Original Article

Deep vein diameters and perivascular space scores are associated with deep medullary vein hypo-visibility in patients with white matter hyperintensity

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Background: Deep medullary vein (DMV) hypo-visibility is correlated with white matter hyperintensity (WMH), but the underlying causes remain unclear. This study aimed to explore the relationship between deep vein diameters and perivascular space (PVS) scores, and DMV hypo-visibility in the presence of WMH.

Methods: This cross-sectional study prospectively analyzed the clinical and imaging data of 190 cerebral small vessel disease patients with WMH and 40 healthy controls from the Lishui Hospital of Traditional Chinese Medicine affiliated with Zhejiang Chinese Medical University. PVS scores ranging from 0 to 4 were determined according to the PVS counts in the basal ganglia area on T2-weighted magnetic resonance images; high-grade PVS was defined as a PVS score >1. The diameters of the deep cerebral veins, including the bilateral septal veins (SVs), thalamostriate veins (TSVs), lateral ventricular veins (LVVs), and internal cerebral veins, were measured using susceptibility weighted imaging (SWI). Left and right DMV scores, ranging from 0 to 9, were calculated based on the visibility of the DMV on SWI in the ipsilateral frontal, parietal, and occipital lobes.

Results: The deep cerebral vein diameters, left and right DMV scores, and high-grade PVS differed between the healthy controls and WMH patients (P<0.05). Left DMV scores were independently associated with age {β [95% confidence interval (CI)]: 0.050 (0.018, 0.082)}, high-grade PVS [β (95% CI): 0.998 (0.262, 1.737)], and the diameters of the ipsilateral SVs [β (95% CI): –1.114 (–1.754, –0.475)], SVs [β (95% CI): –0.734 (–1.191, –0.277)], and LVVs [β (95% CI): –0.921 (–1.567, –0.275)] [all false discovery rate (FDR)-corrected P<0.05]. Right DMV scores were independently associated with age [β (95% CI): 0.071 (0.037, 0.105)], high-grade PVS [β (95% CI): 0.873 (0.111, 1.635)], and the diameters of the ipsilateral SVs [β (95% CI): –0.837 (–1.386, –0.289)], TSVs [β (95% CI): –0.875 (–1.331, –0.419)], and LVVs [β (95% CI): –1.813 (–2.484, –1.142)] (all FDR-corrected P<0.05).

Conclusions: Decreased hypo-visibility of DMVs on SWI was associated with a higher age, the presence of high-grade PVS, and smaller diameters of the ipsilateral deep cerebral veins in individuals with WMH. Our findings provide novel insights into the probable mechanisms leading to high DMV scores.

Keywords: Deep medullary vein (DMV); perivascular space (PVS); deep vein; white matter hyperintensity (WMH); susceptibility weighted imaging (SWI)

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Introduction

White matter hyperintensity (WMH) manifests as hyperintense lamellar signals in the lateral periventricular and deep cerebral white matter regions on fluid attenuated inversion recovery (FLAIR) images. Research has shown that the older the patient, the higher the incidence of WMH (1,2). A previous study showed that the development of WMH is related to venous system dysfunction (3), especially in the deep medullary vein (DMV). As part of the cerebral venous system, the main function of the DMV is to drain venous blood from the deep brain tissues, especially the white matter near the lateral ventricle, into the subependymal vein. On susceptibility weighted imaging (SWI), the DMV appears as a thin strip of low signal, perpendicular to the lateral ventricle, with a fixed position and little variation, which has supported the development of a DMV scoring system based on imaging features to measure the dysfunction of the DMV. As the DMV score increases, the visibility of DMV decreases further, and the dysfunction becomes more pronounced (3). Multiple studies have reported an association between the decreased visibility of DMV or an increased DMV score, and the occurrence and progression of WMH (4-6). However, the specific occurrences and mechanisms leading to the development of a high DMV score are not yet well defined.

Recently, Shi *et al.* (7) found that the pulsatility of venous sinuses was increased, and Chung *et al.* (8) observed the presence of jugular venous reflux in patients with WMH. In this situation, the venous pressure, including the pressure in the deep cerebral veins, is increased. An increase in the wall shearing stress in the deep cerebral veins leads to the remodeling of the vessel wall, resulting in luminal stenosis. Ultimately, luminal stenosis of the deep cerebral veins may cause venous hypertension in the DMV, leading to DMV changes, such as collagen deposition in the wall and hypometabolism, contributing to a higher DMV score. Thus, we hypothesized that luminal stenosis of the deep cerebral veins may occur first, followed by DMV changes in patients with WMH.

The perivascular space (PVS) is another route by which brain interstitial fluid is transferred and drained (9). Dysfunction in the PVS can cause an abnormal microenvironment around the DMV, and changes, such as the accumulation of interstitial fluid, including toxic waste, can promote DMV wall remodeling and luminal stenosis (10). Based on these findings, we hypothesized that a worsening of microenvironment caused by PVS dysfunction may also be responsible for high DMV scores.

Thus, we measured the luminal diameters of deep cerebral veins, PVS scores, and DMV scores on SWI to study the relationship between the deep vein diameters and PVS scores, and DMV hypo-visibility in patients with WMH. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-426/rc).

Methods

Participants

This study adopted a cross-sectional, prospective design, and was approved by the Lishui Hospital of Traditional Chinese Medicine affiliated with Zhejiang Chinese Medical University (No. 2022-LW036). The study was conducted in accordance with the principles of the Declaration of Helsinki (as revised in 2013). All the participants provided informed consent. The participants comprised cerebral small vessel disease patients with WMH and healthy controls. All the participants underwent magnetic resonance imaging (MRI) at the Radiology Department of the Lishui Hospital of Traditional Chinese Medicine affiliated with Zhejiang Chinese Medical University due to headache, transient ischemic attack, dizziness, or cognitive dysfunction.

To be eligible for inclusion in this study, the WMH patients had to meet the following inclusion criteria: (I) be aged >40 years; and (II) have at least one vascular risk factor, such as diabetes, hypertension, smoke, or hyperlipidemia. WMH patients were excluded from the study if they met any of the following exclusion criteria: (I) had >70% stenosis or occlusion of large brain arteries; (II) WMH was not observed on the FLAIR images; (III) had secondary demyelinating lesions (e.g., metabolic, toxic or infectious abnormalities); (IV) had an intracranial tumor, trauma, acute infarction, etc.; and/or (V) had motion artifacts on

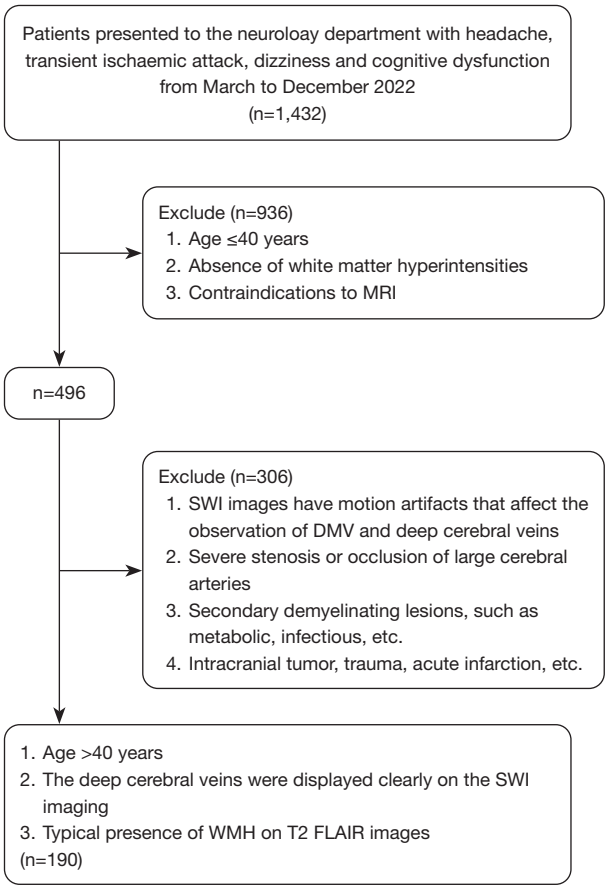

Figure 1 A flowchart of the inclusion process for participants in the study. MRI, magnetic resonance imaging; SWI, susceptibility weighted image; DMV, deep medullary vein; FLAIR, fluid attenuated inversion recovery.

SWI that affected the observation of DMV and the deep cerebral veins (*Figure 1*).

Additionally, 40 healthy controls were enrolled in the study to explore the differences in the DMV scores and deep cerebral vein diameters between the WMH patients and healthy controls. To be eligible for inclusion in this study, the healthy controls had to meet the following inclusion criteria: (I) be aged >40 years; and (II) have no history of diabetes, hypertension, hyperlipidemia, or smoking. Healthy controls were excluded from the study if they met any of the following exclusion criteria: (I) had abnormal brain MRI findings, such as WMH, hemorrhage, infarction, vascular malformation, or space-occupying lesions; (II) had a history of trauma or another confirmed neurological disease; and/or (III) had contraindications to MRI.

Clinical information

The baseline clinical characteristics of the participants were recorded, including their age, gender and vascular risk factors for smoking, diabetes, hypertension, and hyperlipidemia.

MRI protocol

All the participants underwent multimodal MRI, including three-dimensional T1-weighted, T2-weighted, FLAIR, SWI on a 1.5 Tesla scanner (Magnetom Aera, Syngo Platform VD13A, Germany). The SWI parameters were as follows: repetition time: 54 ms; flip angle: 15°; slice thickness: 2 mm; intersection gap: 0.4 mm; field of view: 23×23 cm^2; resolution: 0.5 mm × 0.5 mm in plane; and matrix: 256×256.

High-grade PVS (HPVSs)

A PVS was defined as a small-dot or thin-strip fluid signal shadow on the T2WI images, usually <3 mm in diameter. A HPVS was defined as a PVS score >1. The PVS score was determined by the PVS count in the basal ganglia as follows (11): 0 points for a PVS count of 0; 1 point for a PVS count ≤10; 2 points for a PVS count ≤20; 3 points for a PVS count ≤40; and 4 points for a PVS count >40 (*Figure 2*).

Fazekas scores for WMH

WMH was defined as abnormal signals in deep WMH (DWMH) or periventricular WMH (PWMH) with high signals in FLAIR and low signals in T1WI, which were scored 0 to 3 according to the relevant lesions (12).

DMV scores

The DMV scores were completed on the SWI sequence. Five consecutive slices were selected from the level of the lateral ventricle in the basal ganglia to the disappearance of the lateral ventricle, including most of the DMVs. A section comprised six regions (13): the bilateral frontal, parietal, and occipital lobes. During the evaluation process, a score (from 0 to 3) was given based on the continuity of the DMV signal (*Figure 3*); a score of 0 indicated that the DMV was continuous, clearly visible, and had a uniform signal; a score of 1 indicated that the DMV was continuous but had an

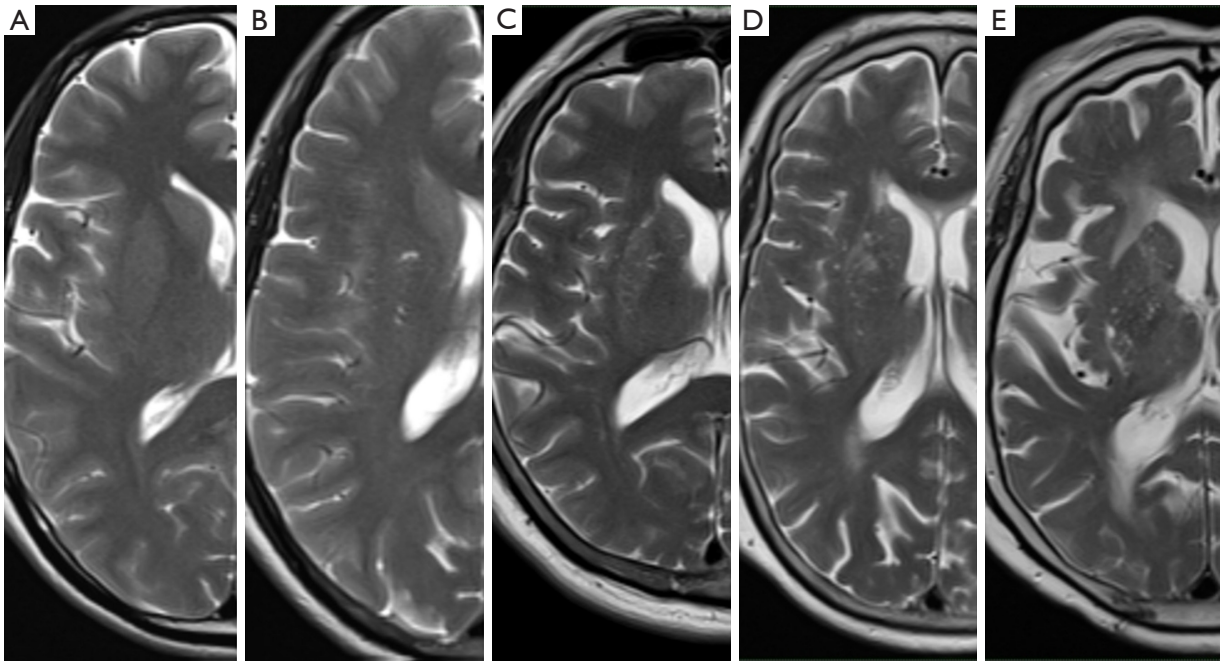

Figure 2 Illustration of the PVS scoring system. (A) No abnormal signal is apparent in the basal ganglia region, and the PVS score is 0 points. In the right basal ganglia region, (B) the PVS count is ≤10 and the PVS score is 1 point; (C) the PVS count is ≤20 and the PVS score is 2 points; (D) the PVS count is ≤40 and the PVS score is 3 points; and (E) the PVS count is >40 and the PVS score is 4 points. PVS, perivascular space.

uneven venous signal; a score of 2 indicated that the DMV showed a weak punctate and had a discontinuous signal; a score of 3 indicated that the DMV was not visible. The left and right DMV scores ranged from 0 to 9 and were obtained by adding the DMV scores of the ipsilateral frontal, parietal, ad occipital lobes. The scores were determined separately by two neuroradiologists with no knowledge of the participants' clinical and radiographic data.

Diameters of the deep cerebral veins

The SWI images were constructed with a thickness of 10 mm using minimum intensity projection. These images were then magnified by 5× (14). Finally, the diameters of the deep cerebral veins, including the left and right septal veins (SVs), the left and right thalamostriate veins (TSVs), the left and right lateral ventricular veins (LVVs), and the left and right internal cerebral veins (ICVs), on the constructed SWI images (15) were measured. The observed vessel origin was selected as the measurement point, the diameters were measured twice separately, and the diameter of the corresponding venous lumen was then represented as the mean of the two measurements (*Figure 4*).

Statistical analysis

The categorical data are presented as ratios. The normally distributed data are presented as means and standard deviation. The non-parametric data are presented as medians and interquartile ranges (IQRs). Interobserver agreement was evaluated using the kappa statistic (κ) or the intraclass correlation coefficient (ICC). Associations between the diameters of the deep cerebral veins and the DMV scores were analyzed using the Spearman correlation coefficient. Differences in the DMV scores between individuals with and without HPVS were analyzed using the Wilcoxon test. To assess the factors associated with the left and right DMV scores, a univariate ordinal regression analysis was first conducted, and factors with P values <0.2 were then selected for the next step. Finally, the multivariate ordinal regression method was used to determine which factors were obviously related to the left and right DMV scores. To correct for multiple comparisons, we applied a Benjamini-Hochberg false discovery rate (FDR) correction. The data were analyzed using SPSS 22.0 (IBM Corp., Armonk, NY, USA). Statistical significance was defined as $P<0.05$ (two-sided).

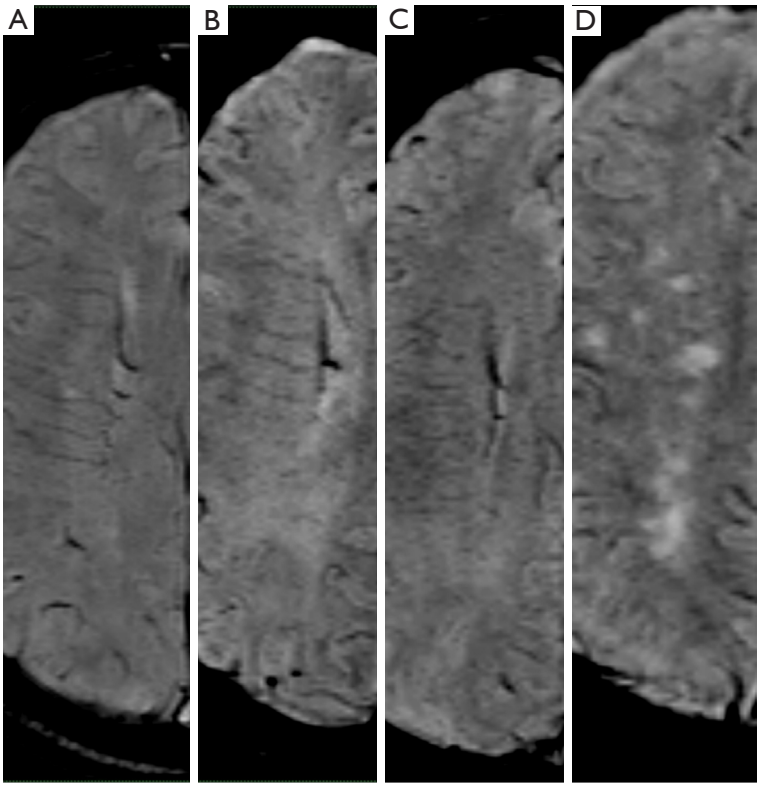

Figure 3 Illustration of the DMV scoring system. (A) The DMV signals are continuous, clear, and uniform, and the DMV score is 0. (B) The DMV signals are continuous, but the venous signals are uneven and the DMV score is 1. (C) The DMVs show weak punctate and discontinuous signals. The DMV score is 2. (D) There is no visible DMV signal. The DMV score is 3. DMV, deep medullary vein.

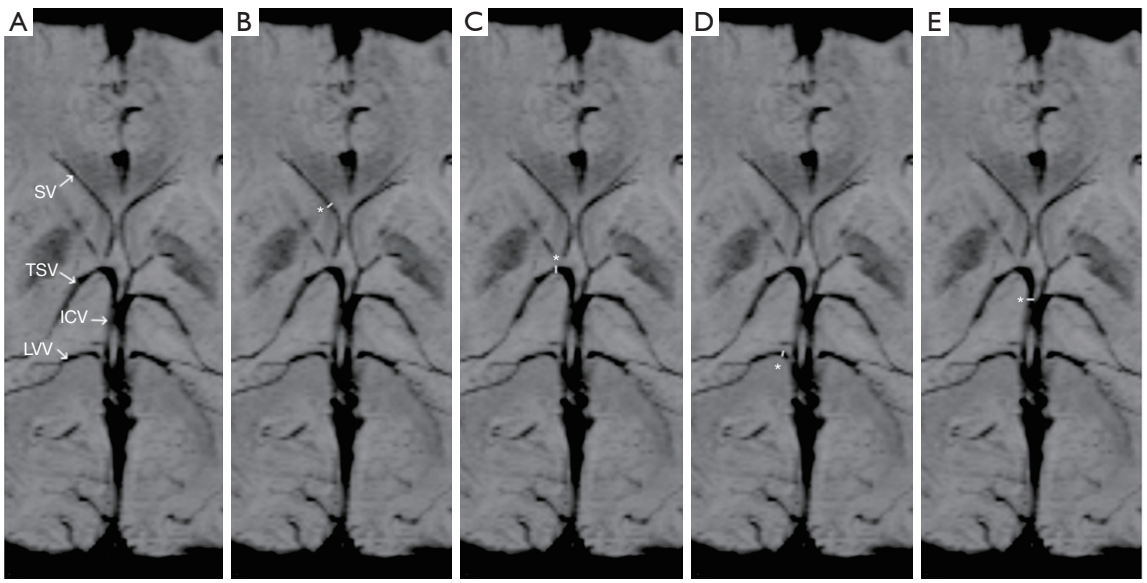

Figure 4 Illustration of the deep cerebral veins and measurement of their diameters. Anatomy of the draining vein, SV, TSV, LVV, ICV. (B-E) Measurement of the draining vein diameters. The starting point of the vein was selected as the measurement point (*), and the results were measured twice. The diameter of the corresponding venous lumen is reported as the mean of the two measurements. SV, septal vein; TSV, thalamostriate vein; LVV, lateral ventricular vein; ICV, internal cerebral veins.

Table 1 Comparison of the baseline characteristics and imaging findings between the healthy controls and WMH participants

Variables	WMH participants, n=190	Healthy controls, n=40	P
Age (years)	63±12	60±7	0.067
Male	88 (46.3)	19 (47.5)	0.892
Hypertension, yes	111 (58.4)	–	–
Diabetes, yes	44 (23.2)	–	–
Hyperlipidemia, yes	59 (31.1)	–	–
Smoking, yes	44 (23.2)	–	–
HPVS	58 (30.5)	4 (10.0)	0.003
Left DMV score	2 [0, 5]	1 [0, 2]	<0.001
Right DMV score	2 [1, 6]	1 [0, 2]	<0.001
Diameters of left deep veins (mm)			
SV	1.25±0.15	1.39±0.07	<0.001
TSV	1.78±0.20	1.84±0.11	0.004
LVV	1.26±0.14	1.40±0.07	<0.001
ICV	2.03±0.21	2.19±0.09	<0.001
Diameters of right deep veins (mm)			
SV	1.25±0.16	1.39±0.08	<0.001
TSV	1.73±0.20	1.84±0.09	<0.001
LVV	1.25±0.14	1.40±0.08	<0.001
ICV	2.00±0.17	2.15±0.08	<0.001

Data are presented as n (%), median [IQR] or mean ± SD. WMH, white matter hyperintensity; HPVS, high-grade perivascular space; DMV, deep medullary vein; SV, septal vein; TSV, thalamostriate vein; LVV, lateral ventricular vein; ICV, internal cerebral vein.

Results

A total of 190 participants (88 male) were included in this study. The participants had a mean age of 63±12 years, and HPVS was observed in 58 (30.5%) participants. The median [IQR] left and right DMV scores were 2 [0, 5] and 2 [1, 6] in individuals with WMH. The deep cerebral vein diameters in the WMH group were significantly smaller than those in the control group (P<0.05) (*Table 1*).

Inter-reader agreement for evaluations of the DMV scores and the deep vein diameters

The agreement between readers was excellent for the left DMV scores (κ=0.900) and right DMV scores (κ=0.908), and the diameters of the left SV (ICC =0.936), right SV (ICC =0.941), left TSV (ICC =0.943), right TSV (ICC =0.939), left LVV (ICC =0.935), right LVV (ICC =0.933), left ICV (ICC =0.928), and right ICV (ICC =0.931).

Comparison of the baseline characteristics and imaging findings between the healthy controls and WMH participants

No obvious differences were observed between the healthy controls and WMH participants in terms of age. The deep cerebral vein diameters, DMV scores, and HPVSs differed between the healthy controls and WMH participants (P<0.05) (*Table 1*).

Factors associated with the left DMV score

According to the univariate analysis, the left DMV score was associated with age, hypertension, HPVS, DWMH, PWMH, and the ipsilateral diameters of the SV, TSV, and LVV (P<0.05), but was not associated with gender, smoking,

Table 2 Univariate and multivariate analyses of the left deep medullary vein score

Variables	Univariate analysis		Multivariate analysis	
	β (95% CI)	P value	β (95% CI)	FDR-corrected P value
Age, years	0.100 (0.075, 0.126)	<0.001	0.050 (0.018, 0.082)	0.016
Gender (male)	0.072 (–0.431, 0.576)	0.778	–	
Hypertension, yes	0.621 (0.105, 1.138)	0.018	0.092 (–0.529, 0.713)	>0.99
Diabetes, yes	–0.446 (–1.040, 0.148)	0.141	0.378 (–0.286, 1.041)	0.795
Hyperlipidemia, yes	0.082 (–0.534, 0.699)	0.793	–	
Smoker, yes	0.186 (0.780, –0.407)	0.539	–	
HPVS	2.113 (1.488, 2.738)	<0.001	0.998 (0.262, 1.737)	0.040
PWMH	1.496 (1.094, 1.899)	<0.001	0.410 (–0.138, 0.958)	0.568
DWMH	1.289 (0.941, 1.637)	<0.001	–0.049 (–0.524, 0.426)	>0.99
Diameters of left deep veins				
SV	–2.502 (–2.070, –2.934)	<0.001	–1.114 (–1.754, –0.475)	0.009
TSV	–2.000 (–2.373, –1.627)	<0.001	–0.734 (–1.191, –0.277)	0.016
LVV	–2.486 (–2.923, –2.050)	<0.001	–0.921 (–1.567, –0.275)	0.030
ICV	0.162 (–0.090, 0.414)	0.208	–	

CI, confidence interval; FDR, false discovery rate; HPVS, high-grade perivascular space; PWMH, periventricular white matter hyperintensity; DWMH, deep white matter hyperintensity; SV, septal vein; TSV, thalamostriate vein; LVV, lateral ventricular vein; ICV, internal cerebral vein.

diabetes, hyperlipidemia, or the ipsilateral diameter of the ICV (P>0.05). According to the ordinal logistic regression analysis, the left DMV score was independently associated with age, HPVS, and the ipsilateral diameters of the SV, TSV and LVV (FDR-corrected P<0.05) (*Table 2*, and *Figures 5*,*6*).

Factors associated with the right DMV score

According to the univariate analysis, the right DMV score was associated with age, hypertension, diabetes, HPVS, DWMH, PWMH, and the ipsilateral diameters of the SV, TSV, and LVV (P<0.05), but was not associated with gender, smoking, hyperlipidemia, or the ipsilateral diameter of the ICV (P>0.05). According to the ordinal logistic regression analysis, the right DMV score was independently associated with age, HPVS, and the ipsilateral diameters of the SV, TSV, and LVV (FDR-corrected P<0.05) (*Table 3*, and *Figures 5*,*7*).

Discussion

This research found that the left and right DMV scores were positively correlated with HPVS and negatively correlated with the ipsilateral diameters of the deep cerebral veins (i.e., the SVs, TSVs, and LVVs). Thus, it appears that enlarged PVS and stenosis of the deep cerebral veins may be responsible for a higher DMV score or decreased hypo-visibility on SWI and may be involved in the process of DMV dysfunction. These findings provide novel insights into the probable mechanisms leading to high DMV scores.

The DMV is mostly distributed in the brain white matter region near the lateral ventricle. The vein into which deep medullary venous blood drains depends on the anatomical location (16). Deep medullary venous blood within the white matter of the deep frontal lobe, deep precentral, postcentral, and angular gyrus, and the deep occipital lobe returns to the deep cerebral veins, separately. Thus, when the lumina of the deep cerebral veins are narrowed, the venous pressure is increased, resulting in a series of changes that may affect DMV hypo-visibility on SWI. Possible explanations are provided below.

As age increases and blood pressure rises, the stiffness of the venous wall increases and venous pulsatility intensifies

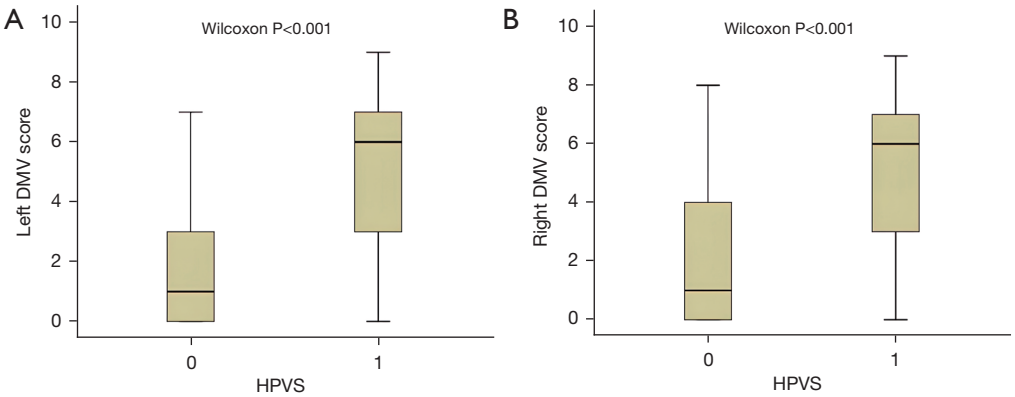

Figure 5 Comparison of high-grade perivascular spaces according to left deep medullary vein score and right deep medullary vein score in individuals with WMH. (A) The left DMV score is different between individuals with or without HPVSs. (B) The right DMV score is different between individuals with or without HPVSs. HPVSs, high-grade perivascular spaces; DMV, deep medullary vein; WMH, white matter hyperintensity.

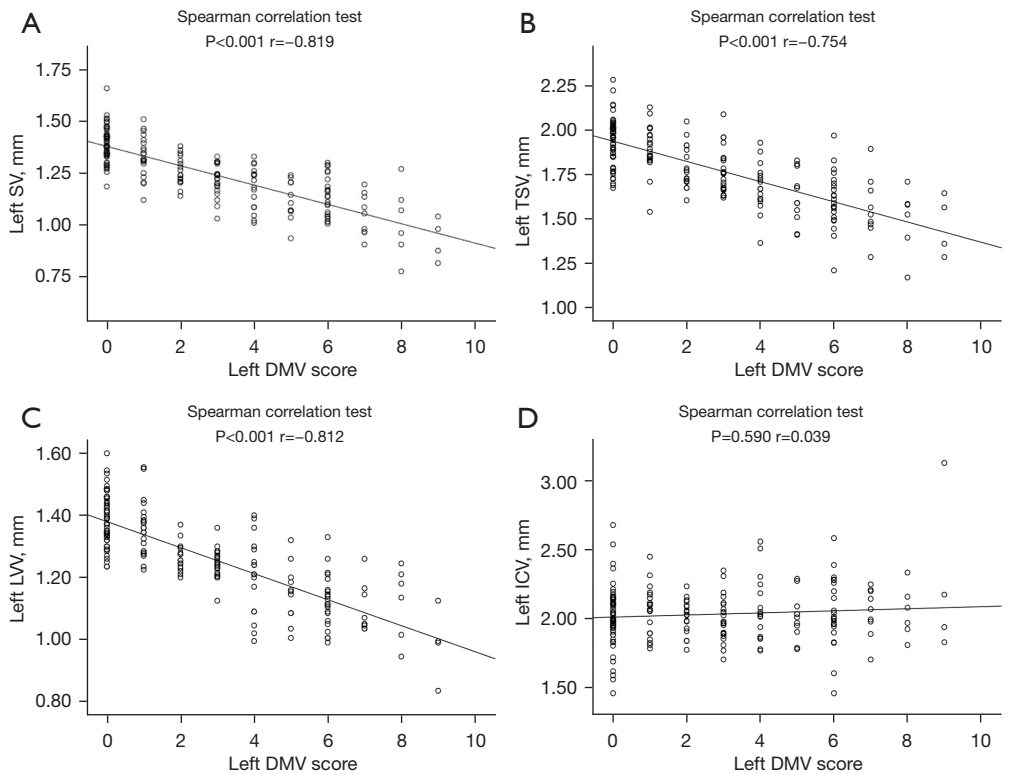

Figure 6 Diameter of the ipsilateral deep cerebral veins among individuals with WMH according to the left deep medullary vein score. (A) Associations between the diameters of the SV and the left DMV score; (B) associations between the diameters of the TSV and the left DMV score; (C) associations between the diameters of the LVV and the left DMV score; (D) associations between the diameters of the ICV and the left DMV score. SV, septal vein; TSV, thalamostriate vein; LVV, lateral ventricular vein; ICV, lateral ventricular vein; DMV, deep medullary vein; WMH, white matter hyperintensity.

Table 3 Univariate and multivariate analyses of the right deep medullary vein score

Variables	Univariate analysis		Multivariate analysis	
	β (95% CI)	P value	β (95% CI)	FDR-corrected P value
Age, years	0.114 (0.087, 0.140)	<0.001	0.071 (0.037, 0.105)	<0.001
Gender (male)	0.093 (–0.594, 0.407)	0.715	–	
Hypertension, yes	0.787 (0.269, 1.304)	0.003	0.130 (–0.487, 0.747)	>0.99
Diabetes, yes	0.635 (0.041, 1.230)	0.036	0.278 (–0.390, 0.946)	>0.99
Hyperlipidemia, yes	0.202 (–0.339, 0.743)	0.465	–	
Smoker, yes	0.032 (–0.559, 0.623)	0.916	–	
HPVS	2.175 (1.546, 2.803)	<0.001	0.873 (0.111, 1.635)	0.045
PWMH	1.448 (1.050, 1.846)	<0.001	0.205 (–0.346, 0.757)	>0.99
DWMH	1.447 (1.091, 1.804)	<0.001	0.159 (–0.320, 0.639)	>0.99
Diameters of right deep veins				
SV	–2.493 (–2.932, –2.063)	<0.001	–0.837 (–1.386, –0.289)	0.018
TSV	–2.197 (–1.805, –2.589)	<0.001	–0.875 (–1.331, –0.419)	<0.001
LVV	–2.785 (–3.242, –2.328)	<0.001	–1.813 (–2.484, –1.142)	<0.001
ICV	–0.044 (–0.294, 0.206)	0.731	–	

CI, confidence interval; FDR, false discovery rate; HPVS, high-grade perivascular space; PWMH, periventricular white matter hyperintensity; DWMH, deep white matter hyperintensity; SV, septal vein, TSV, thalamostriate vein; LVV, lateral ventricular vein; ICV, internal cerebral vein.

(17,18). Such stiffened vessels would be less able to *inhibit* pressure and pulsatility (19,20). Cerebral veins have very thin walls and lack a well-developed smooth muscle layer, the vascular wall thickens due to gradually increasing pressure and the lumen becomes narrower (21). These changes are more obvious in the vessels around the lateral ventricle than in those far from the lateral ventricle (22). Long-term stenosis of the deep cerebral veins around the lateral ventricles leads to a further increase in the circulating pressure of the distal DMV, which causes the deposition of collagen (18) on the venous wall and aggravates the stenosis of the DMV. Stenosis of the DMV results in venous signal discontinuity in the SWI sequence and a higher DMV score.

The hemodynamic changes caused by stenosis in the deep cerebral veins may also be reflected in high DMV scores. The persistence of venous stenosis and chronic cerebral venous hypertension likely decreases cerebral blood flow, promoting local ischemia in the white matter (8). Thus, the level of deoxyhemoglobin in the DMV decreases accordingly, further decreasing the visibility of the DMV on SWI. In addition, increased venous pressure can also lead to increased vascular permeability and result in excessive accumulation of extracellular fluid, which can also lead to abnormal remodeling of venules (23), such as collagen deposition, in the wall of the lumen (18). Thus, a vicious cycle of venous stenosis ischemia—venous pressure increase—aggravated venous ischemia is established. This illustrates how the luminal stenosis of the draining vein is involved in the occurrence and development of DMV dysfunction.

The PVS is an interstitial fluid-filled space around the small blood vessels. Its main function is to remove metabolic wastes by exchanging cerebrospinal fluid with interstitial fluid (9,24). With the expansion or dysfunction of the PVS, the ability to remove harmful substances is reduced, and harmful proteins, such as amyloid, are deposited on the venule wall, thus damaging the vessel wall. DMV wall remodeling then occurs, leading to luminal stenosis and reduced DMV visibility on the SWI images.

This study had several limitations. First, our participants came from a single institution and the sample size was relatively small. Second, the DMV scoring in our study was based on visual observation; however, software-based

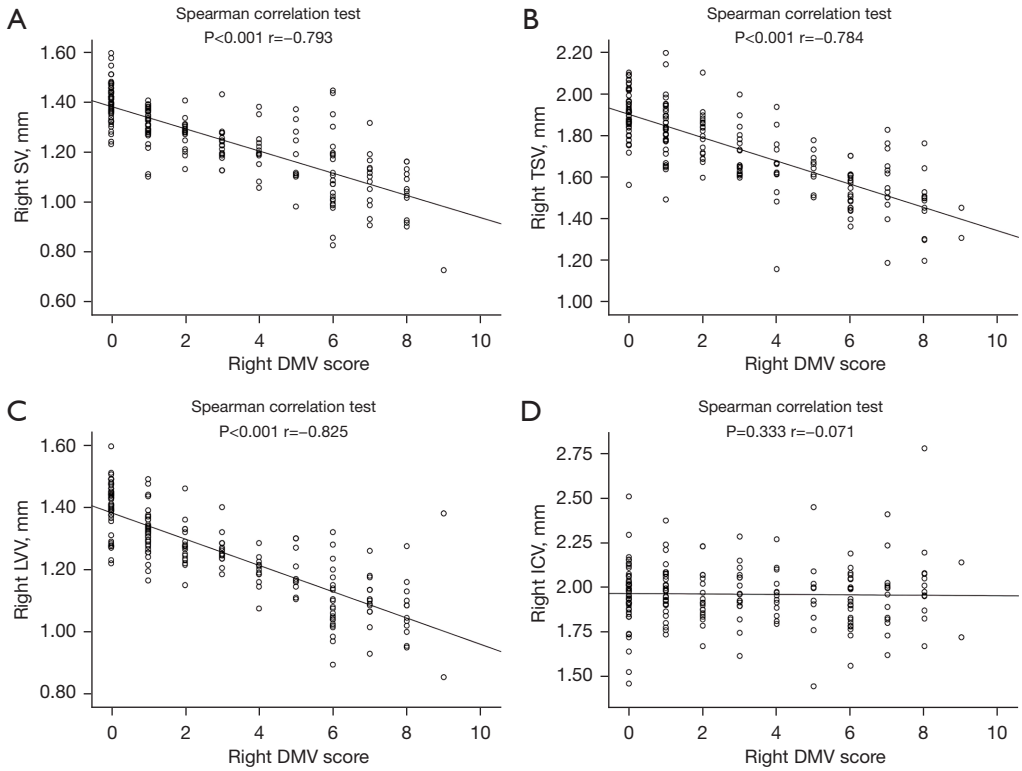

Figure 7 Diameter of the ipsilateral deep cerebral veins among individuals with WMH according to the right deep medullary vein score. (A) Associations between the diameters of the SV and the right DMV score; (B) associations between the diameters of the TSV and the right DMV score; (C) associations between the diameters of the LVV and the right DMV score; (D) associations between the diameters of the ICV and the right DMV score. SV, septal vein; TSV, thalamostriate vein; LVV, lateral ventricular vein; ICV, lateral ventricular vein; DMV, deep medullary vein; WMH, white matter hyperintensity.

automatic identification might more accurate. Third, partial volume effects (large volume WMH surrounding the DMV) might influence the visibility of DMV on SWI. The 7T MR scanner may show small veins better than 1.5T MR scanner. Fourth, we did not perform a long-term follow-up, which impeded our ability to evaluate the natural progression and dynamic changes of deep veins, DMVs, and HPVSs. Fifth, our protocol did not include four-dimensional flow imaging, which can detect vessel pulsatility and pressure on the vessel wall. A multi-center study with a larger sample size is needed to address these limitations.

Conclusions

Decreased hypo-visibility of DMV on SWI was associated with a higher age, the presence of HPVS, and smaller diameters of the ipsilateral deep cerebral veins in individuals with WMH. Our findings provide novel insights into the probable mechanisms leading to high DMV scores.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-23-426/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-426/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. This study was approved by the Lishui Hospital of Traditional Chinese Medicine affiliated with Zhejiang Chinese Medical University (No. 2022-LW036). All the participants provided informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki (as revised in 2013).

References

1. Zhuang FJ, Chen Y, He WB, Cai ZY. Prevalence of white matter hyperintensities increases with age. Neural Regen Res 2018;13:2141-6.
2. Roseborough AD, Langdon KD, Hammond R, Cipriano LE, Pasternak SH, Whitehead SN, Khan AR. Post-mortem 7 Tesla MRI detection of white matter hyperintensities: A multidisciplinary voxel-wise comparison of imaging and histological correlates. Neuroimage Clin 2020;27:102340.
3. 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.
4. Zhang R, Huang P, Jiaerken Y, Wang S, Hong H, Luo X, Xu X, Yu X, Li K, Zeng Q, Wu X, Lou M, Zhang M. Venous disruption affects white matter integrity through increased interstitial fluid in cerebral small vessel disease. J Cereb Blood Flow Metab 2021;41:157-65.
5. Li C, Rusinek H, Chen J, Bokacheva L, Vedvyas A, Masurkar AV, Haacke EM, Wisniewski T, Ge Y. Reduced white matter venous density on MRI is associated with neurodegeneration and cognitive impairment in the elderly. Front Aging Neurosci 2022;14:972282.
6. 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.
7. Shi Y, Thrippleton MJ, Blair GW, Dickie DA, Marshall I, Hamilton I, Doubal FN, Chappell F, Wardlaw JM. Small vessel disease is associated with altered cerebrovascular pulsatility but not resting cerebral blood flow. J Cereb Blood Flow Metab 2020;40:85-99.
8. Chung CP, Hu HH. Pathogenesis of leukoaraiosis: role of jugular venous reflux. Med Hypotheses 2010;75:85-90.
9. Wardlaw JM, Benveniste H, Nedergaard M, Zlokovic BV, Mestre H, Lee H, Doubal FN, Brown R, Ramirez J, MacIntosh BJ, Tannenbaum A, Ballerini L, Rungta RL, Boido D, Sweeney M, Montagne A, Charpak S, Joutel A, Smith KJ, Black SE; colleagues from the Fondation Leducq Transatlantic Network of Excellence on the Role of the Perivascular Space in Cerebral Small Vessel Disease. Perivascular spaces in the brain: anatomy, physiology and pathology. Nat Rev Neurol 2020;16:137-53.
10. Zhang K, Zhou Y, Zhang W, Li Q, Sun J, Lou M. MRI-visible perivascular spaces in basal ganglia but not centrum semiovale or hippocampus were related to deep medullary veins changes. J Cereb Blood Flow Metab 2022;42:136-44.
11. Wardlaw JM, Smith EE, Biessels GJ, Cordonnier C, Fazekas F, Frayne R, et al. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. Lancet Neurol 2013;12:822-38.
12. Fazekas F, Kleinert R, Offenbacher H, Schmidt R, Kleinert G, Payer F, Radner H, Lechner H. Pathologic correlates of incidental MRI white matter signal hyperintensities. Neurology 1993;43:1683-9.
13. Lee C, Pennington MA, Kenney CM 3rd. MR evaluation of developmental venous anomalies: medullary venous anatomy of venous angiomas. AJNR Am J Neuroradiol 1996;17:61-70.
14. Zhang L, Yang B, Wang Z, Li H, Cai X, Duan Y. The research of remodeling pattern in middle cerebral artery atherosclerotic disease: high-resolution magnetic resonance. Apoplexy and Nervous Diseases 2017;34:676-9.
15. Huang Z, Tu X, Lin Q, Zhan Z, Tang L, Liu J. Increased internal cerebral vein diameter is associated with age. Clin Imaging 2021;78:187-93.
16. Taoka T, Fukusumi A, Miyasaka T, Kawai H, Nakane T, Kichikawa K, Naganawa S. Structure of the Medullary Veins of the Cerebral Hemisphere and Related Disorders. Radiographics 2017;37:281-97.
17. Bateman GA, Levi CR, Schofield P, Wang Y, Lovett EC. The venous manifestations of pulse wave encephalopathy: windkessel dysfunction in normal aging and senile

dementia. Neuroradiology 2008;50:491-7.
18. Rivera-Rivera LA, Schubert T, Turski P, Johnson KM, Berman SE, Rowley HA, Carlsson CM, Johnson SC, Wieben O. Changes in intracranial venous blood flow and pulsatility in Alzheimer's disease: A 4D flow MRI study. J Cereb Blood Flow Metab 2017;37:2149-58.
19. Stivaros SM, Jackson A. Changing concepts of cerebrospinal fluid hydrodynamics: role of phase-contrast magnetic resonance imaging and implications for cerebral microvascular disease. Neurotherapeutics 2007;4:511-22.
20. Mitchell GF. Cerebral small vessel disease: role of aortic stiffness and pulsatile hemodynamics. J Hypertens 2015;33:2025-8.
21. 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.
22. Moody DM, Brown WR, Challa VR, Anderson RL. Periventricular venous collagenosis: association with leukoaraiosis. Radiology 1995;194:469-76.
23. Henry-Feugeas MC. Intracranial MR dynamics in clinically diagnosed Alzheimer's disease: the emerging concept of "pulse wave encephalopathy". Curr Alzheimer Res 2009;6:488-502.
24. Yu L, Hu X, Li H, Zhao Y. Perivascular Spaces, Glymphatic System and MR. Front Neurol 2022;13:844938.

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