Rev.int.med.cienc.act.fís.deporte - vol. 23 - número 91 - ISSN: 1577-0354

Zhao, W.; Hu, L.; Lu, W. (2023) A COMPARATIVE STUDY OF 3D-ASL AND DSC-PWI IN THE ASSESSMENT OF ISCHEMIC PENUMBRA AND CEREBRAL BLOOD FLOW IN MALE ATHLETE PATIENTS WITH A FOCUS ON SPORTS-RELATED CASES. Revista Internacional de Medicina y Ciencias de la Actividad Física y el Deporte vol. 23 (91) pp. 500-511
DOI: https://doi.org/10.15366/rimcafd2023.91.031

ORIGINAL

A COMPARATIVE STUDY OF 3D-ASL AND DSC-PWI IN THE ASSESSMENT OF ISCHEMIC PENUMBRA AND CEREBRAL BLOOD FLOW IN MALE ATHLETE PATIENTS WITH A FOCUS ON SPORTS-RELATED CASES

Wensi Zhao[1,#], Lijuan Hu[2,#], Weiheng Lu[3,*]

[1] Department of Radiology, The First People's Hospital of Changde, Changde, 415000, China
[2] Department of Radiology, Hubei Provincial Hospital of Integrated Chinese and Western Medicine, Wuhan, 430015, China
[3] Department of Neurology, Songshan Lake Central Hospital of Dongguan City, Dongguan, 523320, China
E-mail: S17301046@stu.ahu.edu.cn

Recibido 19 de abril de 2022 **Received** April 19, 2022
Aceptado 28 de junio de 2023 **Accepted** June 28, 2023

ABSTRACT

Objective: To compare the evaluation value of 3D-ASL and DSC-PWI on ischemic penumbra and cerebral blood flow in athlete patients with ischemic stroke. **Methods:** Forty-three athlete patients with sudden ischemic stroke were selected. After the athlete patients were admitted to the hospital, they firstly received DWI examination to confirm the disease diagnosis, and then underwent 3D-ASL and DSC-PWI examination respectively. The ischemic penumbra was judged by using the results of 3D-ASL examination and the mismatch between the results of DSC-PWI examination and DWI examination, and the difference between the cerebral blood flows of the two examinations was compared. **Results:** Statistical analysis revealed that the detection rate of 3D-ASL in hypoperfusion area was 90.70%, which was not significantly different from 81.40% of DSC-PWI examination ($P=0.213$). The detection rate of 3D-ASL in ischemic penumbra was 79.07%, which was significantly higher than 58.14% of DSC-PWI examination ($P = 0.037$). On the examination of cerebral blood flow volume, the blood flow volumes in the infarct area and the ischemic penumbra measured by 3D-ASL were significantly higher than those by DSC-PWI ($P < 0.05$). **Conclusion:** Compared with DSC-PWI, 3D-ASL could better detect and locate the ischemic penumbra, and the measured blood flow value of brain tissue is significantly higher than that of DSC-PWI. In addition, 3D-ASL is non-invasive, with short operation time and high application value.

KEYWORDS: Ischemic stroke; Three-dimensional arterial spin labeling imaging; Dynamic magnetic sensitive contrast-enhanced perfusion imaging; Comparative study；Medical Applications; Ischemic penumbra; Cerebral blood flow

1. INTRODUCTION

Ischemic stroke is a serious disease threatening human life, which needs timely rescue treatment. This can lead to varying degrees of neurological dysfunction, including mild sensory loss of the parietal lobe, loss of joint position, and loss of arm and finger mobility. Severe cases result in hemiplegia and almost complete loss of face and arm function(Putaala).

Due to the high incidence and risk of ischemic stroke, the diagnosis and treatment of ischemic stroke has always been a hot research direction (Syahrul et al., 2021). At present, it is generally accepted that athlete patients can be clinically divided into four regions according to the condition of cerebral ischemia: central infarction area, diffuse abnormal area, abnormal perfusion area and benign edema tissue area(Heiss, 2016).

Foreign scholars have given a new name to the diffuse and perfusion abnormal areas, namely, the Ischemic penumbra (IP), which normally lies around the center of an infarction, unlike the central infarct area(Uzdensky & Demyanenko, 2019).

The blood flow in the brain tissue in the infarction area is lower than the normal threshold, and the brain tissue will lose its due function in the long-term ischemia environment, which will cause irreversible damage to the body, and even lead to paralysis. The electrical activity of brain tissue in the ischemic penumbra has been suspended and its physiological structure remains intact (Gaetano et al., 2019).

The tissue cells were also in normal ion equilibrium, and cerebral blood flow decreased slightly, remaining at a high level within the abnormal range. If thrombolysis and reperfusion treatment can be carried out in time, the neurons in this part of the tissue can still be saved and the function of the brain can still be fully recovered (Zeng et al., 2021), which brings hope for the rescue of athlete patients with ischemic stroke. Therefore, special attention should be paid to the rescue of ischemic penumbra brain tissue in the treatment of ischemic stroke(Xin Wu et al., 2022).

If the rescue is timely, good rescue results will be obtained; otherwise, the ischemic penumbra is likely to be transformed into infarction zone, aggravating the symptoms of athlete patients (Ohno, Koyama, Lee, Yoshikawa,

& Sugimura, 2016). In order to carry out effective treatment for athlete patients with ischemic stroke as soon as possible, it is necessary to find and locate the ischemic penumbra region in athlete patients in time(Leonard & Williams, 2021). Researchers have developed various imaging methods, such as computed tomography (CT), magnetic resonance (MR) and so on(Schwamm et al., 2010).

There is now the development of three dimensioned- Arterial Spin labelling, 3D-ASL) and Dynamic Contrast-enhanced Perfusion Weighted imaging (DSC-PWI) (Nachtmann, Stang, Wang, Wondzinski, & Thilmann, 2003). With the assistance of these imaging technologies, the lesions of ischemic penumbra can be accurately located and targeted treatment can be carried out as soon as possible (Hu et al., 2020). The purpose of this study was to compare the application value of 3D-ASL and DSC-PWI in the evaluation of ischemic penumbra and cerebral blood flow in ischemic stroke.

2. Data and methods

2.1 Athlete Patients' data

All subjects were selected from 43 athlete patients with sudden ischemic stroke admitted to our Hospital from July 2020 to July 2021. There were 25/18 males/females, and the athlete patients' ages ranged from 29 to 78 years, with an average age of 60.7±6.8 years. The comorbidities of the athlete patients are shown in Table 1, Figure 1 and Figure 2.

Table 1 Statistics of athlete patients' previous diseases

Disease	Cases (Cases)	Percentage (%)
Hypertension	29	67.44
Diabetes	13	30.23
Heart disease	6	13.95
Hyperlipidemia	15	34.88

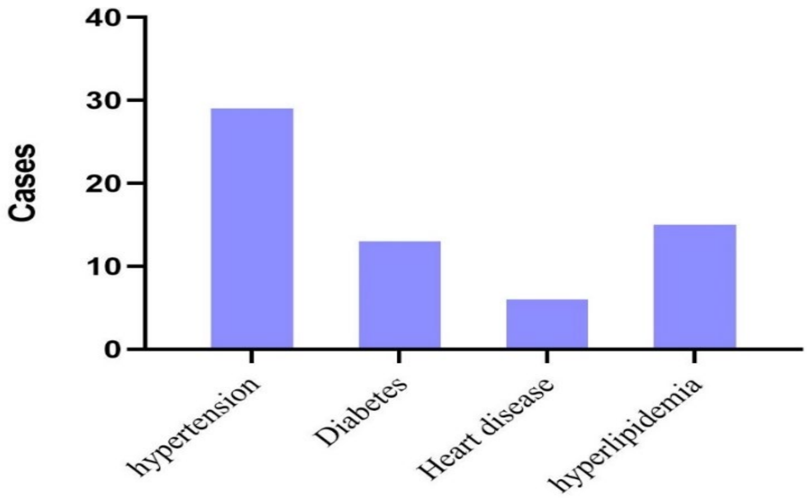

Figure 1. Statistical histogram of patients' past diseases

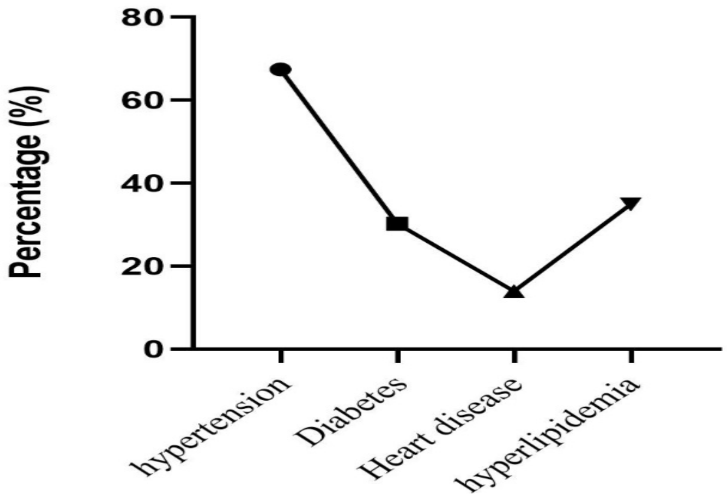

Figure 2. Statistical percentage of previous diseases of patients (%)

2.2 Inclusion criteria and exclusion criteria

Inclusion criteria :(1) the patient's past history investigation, clinical symptoms, physical examination and DWI examination were consistent with the diagnosis of ischemic stroke; (2) The onset time of the patient is less than 6h; (3) All athlete patients had unilateral new cerebral stroke, and the contralateral brain was normal; (4) The patient had no previous cerebrovascular accidents; (5) Patients and their family members were informed and agreed to participate in the instinct study. Exclusion criteria :(1) athlete patients with cerebral hemorrhage, brain tumor, cerebrovascular malformation and other related diseases that may affect the results of this study; (2) The image quality is poor and cannot meet the research requirements; (3) women in pregnancy or lactation; (4) Those who suffer from mental illness and are unable to cooperate with the research.

2.3 Methods

DWI examination was performed first after admission to confirm the diagnosis of ischemic stroke and to determine the infarct site and size. Athlete Patients underwent 3D -- ASL and DSC-PWI examinations, respectively. Normal, low, and high perfusion results were recorded. By comparing DWI with 3D-ASL, a mismatch of more than 20% is considered as ischemic penumbra. The results of PWI and DWI were also compared to locate the ischemic penumbra.

The images were interpreted by two experienced physicians, and the information of ischemic penumbra and cerebral blood flow was obtained. The results of ischemic penumbra in the two groups were statistically analyzed, and the values of cerebral blood flow measured by the two methods were recorded and compared.

2.4 Statistical Methods

SPSS26.0 software was used for data statistics and analysis. The expression of measurement data was mean ± standard deviation (), data comparison was conducted by T test, counting data was expressed by the number of cases (percentage), and comparison between the two groups was conducted by X2 test. P<0.05 was considered as significant difference between groups, which was statistically significant.

3. Results

3.1 Comparison of results of ischemic penumbra

After DWI examination, 43 athlete patients were found to have different degrees of infarction. After 3D-ASL examination, 39 athlete patients were found to have hypoperfusion zone, and the detection rate of hypoperfusion zone was 90.70%. The abnormal perfusion area of 34 athlete patients was inconsistent with DWI results, that is, the presence of ischemic penumbra was detected in 34 athlete patients, and the IP detection rate was 79.07%. Dsc-pwi showed that 35 athlete patients had hypoperfusion zone, the detection rate of hypoperfusion zone was 81.40%, and 25 athlete patients had ischemic penumbra zone, the detection rate of IP was 58.14%. Chi-square test was used to compare the results of low-perfusion zone examination between the two groups, and there was no significant difference between the two values (P=0.213). Compared with the IP detection rate of the two groups, the IP detection rate of 3D-ASL was significantly higher than that of DSC-PWI (P=0.037). Detailed data are shown in Table 2, Table 3, Figure 3 and Figure 4.

Table 2 Comparison of results of 3D-ASL and DSC-PWI examination of hypoperfusion zone ($\bar{x} \pm s$)

Group	N/the number of cases	Hypoperfusion zone (n)	Low perfusion detection rate (%)	X^2/P values
3D-ASL check	43	39	90.70	1.550/0
DSC—PWI check	43	35	81.40	.213

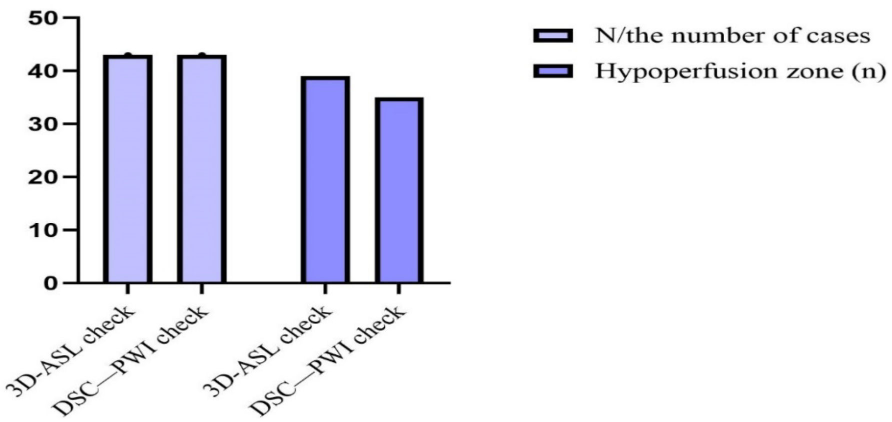

Figure 3. Histogram of examination results of hypoperfusion area

Table 3 Comparison of 3D-ASL and DSC-PWI results of ischemic penumbra ($\bar{x} \pm s$)

Group	N/the number of cases	Number of IP cases (n)	IP detection rate (%)	IP detection rate (%) X2/P value
3D-ASL check	43	34	79.07	4.373/0.037
DSC—PWI check	43	25	58.14	

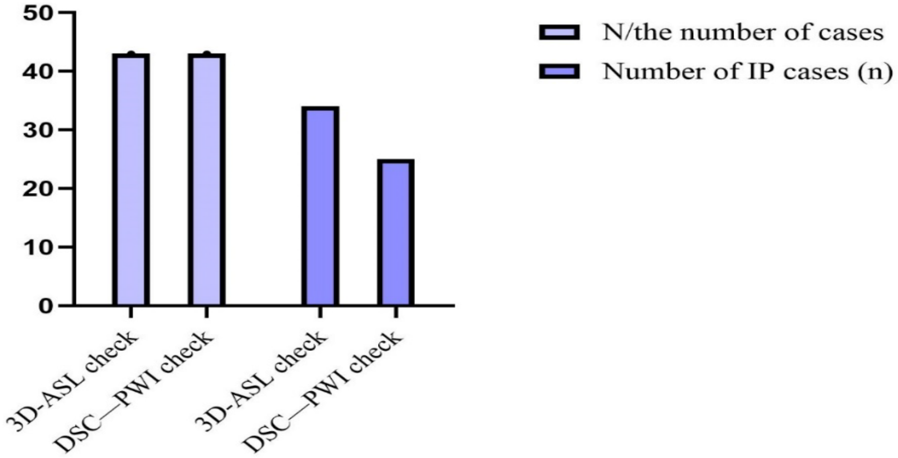

Figure 4. histogram of the results of ischemic penumbra examination

3.2 Blood flow comparison

The mean ratio of blood flow signal intensity of the affected side and the healthy side at the maximum lesion level obtained by 3D-ASL and DSC-PWI were compared, namely, the rCBF condition. Detailed data are shown in Table 4, Figure 5 and Figure 6.

Table 4 Comparison of blood flow measured by 3D-ASL and DSC-PWI ($\bar{x} \pm s$)

Group	3D-ASL check	DSC—PWI check	*t*/P values
CBF infarction area	26.125±6.186	22.843±5.259	2.444/0.017
Ischemic penumbra CBF	41.616±6.918	37.648±6.184	2.275/0.027

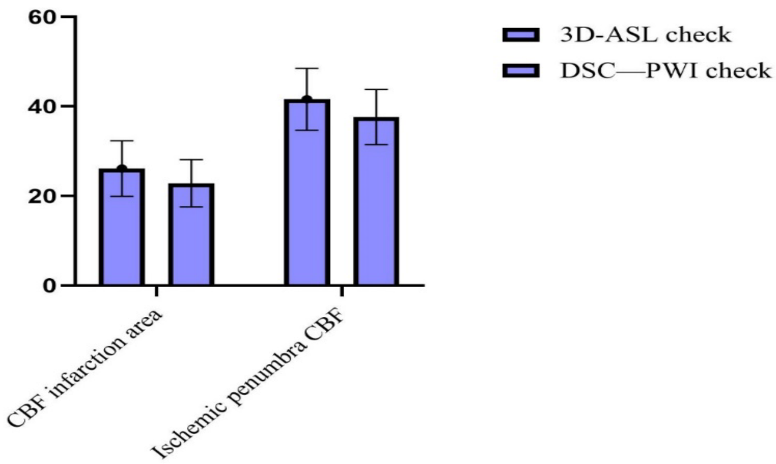

Figure 5. Histogram of blood flow test results

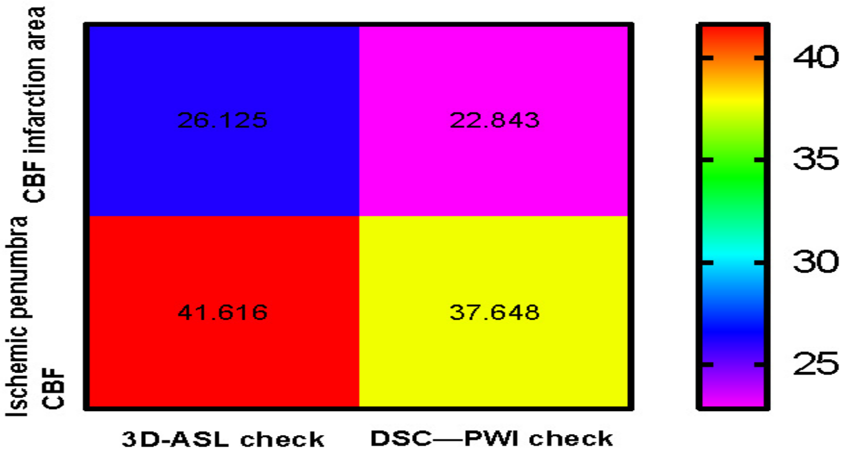

Figure 6. Heat map of blood flow test results

4. Discussion

An ischemic stroke is a series of systemic symptoms caused by a blockage of blood vessels in the brain and a lack of blood supply to brain tissue(Xiujuan Wu et al., 2017). Tissue loss is reversible, and neuronal loss may occur if time ischemia lasts longer. Membrane dysfunction, ranging from electrical loss to calcium influx, leads to calcium-dependent excitatory toxicity that produces reactive oxygen species that ultimately destroy membrane structures and dissolve cells(Sheng, Wang, Jiang, & Zhang, 2022). The 2020 American Heart Association report on Heart Disease and Stroke Statistics estimates that the annual incidence of stroke in the United States is about 2.5 percent(Pigretti et al., 2019). Seven million Americans over the age of 20 have had a stroke, with 800,000 new strokes and nearly 150,000 deaths. According to the survey, the annual incidence of ischemic stroke in adult females is about 1.7 × 100 000, and that in adult males is 212 × 100 000. The average annual incidence is in the range of 0.58 to 0.61%, and the recurrence rate of ischemic stroke is very high, about 12.9% to 21.8% of athlete patients will have a recurrence. As the population ages, the risk of stroke increases. The annual cost of ischemic stroke alone is $45.5 billion between 2021 and 2015. Ischemic stroke not only brings serious life and health threats to patients, but also brings huge expenses to patients' families and society (SU, 2021).

It has been proved that ischemic penumbra appears in brain tissue after ischemic infarction. In the ischemic penumbra, the ion balance of tissue cells was normal and there was still a possibility of recovery. Therefore, clinical treatment of ischemic stroke pays special attention to the treatment of ischemic penumbra. Timely acquisition of imaging data of ischemic penumbra can carry out reperfusion therapy for athlete patients with ischemic stroke as soon as possible, which is very important for rescuing athlete patients. In the past 40 years, the location and treatment of ischemic penumbra has been the focus of ischemic stroke research (Yoshioka, Yaegashi, Yoshioka, & Tsugihashi, 2019).

Imaging techniques for locating the ischemic penumbra have also been developed, such as CT, DWI, 3D-ASL and DSC-PWI (Fisher & Garcia, 1996). DWI is a type of magnetic resonance examination, also known as Diffusion weighted imaging. It takes advantage of the difference in the degree and direction of water diffusion between normal and diseased tissues and is very sensitive to ultra-early cerebral infarction. Infarct sites will show high signal changes in the image, which is more clear and comprehensive compared with traditional CT examination and DWI imaging. PWI is dynamic magnetic sensitive contrast enhanced perfusion imaging, and its inspection principle is to carry out dynamic enhanced scan through contrast agent cluster injection tracking technology. It relies on the principle of image signal changes caused by the change of magnetic susceptibility of contrast agent for imaging. Cerebral blood flow parameters, cerebral blood volume parameters, average passing time and peak time parameters can be obtained after perfusion imaging(Sartoretti et al., 2021). By comparing the results of PWI and DWI, the mismatched area was the ischemic penumbra. Arterial spin labeling (ASL) is another perfusion magnetic resonance imaging technique, which uses water molecules in arterial blood as endogenous contrast agents to develop the image through spin labeling of water molecules. The operation is completely non-invasive and the image quality is high(Cheng, Shen, & QI, 2010).

In this study, 50 athlete patients diagnosed as gliomas by pathological examination were selected as the research objects, including 27 low-grade gliomas (LGGs) and 23 high-grade gliomas (HGGs). Prior to surgery, all athlete patients underwent 3 Tesla magnetic resonance imaging (MRI), 3D ASL, DSC-PWI, and conventional enhanced MRI scans to obtain original 3D ASL and DSC-PWI images. The tumor areas with the most obvious parenchymal perfusion and contralateral normal white matter were selected. After adjusting for individual differences in these regions, parameters of ASL relative cerebral blood flow (ASL-RCBF), DSC relative cerebral blood flow (DSC-RCBF) and DSC relative cerebral blood volume (DSC-RCBV) were obtained(Pollock et al., 2008). The results showed that the values of ASL-CBF, DSC-CBF, DSC-CBV and ASL-RCBF, DSC-RCBF, DSC-RCBV increased with the increase of the grade of the glioma being imaged. And there are significant differences between HGGs and LGGs. Asl-rcbf was positively correlated with DSC-RCBF ($r=0.580$, $P<0.01$).(Oliveira et al., 2017) In addition, asL-RCBF was positively correlated with DSC-RCBV ($r=0.431$, $P<0.01$). Receiver operating characteristic (ROC) curve was applied to compare the diagnostic value of dSC-PWI and 3D ASL perfusion parameters for glioma grading. It was found that the area under ROC curve of ASL-RCBF was the highest (0.836) (Zhu, 2020). Z-test was used to analyze the area under ROC curve of DSC-RCBF and DSC-RCBV, and the difference was not statistically significant(Vupputuri, Ashwal, Tsao, Haddad, & Ghosh, 2017). When the cutoff values of ASL-RCBF, DSC-RCBF and DSC-RCBV were 2.24, 1.85 and 1.68, respectively, the sensitivity of HGG diagnosis was 83.2, 91.3 and 91.3%, and the specificity was 77.7, 63.9 and 667%. It is concluded that DSC-PWI perfusion imaging can be used for preoperative grade diagnosis of glioma, which is helpful to develop the correct surgical procedure and has very good diagnostic value. Greg Zaharchuk et al. conducted a study to compare the performance of spin labeling imaging in athlete patients with TIA with the results of diffusion-weighted imaging and mass perfusion weighted imaging (Saber et al., 2020). DWI, intracranial magnetic resonance angiography (MRA), and ASL, PWI examinations were obtained in a prospective cohort of 76 athlete patients with TIA. Two neuroradiologists evaluate the images blind to determine the frequency of abnormalities in each imaging sequence(Zaharchuk et al., 2012). Using Kappa (leading) statistics to evaluate consistency, leading 2 test is used to detect differences in the proportion of abnormal studies. We found that 62% of the 76 athlete patients had ASL abnormalities, much higher than DWI (24%) and intracranial MRA (13%). ASL significantly increased the yield of MR imaging than the combined yield of DWI and MRA (62% versus 32%, $P < 0.05$). Arterial transport artifacts in the peripheral region were the most common ASL anomaly (51% present). Other abnormalities included focal high or low ASL signaling (11%), abnormal PWI in 31% of athlete patients, and abnormal ASL in 14 of 15 patients (93%). The consensus between neuroradiologists about abnormal studies is that ASL examination is more effective than PWI [LEADING = 0.69 (95% confidence interval 0.53 to 0.86) and LEADING = 0.66 (95% confidence interval 0.43 to 0.89). Finally, leading to the conclusion: In athlete patients with TIA, perfusion related changes are more easily detected with ASL than with PWI or intracranial MRA, and ASL is more helpful in the examination and classification of athlete patients with TIA (MOHAPATRA, MOHANTY, MISHRA, & TUDU, 2020).

The results of this study also proved the excellent value of 3D-ASL technique in the diagnosis of ischemic penumbra and cerebral blood flow in ischemic stroke. The detection rate of 3D-ASL on ischemic penumbra was 79.07%, which was significantly higher than that of DSC-PWI (58.14%) ($P=0.037$). It can also reflect the blood flow in the central infarct area and the ischemic penumbra, providing clinical information of great guiding value for the follow-up treatment of ischemic stroke. Magnetic resonance imaging is powerful in detection, but patients may be allergic because dSC-PWI tests require the use of a mass contrast agent. And it will cause great psychological pressure on athlete patients, which limits the applicable population, for example, athlete patients with pacemakers are not suitable for this examination. While 3D-ASL technology is a completely non-invasive technology, which can be performed even in the presence of bleeding lesions or renal insufficiency. The examination is highly repeatable and easy to perform. There is no gold standard for the diagnosis of IP, although there is still no broad consensus on the selection of the best imaging technique for locating the ischemic penumbra. The choice between CT and MRI still needs to be made based on availability, feasibility, and time pressure. However, the results of this study proved the practical value of 3D-ASL technique in the detection of ischemic penumbra and cerebral blood flow in ischemic stroke, and proved its good clinical application significance. However, 3D-ASL technology also has its limitations. Compared with DSC PWI, 3D-ASL technology has a relatively poor signal-to-noise ratio. Secondly, 3D-ASL technology cannot measure as many parameters as DSC-PWI, and there is only one CBF parameter, which limits its application to some extent. 3D-ASL technology is only in the initial stage of research at present, and the research on 3D-ASL technology is constantly advancing. It is believed that in the near future, the progress of this technology can overcome its shortcomings and make it more widely applicable.

Declaration of conflict of interest

None.

Data Availability Statement

The data used to support the findings of this study are available from the corresponding author upon request.

Acknowledgement

This work was supported by The First People's Hospital of Changde.

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