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Original Article

Diagnostic value of MRI perfusion-weighted imaging and diffusion-weighted imaging parameters in cerebral apoplexy

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Abstract: Objective: To assess the clinical and prognostic value of MRI perfusion-weighted imaging (PWI) versus diffusion-weighted imaging (DWI) parameters for apparent diffusion coefficient (ADC) and cerebral blood flow (CBF) in the diagnosis of patients with ischemic stroke (IS). Methods: Eighty patients diagnosed with IS in the Second Affiliated Hospital of Soochow University from January 2020 to January 2021 were retrospectively analyzed and regarded as a patient group. Meanwhile, 50 patients who underwent physical examination at the Second Affiliated Hospital of Soochow University during the same period were collected, and were identified by physical examination to have atherosclerotic stenosis but not cerebral infarction, they were set as a control group. The differences of ADC and CBF between both groups were compared. The diagnostic value of ADC and CBF in diagnosing acute ischemic stroke was analyzed by receiver operating characteristic (ROC) curve. The changes of ADC and CBF before and after treatment were compared. Patients were sub-grouped according to their mRS scores, and those with scores of 0-2 were grouped into the good prognosis group while those with scores of 3-6 were grouped into the poor prognosis group, and the risk factors affecting patients' prognosis were evaluated by logistic regression. The correlation of ADC and CBF with National Institutes of Health Stroke Scale (NIHSS) scores and modified Rankin Scale (mRS) scores was analyzed. ADC and CBF levels were compared between deceased and surviving patients, and their predictive value was assessed by ROC curves. Results: ADC and CBF were dramatically lower in the patient group compared with the control group ($P<0.05$). The area under the curve (AUC) of ADC and CBF in diagnosing IS was 0.949 and 0.926. The ADC and CBF values after treatment were significantly increased as compared to before treatment (both $P<0.05$). Both ADC and CBF were lower in the patients of the deceased group than in those in the survival group ($P<0.05$). The AUC for ADC and CBF in predicting death in patients diagnosed with IS was 0.866 and 0.766, respectively. ADC, CBF was negatively correlated with patients' NIHSS and mRS scores ($P<0.01$). Higher pre-treatment NIHSS and admission time ≥24 h after onset were risk factors for patient prognosis, whereas higher ADC and CBF values were protective factors (all $P<0.05$). Conclusion: ADC and CBF values are reduced in IS patients and can be used as a diagnostic and prognostic indicator of IS.

Keywords: Ischemic stroke, magnetic resonance imaging, apparent diffusion coefficient, cerebral blood flow, diagnosis, prognosis

Introduction

Stroke is the main clinical manifestation of cerebrovascular disease, including both ischemic and hemorrhagic types. It is a class of organic brain dysfunction with sudden onset and local or diffuse cerebral neurological dysfunction [1]. Acute ischemic stroke (AIS) is caused by disturbance of blood circulation in the brain, resulting in ischemia and hypoxia of the corresponding brain tissue; which leads to local ischemic necrosis or softening of the brain tissue, with clinical manifestations of acute onset with corresponding neurological deficit symptoms [2]. As aging of population increases, the incidence of AIS has increased year by year. Statistics have revealed that AIS accounts for 69.6% to 70.8% of all strokes in China, and it is the most common type of stroke. With the improvement of people's living standards and changes in dietary structure, its incidence is not only increasing in the middle-aged and elderly population, but also in the young population [3-5]. Thus, rapid diagnosis with high sensitivity and specificity is critical to control the disease progression in time and improve patient survival.

In clinical practice, common tests for AIS include computed tomography (CT) and conventional magnetic resonance imaging (MRI) [6, 7]. CT examinations provide timely exclusion of cerebral hemorrhage, and can clearly confirm the diagnosis early in the disease based on clinical features [8]. MRI can show the location and extent of the lesion more clearly and distinctly than CT, and the two complement each other [9]. CT and conventional MRI are mostly limited to disease diagnosis but are insufficient for the prediction of prognosis and recovery of patients [10]. MRI diffusion-weighted imaging (DWI) can minimize the anisotropy of white matter diffusion in the brain and spinal cord, and stereoscopically measure the diffusion in three directions, which has a high diagnostic value for brain diseases [11]. MRI perfusion-weighted imaging (PWI) is an examination technique used to reflect tissue perfusion and microvascular distribution, which provides hemodynamic information and has a high application in the diagnosis of cerebral infarction [12].

However, the clinical value of MRI DWI combined with PWI parameters for the diagnosis and prognosis of patients with ischemic stroke (IS) has not been reported for clarification. To this end, the aim of this research was to assess the diagnostic and prognostic value of the combination of the two in IS patients to provide clinical reference.

Methods and materials

Clinical data

Altogether 80 IS patients diagnosed in the Second Affiliated Hospital of Soochow University from January 2020 to January 2021 were retrospectively enrolled as the patient group. Meanwhile, 50 patients who underwent physical examination during the same period and were identified to have atherosclerotic stenosis instead of cerebral infarction were seen as the control group. This research was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Soochow University (LL2020X54A).

Inclusion and exclusion criteria

Inclusion criteria: All patients in this study were diagnosed by DSA. Patients met the diagnostic criteria of IS developed in the Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2018 [13]. Patients had unilateral IS. Patients' clinical profile was complete. Patients/patients' family members were informed of the treatment schedule.

Exclusion criteria: Patients with unclear time of stroke onset; Patients who had used anticoagulants prior to this episode; Patients who had previous history of hematologic disease; Patients who had severe cardiac, hepatic or renal insufficiency; Patients who were pregnant or breastfeeding; Patients who required vascular intervention for embolization, stenting, and craniotomy due to changes in their condition; Patients with serious complications or adverse events during the course of treatment.

Treatment regimens

Patients were treated with rt PA intravenous thrombolysis (Berlin, Germany, SFDA Approval No. sj20160054) at a drug extraction rate of 0.9 mg/kg according to the treatment guidelines. Of these, 10% were given rapid administration and the remaining 90% were continuously pumped within 1 hour. Saline was routinely given after the intra-pump injection. Thrombolytic drugs such as anticoagulation, antiplatelet aggregation, and fibrinolysis reduction were not used during treatment or within 24 h after administration. Cranial CT was reviewed within 24 h after thrombolysis to eliminate the risk of bleeding. After treatment, patients were given symptomatic supportive therapies such as improving circulation, antiplatelet aggregation, dehydration and lowering cranial pressure, anti-free radicals, neurotrophy and maintaining water and electrical balance. As soon as the condition was stabilized, a rehabilitation program was developed and initiated as soon as possible.

Testing and data processing

All patients underwent PWI after MRI plain scan and MRI DWI (Philips 1.5t Achieva SE). The parameters were 8-channel phased array coil, axial scanning, layer spacing 1.7 mm, layer thickness 4.5 mm, and field of view (FOV) 240

Table 1. Baseline data

Factor	Patient group (n = 80)	Control group (n = 50)	χ^2/t value	*P* value
Age (year)	64.90±8.76	63.24±11.45	0.931	0.353
Gender (male/female)	46/34	30/20	0.079	0.778
BMI (kg/m^2)	21.55±2.97	21.76±2.93	0.381	0.703
Diabetes (Yes/No)	22/58	15/35	0.094	0.758
Hypertension (Yes/No)	35/45	25/25	0.483	0.486
Smoking (Yes/No)	50/30	30/20	0.081	0.775
Excessive drinking (Yes/No)	10/70	10/40	1.330	0.248
NIHSS before treatment	12.37±2.10			
mRS score after 90 days of treatment	3.47±1.34			
Time of admission (≥24 h/<24 h)	38/32			

Note: NIHSS: National Institutes of Health Stroke Scale; MRS: Modified Rankin Scale; BMI: Body Mass Index.

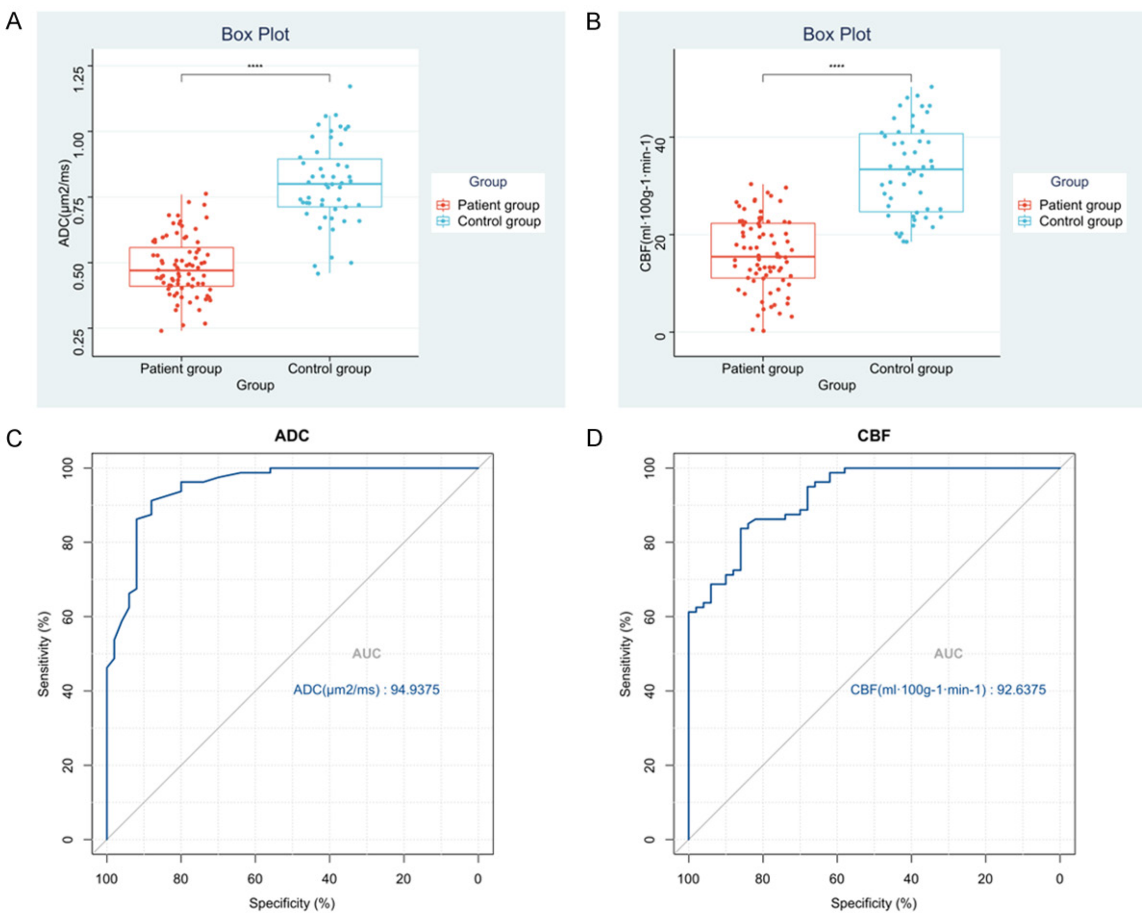

Figure 1. ADC and CBF levels in IS patients and normal subjects. A. Comparison of ADC values in patients and normal subjects. B. Comparison of CBF values between patients and normal subjects. C. ROC curve analysis of the AUC of ADC in diagnosing IS. D. ROC curve analysis of the AUC of CBF in diagnosing IS. Note: **** denotes P<0.0001. ADC: Apparent Diffusion Coefficient; CBF: Cerebral Blood Flow.

mm. Post-processing of the workstation images was evaluated by a neurologist and two radiologists. The region of interest was depicted with reference to the maximum level of high signal in DWI. After that, the Apparent Diffusion coefficient (ADC) of the affected side was measured, and the ADC value of the contralateral mirror area was measured with the midline of

Table 2. Parameters of ADC and CBF in diagnosing IS

Diagnostic variables	AUC	95% CI	Specificity	Sensitivity	Youden's index	Cut-off
ADC	0.866	0.777-0.955	100.00%	71.80%	71.80%	0.43
CBF	0.766	0.640-0.892	100.00%	53.50%	53.50%	15.88

Note: ADC: Apparent Diffusion Coefficient; CBF: Cerebral Blood Flow.

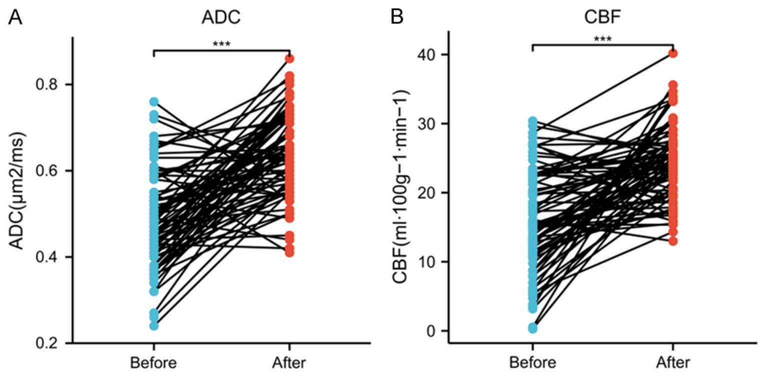

Figure 2. Changes in ADC and CBF before and after treatment. A. Changes in ADC before and after treatment. B. Changes in CBF before and after treatment. Note: *** denotes P<0.001; ADC: Apparent Diffusion Coefficient; CBF: Cerebral Blood Flow.

the brain as the axis. Based on the location and extent of the ROI in DWI, the region of interest for PWI was delineated in the same way, and the cerebral blood flow (CBF) values were calculated for the ipsilateral and contralateral mirror areas, respectively. When measuring quantitative parameters, the ventricles, vessels, brain pools and cranial structures were avoided.

Patient prognostic evaluation criteria

The prognosis of patients with IS was evaluated 90 days after discharge from the hospital by outpatients visit or telephone query, using the onset time of IS as the starting point. The prognosis was evaluated using the m-RS score, with 0-2 denoting a good prognosis and 3-5 representing a poor prognosis.

Outcome measures

Main outcome measures: The differences in ADC and CBF between both groups were compared. The diagnostic value of ADC and CBF in diagnosing AIS was analyzed by ROC curve. The changes in ADC and CBF of patients before and after treatment were assessed. Patients were grouped according to their modified Rankin Scale (mRS) scores [14], and those with scores of 0-2 were divided into the good prognosis group and those with 3-6 were enrolled to the poor prognosis group. Risk factors affecting patients' prognosis were analyzed by logistic regression.

Secondary outcome measures: The differences in clinical data between both groups were compared. The correlation of ADC and CBF with National Institutes of Health Stroke Scale (NIHSS) [15] and mRS score were assessed using Pearson's test. The ADC and CBF levels were compared between deceased and surviving patients, and their predictive value was analyzed by ROC curves.

Statistical analysis

SPSS 20.0 software was used for data analysis and GraphPad Prism 8 software was used for figure rendering. The counting data were expressed as rates and compared using chi-square test. The measurement data were represented as mean ± standard deviation and compared using t-test. The independent sample t-test was used for inter-group comparison, and the paired t-test was applied for intra-group comparison. Logistic regression was used to analyze the risk factors that affected the prognosis. Pearson's test was conducted to evaluate the correlation between the indicators. The diagnostic and prognostic values of ADC and CBF were assessed via ROC curve.

Results

Comparison of clinical data

There were no statistical differences between both groups in terms of age, gender, body mass index (BMI), diabetes, hypertension, and history of smoking and alcoholism (P>0.05, **Table 1**).

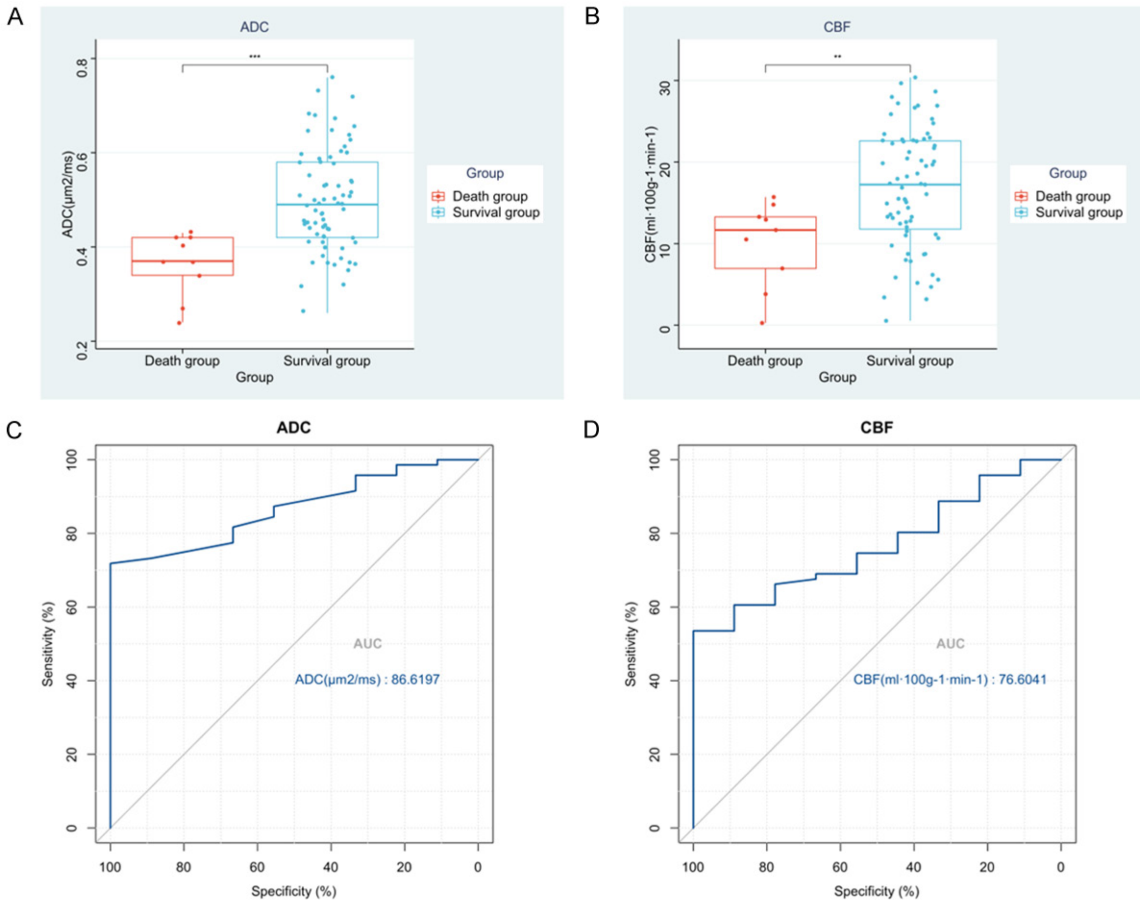

Figure 3. ADC and CBF expression in patients in th death group and survival group. A. Comparison of ADC values between deaths and survivals. B. Comparison of CBF values between deaths and survivals. C. ROC curve analysis of the AUC of ADC in predicting patient survival. D. ROC curve analysis of the AUC of CBF in predicting patient survival. Note: ** denotes P<0.01, *** denotes P<0.001; ADC: Apparent Diffusion Coefficient; CBF: Cerebral Blood Flow.

Levels of ADC and CBF in IS patients and their diagnostic values for IS

In the current study, we compared the differences in ADC and CBF between both groups. The ADC and CBF were found to be dramatically lower in the patient group compared to the control group (both P<0.05, **Figure 1**). In addition, ROC curve analysis revealed that the area under the curve (AUC) of ADC and CBF in diagnosing IS was 0.949 and 0.926, respectively (**Figure 1**; **Table 2**).

Changes in ADC and CBF before and after treatment

ADC and CBF values were examined after 1 week of treatment, which were dramatically higher than those before treatment (P<0.05, **Figure 2**).

Value of ADC and CBF in predicting patient survival

There were 9 deaths and 71 survivers out of 80 IS patients. Further comparison of ADC and CBF value between deceased and surviving patients revealed that ADC and CBF were lower in the deceased group than those in the surviving group (both P<0.05, **Figure 2**). Moreover, ROC curve analysis revealed that the AUC of ADC and CBF in predicting death of IS patients was 0.866 and 0.766, respectively (**Figure 3**; **Table 3**).

Correlation between ADC, CBF and NIHSS, mRS

We analyzed the correlation between ADC, CBF values and NIHSS, mRS scores and found that ADC, CBF were negatively correlated with

Table 3. Univariate analysis of clinical data

Factor	Good prognosis group (n = 35)	Poor prognosis group (n = 45)	χ^2/t value	*P* value
Age (year)	63.68±9.59	65.84±8.03	1.096	0.276
Gender (male/female)	22/13	24/21	0.730	0.392
BMI (kg/m^2)	21.45±3.16	21.64±2.85	0.282	0.778
Diabetes (yes/no)	10/25	12/33	0.035	0.849
Hypertension (yes/no)	15/20	20/25	0.020	0.887
History of smoking (yes/no)	25/10	25/20	2.116	0.145
History of excessive drinking (yes/no)	5/30	5/40	0.181	0.670
NIHSS before treatment	11.40±1.41	13.13±2.25	3.979	0.001
Time of admission (≥24 h/<24 h)	15/20	33/12	7.619	0.006
Systolic pressure (mmHg)	152.57±19.45	150.44±27.84	0.385	0.701
Diastolic pressure (mmHg)	87.94±13.88	84.58±5.99	1.460	0.148
Blood oxygen saturation (%)	94.54±2.88	95.74±2.55	1.973	0.052
White blood cell (10^9/L)	7.84±2.81	8.05±2.73	0.337	0.737
Red blood cell (10^9/L)	4.84±0.58	4.94±0.51	0.819	0.415
Platelet (10^9/L)	168.44±30.47	158.44±25.84	1.587	0.116
Hemoglobin (g/L)	152.47±12.54	144.80±22.84	1.787	0.077
ADC (μm^2/ms)	0.52±0.10	0.45±0.11	2.937	0.004
CBF (ml·100 g^{-1}·min^{-1})	18.26±6.59	14.26±7.52	2.489	0.014

Note: NIHSS: National Institutes of Health Stroke Scale; BMI: Body Mass Index; ADC: Apparent Diffusion Coefficient; CBF: Cerebral Blood Flow.

patients' NIHSS and mRS scores (**Figure 4**, P<0.01).

Analysis of risk factors affecting patients' prognosis

To assess the factors affecting patients' prognosis, we sub-grouped them according to their mRS scores after 90 d and divided them into a good prognosis group (n = 35, 0-2 points) and a poor prognosis group (n = 45, 3-6 points). Subsequently, we collected patients' clinical data and found that there were statistical differences in terms of admission time, NIHSS score, ADC, and CBF (all P<0.05, **Table 4**). The meaningful indicators were then assigned with values (**Figure 5**) and the backward LR method was selected to perform logistic regression analysis on the data. It turned out that higher NIHSS before treatment and patient admission ≥24 h after onset were risk factors for patient prognosis, while higher ADC, CBF values were protective factors (**Figure 5**, all P<0.05).

Discussion

Stroke has become one of the leading causes of death and disability in Chinese people. The identification and prognosis prediction of IS has always been the focus of scholars at home and abroad [16]. Ischemic stroke (IS) is majorly caused by large vessel occlusion; in more severe circumstances, circulation in the large and collateral vessels tends to be poorer, and ischemia is more extensive and severe in these patients [17]. Research has found [18] that IS is an important cause of disability and death in the middle and old age population. Thus, it is vital to find highly accurate and effective diagnostic indicators for IS diagnosis and treatment.

Neuroimaging diagnosis is changing as neuroimaging techniques are gradually improved and updated [19]. Previously, neuroimaging diagnosis mainly focused on the observation of morphological changes in brain tissue; and now, it is a combination of functional and morphological brain diagnosis [20]. DWI can noninvasively reflect the spatial composition of living tissues and the exchange of water molecules between components in pathophysiological states and can show diffusion coefficients that can indicate significant changes within 30 min of stroke, which is essential for localizing and

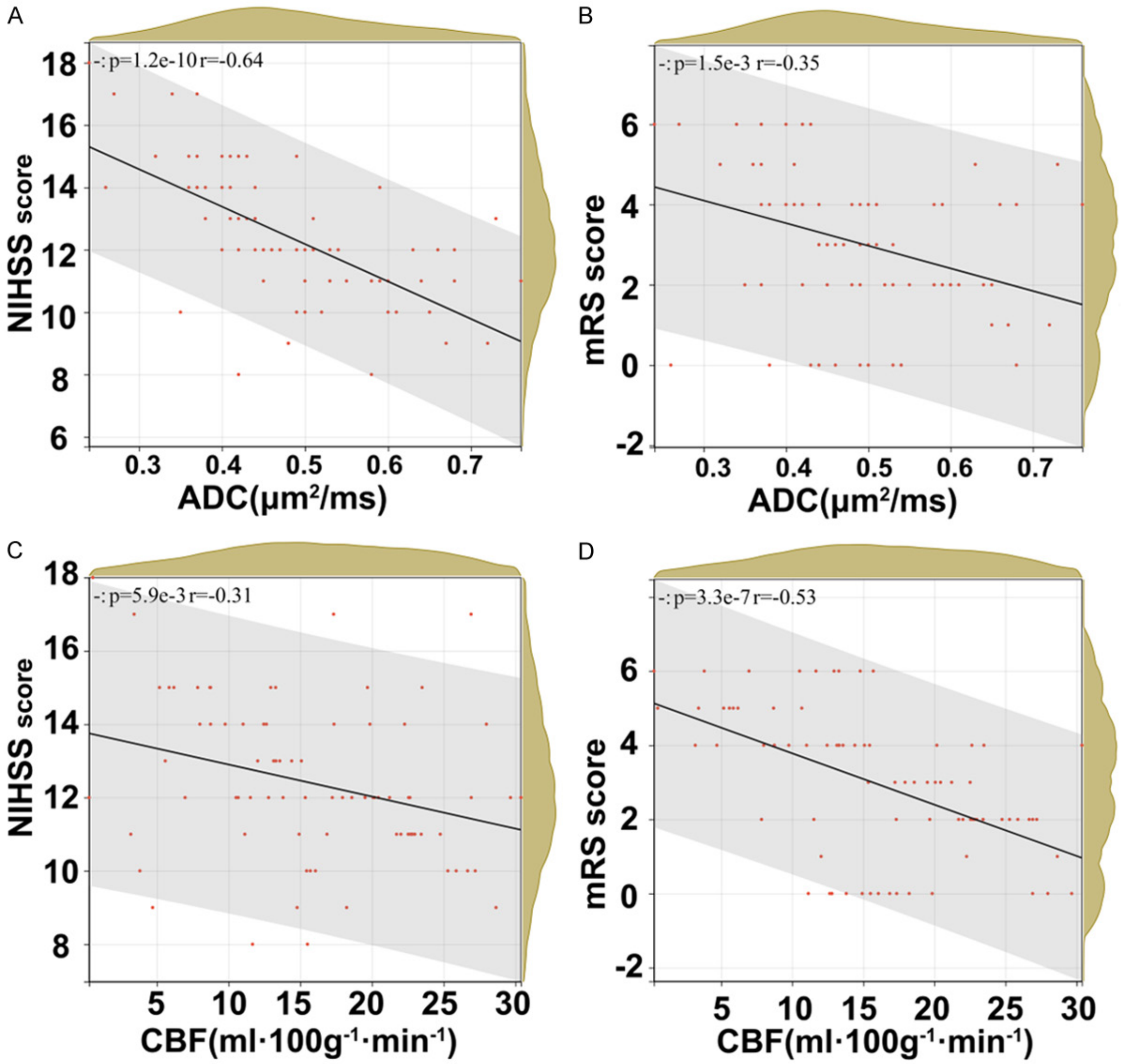

Figure 4. ADC and CBF were negatively correlated with NIHSS and mRS. A. Correlation between ADC values and NIHSS scores. B. Correlation between ADC values and mRS scores. C. Correlation between CBF values and NIHSS scores. D. Correlation between CBF values and mRS scores. Note: NIHSS: National Institutes of Health Stroke Scale; MRS: Modified Rankin Scale; ADC: Apparent Diffusion Coefficient; CBF: Cerebral Blood Flow.

Table 4. Assignment table

Factor	Assignment
NIHSS before treatment	Belonging to continuous variables using original data analysis
Time of admission	≥24 h = 1, <24 h = 0
ADC (μm^2/ms)	Belonging to continuous variables using original data analysis
CBF (ml·100 g^{-1}·min^{-1})	Belonging to continuous variables using original data analysis
Prognosis	Poor prognosis group = 1; Good prognosis group = 0

Note: NIHSS: National Institutes of Health Stroke Scale; ADC: Apparent Diffusion Coefficient; CBF: Cerebral Blood Flow.

determining the extent of lesions [21, 22]. ADC is applied to describe the speed and extent of diffusive motion of molecules in different directions in DWI sequences, and blood perfusion directly affects ADC values when the average ADC value in patients' ischemic lesion is dra-

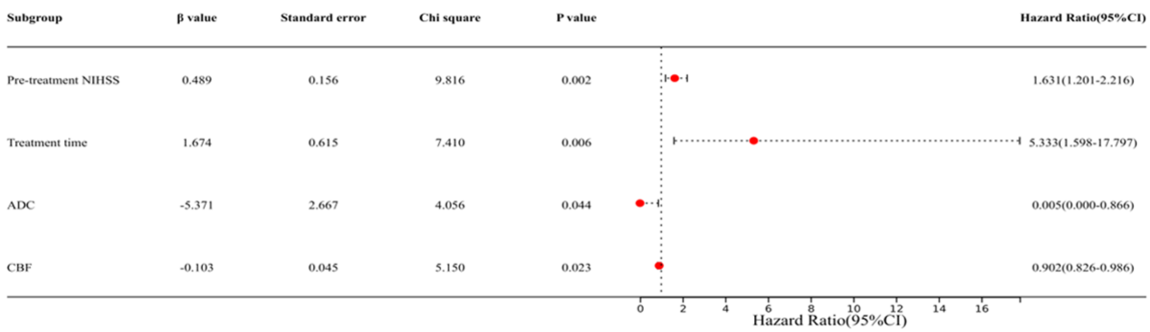

Figure 5. Analysis of risk factors affecting prognosis. Note: NIHSS: National Institutes of Health Stroke Scale; ADC: Apparent Diffusion Coefficient; CBF: Cerebral Blood Flow.

matically reduced [23]. After the formation of an ischemic lesion in brain, blood perfusion decreases dramatically, the diffusion of water molecules in the body slows down, and the ADC value decreases [24]. CBF is an essential parameter to quantify blood flow through local tissues per unit of time, and when IS patients are treated with early thrombolysis, local CBF values increase markedly [25]. In the present study, we found that ADC, CBF values were dramatically lower in IS patients compared with normal subjects. The ROC curve revealed that ADC and CBF could be used as diagnostic indices. Previously, Lestro et al. [26] found in animal models that DWI-ADC maps helped to identify ischemic tissue early and that CBF was higher within the lesion. We further determined the clinical value of ADC and CBF in IS by clinical testing. Shan et al. [27] found no statistical difference in ADC values compared to the normal group in acute stroke lesions. Although 23 IS patients were included in their study, only 8 patients were tested, compared with 22 healthy controls. We can see that there was still an overlapping portion of ADC values between healthy individuals and patients. Therefore, we believe that the absence of differences may be related to the sample size of their study. Furthermore, we compared the changes in ADC and CBF values before and after treatment. In our study, we found that there was a marked increase in ADC and CBF values after treatment, suggesting that ADC and CBF can be used as outcome measures for prognosis.

Because IS has high disability and mortality rates, it seriously affects the life quality and the survivals as well as causes great economic burden to families and society [28]. Thus, it is particularly important to explore effective imaging tools to objectively measure blood-brain barrier permeability to assist in the accurate clinical assessment of patients' conditions to further develop appropriate treatment plans and predict the prognosis. To this end, we analyzed patient survival, which showed that ADC and CBF were dramatically lower in patients who died than in those who survived, and ROC curve further proved the predictive value of ADC and CBF in predicting the survival of patients. In addition, we compared the relationship between ADC, CBF and NIHSS, mRS scores by correlation analysis. The NIHSS score is the most important clinical scale for assessing the neurological function of patients, which is simple in operation and reliable in reflecting the stroke severity [29]. The mRs score is a well-known scale used to assess the outcome of stroke and can assess the independent living skills of patients [30]. Correlation analysis demonstrated that ADC and CBF were negatively correlated with patients' NIHSS and mRS scores. This is a side indication that ADC and CBF are associated with the survival prognosis of patients. In the end, we grouped patients according to their mRS scores. Logistic regression analysis found that higher NIHSS before treatment and admission time ≥24 h after onset were risk factors for patient prognosis, while higher ADC and CBF values were protective factors. Sahin et al. [31] claimed that age, NIHSS were found to be independent predictors of death in patients with AIS. Szmygin et al. [32] found that NIHSS score and time to start reperfusion were independent predictors of clinical outcome. These are consistent with our findings, suggesting that lower NIHSS score at admission and earlier admission are conducive to patients' recovery. Hence, patients must seek medical attention in a timely manner once clinical manifestations appear, which is conducive to clinical treatment and prognostic recovery [33].

We identified ADC and CBF as diagnostic and prognostic indicators of IS, but there are still some limitations in the present study. As a retrospective study, we cannot guarantee that the data are free of bias. Furthermore, the sample size collected was small. For example, the results of Shan et al. [27] were not consistent with our results. Finally, we did not follow the patients for a long period of time. Therefore, we hope to conduct a prospective cohort study to collect a larger sample size to refine our findings.

In conclusion, ADC and CBF values are reduced in IS patients and can be used as diagnostic and prognostic indicators for IS.

Disclosure of conflict of interest

None.

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