



## PROGNOSTIC VALUE OF DEEP MEDULLARY VEIN SIGNS ON MAGNETIC SUSCEPTIBILITY WEIGHTED IMAGING IN ACUTE ISCHEMIC STROKE

Krishna Shrestha<sup>1\*</sup>, Gong Jin Shan<sup>2</sup> and Liu Zhi Yong<sup>3</sup>

<sup>1\*</sup>*School of Clinical Medicine, Inner Mongolia University for Nationalities, 538 West Huolin He Street, Horqin District, Tongliao city, Inner Mongolia, P.R.China.*

<sup>2,3</sup>*Department of Radiology, Affiliated Hospital of Inner Mongolia University for Nationalities, 1742 Huolin He Street, Horqin District, Tongliao city, Inner Mongolia, P.R.China.*

### ABSTRACT

**Objective:** To investigate the correlation between the distribution and grading of deep medullary veins (DMVs) on magnetic susceptibility weighted imaging (SWI) and clinical prognosis in patients with acute anterior circulation cerebral infarction.

**Method:** From December 2018 to December 2019 fifty patients with acute ischemic stroke, who were admitted to our hospital were enrolled in our study. Univariate and multivariate Logistic regression models were used to determine the correlation between distribution of DMVs and clinical prognoses of patients. DMVs on the ipsilateral side of the lesions were further graded and analyzed ; boxplot was used to describe its relation with modified Rankin scale (mRs) scores of the patients.

**Results:** Among the 50 patients, 36 (72%) had DMVs (19 ipsilateral and 17 contralateral). Multivariate logistic regression analysis showed that ipsilateral DMVs was an independent risk factor for poor prognosis (OR =3.380, 95% CI: 1.006-11.393, P= -0.049). However, although the contralateral DMVs could not independently predict the prognosis, most of them appeared in the good prognosis group (44.8%). There were 7 cases of grade 1, 9 cases of grade 2 and 3 cases of grade 3 in ipsilateral DMVs. Box plot analysis showed that DMVs grade 3 had higher Mrs score (average 4 points).

**Conclusion:** The ipsilateral DMVs on SWI are independent predictive biomarkers for poor clinical outcome after stroke, and contralateral DMVs often indicate good prognosis.

**Key words:** Susceptibility-weighted imaging; Deep medullary vein; Acute infarction; Anterior circulation; Clinical prognosis

SWI is a three-dimensional gradient echo MRI sequence 1-3 with high spatial resolution and full velocity correction. Compounds with paramagnetic, diamagnetic, and ferromagnetic properties all interact

with the local magnetic field to deform it, thereby changing the phase of the local tissue and causing signal loss. Paramagnetic compounds include deoxyhemoglobin, ferritin, and hemosiderin. Diamagnetic compounds including bone minerals and dystrophic calcifications. Because of its high sensitivity to paramagnetic materials, susceptibility weighted imaging (SWI) can significantly increase the visualization of intracranial venous system. Studies have shown that SWI can not only clearly show the location and length of venous thrombosis, but also noninvasively assess the ischemic penumbra around the infarct, and early identify the hemorrhagic transformation after thrombolytic therapy. SWI has been widely used in the diagnosis and treatment of acute ischemic stroke<sup>[2-3]</sup>.

Morita et al<sup>[4]</sup>.in 2008, on SWI of a child with ischemic stroke, he found that the white matter area of the affected lateral ventricle was significantly thickened and was perpendicular to the lateral ventricle. With the further study, this sign was quickly confirmed and named as deep medullary veins sign (DMVs) or brush sign<sup>[5]</sup>. In 2015, mucke et al. Included 86 patients with acute ischemic stroke. Combined with the score analysis of modified Rankin Scale (mRS) at 90 days, the results showed that mucke had no significant difference between the two groups. DMVs positive patients have higher mRS scores, suggesting that the worse the prognosis. Since then, there has been an upsurge of research on the relationship between DMVs and the clinical prognosis of patients with acute ischemic stroke. However, there are still some controversies on the clinical evaluation of acute ischemic stroke with DMVs. Some scholars believe that DMVs positive indicates more severe infarction degree and poor prognosis<sup>[6-7]</sup>, but some studies have not found that DMVs positive has predictive value for the prognosis of acute ischemic stroke<sup>[8]</sup>. At present, most of the domestic researchers discuss the venous signs on SWI in the form of significant vascular signs, but pay little attention to the distribution and classification of DMVs in patients with different cerebral infarction. Therefore, our research group takes patients with acute anterior circulation cerebral infarction as the research object, and uses univariate analysis and multivariate logistic regression analysis to explore the predictive value of the distribution and classification of DMVs on the clinical prognosis of patients It is reported as follows.

## MATERIALS AND METHODS

### Object of study:

In this study, 212 patients with acute anterior circulation cerebral infarction who were treated in the Department of Neurology, Affiliated Hospital of Inner Mongolia University for Nationalities from December 2018 to December 2019 were selected as the primary research objects. According to the inclusion and exclusion criteria, the unqualified MRI images and the lost follow-up patients were excluded. Finally, a total of 50 patients were included in the study.

### Inclusion criteria:

- ❖ acute anterior circulation cerebral infarction of the first attack.

- ❖ complete head and neck contrast-enhanced magnetic resonance angiography (CE-MRA) examination within 24 hours after onset, and imaging examination showed stenosis or occlusion of internal carotid artery or middle cerebral artery.
- ❖ All patients were treated with antiplatelet aggregation, statins to stabilize plaque and control risk factors.

**Exclusion criteria:**

- ❖ Acute posterior circulation infarction.
- ❖ Old cerebral infarction (excluding old lacunar infarction and without neurological impairment), cerebral hemorrhage, hemorrhagic infarction, brain tumor, brain trauma and cerebral vascular malformation.
- ❖ No complete diffusion weighted imaging (DWI) was performed Imaging, DWI, SWI, MRA and other imaging data.
- ❖ Intravenous thrombolysis or endovascular treatment.

**MRI examination and Result:**

MRI was performed within 24 hours after admission, including head MRI plain scan, DWI, SWI and MRA. All imaging data were reviewed by a neurologist and a radiologist with double-blind method. According to the method reported in foreign literature [5,7], DMVs were defined as the low signal small vein shadow perpendicular to the lateral ventricle in the white matter area of lateral ventricle on SWI. Whether the sign was found on the same side of the lesion or on the opposite side of the lesion was observed, and it was divided into 3 grades according to Horie et al. [5] Grade 1 (0-5), Grade 2 (6-10), Grade 3 (> 10). The degree of stenosis or occlusion of internal carotid artery and middle cerebral artery was determined according to the results of head and neck CE-MRA. The infarct volume was measured on DWI images using Kingstar wining information system 5.00 (Shanghai Kingstar Weining Software Co., Ltd.). If there is any objection in the above-mentioned judgment results, the author shall reach an agreement through collective discussion.

**Data collection and analysis:**

General data such as gender, age, history of hypertension, diabetes, hyperlipidemia, atrial fibrillation, smoking history, drinking history, etc. were collected: the time from onset to completion of MRI examination, and NIHSS score at admission (completed by experienced neurologist under the condition of unknown imaging manifestations) The imaging data of the patients were analyzed, including infarct volume, distribution of DMVs on SWI (appearing on the same side or opposite side of the lesion) and grading of DMVs on the ipsilateral side of the lesion was collected; According to reference [9], the clinical prognosis of patients was judged by mRS score at follow-up (telephone or outpatient follow-up 1), in which mRS score < 3 was defined as good prognosis, and Mrs score  $\geq 3$  was defined as poor prognosis.

**Statistical methods:**

SPSS 17.0 software was used for statistical analysis. The measurement data of normal distribution was expressed by means  $\pm$  standard deviation ( $\bar{x} \pm s$ ), the comparison between groups was conducted by t test; the

counting data was expressed by the number of cases (percentage) [n(%)], and the comparison between groups was conducted by  $\chi^2$  test. Furthermore, multivariate logistic regression analysis was used to screen out the independent risk factors for poor prognosis; box plot was used to describe the distribution of mRS scores in patients with different grades of ipsilateral DMVs. The difference was statistically significant ( $P < 0.05$ ).

## RESULT

Among the 50 patients included in this study, 31 were male and 19 were female; the age range was 40-85 years old, with an average age of 67 years; there were 37 cases of hypertension, 18 cases of diabetes, 13 cases of hyperlipidemia, 9 cases of atrial fibrillation, 20 cases of smoking and 16 cases of alcohol drinking; the average time from onset to MRI examination was 1065min. 36 cases (72%) were positive for DMVs, including 19 cases on the same side of the lesion and 17 cases on the opposite side of the lesion.

Among the 50 patients included in this study, 29 (58%) had a good prognosis and 21 (42%) had a poor prognosis. There were significant differences in age, NIHSS score, infarct volume and distribution of DMVs between the good prognosis group and the poor prognosis group ( $P < 0.05$ ). The ipsilateral DMVs were more common in the poor prognosis group (52.3%), while the contralateral DMVs in the good prognosis group (44.8%). See Table 1 for details.

Multivariate logistic regression analysis showed that there were significant differences between the two groups. Ipsilateral DMVs (OR = 3.386,  $P = 0.049$ ) and NIHSS score (OR = 1.265,  $P = 0.046$ ) were independent risk factors for poor prognosis. See Table 2 for details.

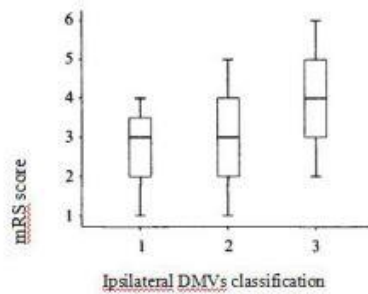
The ipsilateral DMVs were further classified, including 7 cases of grade 1, 9 cases of grade 2, and 3 cases of grade 3. The box plot analysis showed that the patients with grade 3 of DMVs had higher mRS score (with an average of 4 points), suggesting that the worse prognosis. See Figure 1 for details.

	Good prognosis group(n=25)	Poor prognosis group(n=17)	t/x <sup>2</sup>	P
Age	63.6±11.6	72.2±9.3	-2.806	0.007
Male[n(%)]	21(72.4)	10(47.6)	3.178	0.087
Hypertension[n(%)]	21(72.4)	16(76.1)	0.090	1.000
Diabetes mellitus[n(%)]	12(41.3)	6(28.5)	0.867	0.388
Hyperlipidemia[n(%)]	9(31.0)	4(19.0)	0.910	0.515
Smoking[n(%)]	14(48.3)	6(28.5)	1.970	0.243
Drinking[n(%)]	12(41.3)	4(19.0)	2.791	0.129
Arterial fibrillation[n(%)]	5(17.2)	4(19.0)	0.027	1.000
Time from onset to MRI examination(min)	1059±401	1073±292	-1.055	0.297
NIHSS score	5.3±3.3	15.1±8.4	-5.085	0.001
Infarct volume(mm <sup>3</sup> )	15.6±11.8	87.1±63.4	-2.683	0.014
Distribution of DMVs[n(%)]				
Ipsilateral	8(27.6)	11(52.3)		
Contralateral	13(44.8)	4(19.0)	8.121	0.016
Normal	8(27.6)	6(28.7)		

**Table 1:** Clinical and imaging characteristics between good/poor outcomes of patients

	OR	95%CI	Partial regression coefficient	Standard error	Wald	P
Age	1.077	0.967~1.201	0.074	0.060	1.521	0.177
NIHSS score	1.265	1.004~1.593	0.235	0.150	2.454	0.046
Infarct volume	0.980	0.940~1.022	-0.020	0.021	0.907	0.460
Distribution of DMVs						
Ipsilateral lesion	3.386	1.006~11.39	1.220	2.650	0.212	0.049
Contralateral lesion	0.769	0.239~2.470	-0.263	0.570	0.213	0.659

**Table 2:** Results of multivariate Logistic regression analysis of risk factors associated with poor outcome



**Figure 1:** Distributions of modified Rankin scale scores with different grading of ipsilateral deep medullary veins positive patients

## DISCUSSION

In clinical practice, the disability rate of acute anterior circulation cerebral infarction is high. Therefore, it is of great significance to find early prognostic markers and guide clinical treatment. Deep medullary vein is an important part of deep cerebral venous system, but it is difficult to detect by conventional MRI because of its small structure. SWI, with its high resolution, high signal-to-noise ratio and blood oxygen level dependence, improves the detection rate of cerebral venules, especially deep medullary veins<sup>[1-10]</sup>. With the discovery of DMVs and the increase of related research, people's understanding of this sign on SWI is gradually deepening. In recent years, it has been reported that DMVs not only can reflect the local microcirculation, but also can be used to evaluate the early clinical prognosis of acute cerebral infarction <sup>[7,11]</sup>, DMVs may prompt the prognosis of patients with acute cerebral infarction in the early stage of onset, which has an important reference value for clinical selection of appropriate treatment plan and early intervention for patients

Nowadays, There are the following mainstream views about the formation mechanism of DMVs<sup>[12-13]</sup>; one is that the volume of small veins increases and dilates due to thrombosis and blood stasis in the responsible vessels of the infarct; the other is that the oxygen uptake ratio in the local low perfusion area of the infarct increases, resulting in the imbalance of oxygen supply and demand, which is manifested in the increase of the proportion of deoxygenated blood in the blood vessels, resulting in the low signal vein shadow in the deep medulla on SWI.

The distribution of DMVs in SWI of patients with acute anterior circulation cerebral infarction showed three patterns: DMVs appeared on the same side of the lesion. DMVs appeared on the contralateral side of the lesion, and SWI was normal. In this study, 36 cases (72%) of 50 patients were positive for DMVs, including 19 cases on the same side of the lesion and 17 cases on the opposite side of the lesion. It can be seen that the positive rate of DMVs on SWI is not low.

According to the mRS score, the patients were divided into good prognosis group and poor prognosis group. It was found that There were significant differences in age, NIHSS score, infarct volume and DMVs distribution between the good prognosis group and the poor prognosis group ( $P < 0.05$ ), These factors have different degrees of influence on the clinical prognosis of patients. The effect of NIHSS score on short-term

clinical prognosis has been confirmed in many studies<sup>[14]</sup>. Further multivariate logistic regression analysis showed that ipsilateral DMVs (OR = 3.38, 95% CI: 1.006-11.393, P = 0.049) was an independent risk factor for poor prognosis. Then, the ipsilateral DMVs were classified. according to box plot analysis, the patients with DMVs grade 3 had higher mRS score (average 4 points), indicating that the worse the prognosis. The formation of ipsilateral DMVs is mainly due to local blood flow disorder and venous blood stasis on the infarct side, resulting in dilation of deep medullary venules in the ipsilateral cerebral hemisphere. Continuous decompensation of infarct leads to disturbance of energy metabolism of brain cells and increase of oxygen uptake ratio of local brain tissue, which makes ipsilateral deep medullary vein develop on SWI. Therefore, if local blood supply cannot be restored in a short period of time, the prognosis will be poor<sup>[14,15]</sup>. In addition, combined with the formation mechanism of ipsilateral DMVs, it can be inferred that the grade 3 of ipsilateral DMVs is essentially the manifestation of excessive deoxyhemoglobin in the vein of the lesion side and severe local hypoxia. Clinically, it is mostly related to the increased hypoxic changes of surrounding tissues after local cytotoxic edema in the acute phase of cerebral infarction, which is the manifestation of poor prognosis<sup>[16]</sup>. At this time, endovascular treatment within the time window is of great help to improve the prognosis of patients.

In addition, multivariate logistic regression analysis did not find that the contralateral DMVs had a direct predictive value on the clinical prognosis of patients (P = 0.659), but from the clinical outcome, the positive rate of contralateral DMVs was 44.8% in the good prognosis group and only 19.0% in the poor prognosis group. The formation of contralateral DMVs may be related to the increased local blood flow and better collateral circulation <sup>[13,17-18]</sup>. After cerebral infarction, if the cerebral tissue has good collateral circulation compensation, the blood supply is restored in time, and there is no change of oxygen uptake ratio in the injured area, the ipsilateral deep medullary vein can not be visualized on SWI, while the contralateral blood flow compensates for the ischemic area of ipsilateral infarction through Willis ring, so the oxygen uptake ratio increases, forming different signal contrast on SWI, which is manifested as contralateral DMVs.

To sum up, this study found that DMVs is a significant sign on SWI in patients with acute anterior circulation cerebral infarction, and has a certain predictive value for the clinical prognosis of patients: the presence of ipsilateral DMVs on SWI can independently predict poor prognosis, and the occurrence of contralateral DMVs of lesions indicates a good prognosis. However, there are still some deficiencies in this study, such as no follow-up of SWI for patients, lack of dynamic change data of DMVs distribution, and limited sample size of the study. Therefore, it is necessary to increase the number of cases and obtain more comprehensive clinical data to evaluate the clinical prognosis of patients.

## REFERENCES

1. Heyn C, Alcaide-Leon P, Bhamtha A, et al. Susceptibility-weighted imaging in neurovascular disease[J]. Top Magn Reson Imaging, 2016, 25(2): 63-71. DOI: 10.1097/RMR.000000000000079.

2. Luo S, Yang L, Wang L. Comparison of susceptibility-weighted and perfusion-weighted magnetic resonance imaging in the detection of penumbra in acute ischemic stroke[J]. *J Neuromdiol*, 2015, 42(5): 255-260. DOI: 10.10160/j.neumd.2014.07.002.
3. Patzig M, Feddersen B, Haegler K et al. Susceptibility-weighted angiography visualizes hypoxia in cerebral veins[J]. *Invest Radiol*, 2015, 50(6):397-400. DOI: 10.1097/RLI.000000000000143.
4. Morita N, Harada M, Uno M, et al. Ischemic findings of T2+-weighted 3-tesla Mlu in acute stroke patients[J]. *Cerebrovasc Dis*, 2008, 26(4):367-375. DOI: 10.1159/000151640.
5. Hofie N, Mofikawa M, Nozaki A, et al. "Brush Sign" on susceptibility-weighted MR imaging indicates the severity of moyamoya disease[J]. *AJNR Am J Neuroradiol*, 2011, 32(9): 1697-1702. DOI: 10.3174/ajnr.A2568.
6. Mucke J, Mohlenbruch M, Kickingereder P, et al. Asymmetry of deep medullary veins on susceptibility weighted MRI in patients with acute MCA stroke is associated with poor outcome [J]. *PLoS One*, 2015, 10(4): e0120801. DOI: 10.1371/journal.pone.0120801.
7. Lou M, Chen Z, Wan J, et al. Susceptibility-diffusion mismatch predicts thrombolytic outcomes: a retrospective cohort study[J]. *AJNR Am J Neuroradiol*, 2014, 35(11):2061-2067. DOI: 10.3174/ajnr.A4017.
8. Payabvash S, Benson JC, Taleb S, et al. Prominent conical and medullary veins on susceptibility-weighted images of acute ischaemic stroke[J]. *Br J Radiol*, 2016, 89(1068): 20160714. DOI: 10.1259/bjr.20160714.
9. Kasner SE. Clinical interpretation and use of stroke scales[J]. *Lancet Neurol*, 2006, 5(7): 603-612. DOI: 10.1016/S1474-4422(06)70495-1.
10. Egger K, Dempfle AK, Yang S, et al. Reliability of cerebral vein volume quantification based on susceptibility-weighted imaging[J]. *Neuroradiology*, 2016, 58(9): 937-942. DOI: 10.1007/s00234-016-1712-z.
11. Terasawa Y, Yamamoto N, Morigaki R, et al. Brush sign on 3-T T2\*-weighted MRI as a potential predictor of hemorrhagic transformation after tissue plasminogen activator therapy[J]. *Stroke*, 2014, 45(1):274-276. DOI: 10.1161/STROKEAHA.113.002640.
12. Taoka T, Fukusumi A, Miyasaka T, et al. Structure of the medullary veins of the cerebral hemisphere and related disorders[J]. *Radiographics*, 2017, 37(1): 281-297. DOI: 10.1148/rg.2017160061
13. Yu X, Yuan L, Jackson A, et al. Prominence of medullary veins on susceptibility-weighted images provides prognostic information in patients with subacute stroke[J]. *AJNR Am J Neuroradiol*, 2016, 37(3):423-429. DOI: 10.3174/ajnr.A4541.
14. Tan S, Chang SW, Song B, et al. Predictive value of the early modified National Institutes of Health Stroke Scale for the prognosis of ischemic stroke[J]. *Chin J Neurol*, 2012, 45(3): 154-157. DOI:10.3760/cma.j.issn.1006-7876.2012.03.003.
15. Wang Y, Shi T, Chen B, et al. Prominent hypointense vessel sign on susceptibility-weighted imaging is associated with clinical outcome in acute ischaemic stroke[J]. *Eur Neurol*, 2018, 79(5-6): 231-239. DOI: 10.1159/000488587.



16. Meoded A, Poretti A, Benson JE, et al. Evaluation of the ischemic penumbra focusing on the venous drainage : the role of susceptibility weighted imaging(SWI) in pediatric ischemic cerebral stroke[J]. J Neuroradiol, 2014, 41(2): 108-116. DOI: 10.1016/j.neurad.2013.04.002.
17. Kaku Y, lihara K, Nakajima N, et al. Cerebral blood flow and metabolism of hyperperfusion after cerebral revascularization in patients with moyamoya disease[J]. J CerebBlood Flow Metab, 2012, 32(11): 2066-2075. DOI: 10.1038/jcbfm.2012.110.
18. Bivard A, Stanwell P, Levi C, et al. Arterial spin labeling identifies tissue salvage and good clinical recovery after acute ischemic stroke[J].J Neuroimaging,2013,23(3): 391-396.DOI:10.1111j.1552-6569.2012.00728.x.