



Deep medullary veins as an important imaging indicator of poor prognosis in acute ischemic stroke: a retrospective cohort survey

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Background: The deep medullary veins (DMVs), which constitute a component of the intracerebral venous circulation system and are part of intracerebral reperfusion mechanisms, have been suggested as a novel imaging marker for cerebral white matter hypersignal and cerebral small vessel disease based on their discontinuous and reduced visual representation. However, the correlation between the number and continuity of visible DMVs and the poor prognosis of acute ischemic stroke (AIS) remains undefined. Magnetic susceptibility-weighted imaging was applied in this study to assess the distribution and structural characteristics of DMVs in patients with AIS and to investigate its relationship with the poor prognosis of those with AIS.

Methods: This retrospective study included 90 patients diagnosed with AIS in the middle cerebral artery region by the Neurology Department of Liaoning Provincial People's Hospital. Clinical, laboratory, and cranial magnetic resonance imaging data were collected. After the 3-month follow-up visit, patients were dichotomized into good (0–2 points) and poor (≥ 3 points) prognosis groups based on the modified Rankin Scale score, and the DMV imaging characteristics were evaluated using a 3-level visual rating scale. The association between DMV and AIS prognosis was determined through Mann-Whitney test and multivariate logistic regression analysis.

Results: In univariate analysis, factors that were statistically significant between the different prognostic groups were DMV score ($P=0.007$), DMV symmetry ($P=0.016$), infarct size ($P=0.029$), and admission National Institutes of Health Stroke Scale (NIHSS) score ($P<0.001$). DMV score had a positive correlation with NIHSS score, ($r_s=0.209$; $P=0.048$). Logistic regression analysis showed that the DMV score [odds ratio (OR), 1.356; 95% confidence interval (CI): 1.114–1.650; $P=0.002$], NIHSS score (OR, 1.280; 95% CI: 1.117–1.466; $P<0.001$), and fasting glucose (OR, 1.220; 95% CI: 1.023–1.456; $P=0.027$) were risk factors for poor prognosis in those with AIS.

Conclusions: Discontinuity in DMV visualization was found to be associated with an unfavorable prognosis for patients AIS. The visual assessment of DMV through susceptibility-weighted imaging has the

potential to predict AIS prognosis and furnish valuable insights for clinical treatment.

Keywords: Ischemic stroke; susceptibility-weighted imaging (SWI); deep medullary veins (DMVs)

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Introduction

Acute ischemic stroke (AIS) refers to brain tissue in the blood supply area becoming ischemic due to occlusion or narrowing of an intracranial artery, leading to brain cell necrosis. It is associated with a poor prognosis, a high disability rate, and a recurrence rate of about 11–12%, and is currently recognized as the second leading cause of death worldwide (1,2). The prognosis of AIS is influenced by various factors, such as age, hypertension, diabetes mellitus, hyperuricemia (3), proprotein convertase subtilisin/kexin type 9 (PCSK9) levels, and genetic polymorphisms (4). The neuroimaging factors related to AIS include ischemic semidark zone, infarct size, hemorrhagic transformation, and collateral circulation formation. Among these, collateral circulation may be particularly significant, as it improves the reperfusion rate of brain tissue, reduces the rate of hemorrhagic transformation, decreases mortality, and ultimately leads to a better clinical outcome for AIS patients (5-8).

The current assessment of collateral circulation is divided into structural and functional assessments, multiphase computed tomography angiography (mCTA), magnetic resonance angiography (MRA), susceptibility-weighted imaging (SWI), and digital subtraction angiography (DSA), with the latter comprising computed tomography perfusion (CTP), arterial spin labeling (ASL), and magnetic resonance (MR) perfusion-weighted imaging (PWI). In contrast, the advantage of SWI is the display of tiny intracerebral veins, the sensitivity to paramagnetic substance, the accurate reflection of changes in deoxygenated hemoglobin content (9), and the ability to reveal prominent veins that contain high levels of deoxyhemoglobin. When there is a mismatch between the oxygen supply and oxygen demand of brain tissue in the hypoperfused area of AIS, the soft meningeal or medullary veins on the infarcted side appear dilated and enlarged compared to the healthy side of the same layer, thus reflecting poor compensation of the collateral circulation; therefore, these 2 manifestations are currently considered to be imaging markers of the status

of the collateral circulation (10-15). However, the imaging evaluation criteria regarding collateral circulation have not been standardized, and the evaluation of the collateral circulation by the soft meningeal veins remains problematic in clinical application.

Over recent years, the small cerebral veins involved in the formation of the deep lateral circulation in the brain have gradually received increased attention, especially the deep medullary veins (DMVs), which drains the white matter of the lateral paraventricular brain and has been widely used in the study of various diseases. DMVs are located in the periventricular white matter region, with the vast majority being distributed in the head and body of the caudate nucleus or next to the body of the lateral ventricle (16). Computed tomography (CT) and conventional MR examination sequences are unable to show DMVs, and they are only visible on SWI images. The degree of DMV visualization is subject to influence by intracerebral blood flow, making it capable of reflecting brain tissue reperfusion and the quality of collateral circulation from a venous perspective after the onset of AIS. Previous studies (16-18) have demonstrated that a reduced number of DMV visualizations can be used as an imaging marker for cerebral white matter hypersignal and cerebral small vessel disease. However, whether DMV morphological changes and reduced visualizations can be utilized as imaging markers for AIS remains to be investigated.

The objective of this study was thus to evaluate the distribution and morphological features of DMVs in the brains of patients with AIS using SWI imaging. First, visualization scoring criteria were developed based on the degree of DMV visualization continuity, and then symmetry was judged based on the degree and numbers of DMV expansion so as to determine whether DMVs could be a new imaging index to predict the prognosis of AIS from various perspectives. The study aims to provide robust support for the clinical management and evaluation of patients with AIS. We present this article in accordance with the STROBE reporting checklist (available at <https://qims.amegroups.com/>

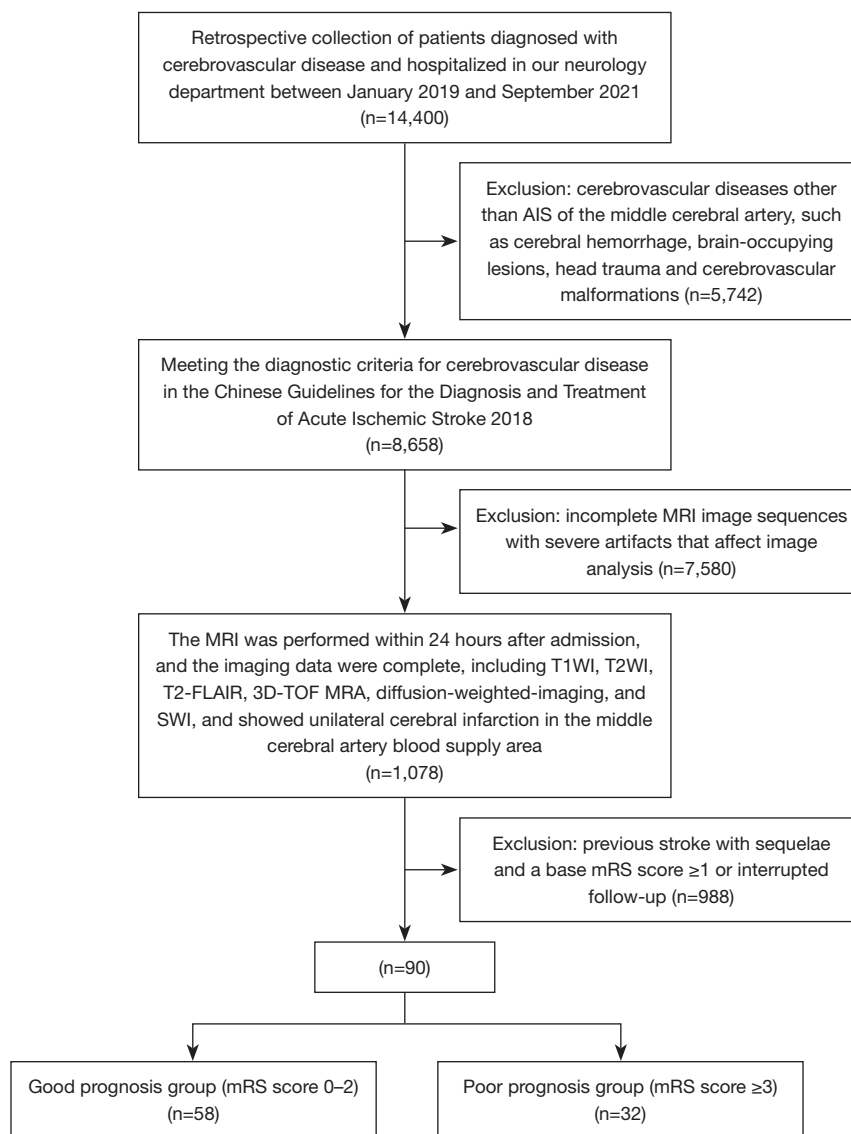


Figure 1 Case screening flowchart. AIS, acute ischemic stroke; MRI, magnetic resonance imaging; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; FLAIR, fluid-attenuated inversion recovery; 3D-TOF, 3-dimensional time of flight; MRA, magnetic resonance angiography; SWI, susceptibility-weighted imaging; mRS, modified Rankin Scale.

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Methods

Study design and population

A retrospective cohort study was conducted on patients who were hospitalized in the Department of Neurology of Liaoning Provincial People's Hospital and diagnosed with AIS between January 2019 and September 2021. After

screening based on inclusion and exclusion criteria was applied, a total of 90 individuals were included in this study (*Figure 1*). The study was conducted in accordance with the Declaration of Helsinki (revised in 2013) and was approved by the medical ethics committee of The People's Hospital of Liaoning Province (No. 2022-K001). Informed consent was obtained from all individual participants. The sample size was calculated using the 10-fold events per variable (EPV) principle, which is a common method for multifactorial regression analysis (19).

Table 1 MR scan parameters by sequence

Parameters	TR (ms)	TE (ms)	FOV (mm)	Layer thickness (mm)	Matrix
T1WI	1,750	25	240×240	6	512×512
T2WI	5,690	105.8	240×240	6	512×512
FLAIR	8,400	93.5	240×240	5	512×512
DWI	3,000	65.4	240×240	6	256×256
SWI	44	23	240×240	1	512×512
MRA	21	2.5	220×220	1.4	512×512

MR, magnetic resonance; TR, repetition time; TE, echo time; FOV, field of vision; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; FLAIR, fluid-attenuated inversion recovery; DWI, diffusion-weighted imaging; SWI, susceptibility-weighted imaging; MRA, magnetic resonance angiography.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (I) patients meeting the diagnostic criteria for cerebrovascular disease in the Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2018 (20); and (II) patients who underwent magnetic resonance imaging (MRI) performed within 24 h after admission with complete imaging data, including T1-weighted imaging (T1WI), T2-weighted imaging (T2WI), fluid-attenuated inversion recovery (FLAIR), 3-dimensional time-of-flight (3D-TOF) MRA, diffusion-weighted imaging (DWI), and SWI that showed unilateral cerebral infarction in the middle cerebral artery blood supply area.

The exclusion criteria were as follows: (I) patients with cerebrovascular diseases other than AIS, such as cerebral hemorrhage, brain-occupying lesions, head trauma, and cerebrovascular malformations; (II) MRI images showing severe artifacts that affect imaging analysis; (III) previous stroke with sequelae and a base modified Rankin Scale (mRS) score ≥ 1 ; (IV) inadequate clinical data or interrupted follow-up.

MRI examination

A Discovery 750 3.0T MRI scanner with an 8-channel coil in the head (GE HealthCare) was applied to scan the patient. The patient was scanned in the supine position, head first, with the scan baseline parallel to the anterior-posterior joint line, up to the cranial vault and down to the level of the greater occipital foramen. The scan sequences included conventional sequences and DWI and SWI sequences. The scanning parameters of each sequence are shown in *Table 1*. All scanned data were uploaded to the

ADW 4.7 workstation (GE HealthCare) for postprocessing and analysis.

Baseline data and imaging index

The baseline data were obtained through electronic medical records. The clinical parameters included in the analysis were age at admission, sex, systolic and diastolic blood pressure, fasting glucose, cholesterol, total homocysteine (tHcy), National Institutes of Health Stroke Scale (NIHSS) score at admission, and mRS score obtained via telephone or outpatient follow-up at 3 months. Based on the mRS score, patients were divided into 2 groups: those with good prognosis (0–2 points) and those with poor prognosis (≥ 3 points). Imaging metrics analyzed included DMV symmetry at admission, DMV score, scores for white matter hyperintensities (WMHs), paraventricular WMHs (PVWMHs), deep WMHs (DWMHs), and infarct size. All image data analysis was performed by 3 radiologists with more than 10 years of experience in reviewing cerebrovascular disease. In cases where there was disagreement, agreement was reached after discussion.

Imaging index scoring criteria

DMV visual assessment

According to the anatomical distribution characteristics of the DMVs, the centrum semiovale level and the parietal ventricular level were selected for observation, and 6 regions were divided according to the above levels (*Figure 2*), including the bilateral frontal regions, parietal regions, and occipital regions. The DMV score was then evaluated within each region, and the sum was added as

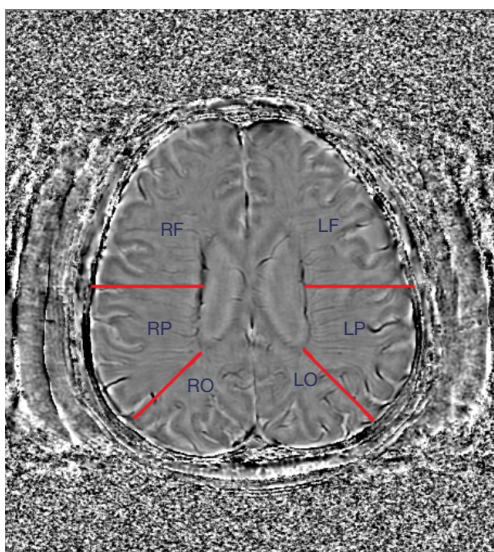


Figure 2 DMV scoring area division map. Divided into six regions: LF region, RF region, LP region, RP region, LO region, and RO region. DMV, deep medullary vein; LF, left frontal; RF, right frontal; LP, left parietal; RP, right parietal; LO, left occipital; RO, right occipital.

the final score, based on the visual scoring criteria for DMVs proposed in the literature (*Figure 3*) (17,21). The scores were calculated as follows: (I) 0 points = each vein is continuous, with a uniform signal; (II) 1 point = each vein is continuous, but 1 or more veins have an uneven signal; (III) 2 points = 1 or more veins are discontinuous and show punctiform low signal; and (IV) 3 points = no continuous veins are observed. The DMV visual score ranges from 0 to 18, with higher scores indicating intermittent and unclear vein display.

DMV symmetry was indicated as follows: both lateral parietal ventricles showed DMVs in the same area and were similarly dilated, with a difference in number of no more than 5 (*Figure 4*).

WHM score

On the FLAIR sequence according to the Fazekas scale (0–6 points) (22), the PVWMH and DWMH were scored separately, and the scores of the 2 components were added together to form the WMH score. The PVWMH score was determined as follows: 0, no lesion; 1, cap or pencil-like thin lesion; 2, a smooth halo of the lesion; and 3, irregular paraventricular high signal extending into the DWM. Meanwhile, the DWMH score was determined as follows, 0, no lesion; 1, punctate lesion; 2, lesion starting to fuse; and 3,

lesion extensively fused.

Infarct area grouping

The patients were staged according to the maximum infarct size corresponding to the symptoms shown on T2WI: (I) lacunar cerebral infarction: $\leq 1.5 \text{ cm}^2$; (II) small infarction: $1.6\text{--}3.0 \text{ cm}^2$; (III) medium infarction: $3.1\text{--}5.0 \text{ cm}^2$ and less than one lobe area; (IV) large infarction: more than one lobe or greater than 5.0 cm^2 .

Statistical methods

All of the data were analyzed using SPSS 23.0 (IBM Corp.). The results are reported using descriptive statistics for continuous variables, including mean and standard deviation for normally distributed data and median and interquartile range (IQR) for nonnormally distributed data. Categorical data are reported as frequencies and percentages and were analyzed using the independent samples *t*-test, Mann-Whitney test, Fisher exact test, and Pearson chi-squared test. Correlation analysis was performed with Spearman correlation test. The forward Ward method was used and corrected for confounding factors. Subsequently, variables with $P < 0.15$ and factors that might cause poor prognosis in acute cerebral infarction (despite $P > 0.15$) were selected in the univariate analysis for inclusion in the multivariate logistic regression analysis. The level of statistical significance was set at a two-tailed *P* value of less than 0.05.

Results

Patient baseline information

A total of 90 patients with AIS were included in this study, comprising 63 males and 27 females, with a mean age of 65.9 ± 9.8 years. In the good prognosis group, there were 58 cases (64.4%), including 42 males and 16 females, with a mean age of 64.9 ± 9.9 years; in the poor prognosis group, there were 32 cases (35.6%), including 21 males and 11 females, with a mean age of 67.7 ± 9.5 years. Among all cases, 18 were treated with recombinant tissue plasminogen activator (rt-PA), 2 with intraarterial thrombectomy (IAT), 2 with rt-PA followed by IAT, and 68 with antithrombotic drugs.

As shown in *Table 2*, there were statistical differences in the admission NIHSS score, DMV symmetry, DMV score, and infarct size between the 2 groups but no statistical differences in age, sex, diastolic blood pressure, fasting

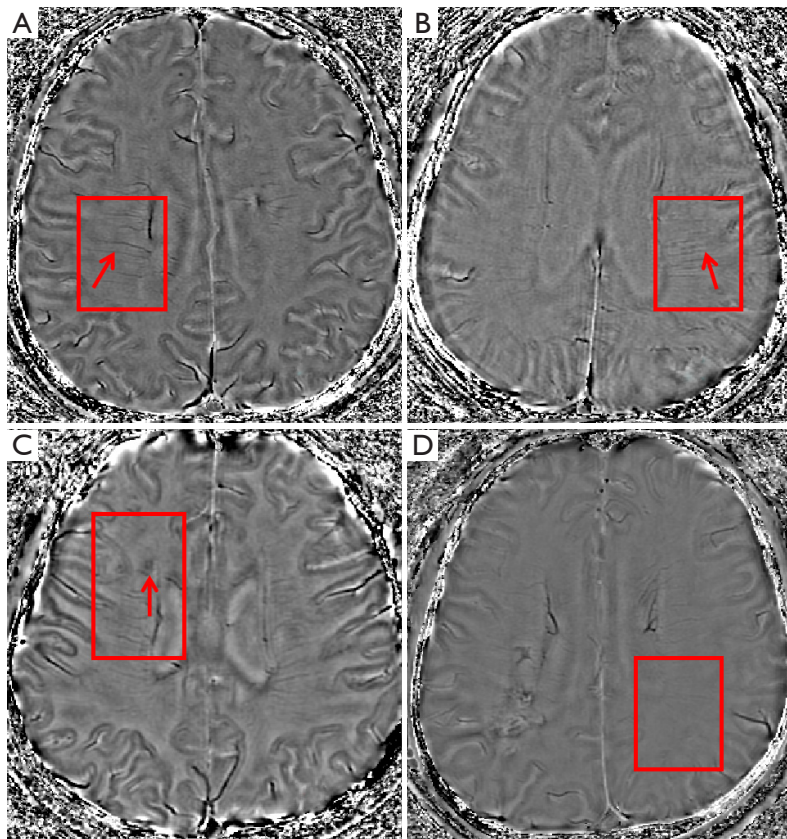


Figure 3 Schematic of the DMV scoring criteria. (A) DMV 0 points: each vein is continuous with a uniform signal; the box shows part of the RF and all of RP area; and the arrow shows the continuous and uniform development of DMV in the RP area. (B) DMV 1 point: each vein is continuous but 1 or more veins have an uneven signal, the box shows part of the LF and all of the LP area, and the arrow shows the DMV development is continuous with an uneven signal in the LP area. (C) DMV 2 points: 1 or more veins are discontinuous and show punctiform low signal, the box shows all the RF and part of the LP region, and the arrow shows DMV discontinuity in the RF region as a point-like low signal. (D) DMV 3 points: no continuous veins are observed, and the box shows blurring of the DMVs in the LO area. DMV, deep medullary vein; RF, right frontal; RP, right parietal; LF, left frontal; LP, left parietal; LO, left occipital.

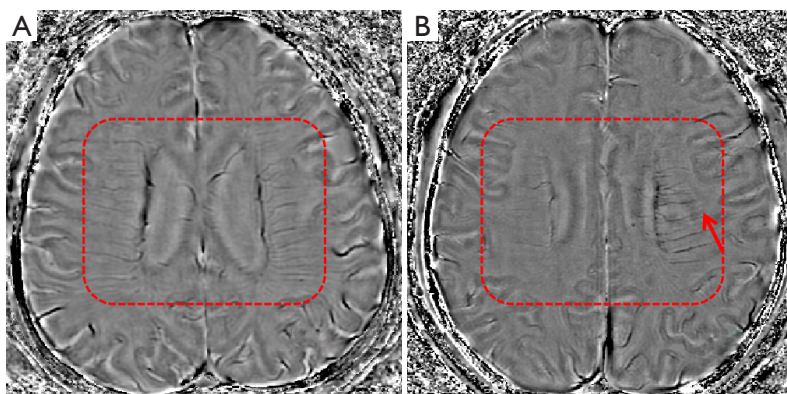


Figure 4 Schematic of DMV symmetry determination. (A) The dotted box shows DMV symmetric distribution, with the degree and number of DMV visualization on both sides of the lateral ventricles being close. (B) The dotted box shows DMV asymmetric distribution, uneven thickening, and an increase in the number of DMVs on the left side of the lateral ventricle (arrow). DMV, deep medullary vein.

Table 2 Clinical data and imaging features of the different prognostic groups

Variables	Good prognosis group (n=58)	Poor prognosis group (n=32)	Statistical values ($\chi^2/t/Z$)	P value
Gender			0.453	0.501
Male	42 (72.4)	21 (65.6)		
Female	16 (27.6)	11 (34.4)		
Age (years)	64.9±9.9	67.7±9.5	-1.300	0.197
Admission NIHSS score	3	8	-5.070	<0.001
Systolic blood pressure (mmHg)	161.1±24.2	163.2±22.9	-0.378	0.700
Diastolic blood pressure (mmHg)	90.2±14.2	90.7±15.0	-0.171	0.865
Total homocysteine (μ mol/L)	21.9±15.5	20.3±11.0	0.510	0.611
Cholesterol (mmol/L)	4.6±1.1	4.5±1.3	0.526	0.600
Fasting glucose (mmol/L)	6.7±2.9	7.5±2.9	-1.384	0.170
Mode of treatment			1.463	0.750
rt-PA only	13 (22.4)	5 (15.7)		
IAT only	1 (1.7)	1 (3.1)		
rt-PA followed by IAT	1 (1.7)	1 (3.1)		
Antithrombotic drugs	43 (74.2)	25 (78.1)		
Infarct area			9.022	0.029
Lacunar cerebral infarction	27 (46.5)	7 (21.8)		
Small infarction	12 (20.7)	5 (15.6)		
Medium infarction	3 (5.2)	6 (18.8)		
Large infarction	16 (27.6)	14 (43.8)		
DMV score	2	4	-2.719	0.007
DMV symmetry			5.792	0.016
DMV symmetry	42 (72.4)	15 (46.9)		
DMV asymmetry	16 (27.6)	17 (53.1)		
WMH score	3	3.5	-1.403	0.161
PVWMH score	2	2	-1.545	0.122
DWMH score	1	1	-0.460	0.646

Data are presented as mean \pm standard deviation or n (%). NIHSS, National Institutes of Health Stroke Scale; rt-PA, recombinant tissue plasminogen activator; IAT, intra-arterial thrombectomy; DMV, deep medullary vein; WMH, white matter hyperintensity; PVWMH, paraventricular white matter hyperintensity; DWMH, deep white matter hyperintensity.

glucose, cholesterol, tHcy, PVWMH score, WMH score, or DWMH score. The results showed that the median DMV scores in patients with poor prognosis were higher than those with good prognosis, implying that DMV morphological discontinuities and inhomogeneous signal were more prominent. In the good prognosis group,

72.4% had symmetrical DMV distribution and 27.6% had asymmetrical distribution, while in the poor prognosis group, 46.9% had symmetrical DMV distribution and 53.1% had asymmetrical distribution, indicating a higher occurrence of asymmetrical DMV distribution in the poor prognosis group. The highest percentage of lacunar cerebral

Table 3 Multifactorial logistic regression analysis of factors influencing poor prognosis in patients with AIS

Plaque characteristics	P value	OR (95% CI)
DMV score	0.002	1.356 (1.114–1.650)
NIHSS score	<0.001	1.280 (1.117–1.466)
Fasting glucose	0.027	1.220 (1.023–1.456)

AIS, acute ischemic stroke; OR, odds ratio; CI, confidence interval; DMV, deep medullary vein; NIHSS, National Institutes of Health Stroke Scale.

infarction was found to be 46.5% in the good prognosis group, while the highest percentage of large infarction was 43.8% in the poor prognosis group ($\chi^2=9.022$; $P=0.029$). DMV score had a positive correlation with NIHSS score ($r_s=0.209$; $P=0.048$).

Logistic regression analysis

Age, diastolic blood pressure, fasting glucose, admission NIHSS score, DMV symmetry, DMV score, PVWMH score, and infarct area were selected for inclusion in the multivariate logistic regression analysis, which showed that the logistic model was statistically significant ($\chi^2=32.063$; $P<0.05$). As shown in *Table 3*, the independent risk factors for poor prognosis of AIS were DMV score [odds ratio (OR), 1.356; 95% confidence interval (CI): 1.114–1.650; $P=0.002$], NIHSS score (OR, 1.280; 95% CI: 1.117–1.466; $P<0.001$), and fasting glucose (OR, 1.220; 95% CI: 1.023–1.456; $P=0.027$).

Discussion

The principal results of our study are as follows: (I) DMV can be used as an imaging indicator of AIS prognosis, and patients with asymmetric distribution of DMV and discontinuous visualization of DMVs have a poor prognosis; (II) fasting glucose values are higher in patients with poor AIS prognosis.

In addition to acute stroke studies, the DMV marker is currently being applied in studies of cerebral white matter hypersignal, smog, and cerebral small vessel disease. For example, the DMVs are involved in the pathogenesis and prognosis of cerebral white matter hypersignal as a draining vein. There is also a noninflammatory periventricular venous lesion in the WMH, which arises due to collagen deposition in the wall, resulting in the narrowing or even

occlusion and rupture of the lumen of the vein. This venous lesion leads to local brain tissue ischemia and increases the volume of white matter hypersignal in the lateral ventricles (17,21,23,24). The characteristics of DMVs are associated with the severity of smog and cerebral small vessel disease: the greater the number of dilatations, the lower the cerebral blood flow and cerebrovascular reserve in the middle cerebral artery supply area (18,25). In contrast, in cerebral venous thrombotic disease, the brush sign of DMV expansion formation is associated with ipsilateral brain parenchymal lesions, the degree of thrombosis, and the severity of focal neurological deficits (26).

In recent years, SWI sequences have been widely used in clinical research; in stroke, they are mainly used for the prediction of hemorrhagic transformation after ischemic stroke as well as the establishment and assessment of collateral circulation. SWI combined with DWI can be applied to assess infarct area growth; however, developing methods of effectively monitoring the collateral circulation remodeling in the infarct area is a key issue in the clinical treatment of cerebral infarction. Verma *et al.* (27) showed the importance of soft cerebral collateral circulation on brain tissue perfusion, validating the importance of collateral circulation in stroke. The assessment of collateral circulation plays an important role in treatment decisions. The main imaging indicators studied in collateral circulation are asymmetric cortical vein (ACV) sign and FLAIR high-signal vascular sign (HVS), among which HVS can reflect the status of soft meningeal collateral vessels (28,29). A previous study has confirmed there to be a correlation between ACV, HVS, and DMV (30), but overall, there are relatively few studies on DMVs.

Our research determined that DMVs are a crucial factor in the prognosis of patients with AIS. A high DMV score predicts poor prognosis for patients with AIS. In the poor prognosis group, DMV demonstrated inhomogeneous signals, visual discontinuity, and blurred displays. The visibility of veins on SWI is dependent on the degree of deoxyhemoglobin within the blood (17), and the decrease in cerebral blood flow leads to an increase in oxygen uptake by brain tissue and an increase in the amount of deoxyhemoglobin within the blood, thus resulting in a significantly low or inhomogeneous signal of venous appearances on SWI images (31). When the collateral circulation is well compensated, the ischemic brain tissue maintains a certain perfusion pressure and blood flow through compensatory blood flow. Although the oxygen content in local capillaries and small veins is lower than

that in normal brain tissue, their oxygen uptake fraction is improved and deoxyhemoglobin content is relatively low, so the incidence of insignificant DMV dilation or inhomogeneous low signal is low (12,32,33). Previous studies have also provided explanations from a pathological point of view (16,34), suggesting that with an increase in venous wall thickening and luminal narrowing, luminal occlusion may occur as the final stage of disruption of DMVs, leading to discontinuous, speckled visualization or blurring of DMVs. Therefore, we conducted a dual examination in this study in terms of DMV dilatation symmetry and vein morphology. In addition, venous outflow is affected by varying degrees of reduced arterial flow, and slow venous return is accompanied by collateral circulation formation when arteries are obstructed; therefore, we can infer that the degree of upstream arterial ischemia also affects the change in DMV score. To conclude, a low DMV venous inhomogeneous signal may be the result of altered venous hemodynamics or venous obstruction (35), and its expansion may reflect the poor compensatory capacity of the intracerebral collateral circulation.

Several studies indicate that asymmetric signs of the soft meningeal vein or DMV visualization in SWI images can predict a poor prognosis (36-38); however, these studies did not exclude the effect of other confounding factors on the outcome variables. The present study was refined on this basis, and we found that the DMV asymmetric signs were associated with AIS prognosis in univariate analysis, but logistic regression analysis showed that they were not an influential factor in the prognosis of AIS. The reasons for this may be related to the definition of DMV symmetry and the time interval between the onset and completion of the MR examination. In the present study, we defined asymmetric distribution as the degree of bilateral lateral paraventricular DMV being different, and we did not quantify the degree of DMV development; moreover, we did not limit the time window between onset and MR examination, so we speculated that the change in the degree of DMV development was not obvious because the change in brain tissue hypoperfusion was mild and because the increase in deoxyhemoglobin content was not significant at the early stage of infarction. In this study, most patients had significant DMVs on the affected side, and only a few patients had significant DMVs on the healthy side. We speculate that this may be due to the following reasons: first, the brain tissue on the infarct side is hypoperfused, and the intravascular deoxygenated hemoglobin content is increased, which aggravates the DMV shadowing on the

affected side; second, with regard to the pathogenesis of WMH, if the periventricular venous lumen is obstructed or ruptured, the DMV dilation is not significant or the DMV shadowing is reduced at the time of infarction even if the oxygen uptake rate of the brain tissue on the affected side is increased (39); third, the collateral circulation within the brain tissue on the infarct side is well compensated, and the intravascular deoxygenated hemoglobin content is relatively low and thus not significantly dilated.

The reason that WMH was not found to be an imaging factor for AIS prognosis in this study is because the Fazekas scale scoring scale used in this study is too superficial and sufficiently refined, for example, in the aspect of volumetric measurements. Nonetheless, the relationship between WMH as an MRI imaging marker of cerebral small vessel disease and the prognosis of AIS warrants further in-depth study.

In this study, the prognosis of AIS patients was used as the outcome variable to analyze the factors related to prognosis. The findings suggest that NIHSS, DMV score, and fasting glucose are factors affecting prognosis. However, it should be noted that the clinical factors included were not comprehensive, with the focus mainly being on the analysis of the DMV imaging index, and further grading of fasting glucose or qualification of the glycemic control and medication for patients was not applied. Nonetheless, previous studies (40,41) have confirmed that fasting glucose is one of the factors of AIS prognosis and that hyperglycemia is associated with poor prognosis, which is consistent with the results of this study.

Conclusions

DMVs constitute a crucial indicator of poor prognosis in patients with AIS. DMV score, as evaluated using the 3-level visualization scale, can serve as a predictor of poor prognosis, offering valuable information for early assessment of a patient's clinical situation and providing a basis for determining clinical treatment plans.

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Footnote

Reporting Checklist: The authors have completed the

STROBE reporting checklist. Available at <https://qims.amegroupp.com/article/view/10.21037/qims-23-321/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://qims.amegroupp.com/article/view/10.21037/qims-23-321/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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the medical ethics committee of The People's Hospital of Liaoning Province (No. 2022-K001). Informed consent was obtained from all individual participants.

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References

1. Feigin VL, Brainin M, Norrving B, Martins S, Sacco RL, Hacke W, Fisher M, Pandian J, Lindsay P. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. *Int J Stroke* 2022;17:18-29.
2. Jang KM, Choi HH, Jang MJ, Cho YD. Direct Endovascular Thrombectomy Alone vs. Bridging Thrombolysis for Patients with Acute Ischemic Stroke : A Meta-analysis. *Clin Neuroradiol* 2022;32:603-13.
3. Chen W, Wang Y, Meng X, Pan Y, Wang M, Li H, Wang Y, Wang Y. Association of PCSK9 levels and genetic polymorphisms with stroke recurrence and functional outcome after acute ischemic stroke. *Ann Transl Med* 2022;10:729.
4. Bai H, Nie X, Leng X, Wang D, Pan Y, Yan H, Yang Z, Wen M, Pu Y, Zhang Z, Duan W, Ma N, Miao Z, Liu X, Lu Q, Wei Y, Liu L, Liu J. Increased serum uric acid level is associated with better outcome after endovascular treatment for acute ischemic stroke-a prospective cohort study. *Ann Transl Med* 2022;10:1111.
5. Leng X, Lan L, Liu L, Leung TW, Wong KS. Good collateral circulation predicts favorable outcomes in intravenous thrombolysis: a systematic review and meta-analysis. *Eur J Neurol* 2016;23:1738-49.
6. Wufuer A, Wubuli A, Mijiti P, Zhou J, Tuerxun S, Cai J, Ma J, Zhang X. Impact of collateral circulation status on favorable outcomes in thrombolysis treatment: A systematic review and meta-analysis. *Exp Ther Med* 2018;15:707-18.
7. Leng X, Fang H, Leung TW, Mao C, Xu Y, Miao Z, Liu L, Wong KS, Liebeskind DS. Impact of Collateral Status on Successful Revascularization in Endovascular Treatment: A Systematic Review and Meta-Analysis. *Cerebrovasc Dis* 2016;41:27-34.
8. Lee HJ, Roh HG, Lee SB, Jeon YS, Park JJ, Lee TJ, Jung YJ, Choi JW, Chun YI, Ki HJ, Cho J, Lee JS, Kim HJ. Collateral estimation by susceptibility-weighted imaging and prediction of functional outcomes after acute anterior circulation ischemic stroke. *Sci Rep* 2021;11:21370.
9. Liu YL, Yin HP, Qiu DH, Qu JF, Zhong HH, Lu ZH, Wang F, Liang MQ, Chen YK. Multiple hypointense vessels on susceptibility-weighted imaging predict early neurological deterioration in acute ischaemic stroke patients with severe intracranial large artery stenosis or occlusion receiving intravenous thrombolysis. *Stroke Vasc Neurol* 2020;5:361-7.
10. Horie N, Morikawa M, Nozaki A, Hayashi K, Suyama K, Nagata I. "Brush Sign" on susceptibility-weighted MR imaging indicates the severity of moyamoya disease. *AJNR Am J Neuroradiol* 2011;32:1697-702.
11. Sun W, Liu W, Zhang Z, Xiao L, Duan Z, Liu D, Xiong Y, Zhu W, Lu G, Liu X. Asymmetrical cortical vessel sign on susceptibility-weighted imaging: a novel imaging marker for early neurological deterioration and unfavorable prognosis. *Eur J Neurol* 2014;21:1411-8.
12. Mucke J, Möhlenbruch M, Kickingereider P, Kieslich PJ, Bäumer P, Gumbinger C, Purrucker J, Mundiyanapurath S, Schlemmer HP, Bendszus M, Radbruch A. Asymmetry of deep medullary veins on susceptibility weighted MRI in patients with acute MCA stroke is associated with poor outcome. *PLoS One* 2015;10:e0120801.
13. Jing L, Sui B, Shen M, Qin H, Gao P. Are prominent medullary veins better than prominent cortical veins as predictors of early clinical outcome in patients with acute ischemic stroke? *Diagn Interv Radiol* 2021;27:285-92.
14. Chen CY, Chen CI, Tsai FY, Tsai PH, Chan WP. Prominent vessel sign on susceptibility-weighted imaging

- in acute stroke: prediction of infarct growth and clinical outcome. *PLoS One* 2015;10:e0131118.
15. Duan Y, Xu Z, Li H, Cai X, Chang C, Yang B. Prominent deep medullary veins: a predictive biomarker for stroke risk from transient ischemic attack? *Acta Radiol* 2018;59:606-11.
 16. Chen X, Wei L, Wang J, Shan Y, Cai W, Men X, Liu S, Kang Z, Lu Z, Mok VCT, Wu A. Decreased visible deep medullary veins is a novel imaging marker for cerebral small vessel disease. *Neurol Sci* 2020;41:1497-506.
 17. Zhang R, Zhou Y, Yan S, Zhong G, Liu C, Jiaerken Y, Song R, Yu X, Zhang M, Lou M. A Brain Region-Based Deep Medullary Veins Visual Score on Susceptibility Weighted Imaging. *Front Aging Neurosci* 2017;9:269.
 18. Xu Z, Li F, Wang B, Xing D, Pei Y, Yang B, Duan Y. New Insights in Addressing Cerebral Small Vessel Disease: Association With the Deep Medullary Veins. *Front Aging Neurosci* 2020;12:597799.
 19. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996;49:1373-9.
 20. Peng B, Wu B. Chinese guidelines for diagnosis and treatment of acute ischemic stroke 2018. *Chinese Journal of Neurology* 2018;51:666-82.
 21. Yan S, Wan J, Zhang X, Tong L, Zhao S, Sun J, Lin Y, Shen C, Lou M. Increased visibility of deep medullary veins in leukoaraiosis: a 3-T MRI study. *Front Aging Neurosci* 2014;6:144.
 22. Wang Y, Liu X, Hu Y, Yu Z, Wu T, Wang J, Liu J, Liu J. Impaired functional network properties contribute to white matter hyperintensity related cognitive decline in patients with cerebral small vessel disease. *BMC Med Imaging* 2022;22:40.
 23. Rusanen H, Saarinen JT, Sillanpää N. Collateral Circulation Predicts the Size of the Infarct Core and the Proportion of Salvageable Penumbra in Hyperacute Ischemic Stroke Patients Treated with Intravenous Thrombolysis. *Cerebrovasc Dis* 2015;40:182-90.
 24. Marsh EB, Leigh R, Radvany M, Gailloud P, Llinas RH. Collaterals: an important determinant of prolonged ischemic penumbra versus rapid cerebral infarction? *Front Neurol* 2014;5:208.
 25. Lu J, Zhao Y, Li M, Ma L, Chen Y, Wang R, Ye X, Wang H, Chen X, Zhao Y. Clinical Implications of the "Brush Sign" in Susceptibility-Weighted Imaging for Moyamoya Disease. *Cerebrovasc Dis* 2021;50:147-55.
 26. Aguiar de Sousa D, Lucas Neto L, Jung S, Penas S, Panos L, Heldner MR, Fischer U, Arnold M, Canhão P, El-Koussy M, Ferro JM, Hakim A. Brush Sign Is Associated With Increased Severity in Cerebral Venous Thrombosis. *Stroke* 2019;50:1574-7.
 27. Verma RK, Hsieh K, Gratz PP, Schankath AC, Mordasini P, Zubler C, Kellner-Weldon F, Jung S, Schroth G, Gralla J, El-Koussy M. Leptomeningeal collateralization in acute ischemic stroke: impact on prominent cortical veins in susceptibility-weighted imaging. *Eur J Radiol* 2014;83:1448-54.
 28. Derraz I, Ahmed R, Benali A, Corti L, Cagnazzo F, Dargazanli C, Gascou G, Riquelme C, Lefevre PH, Bonafe A, Arquizan C, Costalat V. FLAIR vascular hyperintensities and functional outcome in nonagenarians with anterior circulation large-vessel ischemic stroke treated with endovascular thrombectomy. *Eur Radiol* 2021;31:7406-16.
 29. Bunker LD, Walker A, Meier E, Goldberg E, Leigh R, Hillis AE. Hyperintense vessels on imaging account for neurological function independent of lesion volume in acute ischemic stroke. *Neuroimage Clin* 2022;34:102991.
 30. Xu Z, Duan Y, Yang B, Huang X, Pei Y, Li X. Asymmetric Deep Medullary Veins in Patients With Occlusion of a Large Cerebral Artery: Association With Cortical Veins, Leptomeningeal Collaterals, and Prognosis. *Front Neurol* 2019;10:1292.
 31. Yu X, Yuan L, Jackson A, Sun J, Huang P, Xu X, Mao Y, Lou M, Jiang Q, Zhang M. Prominence of Medullary Veins on Susceptibility-Weighted Images Provides Prognostic Information in Patients with Subacute Stroke. *AJNR Am J Neuroradiol* 2016;37:423-9.
 32. Payabvash S, Benson JC, Taleb S, Rykken JB, Hoffman B, Oswood MC, McKinney AM. Prominent cortical and medullary veins on susceptibility-weighted images of acute ischaemic stroke. *Br J Radiol* 2016;89:20160714.
 33. Liu YL, Xiao WM, Lu JK, Wang YZ, Lu ZH, Zhong HH, Qu JF, Fang XW, Liang MQ, Chen YK. Asymmetrical cortical vessel sign predicts prognosis after acute ischemic stroke. *Brain Behav* 2020;10:e01657.
 34. Moody DM, Brown WR, Challa VR, Anderson RL. Periventricular venous collagenosis: association with leukoaraiosis. *Radiology* 1995;194:469-76.
 35. Zeng C, Chen X, Li Y, Ouyang Y, Lv F, Rumzan R, Wang Z. Cerebral vein changes in relapsing-remitting multiple sclerosis demonstrated by three-dimensional enhanced T₂-weighted angiography at 3.0 T. *Eur Radiol* 2013;23:869-78.
 36. Mundiyanapurath S, Ringleb PA, Diatschuk S, Burth

- S, Möhlenbruch M, Floca RO, Wick W, Bendszus M, Radbruch A. Cortical vessel sign on susceptibility weighted imaging reveals clinically relevant hypoperfusion in internal carotid artery stenosis. *Eur J Radiol* 2016;85:534-9.
37. Wang Y, Xiao J, Zhao L, Wang S, Wang M, Luo Y, Liang H, Jin L. The Frequency and Associated Factors of Asymmetrical Prominent Veins: A Predictor of Unfavorable Outcomes in Patients with Acute Ischemic Stroke. *Neural Plast* 2021;2021:9733926.
38. Wang Y, Shi T, Chen B, Lin G, Xu Y, Geng Y. Prominent Hypointense Vessel Sign on Susceptibility-Weighted Imaging Is Associated with Clinical Outcome in Acute Ischaemic Stroke. *Eur Neurol* 2018;79:231-9.
39. Lahna D, Schwartz DL, Woltjer R, Black SE, Roese N, Dodge H, Boespflug EL, Keith J, Gao F, Ramirez J, Silbert LC. Venous Collagenosis as Pathogenesis of White Matter Hyperintensity. *Ann Neurol* 2022;92:992-1000.
40. Ling X, Shen B, Li K, Si L, Yang X. Development of a prediction model for 1-year poor prognosis in patients with acute ischemic stroke. *J Investig Med* 2019;67:957-63.
41. Yao T, Zhan Y, Shen J, Xu L, Peng B, Cui Q, Liu Z. Association between fasting blood glucose and outcomes and mortality in acute ischaemic stroke patients with diabetes mellitus: a retrospective observational study in Wuhan, China. *BMJ Open* 2020;10:e037291.

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