acute ischemic stroke (AIS) caused by cerebral artery occlusion. Our aim was to determine the reliability of CIS calculated from MIP-CTA images as an alternative to DSA-based CIS, as CTA is less invasive and less expensive. Methods Clinical and imaging data of 40 patients with AIS caused by cerebral artery occlusion within 6 h from symptom onset were collected. CIS was calculated from CTA and DSA images. Patients were classified into the favorable collateral flow group if CIS was ≥2 (fCIS), and into the poor collateral flow group if CIS was <2 (pCIS). Agreement between the methods was evaluated using the Kappa test. Logistic regression was performed to explore the relationship between CTA-based CIS and clinical outcomes. Results The two methods had high consistency (Kappa = 0.72), and the diagnostic accuracy of CTA for CIS classification was 87.5%. The decrease in the NIHSS score at discharge was not significantly different between the fCIS and pCIS groups according to CTA (p = 0.156), while the 90-day mRS was higher in the pCIS group (p = 0.04). High CTA-based CIS and low blood glucose at admission were significantly correlated with good outcome. Conclusion CIS calculated using CTA is as reliable as DSA-based CIS for assessing collateral flow in AIS, and is also a good predictor of clinical outcome. This index could be useful for guiding patient selection and treatment strategies for AIS.

Background

Acute ischemic stroke (AIS) caused by cerebral artery occlusion is prevalent. AIS is managed by endovascular treatment (EVT), which is a highly feasible method that is widely used in clinical practice and has seen great improvements in recent years [1-3]. The therapeutic outcome of AIS is associated with cerebral collateral flow [4]. Good collateral circulation contributes to increase in the ischemic penumbra, reduces infarct size and improves prognosis [5]. After AIS, the activity of ischemic brain tissue is maintained by residual cerebral blood flow (rCBF), and a higher number and greater diameter of collateral vessels is associated with greater rCBF. In patients with insufficient rCBF, the treatment time window is greatly reduced. Therefore, patients with poor collateral flow benefit lesser, even when therapeutic revascularization (through EVT and thrombolysis treatment) is achieved. On the contrary, patients with good collateral flow have higher rates of vascular recanalization and good clinic outcome after EVT [6-8]. Thus, collateral flow after AIS seems to be a good indicator of clinical outcome.

Collateral flow has been used in the selection of patients for EVT and studies on extension of the treatment time window. According to the guidelines for EVT in China, the time window for treatment is within 6 h of AIS. However, large multi-center studies have demonstrated that performing EVT beyond the treatment time window may partially benefit patients with favorable collateral flow. For example, Motyer et al. [9] suggested that patient selection be based on ASPECTS and collateral assessment, and that good clinical outcome can be achieved even beyond 12 h from AIS onset. Further, in the DAWN clinical trial [10], patients were selected based on collateral flow assessment with MRI and CTP, and it was found that EVT was beneficial even up to 24 h after onset. Therefore, preoperative evaluation of collateral circulation seems to be a promising approach for patient selection for EVT after AIS.

Capillary index score (CIS) was first introduced by Al-Ali et al. [4, 11] for the evaluation of collateral flow in ischemic areas on DSA images in cases of AIS caused by artery occlusion. CIS is calculated on a 4-point scale ranging from 0 to 3, based on the anteroposterior position of the occluded artery at the peak period. The ischemic territory is divided into three equal flabellate segments. Each segment is assigned 1 point if normal capillary blush is observed and 0 if it is not observed. The scores of each segment are then added to determine the final CIS for the ischemic area. A CIS≤2 is considered to be unfavorable or poor (pCIS), and a CIS 2 is considered favorable (fCIS). A CIS of 0 indicates that there is no viable tissue in the ischemic area, while a score of 3 implies that all the tissue may be salvageable. CIS is only used in occlusions of the ICA and M1 segment of the MCA. Previous research has shown that CIS calculated from DSA images is strongly associated with clinical outcome [4, 11-13]. Further, CIS can be easily calculated with a rapid, semi-quantitative, objective method. Therefore, CIS could be developed as a tool to identify patients with sufficient collateral circulation prior to treatment and help guide decision making in the clinic.

DSA was earlier considered the gold standard for collateral circulation evaluation, but it is a complex, invasive, and expensive method that uses highly deleterious radiation. MIP images reconstructed from head CTA images are similar to DSA images, and CIS can be calculated from these images. CTA is usually the first choice for emergency examination because it is rapid and non-invasive and involves simple post-processing. Single-phase head CTA can be used to identify the location of vessel obstruction and also to calculate CIS. Given these features of MIP-CTA, it might be useful to explore whether CTA images can be used as an alternative to DSA images for the calculation of CSI. Therefore, this study attempted to calculate CIS from CTA-MIP images, and to determine whether CIS calculated from the CTA and DSA images were consistent.

1. Methods

1.1 Patients

This was a retrospective analysis of AIS patients treated at our hospital between 2016 and 2017. Patients who underwent EVT within 6 h from the onset of AIS caused by occlusion of the distal ICA or M1 segment and who had undergone head non-contrast CT, CTA and DSA were included. Patients were excluded if (1) the occlusion site was an extracranial segment of the internal carotid artery, (2) spontaneous recanalization of the occluded vessel had occurred, or (3) the quality of the images was too poor for analysis. Informed consent was obtained from patients or their relatives. As our study was retrospective, ethics approval and consent to participate is not required.

1.2 CTA and DSA

CTA: CTA imaging of the head was performed with a 64-slice CT scanner (PHILIPS Brilliance iCT machine). Contrast material (5065 mL) was intravenously administered through the elbow at an injection rate of 3 to 5 mL/s, with the aid of a high-pressure injector. The aortic arch was labeled as a region of interest. The scan was triggered with a 4s delay, in order to allow the concentration of contrast material at

the region of interest to reach 100150 Hu. The acquisition parameters were 120 kVp (voltage) and 230 mA·s (current rate). The transversal scanning range was from the neck to the crown of the head parallel to the orbitomeatal line and in the direction of blood flow, which guaranteed clear visualization of the vessels. The slice thickness was 0.8 mm, and the reconstruction interval was 0.51 mm. Anteroposterior MIP reconstruction imaging was performed with the systemic software, with posterior circulation removed. The reconstructed images were included only if (1) the ICA, the anterior cerebral artery, the MCA and its main branches (including the ophthalmic artery, the posterior communicating artery, and the anterior communicating artery), and the basilar and posterior cerebral artery and their main branches were clearly visualized; (2) superficial sagittal sinus and sigmoid sinus development was observed; and (3) CIS of the contralateral hemisphere with CTA was 3.

DSA: All the patients underwent comprehensive diagnostic cerebral angiography of both the internal carotid arteries and the vertebral arteries. Contrast medium at a volume of 10 mL was injected into the ICA at a rate of 4–5 mL/s, and a volume of 7 mL was injected into the vertebral artery at a rate of 2–3 mL/s. Imaging was performed through the entire arterial and late venous phases to calculate the CIS.

1.3 Imaging and clinical assessment

The CTA and DSA images were assessed in random order, and the assessors were blinded to the clinical information of the patients. The assessors were two reviewers with more than 10 years of clinical experience in radiography, and they independently calculated CIS based on the anteroposterior DSA and CTA-MIP images. Based on CIS, the patients were divided into two groups: CIS 2 (fCIS) and CIS 2 (pCIS). The extent of recanalization after EVT was assessed based on the modified TICI (mTICI) score, based on which revascularization was classified as poor (0, 1, or 2a) or good (2b or 3). The opinion of a third doctor was sought to resolve any disagreements.

An experienced neurologist evaluated the patients using NIHSS and mRS. A 90-day mRS score ≤ 2 was considered to indicate good clinical outcome.

The reviewers were all blinded to the patients' information throughout the assessment process.

1.4 Statistical analysis

Analyses were conducted using the statistical analysis software SPSS (version 19). Continuous data are presented as mean SD values, while categorical variables are presented as absolute and relative frequencies. Continuous variables were compared using *t*-tests, and categorical variables were compared using the χ^2 or Fisher's exact test, as appropriate. The Mann-Whitney *U*-test was used to analyze the relationship between CIS with CTA and good clinical outcome (90-day mRS 2). Consistency between CIS determined from CTA and DSA was analyzed using the Kappa correlation test. The association between CIS determined from CTA and functional outcome (90-day mRS 2) was determined by multivariate logistic regression, with adjustment for factors that were found to be significant on univariate analysis.

2. Results

A total of 45 patients with AIS caused by MCA occlusion were selected, but 5 were excluded because of poor image quality (3 patients), spontaneous recanalization (1 patient) and loss to follow-up (1 patient). Therefore, 40 patients were included eventually. The characteristics of the 40 patients are listed at Table 1. There were 30 males (75.0%) and 10 females (25.0%). The median age was 68 years, and the average onset time was 214.27±72.71min. Good recanalization (mTICI 2b/3) was achieved in 26 patients, and good clinical outcomes in 18 patients. However, 5 patients died, and two for hemorrhagic transformation at basal ganglia, two for large infarction core of the middle cerebral artery area, and one for timeout treatment time window combined with failed recanalization.

2.1 Consistency between CIS determined using CTA and DSA

CIS classification (fCIS and pCIS) based on CTA and DSA had high consistency, with a Kappa value of 0.72 (p□0.05). Tables 2 and 3 illustrate the good diagnostic performance of CTA-based CIS classification, especially for the fCIS subgroup.

2.2 Logistic regression analysis

The mRS scores were significantly different between the pCIS and fCIS groups on CTA (p = 0.04). Multiple logistic regression analysis indicated that fCIS (OR, 8.16; 95% CI, 1.06-62.90; P = 0.044), lower blood glucose levels at admission (OR, 0.73; 95% CI, 0.54-0.98; P = 0.039) and good recanalization (OR, 3.56; 95% CI, 1.37-9.27; P = 0.009) were predictors of better clinical outcome, as indicated by the 90-day mRS score (Table 4).

3. Discussion

The present study sought to explore whether CTA can be used as a substitute for the more invasive DSA technique for calculating CIS for the evaluation if collateral circulation in cases of AIS. The findings showed that classification of patients as fCIS and pCIS based on CIS determined from CTA and DSA images had high consistency, with a Kappa value of 0.72 (p□0.05). Further, CIS calculated using both imaging methods was also significantly associated with prognosis.

We found that CIS was higher with CTA than with DSA in some cases. There could be several reasons for this, as listed below. (1) Head CTA provides an image of both cerebral hemispheres at the same time. If the ischemic area was compensated by the contralateral cerebral vasculature, the collateral flow as observed on CTA would be greater. (2) Further, the time of CTA acquisition is associated with the concentration of contrast material in the cerebral vessels, which could have influenced the observed collateral flow [14-16]. (3) As single-phase head CTA captures one snapshot at a set time point, small errors in the scanning time could have also influenced the collateral flow apparent on the images [17]. (4) Assessment of collateral circulation would also be affected if the veins are excessively developed and difficult to remove in the post-processing phase, and this might result in a false increase in CIS. In our

study, the diagnostic accuracy for fCIS was higher with CTA than with DSA. Therefore, CTA seems to have an advantage with regard to the assessment of functional collateral flow. Based on these findings, it can be speculated that in patients with AIS caused by occlusion of the MCA or the distal ICA, a CIS of 2 or 3 points obtained with CTA indicates that EVT should be the first choice for treatment for better outcome, provided the patient has not undergone other procedures and does not have any contraindications.

In some cases, CIS was lower with CTA than with DSA. The possible reasons are discussed here. (1) The time required for visualization of collateral circulation on the affected side is usually longer than that required for the healthy side, because of the slow blood flow caused by artery occlusion on the affected side. This means that slightly early scan acquisition may not depict the entire collateral flow [17]. (2) If a stagnant column of unopacifed blood caused by MCA occlusion results in the blockage of distal contrast penetration [18], the occlusion site and collateral flow may be misinterpreted. (3) The low spatial resolution of CTA limits the display of distal vessels that have a diameter less than 1 mm and leads to underestimation of collateral flow. (4) Some details about collateral flow could be missing in the reconstructed MIP images as compared with the primary axial images, and this may also lead to a lower CIS with CTA [19]. Because of these limitations, the reliability of CTA for assessing poor collateral flow was relatively low. For patients with a CIS of 0 or 1, it was necessary to use other methods, such as CTP and MR, to evaluate collateral flow, so as to ensure that treatment is administered within the optimal time window. Therefore, when low CIS is determined from CTA images of AIS patients, further examination should be conducted to obtain a better picture of the collateral flow status.

Logistic regression analysis showed that high CIS with CTA, low blood glucose levels at admission and good recanalization were significantly correlated with good outcomes (as evident from the 90-day mRS). High CIS with CTA was a protective factor and high blood glucose levels on admission was a risk factor for poor clinical outcome. The relationship between blood glucose level at admission and prognosis is controversial, as some researchers have reported that the blood glucose level at the time of admission had no significant influence on the treatment effect of EVT for AIS[20]. In contrast, other researchers have suggested that high blood glucose and high systolic blood pressure at admission are independent predictors of malignant MCA infarction [21]. Given these contradictory findings, it seems that more comprehensive research is required into the predictive factors for clinical outcome after EVT in AIS patients.

Previous studies have analyzed other factors related to prognosis after EVT. For example, it has been reported that a high ASPECT score and a high recanalization rate are indicative of good outcome, while older age, hypertension, high NIHSS score and hemorrhagic transformation are strong risk factors for poor outcome [22]. As the head non-contrast CT scans of the included patients in our study showed no obvious low density, the ASPECT score was not considered.

There are several limitations to this study. First, the study was a single-center retrospective study with a relatively small number of cases; this might have caused an inclusion bias. Therefore, the reliability of CIS determined with CTA should be tested by more multi-center case studies. Second, the relationship

between CIS with CTA and the mRS scores was analyzed only at 90 days, and no long-term follow-up (i.e., 6-month or 1-year mRS scores) findings are available. It is important to collect long-term data, as it is known that the 3-month mRS scores are highly relevant in severe cerebral infarctions.

4. Conclusion

The CIS obtained with CTA was highly consistent with the CIS determined with DSA. Based on the present findings, it appears that CTA is feasible as an alternative to DSA for evaluating collateral flow in AIS caused by MCA or distal ICA occlusion, and for predicting the clinical outcomes after EVT. Compared to other methods for the evaluation of collateral flow, including multiphase CTA, CTP and MRP, CIS on CTA is easy to obtain. As CTA technology is relative popularity, CIS on CTA can be wildly used. Thus, it could be used as a surrogate index for selecting AIS patients who can potentially benefit from EVT and therefore be useful for making good treatment decisions.

Declarations

Ethics approval and consent to participate

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Our study was retrospective. For this type of study formal consent is not required.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

SK and ZXX collected and analysed the patient data regarding the acute ischemic stroke. SK accomplished most tasks on data processing and analyzing, and was a major contributor in writing the manuscript. LYH helped to design of the work and improved the methods. All authors have certified the author list and contribution description. And all authors read and approved the final manuscript.

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Tables

Table 1

Characteristics of the patients according to CIS determined from CTA

	CIS on CTA		p
	pCIS (CIS≤2)	fCIS (CIS > 2)	
Patients	14	26	
Age (y)	71.79±11.29	67.04±12.61	0.23
Sex (male/female)	10/4	20/6	
Affected hemisphere (L/R)	8/6	15/11	8/6
Time to onset (min)	200.83±69.06	220.72±74.91	0.80
Body mass index (BMI)	16.76±11.61	20.97±8.56	0.24
LDL at admission (mmol/L)	2.22±1.05	2.28±1.25	0.87
Blood glucose at admission (mmol/L)	5.68±3.65	8.02±4.54	0.10
Diabetes	2	7	0.35
Hypertension	11	20	0.91
Atrial fibrillation	9	9	0.07
Percentage decrease in NIHSS at discharge (%)	0.30 ± 0.34	0.49 ± 0.34	0.156
Good clinical outcome[2]	3	14	0.04*
Hemorrhagic transformation	3	6	0.90

[2]Good clinical outcome: 90-day mRS £ 2

*p≤0.05 (significant difference between the groups)

Table 2

Comparison of CIS determined from CTA and DSA

CIS from CTA	CIS from DSA				Total
	0 point	1 point	2 point	3 point	
0 point	3	2	0	0	5
1 point	3	3	2	1	9
2 point	0	2	5	8	15
3 point	0	0	1	10	11
In total	6	7	8	19	40

Table 3

Diagnostic accuracy of CTA and consistency between CIS obtained with CTA and DSA

Grouping according to CTA	Grouping according to DSA	
	pCIS (CIS□2)	fCIS (CIS □ 2)
pCIS	11	3
fCIS	2	24
Diagnostic accuracy	87.5%	
Kappa value	0.72(p□0.001)	

Table 4

Results of multivariable logistic regression for good outcome (90-day mRS £ 2)

Variable	Regression coefficient	OR	95% CI	p
CIS classification on CTA[1]	2.10	8.16	1.06-62.90	0.044*
LDL at admission	-0.28	0.75	0.28-2.03	0.576
Blood glucose at admission	-0.32	0.73	0.54-0.98	0.039*
mTICI grade	1.27	3.56	1.37-9.27	0.009*

[1] CIS classification into fCIS and pCIS

*p□0.05 (significant association with clinical outcome)