



Evaluation of collateral circulation and short-term prognosis of patients with acute cerebral infarction by perfusion-weighted MRI

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Background: Perfusion-weighted magnetic resonance imaging (MRI) can evaluate collateral circulation in patients with acute cerebral infarction by reflecting hemodynamic signals in the brain. The purpose of this study was to evaluate the collateral circulation and short-term prognosis of patients with acute cerebral infarction, using perfusion-weighted MRI.

Methods: The study enrolled 206 patients with acute cerebral infarction due to unilateral cerebral artery occlusion diagnosed by digital subtraction angiography (DSA) and computed tomography angiography (CTA). The relative cerebral blood volume (rCBV), relative cerebral blood flow map (rCBF), relative peak time (rTTP), and relative mean transit time (rMTT) were calculated based on the ratio of the perfusion-weighted MRI reference values of the infarcted side and the control side of the patient. According to the results of perfusion-weighted MRI, patients were divided into a high perfusion group (n=121) and a low perfusion group (n=85). The Thrombolysis in Cerebral Infarction scale proposed by Higashida *et al.* in 2003 (Higashida scale) was used to evaluate the establishment of collateral circulation on the day of admission and 15 days after admission. The National Institutes of Health Stroke Scale (NIHSS) score and the modified Rankin scale assessed the short-term prognosis of patients with cerebral infarction. The Spearman correlation analysis examined the correlation between the rCBV, rCBF, and NIHSS scores, and the modified Rankin scale (mRS).

Results: Compared with the patients in the low perfusion group, the rCBV and rCBF in the infarcted area of the patients in the high perfusion group were significantly increased and the rTTP and rMTT were significantly decreased. On day 15 after admission, the collateral circulation rate of the high perfusion group was significantly higher than that of the low perfusion group, and the NIHSS score and the mRS score were significantly lower than those scores of the low perfusion group. Perfusion-weighted MRI indexes, rCBV, and rCBF were negatively correlated with the NIHSS score and Rankin scale.

Conclusions: Perfusion-weighted MRI can effectively evaluate the compensatory ability of collateral circulation and the prognosis of patients with acute cerebral infarction.

Keywords: Perfusion-weighted MRI; acute cerebral infarction; collateral circulation; short-term prognosis

Submitted Nov 08, 2021. Accepted for publication Mar 01, 2022.

doi: 10.21037/apm-21-3589

View this article at: <https://dx.doi.org/10.21037/apm-21-3589>

Introduction

Cerebral infarction, also known as cerebral arterial thrombosis, refers to ischemic necrosis or encephalomalacia of brain tissue caused by cerebral blood circulation disorder (1). Acute cerebral infarction is a disease with high morbidity and mortality. About 75% of patients have varying degrees of disability (2), which adds a serious burden to society and families. Hyperlipidemia, cerebral artery stenosis, smoking history or drinking history are the risk factors of acute cerebral infarction.

Cerebral collateral circulation refers to the auxiliary vascular network formed by other blood vessels (proper collateral or newly formed blood vessels) when an artery supplying blood is severely narrowed or occluded (3,4). The formation of collateral circulation in acute cerebral infarction is an effective indicator of the restoration of blood flow to the ischemic area and is a sign of good clinical prognosis, especially in patients who fail to receive intravenous thrombolysis or endovascular treatment within the effective therapeutic time window (5,6). Studying the prognosis of acute cerebral infarction has important clinical significance.

At present, digital subtraction angiography (DSA) is the gold standard for the clinical diagnosis of internal carotid artery stenosis or occlusion. It is highly valuable for evaluating collateral pathways, but the examination is invasive and cannot show brain parenchymal changes (7-9). Computed tomography angiography (CTA) technology and magnetic resonance angiography (MRA) have also been widely used in the study of cerebrovascular stenosis or occlusive diseases, and both can provide information, to a certain extent, on collateral circulation (10,11). Perfusion-weighted magnetic resonance imaging (PWI) can evaluate collateral circulation in patients with acute cerebral infarction by reflecting hemodynamic signals in the brain. However, there is no report on the relationship between PWI indexes and the establishment of collateral circulation and prognosis. In this study, perfusion-weighted magnetic resonance imaging (MRI) was used to evaluate the establishment and prognosis of collateral circulation in patients with acute cerebral infarction, and to explore the value of perfusion-weighted MRI in the assessment of collateral circulation and the short-term prognosis of patients with acute cerebral infarction. We present the following article in accordance with the MDAR reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-21-3589/rc>).

Methods

Patients

We selected 273 patients with acute cerebral infarction who were admitted to the Department of Neurology in Weifang Sunshine Union Hospital from July 2017 to March 2021, including 168 males and 105 females. The ages of the patients ranged from 49 to 77 years, with an average age of 63.71 ± 6.89 years. All patients were admitted to the hospital and diagnosed with acute cerebral infarction by DSA, CTA, and MRA. According to the National Institutes of Health Stroke Scale (NIHSS) score, patients with an NIHSS score ≤ 8 were classified as patients with mild cerebral infarction, patients with an NIHSS score of 8–15 were classified as patients with moderate cerebral infarction, and patients with an NIHSS score >15 were classified as patients with severe cerebral infarction (12). In total, there were 63 patients with mild cerebral infarction, 97 patients with moderate cerebral infarction, and 113 patients with severe cerebral infarction. All patients signed an informed consent form. This study was approved by the Ethics Committee of Jiangsu Vocational College of Medicine (No. JVCM-SMI-2017-05). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Inclusion criteria

Patients were included in the study if they met the diagnostic criteria for patients with acute cerebral infarction, were admitted to the hospital within 72 h after the onset of acute cerebral infarction, had undergone DSA, CTA, MRA, and perfusion-weighted imaging (PWI) examinations within 1 week after admission, had complete sets of images and clinical data, had NIHSS scores between 3 and 25 at the time of admission, and suffered only acute, unilateral cerebral infarction.

Exclusion criteria

Patients were excluded from the study if they had incomplete clinical data or unclear image sets, had a brainstem infarction that could not be examined by MRI, were a tumor stroke, inflammatory stroke, traumatic stroke, or another type of stroke patient, had a history of neurological disease and sequelae, or other serious physical diseases, were infarct patients with severe complications (such as heart and lung failure, liver and kidney failure, or

hernia), had advanced cancer, were pregnant, or lactating, had abnormal liver, kidney, and lung functions, were allergic to contrast agents, had bilateral cerebral infarction, or had cardiogenic cerebral infarction caused by rheumatic heart disease, atrial fibrillation, arrhythmia, or other causes.

Perfusion-weighted MRI image acquisition

All patients were imaged on a 3.0 T superconducting MRI scanner (TrioTim, Siemens Systems, Erlangen, German) using a T2* MRI technology sequence for 50 consecutive scans, with the first 6 scans without injection of contrast agent as the plateau period of the time signal curve. After the sixth scan, a high-pressure syringe was used to inject a fast bolus of 0.5 mmol/kg of body weight of Magnevist (gadolinium-diethylenetriamine pentaacetate, Gd-DTPA; Bayer Healthcare Pharmaceuticals Inc., Wayne, NJ, USA) through the elbow vein at a speed of 5 mL/s. Each scanning plane comprised 50 consecutive images. A total of 950 layers of 19×20 images were obtained and delivered to a Leonardo workstation (Siemens Medical Solutions, Erlangen, Germany) for the cerebral blood perfusion analysis. The scan time was 77 s.

Perfusion-weighted MRI indexes analysis

The original images obtained by the perfusion-weighted MRI scan were imported into perfusion software in the Siemens Leonardo workstation for image post-processing, and the mean transit time (MTT), time to peak (TTP), and cerebral blood volume (CBV) of the infarct side of the brain were calculated. The blood flow (CBF) map was analyzed by two experienced neuroimaging diagnosticians to determine the abnormal area of perfusion and quantify the perfusion parameters. Simultaneously, mirror measurements of the unaffected cerebral hemisphere were taken to calculate the ratio between each index on the infarct side and the region of interest (ROI) on the control side, to obtain the relative mean transit time (rMTT), relative peak time (rTTP), relative cerebral blood volume (rCBV), and relative cerebral blood flow (rCBF) index data.

Assessment of establishment of collateral circulation

We used the Thrombolysis in Cerebral Infarction scale proposed by Higashida *et al.* in 2003 to assess the establishment of collateral circulation in each patient, as follows: no visible collaterals at the ischemic site (grade 0);

slow collateral circulation around the ischemic site with persistent partial defects (grade 1); rapid collateral circulation, part of the defect persists, in only part of the ischemic area (grade 2); late vein (grade 3), the collateral blood flow of the ischemic bed is slow but complete; thorough retrograde perfusion (grade 4), throughout the entire ischemic area, with complete and rapid collateral blood flow to the vascular bed. The above criteria were used to, determine whether the patient's collateral circulation was open.

Follow-up

NIHSS scores were performed on patients when they were admitted to the hospital and 15 days after onset. The NIHSS score assessed the patient's neurological deficit. The higher the score, the more serious the neurological deficit. On day 15 after the onset of disease, the patient's modified Rankin scale (mRS) was used to evaluate the patient's neurological functional recovery. The higher the score, the worse the neurological functional recovery. Through the comprehensive NIHSS score and mRS score, the prognosis of each patient was evaluated.

Statistical analysis

The data of this study were analyzed by SPSS v. 21.0 statistical software (SPSS, Inc., Chicago, IL, USA). The count data in this study are expressed in the form of n (%), using the chi-squared (χ^2) test. The measurement data were expressed in the form of mean \pm variance, and the data analysis was performed using the *t*-test. A result of $P < 0.05$ indicated a statistically significant difference. Spearman correlation analysis was used to analyze the correlation between rCBV, rCBF, and NIHSS scores, and the modified Rankin scale. The correlation coefficient (*r*) ranges were from -1 to 1. If $|r|$ was less than 0.3, a poor correlation conclusion was drawn. If $|r|$ was greater than 0.3 but less than 0.5, a weak correlation conclusion was drawn. If $|r|$ was greater than 0.5 but less than 0.8, a conclusion of medium correlation was drawn. If $|r|$ was greater than 0.8, a strong correlation conclusion was drawn.

Results

Baseline characteristics and general clinical data

Of the 273 participants, a total of 206 patients were

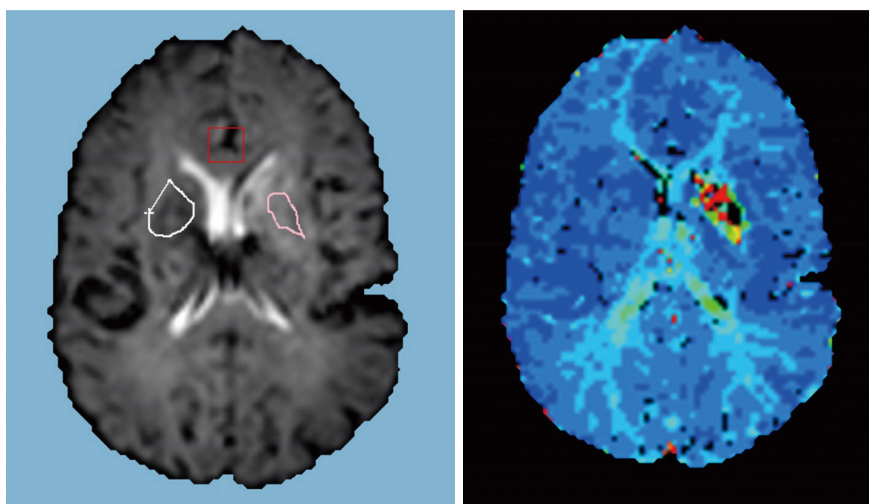


Figure 1 Representative images of perfusion-weighted MRI. The red box marked in the left panel represents the brain stem region; the left marked area indicates the signal characteristics under normal conditions; the marked area on the right represents the high signal characteristics of cerebral infarction. MRI, magnetic resonance imaging.

Table 1 Comparison of cerebral perfusion parameters of patients in each group

Group	n	rCBV	rCBF	rTTP	rMTT
Low perfusion group	85	0.89±0.19	0.94±0.14	1.19±0.28	1.31±0.29
High perfusion group	121	0.96±0.28	1.05±0.33	1.07±0.36	1.19±0.26
<i>t</i>		2.003	2.894	2.574	3.109
<i>P</i>		0.047	0.004	0.011	0.002

rCBV, relative cerebral blood volume; rCBF, relative cerebral blood flow map; rTTP, relative peak time; rMTT, relative mean transit time.

eventually enrolled. Among them, 23 patients had incomplete clinical data, 10 patients had a history of neurological diseases, 5 patients had liver and kidney failure, 14 patients also had advanced cancer, 9 patients had cardiogenic cerebral infarction, and 6 patients had bilateral cerebral infarction. Eventually, 121 patients were included in the high perfusion group and 85 patients in the low perfusion group. The patients were 49–76 years old, with an average age of 64.68±6.11 years. On the day of admission, the NIHSS score of the patients in the high perfusion group was 15.04±2.94 and the NIHSS score of the patients in the low-perfusion group was 14.89±2.37. There was no significant difference in the NIHSS score between the two groups ($P>0.05$). Representative images of perfusion-weighted MRI were shown in *Figure 1*.

Cerebral perfusion parameters

The cerebral perfusion parameter indexes of the high perfusion group and the low perfusion group were compared. As shown in *Table 1*, compared with the low perfusion group, the rCBV and rCBF of the high perfusion group were significantly increased, and the rTTP and rMTT were significantly decreased; the difference was statistically significant ($P<0.05$). This shows that the cerebral hemodynamic indexes of the high perfusion group were significantly better than those of the low perfusion group.

Collateral circulation establishment

According to the evaluation criteria of the Higashida scale

Table 2 The establishment of collateral circulation in each group of patients

Group	n	Day of admission, n (%)	15 days after admission, n (%)
Low perfusion group	85	6 (7.06)	37 (43.53)
High perfusion group	121	10 (8.26)	80 (66.12)
χ^2		0.101	10.380
P		0.750	0.001

Table 3 Comparison of prognosis of patients in each group

Group	n	NIHSS		mRS	
		Day of admission	15 days after admission	Day of admission	15 days after admission
Low perfusion group	85	14.89±2.37	12.38±3.67	3.85±0.69	2.71±0.89
High perfusion group	121	15.04±2.94	10.34±2.62	3.76±0.84	2.32±0.76
<i>t</i>		0.405	4.396	0.842	3.285
P		0.686	0.000	0.401	0.001

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

(Table 2), the establishment of collateral circulation on the day of admission and 15 days after admission was evaluated. There was no significant difference in the proportion of established collateral circulation between the two groups on the day of admission, but 15 days after admission, the establishment of collateral circulation in the high perfusion group was significantly better than that in the low perfusion group ($P < 0.05$).

Assessment of prognosis

The NIHSS and mRS scores were used to comprehensively evaluate the prognosis of the high perfusion group and the low perfusion group. On the day of admission, there was no significant difference in the NIHSS score and the mRS score of the high perfusion group and the low perfusion group ($P > 0.05$), but 15 days after admission, compared with patients in the low perfusion group, the NIHSS score and the mRS score of the patients in the high perfusion group were significantly lower (Table 3; $P < 0.05$).

Correlation analysis of perfusion parameter index and NIHSS and mRS scores

Spearman correlation analysis showed that the patient rCBV was weakly negatively correlated with the NIHSS score ($r = -0.427$; $P = 0.000$; Figure 2A), and weakly negatively

correlated with the mRS score ($r = -0.324$; $P = 0.000$; Figure 2B). The rCBF was moderately negatively correlated with the NIHSS score ($r = -0.594$; $P = 0.000$; Figure 2C) and was weakly negatively correlated with the mRS score ($r = -0.305$; $P = 0.000$; Figure 2D).

Discussion

Acute cerebral infarction is a local, cerebral, blood supply disorder. Caused by a variety of reasons, it can lead to cerebral ischemia and hypoxia, with the corresponding clinical manifestations of neurological dysfunction (13). Acute cerebral infarction mostly occurs in the elderly. In patients with acute cerebral infarction, thrombolytic therapy is most effective within 1 to 6 hours after the onset of cerebral ischemia (14). Missing this therapeutic time window means losing the opportunity for successful treatment. Early clinical diagnosis is the key to ensuring the cure of acute cerebral infarction, and is also a prerequisite for the implementation of thrombolytic therapy. Cerebral vascular stenosis or occlusion is an important cause of the occurrence and development of acute cerebral infarction (15). When cerebral vessels are narrowed or occluded due to the change of blood perfusion pressure in an ischemic area, blood can flow from high pressure to low pressure points through collateral circulation pathways to compensate for the lack of blood supply to the ischemic area. In this way,

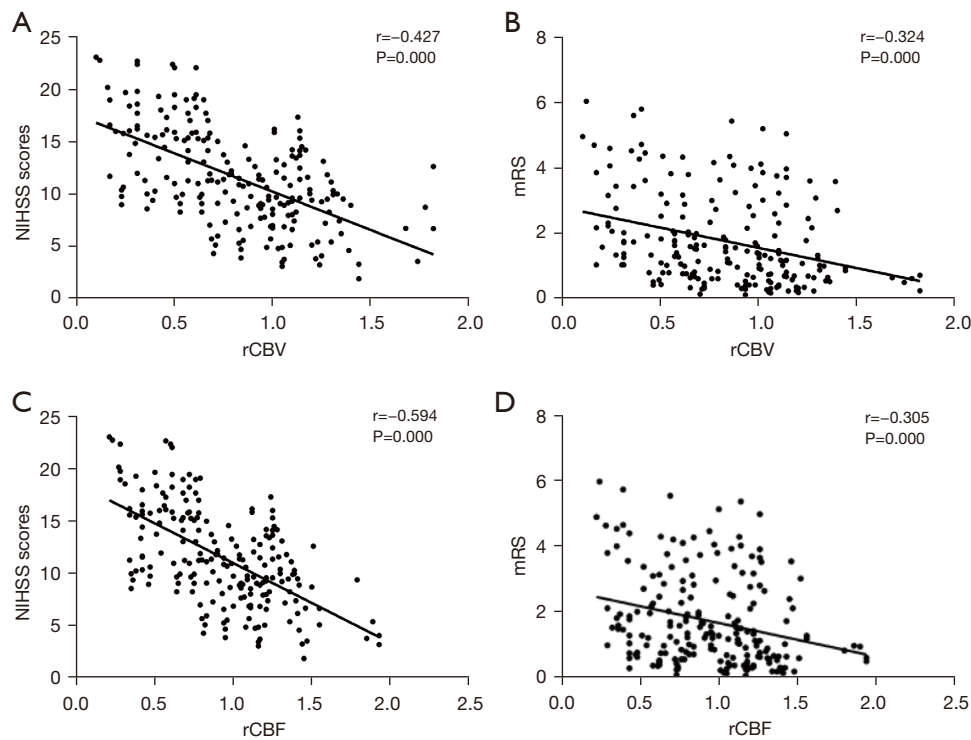


Figure 2 Correlation analysis of perfusion parameters and the NIHSS and mRS scores. (A) rCBV is weakly negatively correlated with the NIHSS score ($r=-0.427$; $P=0.000$). (B) There is a weak negative correlation between the rCBV and mRS score ($r=-0.324$; $P=0.000$). (C) The rCBF and NIHSS scores were moderately negatively correlated ($r=-0.594$; $P=0.000$). (D) The rCBF and mRS scores were weakly negatively correlated ($r=-0.305$; $P=0.000$). NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin scale; rCBV, relative cerebral blood volume; rCBF, relative cerebral blood flow map.

perfusion can compensate for brain tissue ischemia, and corresponding nerve functions can be retained (16-18). The compensation of blood flow via the collateral circulation can increase blood supply to the ischemic area and also enable therapeutic drugs to reach the ischemic area without being compromised by narrowed or occluded blood vessels (19,20). Different patients experience individual differences in the thrombolytic treatment window, which is dependent on the presence or absence of collateral circulation. Studies have shown that patients with good collateral circulation and compensatory reserve can extend the time window for intra-arterial treatment, correspondingly. Thrombolysis is not only effective in the short term but also in the long term, and the clinical prognosis is also usually good (21,22).

There are many methods used to assess carotid artery stenosis and cerebral collateral circulation, and DSA is the gold standard for the assessment of carotid artery stenosis and collateral circulation (23). This is largely due to the fact that DSA provides a high level of spatial

resolution, providing visibility of the position and degree of vascular stenosis, the shape of collateral vessels, the direction of blood flow, and any compensatory changes. The high level of spatial resolution is useful for evaluating the perfusion status associated with the pial collateral vessels, deep perforating arteries, ophthalmic arteries and other secondary collateral circulation pathways providing obvious advantages (24-26). However, DSA is an invasive examination. In the process of cerebral angiography, it can cause arterial dissection or rupture of blood vessels, vasospasm, embolism, intracranial hemorrhage, and even death. In addition, differences in contrast agent dosage and pressure may affect the display of distal blood vessels. (27-29). Furthermore, DSA examination is expensive and technically difficult (30), which makes it difficult to use widely in clinical practice.

PWI is a functional imaging approach that can sensitively reflect the blood perfusion of brain tissue (31). PWI technology is very sensitive to changes in tissue capillary

perfusion, and it can provide hemodynamic information that cannot be obtained by conventional MRI (32). PWI is used to detect early ischemic changes in patients with acute cerebral infarction and is more sensitive than conventional magnetic resonance imaging. The magnetic resonance (MR) signal of tissue with normal blood supply is relatively strong due to the relatively fast blood flow, and the MR signal of ischemic tissue is weakened due to poor blood supply, slow blood flow, and significant area of persistent ischemia (33,34). Within minutes of a stroke, a high signal can be observed on PWI with a prolonged peak time (35). PWI can semi-quantitatively study the changes of blood flow after cerebral infarction, and provide necessary hemodynamic parameters (36). Through the comprehensive analysis of these parameters, a specific assessment of blood supply in the area of cerebral infarction can be made. Because PWI can sensitively observe blood flow signals, it can better predict the collateral circulation and prognosis of patients than conventional CT and magnetic resonance imaging. In this study, compared with the low perfusion group, the rCBV and rCBF in the infarcted area of the high perfusion group were significantly increased, the rTTP and rMTT were significantly reduced, and the collateral circulation patency rate was significantly increased. The changes of hemodynamic parameters in the infarcted area in the hyperperfusion group were consistent with the rate of opening of collateral circulation. At the same time, the prognosis of patients in the high perfusion group was significantly better than those in the low perfusion group. A number of studies have shown the same. The opening of collateral circulation is related to the prognosis of patients with acute cerebral infarction. The results of this study are consistent with previous studies.

In summary, perfusion-weighted MRI can accurately provide relevant information on cerebral blood flow in patients with acute cerebral infarction, contributing to the assessment of a patient's collateral circulation and prognosis, and providing an important basis for clinical treatment.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the MDAR reporting checklist. Available at <https://apm.amegroups.com/article/view/10.21037/apm-21-3589/rc>

Data Sharing Statement: Available at <https://apm.amegroups.com/article/view/10.21037/apm-21-3589/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://apm.amegroups.com/article/view/10.21037/apm-21-3589/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All patients signed an informed consent form. This study was approved by the Ethics Committee of Jiangsu Vocational College of Medicine (No. JVCM-SMI-2017-05). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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(English Language Editor: K. Gilbert)

Cite this article as: Shang W, Zhang Y, Xue L, Li W. Evaluation of collateral circulation and short-term prognosis of patients with acute cerebral infarction by perfusion-weighted MRI. *Ann Palliat Med* 2022;11(4):1351-1359. doi: 10.21037/apm-21-3589