International Journal of General Medicine

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Association Between Cognitive Impairment and Multimodal MRI Markers in Patients with Cerebral Microbleeds: A Retrospective Case–Control Study

Peiqing Zhuang[1], Jiyang Liu[2], Xuehua Cai[2], Biyu Wu[2]

[1]Department of Medical Imaging, Quanzhou First Hospital, Quanzhou First Hospital, Quanzhou, Fujian, 362000, People's Republic of China; [2]Quanzhou First Hospital, Quanzhou, Fujian, 362000, People's Republic of China

Correspondence: Biyu Wu, Email 13506929618@163.com

Objective: To investigate the association between cognitive impairment and multimodal magnetic resonance imaging (MRI) markers in patients with cerebral microbleeds (CMBs), and to identify imaging predictors of CMB-related cognitive dysfunction.

Methods: This retrospective case–control study included 71 patients with CMBs confirmed by MRI between August 2022 and February 2024 and 65 age-matched healthy controls. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA). All participants underwent multimodal MRI, including susceptibility-weighted imaging (SWI) for CMB detection and diffusion tensor imaging (DTI) for quantitative assessment of fractional anisotropy (FA) and apparent diffusion coefficient (ADC) in predefined brain regions. Spearman correlation analysis was performed to evaluate associations between CMB burden, DTI parameters, and cognitive scores. Multivariate linear regression analysis was used to identify independent risk factors for cognitive impairment.

Results: Compared with controls, patients with CMBs had significantly lower MoCA scores and higher CMB burden (both $P < 0.05$). FA values in the frontal–temporal lobe, parietal lobe, and basal ganglia were significantly reduced, while ADC values were increased (all $P < 0.05$). CMB number was negatively correlated with MoCA scores ($r = -0.643$, $P < 0.001$). Decreased FA and increased ADC in the frontal–temporal lobe and basal ganglia were significantly associated with cognitive decline. Regression analysis showed that CMB burden ≥10, reduced FA, elevated ADC, and basal ganglia involvement were independent risk factors for cognitive impairment.

Conclusion: Cognitive impairment in CMB patients is closely associated with lesion burden and microstructural white matter alterations detected by multimodal MRI. These imaging markers may facilitate early risk stratification and targeted monitoring, although longitudinal validation is warranted.

Keywords: cerebral microbleeds, cognitive impairment, multimodal mri, diffusion tensor imaging, fractional anisotropy, apparent diffusion coefficient

Introduction

Cerebral microbleeds (CMBs) are small hemosiderin deposits caused by cerebral small vessel disease (CSVD), typically defined as round or ovoid hypointense lesions with a diameter of 2–10 mm on susceptibility-weighted imaging (SWI).[1,2] They are predominantly distributed in the subcortical white matter, basal ganglia, thalamus, and brainstem, and are increasingly recognized as one of the core neuroimaging markers of CSVD. CMBs are frequently observed in patients with hypertension, ischemic stroke, intracerebral hemorrhage, and neurodegenerative disorders, as well as in the aging population.[3] With the widespread application of high-resolution MRI, the detection rate of CMBs has risen steadily, and their broader clinical implications have attracted growing attention. While early research primarily focused on the association between CMBs and hemorrhagic risk, accumulating evidence suggests that CMBs may also contribute to cognitive impairment. Proposed mechanisms include disruption of white matter microstructure, impairment of structural

https://doi.org/10.2147/IJGM.S556275
Received: 25 July 2025
Accepted: 24 January 2026
Published: 17 February 2026

brain networks, and secondary effects on functional connectivity.[4,5] Several studies have demonstrated that a higher CMB burden and wider anatomical distribution are associated with poorer global cognition and deficits in executive function, attention, and processing speed.[6,7] These findings support the concept that CMBs may represent not merely focal vascular lesions but markers of diffuse network-level brain injury.

Advances in multimodal MRI, particularly diffusion tensor imaging (DTI), have provided new opportunities to investigate the microstructural basis of CMB-related cognitive dysfunction. DTI-derived parameters, including fractional anisotropy (FA) and apparent diffusion coefficient (ADC), enable quantitative assessment of white matter integrity and microstructural damage beyond what can be detected by conventional MRI.[8] Prior DTI-based studies have shown that decreased FA and increased ADC are associated with cognitive decline in CSVD and mild cognitive impairment, indicating potential predictive value.[9,10] However, most existing studies have examined DTI abnormalities or CMB burden in isolation, with limited integration of multimodal imaging parameters and standardized cognitive assessments. Importantly, it remains unclear whether regional white matter microstructural alterations mediate the relationship between CMB burden and cognitive impairment, and which brain regions are most strongly associated with cognitive decline. Moreover, the independent predictive value of combined CMB characteristics and DTI parameters has not been fully elucidated. From a network disruption perspective, CMB-related microstructural damage may impair information transfer efficiency across key cognitive networks, thereby contributing to global cognitive dysfunction. Therefore, we hypothesized that increased CMB burden and region-specific white matter microstructural damage, as quantified by multimodal MRI-derived FA and ADC parameters, are independently associated with cognitive impairment. Accordingly, this retrospective case–control study aimed to compare cognitive performance and multimodal MRI parameters between patients with CMBs and healthy controls, to analyze the associations between CMB burden, regional FA/ADC values, and cognitive scores, and to identify independent predictors of cognitive dysfunction, thereby providing imaging-based evidence for early risk stratification and intervention.

Materials and Methods

Study Design and Participants

This study was a single-center, retrospective case–control study. All MRI examinations and clinical data were obtained from routine clinical practice, and cognitive assessments were completed within 7 days after MRI as part of standardized clinical evaluation, without any prospective intervention. A total of 71 consecutive patients diagnosed with CMBs by MRI and hospitalized in the Neurology Department of our hospital between August 2022 and February 2024 were enrolled as the observation group. Meanwhile, 65 age- and sex-matched healthy individuals undergoing routine health examinations during the same period were recruited as the control group. No subject was enrolled or assessed based on future outcomes, ensuring the retrospective nature of the study.

The study protocol was approved by the Medical Ethics Committee of Quanzhou First Hospital (Approval No.: SNYX24-19) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants or their legal representatives. The research overview flowchart is shown in Figure 1.

Sample Size Consideration

Given the retrospective design, no a priori sample size calculation was performed. However, the final sample size was comparable to or larger than that of previous multimodal MRI studies investigating CMBs-related cognitive impairment, and was considered adequate to detect moderate-to-large effect sizes in correlation and multivariate regression analyses.

Inclusion and Exclusion Criteria

Inclusion criteria: Observation group: (1) Age ≥50 years; (2) Diagnosis of CMBs confirmed by cranial MRI including SWI; (3) Ability to complete cognitive assessment and MRI examination. Control group: (1) Age- and sex-matched with the observation group; (2) No history of neurological or psychiatric disorders; (3) No structural abnormalities on cranial MRI.

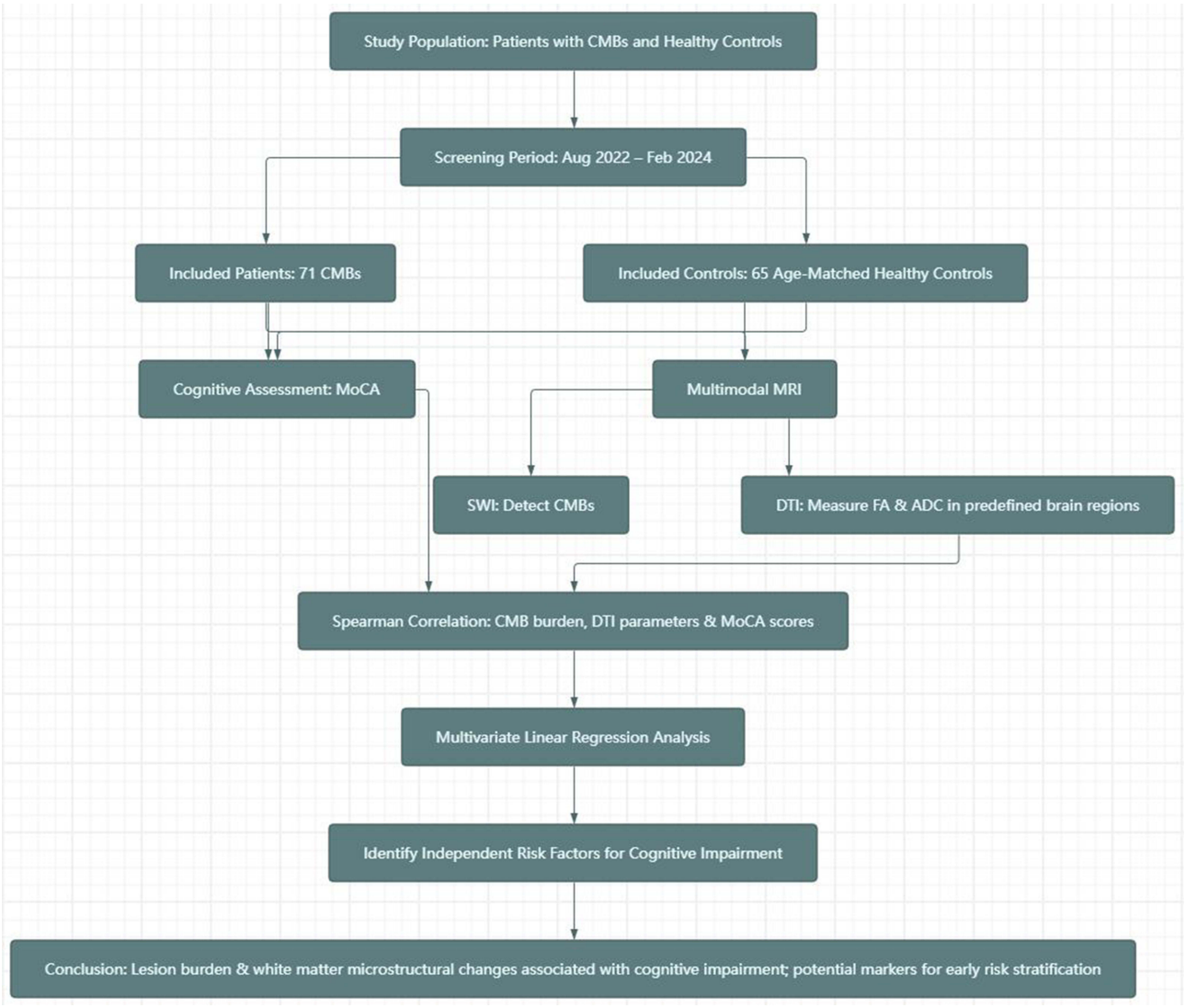

Figure 1 Research Overview Flowchart.

Exclusion criteria: (1) Neurodegenerative diseases (eg, Alzheimer's disease, Parkinson's disease); (2) Severe sensory, psychiatric, or communication disorders; (3) Recent stroke, traumatic brain injury, or intracranial surgery; (4) Poor image quality or severe motion artifacts; (5) Severe systemic diseases or acute metabolic disorders affecting cognition.

Cognitive Function Assessment

Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) by trained neurologists within 7 days after MRI. The MoCA evaluates executive function, attention, memory, language, abstraction, and orientation (total score: 30). Scores ≤26 indicated cognitive impairment, with one additional point added for individuals with ≤12 years of education. All assessments were performed by the same evaluator in a quiet environment.

MRI Acquisition and Post-Processing

MRI scans were performed on a 3.0-T scanner (GE SIGNA EXCITE II). Sequences included T1WI, T2WI, FLAIR, SWI, and DTI. DTI was acquired with 32 diffusion directions ($b = 1000$ s/mm^2). DTI data were processed using FSL (version 6.0). Preprocessing steps included eddy current and head motion correction, brain extraction, and tensor fitting. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) maps were generated. Regions of interest (ROIs)

including the frontal–temporal lobe, parietal lobe, occipital lobe, and basal ganglia were defined using a standard neuroanatomical atlas. Automated extraction was followed by manual verification to ensure anatomical accuracy and consistency across subjects.

Assessment of CMBs

CMBs were identified on SWI as round or ovoid hypointense lesions with diameters of 2–10 mm. Two experienced neuroradiologists independently evaluated all images. Discrepancies were resolved by consensus with a third reviewer.

Data Preprocessing and Variable Transformation

Prior to regression modeling, continuous variables were assessed for normality. The number of CMBs was dichotomized using a threshold of ≥10 lesions, based on prior literature and observed distribution, to reflect high lesion burden. FA and ADC values were entered as continuous variables after z-score normalization. ROI-specific rules were applied uniformly across all regions.

Covariates and Multicollinearity Assessment

Potential vascular confounders, including hypertension and diabetes mellitus, were collected and entered as covariates. Multicollinearity was assessed using variance inflation factors (VIF), with VIF < 5 considered acceptable.

Statistical Analysis

Statistical analyses were conducted using SPSS 26.0. Group comparisons were performed using independent-sample t-tests or χ^2-tests as appropriate. Spearman correlation analysis assessed associations between imaging parameters and cognitive scores. Multivariate linear regression was used to identify independent predictors of cognitive impairment. Model assumptions were checked, and missing data (<5%) were handled by complete-case analysis. A two-tailed $P < 0.05$ was considered statistically significant.

Results

Comparison of General Data

The observation group consisted of 71 patients with CMBs, including 38 males and 33 females; the average age was (66.42 ± 8.75) years. The control group included 65 individuals, 35 males and 30 females; the average age was (65.83 ± 9.12) years. There were no statistically significant differences between the two groups in terms of gender, age, body mass index (BMI), or years of education ($P > 0.05$), indicating good baseline comparability. In addition, the prevalence of hypertension and diabetes mellitus did not differ significantly between the two groups (both $P > 0.05$). See Table 1.

Table 1 Comparison of General Data Between the Two Groups

General Data	Observation (n=71)	Control (n=65)	t/x^2	P
Gender	–	–	0.005	0.938
Male	38 (53.52)	35 (53.85)	–	–
Female	33 (46.48)	30 (46.15)	–	–
Age (years)	66.42±8.75	65.83±9.12	0.384	0.700
BMI (kg/m^2)	22.53±2.49	22.76±2.41	0.546	0.585
Years of Education	10.03±3.55	9.85±3.72	0.288	0.773
Hypertension	29 (40.85)	24 (36.92)	0.214	0.644
Diabetes mellitus	18 (25.35)	15 (23.08)	0.095	0.758

Cognitive Function Score Results

The MoCA score in the observation group was (21.63 ± 1.59), whereas that in the control group was (26.58 ± 1.97). The MoCA score in the observation group was significantly lower than that in the control group (mean difference: −4.95 points; 95% CI: −5.56 to −4.34; P < 0.001), as shown in Figure 2.

Comparison of CMBs Count and Imaging Indicators

The total number of CMBs in the observation group was (12.41 ± 6.85), which was significantly higher than that in the control group (0.53 ± 0.26) (P < 0.001; Cohen's d = 2.41), as shown in Figure 3. In the observation group, CMBs were mainly distributed in the frontal–temporal lobe, parietal lobe, and basal ganglia, with basal ganglia involvement accounting for 54.0%, representing the most common site.

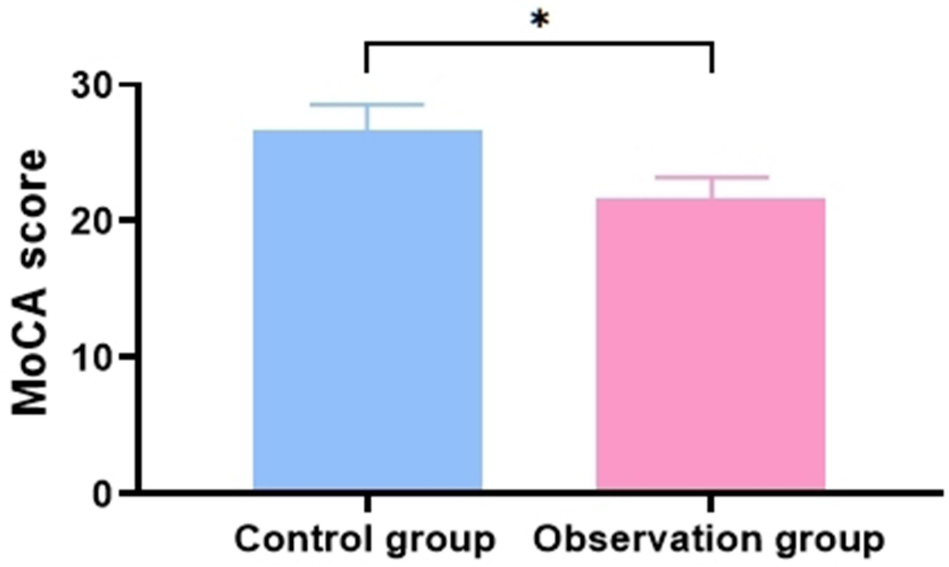

Figure 2 Comparison of MoCA Scores Between the Two Groups.
Note: Intergroup comparison, *P < 0.05.

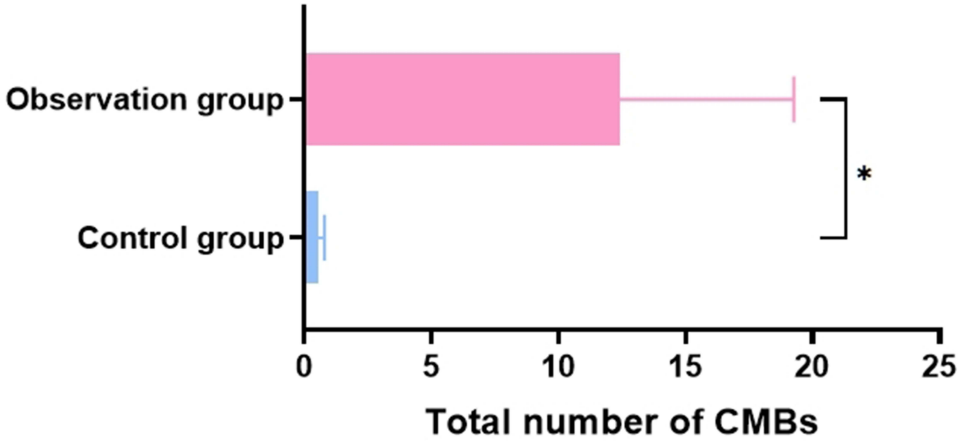

Figure 3 Comparison of the number of CMBs between the two groups.
Note: Intergroup comparison, *P < 0.05.

https://doi.org/10.2147/IJGM.S556275

Comparison of FA and ADC Values in Brain Regions

In the multimodal MRI analysis, FA values in the frontotemporal lobe, parietal lobe, and basal ganglia in the observation group were significantly lower than those in the control group, while ADC values were significantly higher (all $P < 0.001$; effect sizes ranged from Cohen's $d = 0.82$ to 1.46). There was no statistically significant difference in FA or ADC values in the occipital lobe between the two groups ($P > 0.05$). The lack of significance in the occipital lobe was accompanied by small effect sizes (FA: $d = 0.12$; ADC: $d = 0.10$), suggesting limited clinical relevance, as shown in Table 2.

Spearman Correlation Analysis Results

Spearman correlation analysis showed that the number of CMBs was significantly negatively correlated with the MoCA score ($r = -0.643$, 95% CI: −0.76 to −0.50; $P < 0.001$). FA values in the frontal–temporal lobe were positively correlated with the MoCA score ($r = 0.529$, 95% CI: 0.32–0.69; $P = 0.002$), whereas ADC values were negatively correlated with the MoCA score ($r = -0.597$, 95% CI: −0.73 to −0.41; $P < 0.001$). FA values in the basal ganglia were positively correlated with the MoCA score ($r = 0.563$, 95% CI: 0.36–0.71; $P < 0.001$), while ADC values were negatively correlated with the MoCA score ($r = -0.626$, 95% CI: −0.75 to −0.46; $P < 0.001$), as shown in Table 3 and Figures 4–6. No significant correlations were observed between parietal lobe FA/ADC values and MoCA scores (both $P > 0.10$), which may partly reflect limited statistical power for region-specific analyses.

Multiple Linear Regression Analysis Results

Using MoCA scores as the dependent variable, and gender, age, years of education, hypertension, diabetes mellitus, CMBs count (≥10), and FA/ADC values in the frontotemporal lobe and basal ganglia as independent variables, a multiple linear regression model was constructed. Results indicated that having ≥10 CMBs lesions, reduced FA values, increased ADC values, and involvement of the basal ganglia were independent risk factors for cognitive impairment (all $P < 0.05$),

Table 2 Comparison of FA and ADC Values Between the Two Groups by Brain Region

	Observation (n=71)	Control (n=65)	*t*	*P*
FA Values	–	–	–	–
Frontotemporal lobe	0.321±0.056	0.367±0.042	5.380	<0.001
Parietal lobe	0.348±0.049	0.384±0.038	4.756	<0.001
Occipital lobe	0.374±0.043	0.379±0.041	0.692	0.489
Basal ganglia	0.301±0.061	0.362±0.047	6.488	<0.001
ADC Values ($\times 10^{-3}$ mm^2/s)	–	–	–	–
Frontotemporal lobe	0.941±0.087	0.812±0.061	9.926	<0.001
Parietal lobe	0.914±0.079	0.835±0.057	6.634	<0.001
Occipital lobe	0.805±0.062	0.799±0.058	0.581	0.562
Basal ganglia	0.962±0.092	0.821±0.066	10.186	<0.001

Table 3 Correlation Analysis of CMBs Count, FA/ADC Values, and Cognitive Scores

Indicator	MoCA (r)	P
CMBs count	−0.643	<0.05
FA value (Frontotemporal)	0.529	<0.05
ADC value (Frontotemporal)	−0.597	<0.05
FA value (Basal ganglia)	0.563	<0.05
ADC value (Basal ganglia)	−0.626	<0.05

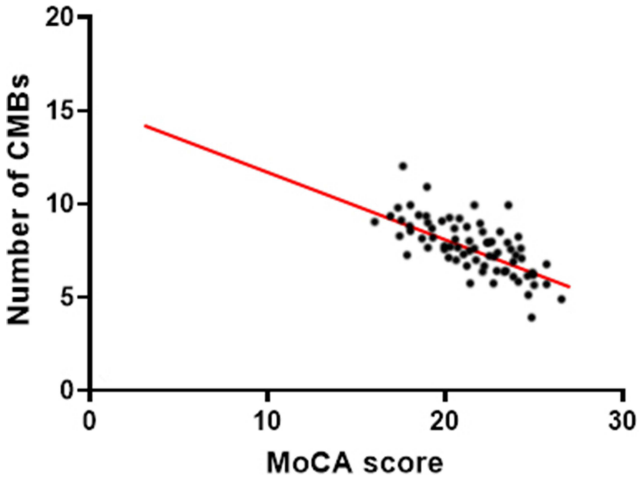

Figure 4 Scatter plot of correlation between CMBs count and cognitive scores.

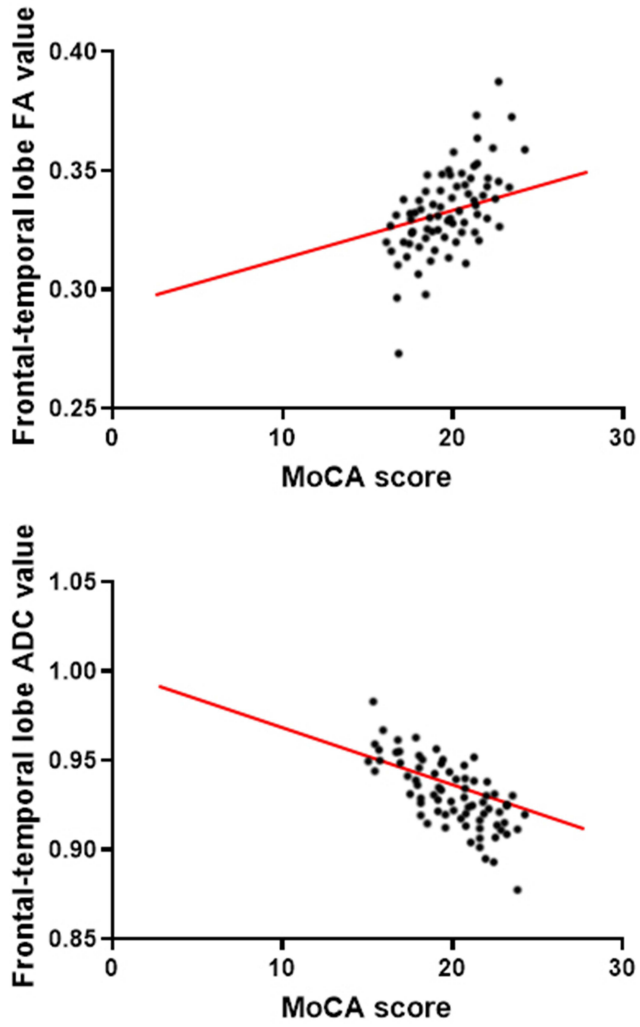

Figure 5 Scatter plot of correlation between FA/ADC values in frontotemporal lobe and cognitive scores.

https://doi.org/10.2147/IJGM.S556275

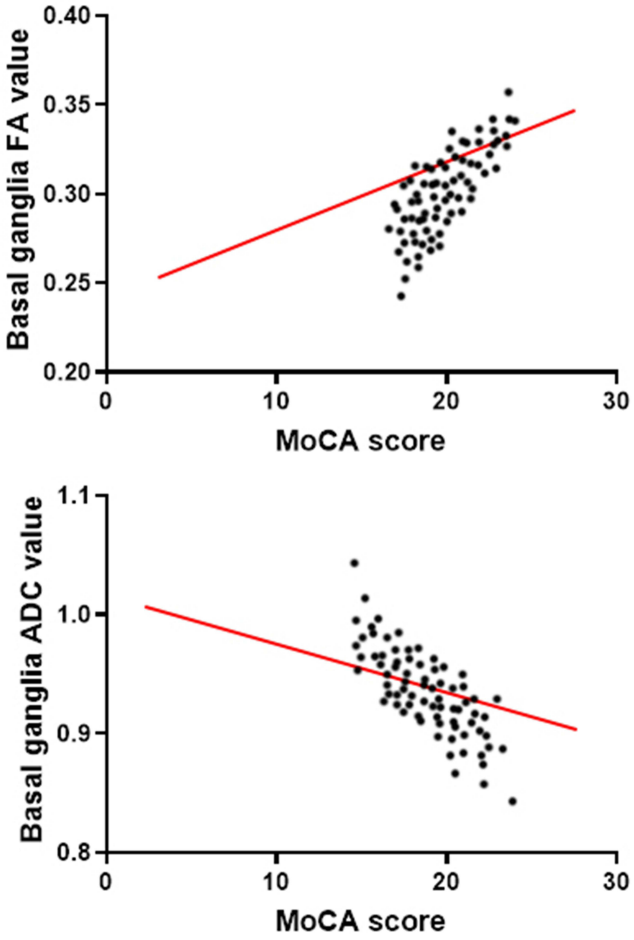

Figure 6 Scatter plot of correlation between FA/ADC values in basal ganglia and cognitive scores.

whereas hypertension and diabetes mellitus were not independently associated with MoCA scores (both $P > 0.05$). The final model explained 58.4% of the variance in cognitive performance (adjusted $R^2 = 0.584$). Model diagnostics demonstrated acceptable residual normality and no evidence of multicollinearity (all VIFs < 2.5), as shown in Table 4.

Table 4 Multiple Linear Regression Analysis: Independent Predictors of Cognitive Function (MoCA Score)

Variable	Standardized β	SE	95% CI for β	t	P	VIF
Age (years)	−0.084	0.031	−0.145 to −0.023	−1.72	0.089	1.42
Gender (male)	0.067	0.284	−0.49 to 0.62	0.83	0.408	1.18
Years of education	0.214	0.067	0.08 to 0.35	3.19	0.002	1.36
Hypertension	−0.091	0.312	−0.70 to 0.52	−0.29	0.774	1.51
Diabetes mellitus	−0.103	0.341	−0.77 to 0.56	−0.30	0.763	1.47
CMBs count ≥10	−1.873	0.521	−2.89 to −0.86	−3.594	<0.001	1.88
FA value (frontotemporal lobe)	2.112	0.604	0.93 to 3.29	3.497	<0.001	2.21
ADC value (frontotemporal lobe)	−1.538	0.431	−2.38 to −0.69	−3.568	<0.001	2.34
Basal ganglia involvement	−1.705	0.627	−2.93 to −0.48	−2.719	0.008	1.79

Discussion

This study aimed to explore the characteristics of cognitive impairment in patients with CMBs and its association with multimodal MRI parameters, further identifying independent risk factors influencing cognitive function. The results showed that patients with CMBs scored significantly lower on the MoCa scale compared to healthy controls, indicating notable cognitive impairment. Moreover, this study confirmed that the number, distribution, and microstructural changes in white matter (decreased FA, increased ADC) were closely related to the severity of cognitive deficits. A CMBs lesion count ≥10, basal ganglia involvement, and abnormal changes in FA/ADC values were identified as significant predictors of cognitive dysfunction.

Association Between CMBs and Cognitive Impairment

CMBs are key neuroimaging manifestations within the spectrum of CSVD, typically representing hemosiderin deposition from chronic hemorrhage in the brain parenchyma, commonly observed in SWI sequences.[11] The pathological basis includes microarteriolosclerosis, fibrinoid necrosis, microaneurysm formation, and blood-brain barrier dysfunction.[12] Persistent hypertension, cerebral arteriosclerosis, and cerebral amyloid angiopathy are major contributing factors for the formation of CMBs, which in turn may affect cerebral functional homeostasis through multiple mechanisms.[13] Although our study accounted for hypertension and diabetes in the regression model, further assessment of cerebrovascular comorbidities, including amyloid burden, is warranted to fully clarify the independent impact of CMBs.

Recent neuroimaging studies[14–16] have indicated that CMBs not only cause local microstructural damage but also disrupt the integrity of neural network connectivity, leading to dysfunction in remote brain areas. This is particularly evident in the cognitive systems of the elderly. Notably, DTI-based connectome studies have shown that CMBs can disrupt large-scale networks, including the default mode network and executive control network, contributing to domain-specific deficits such as impaired executive function and memory retrieval.[17,18] In this study, a significant negative correlation was observed between total CMBs count and cognitive scores (MoCA), suggesting a progressive decline in cognitive levels with increasing microbleed burden. This supports the currently proposed "lesion burden-related damage model",[19] where the number and cumulative impact of CMBs are positively associated with the extent of cognitive impairment.

Furthermore, the anatomical distribution of microbleeds may play a crucial role in the mechanism of cognitive decline. This study highlighted that the basal ganglia region was among the most common sites for microbleed occurrence, and its involvement was strongly associated with cognitive dysfunction. The basal ganglia are not only involved in motor control but also form cognitive function-related loops through connections with the prefrontal cortex, thalamus, and limbic system, governing executive control, motivation, working memory, and behavioral flexibility.[20] Therefore, when CMBs affect the basal ganglia, they may impair signal transmission within these circuits, resulting in inefficient information processing and executive dysfunction, manifested clinically as inattention, reduced planning ability, and poor adaptability.

Relationship Between White Matter Microstructure and Cognitive Function

White matter serves as the critical infrastructure for high-speed communication between brain regions, and its microstructural integrity is fundamental to higher-order cognitive activities.[21] DTI, a sophisticated technique for assessing white matter microstructure, has been widely applied in various neurological disorders. FA reflects the directional preference of water molecule diffusion along axons, representing axonal alignment and myelin integrity,[22] while ADC measures the overall diffusion level of water molecules and correlates with cell density and tissue complexity.[23] In this study, quantitative DTI analysis revealed significantly decreased FA values and increased ADC values in the frontal-temporal lobes, parietal lobes, and basal ganglia of CMBs patients compared to healthy controls, indicating microstructural damage in these brain regions. These alterations may reflect underlying pathologies such as axonal disruption, demyelination, or glial activation, suggesting that CMBs may induce not only focal deposition of blood components but also secondary damage to white matter structures, impairing the speed and accuracy of information transmission. From a network perspective, the observed regional FA/ADC changes likely reflect disruptions in large-scale networks, such as the default mode and executive control networks, which may underlie the domain-specific cognitive deficits observed in

these patients. From a functional localization perspective, the frontal-temporal lobes are central to executive functions, working memory, and language processing. Damage to these areas can directly lead to impairments in task-switching, contextual integration, and strategy formulation.[24] The parietal lobes are involved in spatial orientation and visual attention; white matter damage in these areas often results in reduced directional sense and diminished visual search efficiency.[25] The basal ganglia modulate executive control, emotional regulation, and reward mechanisms through loops connecting to the prefrontal cortex, thalamus, and limbic system, functioning as a core hub of the cognitive network. Structural abnormalities in this region can disrupt subcortical circuitry and lead to reduced behavioral motivation and delayed response speed.[26]

Further correlation analysis revealed that FA values in the frontal-temporal lobes and basal ganglia were positively correlated with MoCA scores, while ADC values were negatively correlated, supporting their role as sensitive imaging markers for cognitive impairment. These findings indicate a clear linear relationship between the degree of white matter damage in these regions and overall cognitive performance, suggesting potential utility for early risk identification and quantitative assessment of cognitive decline. Notably, this study did not find statistically significant correlations between FA/ADC values in the parietal lobes and cognitive scores, which may be attributed to several factors: First, damage in the parietal region may affect specific cognitive domains (eg, visuospatial abilities, sustained attention),[27] which are not fully captured by global cognitive measures such as MoCA. Second, the degree of parietal white matter damage in this study cohort might have been relatively mild, not reaching the threshold to impact overall cognitive function. Lastly, the parietal lobes may exhibit greater neuroplasticity and compensatory capacity, masking early damage in standard cognitive assessments.[28]

These findings are consistent with studies by Hernández-Díaz et al[29] and Hristovska et al[30] on CSVD-related white matter lesions and cognitive decline, reinforcing the concept that microstructural white matter damage, particularly within key functional hub regions, acts as a critical intermediary in CMBs-related cognitive impairment. Therefore, DTI not only offers superior sensitivity in detecting microstructural brain changes but also holds promise as a frontline imaging tool for cognitive risk assessment.

Clinical Application Value of Multivariate Regression Analysis in Cognitive Risk Assessment

By constructing a multivariate linear regression model, this study incorporated multiple variables that may affect cognitive function, including demographic factors (such as gender, age, and years of education), imaging characteristics (such as the number and distribution of CMBs), and microstructural white matter indicators (FA, ADC values, etc). The results showed that having ≥10 CMB lesions, involvement of the basal ganglia, decreased FA values, and increased ADC values were significant independent predictors of cognitive decline. These findings not only deepen the understanding of the mechanisms linking CMBs and cognitive impairment but also provide quantitative evidence for clinically identifying high-risk populations.

Unlike traditional methods that rely solely on cognitive scale scores or subjective clinical judgment, this study emphasized the value of quantitative imaging parameters in cognitive function assessment. Particularly in the early stages when some patients have not yet shown obvious symptoms of cognitive impairment, structural burden indicators based on MRI combined with DTI microstructural parameters can objectively predict the risk of potential cognitive damage, thereby improving the sensitivity and foresight of disease screening. Moreover, this integrative multifactor analysis model supports the formulation of individualized intervention strategies and helps in accurately identifying patient groups that require enhanced management and intervention. In addition, the progression of cognitive impairment in CMBs patients is often insidious and diverse,[31] and the independent predictive capabilities of the indicators in the regression model suggest that cognitive decline is not caused by a single factor but is the result of multiple brain structural damage mechanisms acting in concert.[32]

Strengths and Limitations of This Study

The main strength of this study lies in the use of multimodal MRI technology for a systematic assessment of patients with cerebral microbleeds. It not only focused on lesion count and distribution but, for the first time, incorporated microstructural indicators

such as FA and ADC to quantitatively explore their relationship with cognitive impairment, enhancing both precision and scientific rigor. Importantly, the findings suggest that patients with a high CMB burden or abnormal FA/ADC values in critical regions could be prioritized for enhanced cognitive monitoring. As a preliminary guideline, clinicians may consider follow-up intervals of 6–12 months and pay special attention when FA decreases by ≥ 0.05 or ADC increases by $\geq 0.1 \times 10^{-3}$ mm^2/s relative to baseline, although these thresholds require validation in larger cohorts.

In addition, future studies could leverage artificial intelligence and advanced computational modeling to integrate multimodal MRI parameters, cognitive assessments, and clinical features to develop early predictive models for cognitive decline. For example, recent computational neuroimaging frameworks demonstrate the feasibility of combining structural and functional MRI data to simulate network-level brain dynamics and predict domain-specific cognitive deficits.

There are also several limitations. First, this was a single-center retrospective study, and subtle differences in scanner hardware or protocols may introduce systematic bias, highlighting the need for multicenter validation. Second, the study did not conduct domain-specific cognitive analyses, which could help refine patterns of impairment across executive function, memory, attention, and visuospatial processing. Third, other CSVD markers (eg, white matter hyperintensities, lacunar infarctions) were not included, possibly underestimating cumulative pathological burden. Future work should integrate multimodal neuroimaging, electrophysiology, biomarkers, and longitudinal follow-up to construct multifactorial predictive models and evaluate whether interventions—such as neuroprotection, anti-inflammatory therapy, or vascular remodeling—can mitigate white matter damage and cognitive decline in CMBs patients.

Conclusion

This study systematically investigated the associations between CMBs, white matter microstructure, and cognitive function using cognitive assessments combined with multimodal MRI. The findings indicate that higher CMB burden, basal ganglia involvement, and region-specific alterations in FA and ADC are independently associated with cognitive impairment. These neuroimaging markers may serve as potential indicators for early risk stratification and for identifying patients who could benefit from closer cognitive monitoring.

The study highlights the clinical relevance of combining conventional MRI and DTI to detect microstructural white matter damage and to quantify alterations in brain integrity in CMBs patients. From a mechanistic perspective, the results support the role of CMB-related microstructural disruption in cognitive decline, providing a foundation for future longitudinal studies and interventional trials aimed at mitigating cognitive deterioration.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Liu SX, Song KY, Li Y, et al. Analysis of imaging features of age-related cerebral small vessel disease with idiopathic normal pressure hydrocephalus. *Zhonghua Yi Xue Za Zhi*. 2020;100(43):3402–3406. doi:10.3760/cma.j.cn112137-20200615-01853 Danish
2. Martínez Camblor L, Peña Suárez JM, Martínez-Cachero García M, et al. Cerebral microbleeds. Utility of SWI sequences. *Radiologia*. 2023;65(4):362–375. doi:10.1016/j.rx.2022.12.003
3. Ji FS. [The impact of cerebral microhemorrhage on antithrombotic strategies in patients with cardiovascular and cerebrovascular diseases]. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2024;52(8):879–883. doi:10.3760/cma.j.cn112148-20230828-00112 Polish
4. Litvinenko IV, Naumov KM, Lobzin VY, et al. [Traumatic brain injury as risk factor of Alzheimer's disease and possibilities of pathogenetic therapy]. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2024;124(1):45–54. doi:10.17116/jnevro202412401145 Hungarian
5. Schirò G, Balistreri CR. The close link between brain vascular pathological conditions and neurodegenerative diseases: focus on some examples and potential treatments. *Vascul Pharmacol*. 2022;142:106951. doi:10.1016/j.vph.2021.106951
6. Barus R, Bergeron S, Auger F, et al. Sex differences in cognitive impairment induced by cerebral microhemorrhage. *Transl Stroke Res*. 2021;12(2):316–330. doi:10.1007/s12975-020-00820-1
7. Eligulashvili A, Gordon M, Lee JS, et al. Long-term outcomes of hospitalized patients with SARS-CoV-2/COVID-19 with and without neurological involvement: 3-year follow-up assessment. *PLoS Med*. 2024;21(4):e1004263. doi:10.1371/journal.pmed.1004263
8. Dykan IM, Golovchenko Y, Loganovsky K, et al. Diffusion tensor magnetic resonance imaging in early diagnosis of structural changes in brain white matter in small vessel disease associated with arterial hypertension and ionizing radiation. *Probl Radiac Med Radiobiol, 2020*. 2020;25:558–568. doi:10.33145/2304-8336-2020-25-558-568
9. Jiang W, Wu Q, Zhou C, et al. Gray matter nuclei damage in acute carbon monoxide intoxication assessed in vivo using diffusion tensor MR imaging. *Radiol Med*. 2020;125(1):80–86. doi:10.1007/s11547-019-01078-w

10. Eleftheriou A, Blystad I, Tisell A, et al. Indication of thalamo-cortical circuit dysfunction in idiopathic normal pressure hydrocephalus: a tensor imaging study. *Sci Rep*. 2020;10(1):6148. doi:10.1038/s41598-020-63238-7
11. Wu ZR, Zong C, Zhang K, et al. [Analysis of coexisting and associated factors of intracerebral hemorrhage lesions in patients with recent subcortical small infarct]. *Zhonghua Yi Xue Za Zhi*. 2025;105(7):529–536. doi:10.3760/cma.j.cn112137-20241231-02976 Danish
12. Huang XH, Gao F, Yuan J, et al. Association of serum neurofilament light and glial fibrillary acidic protein with cerebral small vessel disease in nondemented middle-to-old aged population. *Transl Stroke Res*. 2025;16:1956–1965. doi:10.1007/s12975-025-01359-9
13. Luo Q, Tang H, Xu X, et al. *The* prevalence and risk factors of cerebral microbleeds: a community-based study in China. *Ther Clin Risk Manag*. 2021;17:165–171. doi:10.2147/TCRM.S297708
14. Xin H, Liang C, Fu Y, et al. Disrupted brain structural networks associated with depression and cognitive dysfunction in cerebral small vessel disease with microbleeds. *Prog Neuropsychopharmacol Biol Psychiatry*. 2024;131:110944. doi:10.1016/j.pnpbp.2024.110944
15. Yin J, Zhou X, Chen Y, et al. Cerebral microbleeds linked to structural network disruption and cognitive impairment in white matter hyperintensities. *Neuroscience*. 2025;564:31–40. doi:10.1016/j.neuroscience.2024.11.027
16. Fang Z, Chen X, Zhao Y, et al. Quantitative assessments of white matter hyperintensities and plasma biomarkers can predict cognitive impairment and cerebral microbleeds in cerebral small vessel disease patients. *Neuroscience*. 2025;564:41–51. doi:10.1016/j.neuroscience.2024.11.014
17. Feng M, Wen H, Xin H, et al. Decreased local specialization of brain structural networks associated with cognitive dysfuntion revealed by probabilistic diffusion tractography for different cerebral small vessel disease burdens. *Mol Neurobiol*. 2024;61(1):326–339. doi:10.1007/s12035-023-03597-0
18. Beaman C, Kozii K, Hilal S, et al. Cerebral microbleeds, cerebral amyloid angiopathy, and their relationships to quantitative markers of neurodegeneration. *Neurology*. 2022;98(16):e1605–e1616. doi:10.1212/WNL.0000000000200142
19. Duckworth H, Azor A, Wischmann N, et al. A finite element model of cerebral vascular injury for predicting microbleeds locatioN. *Front Bioeng Biotechnol*. 2022;10:860112. doi:10.3389/fbioe.2022.860112
20. Cherkasov NS, Tomyshev AS, Lebedeva IS, et al. [Structural features of the brain in amnestic mild cognitive impairment and their correlation with mild behavioral impairment]. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2025;125(6):112–119. doi:10.17116/jnevro2025125061112 Hungarian
21. Du RJ, Xue YT, Lu CQ. [A quantitative MRI comparative study of imaging markers for cerebral small vessel disease in the middle-aged and elderly patients with and without hypertension]. *Zhonghua Yi Xue Za Zhi*. 2024;104(28):2619–2625. doi:10.3760/cma.j.cn112137-20240110-00076 Danish
22. Feng HR, Wei YK, Lin QT, et al. [Correlation between postoperative microstructural changes in cerebral white matter and early postoperative cognitive function in patients undergoing meningioma resection]. *Zhonghua Yi Xue Za Zhi*. 2024;104(5):357–364. doi:10.3760/cma.j.cn112137-20231025-00900 Danish
23. Wang YJ, Liu -S-S, Liu Y-C, et al. [An assessment of white matter development in preterm infants with bronchopulmonary dysplasia using diffusion tensor imaging]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2020;22(10):1079–1084. doi:10.7499/j.issn.1008-8830.2004236 Xhosa
24. Mao LY, Cai Y, Zhang QQ, et al. [The association between frontotemporal connecting fibers and seizure severity in patients with temporal lobe epilepsy]. *Zhonghua Yi Xue Za Zhi*. 2024;104(21):1994–1997. doi:10.3760/cma.j.cn112137-20230919-00495 Danish
25. Yang YF, Jin B, Liu LZ, et al. [Changes of brain network characteristics in patients with depression before and after precise repetitive transcranial magnetic stimulation]. *Zhonghua Yi Xue Za Zhi*. 2022;102(43):3449–3456. doi:10.3760/cma.j.cn112137-20220415-00813 Danish
26. Song C, Li J, Xu H, et al. [Combination of apparent diffusion coefficient and amplitude-integrated electroencephalogram to predict the outcome of comatose patients with severe traumatic brain injury]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2021;33(5):609–612. doi:10.3760/cma.j.cn121430-20200611-00462 Dutch
27. Federico G, Reynaud E, Navarro J, et al. The cortical thickness of the area PF of the left inferior parietal cortex mediates technical-reasoning skills. *Sci Rep*. 2022;12(1):11840. doi:10.1038/s41598-022-15587-8
28. Zuber P, Gaetano L, Griffa A, et al. Additive and interaction effects of working memory and motor sequence training on brain functional connectivity. *Sci Rep*. 2021;11(1):23089. doi:10.1038/s41598-021-02492-9
29. Hernández-Díaz ZM, Peña-Sánchez M, González-Quevedo A, et al. Cerebral small vessel disease associated with subclinical vascular damage indicators in asymptomatic hypertensive patients. *Behav Sci*. 2019;9(9):91. doi:10.3390/bs9090091
30. Hristovska I, Binette AP, Kumar A, et al. Identification of distinct and shared biomarker panels in different manifestations of cerebral small vessel disease through proteomic profiling. *medRxiv*. 2024;23:2024–06
31. Nakamori M, Hosomi N, Tachiyama K, et al. Lobar microbleeds are associated with cognitive impairment in patients with lacunar infarction. *Sci Rep*. 2020;10(1):16410. doi:10.1038/s41598-020-73404-6
32. Liang YL, Wei WZ, Hou QZ, et al. [Screening and evaluation of clinical predictors of type 2 diabetes mellitus with cognitive impairment]. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2024;58(8):1184–1190. doi:10.3760/cma.j.cn112150-20240104-00016