

# FLAIR Vascular Hyperintensity: An Important MRI Marker in Patients with Transient Ischemic Attack

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**Purpose:** We aimed to investigate the prevalence of fluid-attenuated inversion recovery (FLAIR) vascular hyperintensities (FVHs) and the clinical–radiological correlation in transient ischemic attack (TIA) patients.

**Materials and Methods:** We performed a retrospective analysis of TIA patients who had undergone magnetic resonance imaging (MRI) within 24 h of symptom onset. Two independent neuroradiologists investigated the presence of FVHs, large-artery severe stenosis or occlusion (LASO) in magnetic resonance angiograms, and the nature of factors associated with FVH.

**Results:** A total of 207 patients were enrolled in this study. FVHs were detected in 42 (20.3%) patients, in whom atrial fibrillation (AF) was confirmed in 25 (59.5%) cases and LASO was confirmed in 30 (71.4%) cases. The corresponding figures were 33 (20.0%) and 10 (6.1%), respectively, for the 165 FVH-negative patients. Logistic regression analysis showed that time from symptom onset to MRI (odds ratio [OR] = 0.82, 95% CI 0.76–0.97,  $p = 0.042$ ), previous stroke (OR = 2.95, 95% CI 1.58–6.74,  $p = 0.002$ ), AF (OR = 5.83, 95% CI 2.24–9.46,  $p < 0.001$ ), and LASO (OR = 4.28, 95% CI 2.96–10.28,  $p < 0.001$ ) were independently associated with FVH. Overall, the sensitivity and specificity of FVH for predicting LASO were 0.75 and 0.93, respectively, and the positive predictive value, negative predictive value, and accuracy were 0.71, 0.94, and 0.89, respectively. The area under the receiver operating characteristic curve was 0.839. FVH-positive TIA patients with LASO had less AF (14 [46.7%] versus 11 [91.7%],  $p = 0.019$ ) and longer times from symptom onset to MRI ( $6.8 \pm 2.8$  h versus  $4.8 \pm 1.3$  h,  $p = 0.004$ ) than those without LASO.

**Conclusion:** The presence of FVH could be an important marker in TIA patients. Many factors, including LASO, AF, and time from symptom onset to MRI, are associated with the detection of FVH.

**Keywords:** FLAIR vascular hyperintensity, hyperintense vessel, transient ischemic attack, magnetic resonance imaging

## Background

Transient ischemic attack (TIA) is traditionally defined as the sudden onset of a focal neurological deficit of presumed vascular origin that resolves completely within 24 h.<sup>1–3</sup> Several neuroimaging-based evaluation techniques, including computed tomography, digital subtraction angiography, magnetic resonance imaging (MRI), and nuclear medical imaging, have been proposed to help identify patients at high risk of true ischemic events.<sup>1,4,5</sup> MRI is a relatively sensitive imaging modality that has high predictive value for diagnosing ischemic insults. However, if the severity or duration of ischemia is not sufficient to cause permanent damage, conventional magnetic resonance (MR) findings may be negative, which makes early diagnosis of true TIA or nonischemic etiologies difficult.<sup>6,7</sup>

Large-artery severe stenosis or occlusion (LASO) is considered to involve a remarkable reduction in flow velocity because of vascular stenosis or occlusion and the occurrence of collateral blood flow.<sup>8</sup> It has been identified

that the presence of LASO has the highest predictive value, and LASO has long been recognized as a major risk factor for future stroke after TIA.<sup>9</sup> Fluid-attenuated inversion recovery (FLAIR) vascular hyperintensities (FVHs) are serpentine or linear hyperintensities that are best visualized within the Sylvian fissure ipsilateral to acute ischemic stroke.<sup>10,11</sup> FVH has demonstrated good diagnostic performance for the identification of LASO in stroke, but the relationship between FVH and TIA is still undetermined. The purpose of this study was to investigate the prevalence of FVH and the clinical–radiological correlation in patients with TIA.

## Materials and Methods

### Subjects

We retrospectively investigated the records of patients with TIA in our hospital from January 2015 to December 2021. TIA was defined as a sudden focal neurological deficit with a duration of less than 24 h without acute infarction on imaging. Each diagnosis of TIA was made jointly by at least two neurologists. Enrollment criteria included: (a) transient neurological symptoms thought by a clinical neurologist at the end of evaluation to have a possible vascular etiology; (b) MR scans performed within 24 h of symptom onset; (c) without prior history of stroke, and nonspecific findings on general MR and diffusion-weighted exams; and (d) the patient underwent a magnetic resonance angiography (MRA) study. Exclusion criteria were as follows: (a) a history of stroke, cranial trauma, brain tumors, mental illness, or other known brain abnormality; (b) the patient had severe coexisting or terminal systemic disease; and (c) the image quality was insufficient to assess FVH. The clinical background characteristics of patients, including cardiovascular risk factors, time from symptom onset to MRI, and clinical symptoms of TIA, were collected. Atrial fibrillation (AF) was diagnosed on the basis of either an electrocardiogram performed within 24 h or a confirmed history. ABCD<sup>2</sup> scores were generated according to the presence of pre-existing conditions in TIA patients. This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Hospital of Chengdu University of Traditional Chinese Medicine Research Ethics Committee.

### MRI Protocol

All patients underwent MRI with a Discovery MR750 3.0 T system (GE Healthcare, Milwaukee, WI, USA) and an eight-channel phased-array head coil. The imaging protocol consisted of T2 weighting (repetition time/echo time, 3480/110 ms; field of view [FOV], 240 mm × 240 mm; matrix, 256 × 256; section thickness, 6 mm; gap, 2 mm), T1 weighting (repetition time/echo time/inversion time, 1780/20/860 ms; FOV, 240 mm × 240 mm; matrix, 256 × 256; section thickness, 6 mm; gap, 2 mm), T2-FLAIR (repetition time/echo time/inversion time, 8400/140/2370 ms; FOV, 260 mm × 260 mm; matrix, 256 × 256; section thickness, 5 mm; gap, 1.5 mm), diffusion-weighted imaging (repetition time/echo time, 3000/74 ms; FOV, 240 mm × 240 mm; matrix, 260 × 260; section thickness, 5 mm with no gap; b = 0 and 1000 s/mm<sup>2</sup>), and MRA (repetition time/echo time, 8.2/3.2 ms; FOV, 240 mm × 240 mm; matrix, 256 × 256; slice thickness, 1 mm).

### Image Evaluation

FVHs were defined as linear or serpentine hyperintensities with respect to gray matter in the subarachnoid space that corresponded to typical arterial courses on the T2-FLAIR image. Two independent neuroradiologists who were blinded to clinical information reviewed FLAIR images to identify FVHs and MRA images to locate large-vessel occlusions when present. Patients were divided into FVH-positive and FVH-negative groups on the basis of the presence of an FVH sign. Large vessels were defined as the internal carotid artery, middle cerebral artery (MCA) M1, and MCA M2. Patients who were FVH-positive were divided into two groups, namely, those with LASO and those without large-vessel occlusion, according to the occlusion sites identified by MRA.

### Statistical Analysis

Interobserver agreement was assessed using the kappa ( $\kappa$ ) statistic. A value of  $\kappa > 0.6$  was considered to represent good agreement, while  $\kappa > 0.8$  was considered to represent excellent agreement. Continuous variables with a normal

distribution were described as the mean  $\pm$  SD, and categorical variables were described in terms of frequency (%). The difference in each categorical variable between patients with and without FVH was analyzed using the Mann–Whitney *U*-test, Student's *t*-test, chi-squared tests, and Fisher's exact test (when the expected cell frequency was  $<5$ ). Logistic regression analysis was used to test for independence among predictors for the presence of FVH. Diagnostic parameters (sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate) were also calculated for FVH in predicting LASO tested against MRA as the gold standard. The predictive values were determined by receiver operating characteristic (ROC) analysis. A two-tailed *p*-value of  $<0.05$  was considered to indicate a statistically significant difference. All statistical analyses were performed using SPSS software version 20.0 (SPSS, Inc., Chicago, IL, USA).

## Results

### Demographic and Clinical Information

A total of 272 patients with TIA were retrospectively identified, of whom 65 were excluded. Thirty-six patients were excluded as there were no available angiography findings; 20 patients were excluded as a result of delays in MRI or angiography; and nine patients were excluded because of severe artifacts on FLAIR. Finally, the remaining 207 patients (mean age,  $60.8 \pm 9.0$  years; 120 female/87 male) met the inclusion criteria and were retrospectively enrolled in this study. Agreement between two readers on the presence of FVHs ( $\kappa = 0.84$ ) and the location of occlusions ( $\kappa = 0.89$ ) was good. Characteristics of TIA patients with and without FVH are listed in Table 1.

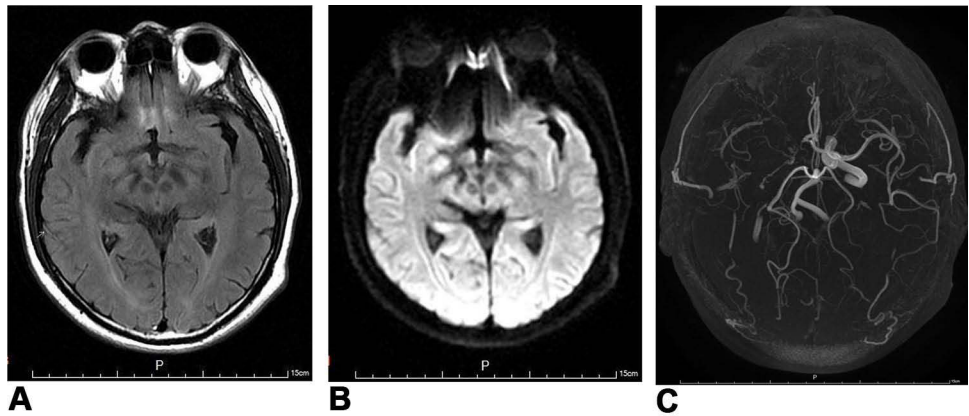
FVHs were detected in 42 (20.3%) patients. The commonest presenting symptoms were focal weakness, speech disturbance, dizziness, and vertigo. The median time between symptom onset and imaging was  $8.1 \pm 3.5$  h. The majority of FVH-positive patients (32/42, 76.2%) had symptoms thought to represent hemispheric TIA. Among these 42 patients, AF was confirmed in 25 (59.5%) cases, and LASO was confirmed in 30 (71.4%) cases. The corresponding figures were 33 (20.0%) and 10 (6.1%), respectively, for the 165 FVH-negative patients. The FVH-positive patients and FVH-negative patients exhibited significant differences in history of TIA, time from symptom onset to MRI, history of previous stroke, AF, and LASO. A representative case of an FVH-positive patient with LASO is shown in Figure 1. Univariate analyses revealed that FVH-positive patients were significantly more likely to have a history of

**Table 1** Characteristics of TIA Patients with and without FLAIR Vascular Hyperintensity

	FVH-Positive (n=42)	FVH-Negative (n=165)	<i>p</i> -value
Age (y)	58.4 $\pm$ 6.8	61.4 $\pm$ 9.4	0.054
Female sex	26 (61.9%)	94 (57.0%)	0.563
Characteristics of TIA			
History of TIA	17 (40.5%)	24 (15.5%)	$<0.001^*$
Median ABCD <sup>2</sup> score	3.7 $\pm$ 0.8	3.6 $\pm$ 0.7	0.306
Symptoms onset to MRI (hours)	6.2 $\pm$ 2.6	8.5 $\pm$ 3.6	$<0.001^*$
Duration of TIA ( $\geq 1$ h)	12 (28.6%)	52 (31.5%)	0.712
Risk factor			
Previous stroke	17 (40.5%)	32 (19.4%)	0.004*
Hypertension	26 (61.9%)	94 (57.0%)	0.563
Diabetes mellitus	7 (16.7%)	31 (18.8%)	0.751
Hyperlipidemia	21 (50.0%)	89 (53.9%)	0.648
Current smoking	8 (19.0%)	42 (25.5%)	0.386
Atrial fibrillation	25 (59.5%)	33 (20.0%)	$<0.001^*$
LASO	30 (71.4%)	10 (6.1%)	$<0.001^*$

**Note:** \*There is significant difference between two groups.

**Abbreviations:** LASO, large artery severe stenosis or occlusion; ABCD<sup>2</sup>, age, blood pressure, clinical features, duration of TIA, diabetes.



**Figure 1** A 53-year-old male with a history of hypertension, hyperlipidemia, and recurrent transient ischemic attack underwent a magnetic resonance scan 4 h after sudden-onset vertigo. **(A)** T2 fluid-attenuated inversion recovery (FLAIR) showing FLAIR vascular hyperintensity (FVH) in the region of the right middle cerebral artery (arrow) and **(B)** diffusion-weighted imaging demonstrated no abnormal findings. **(C)** Magnetic resonance angiogram showing occlusion of the right intracranial internal carotid and middle cerebral arteries.

TIA, previous stroke, AF, and LASO and shorter times from symptom onset to MRI than patients without FVH. Logistic regression analysis showed that time from symptom onset to MRI (odds ratio [OR] = 0.82, 95% CI 0.76–0.97,  $p = 0.042$ ), previous stroke (OR = 2.95, 95% CI 1.58–6.74,  $p = 0.002$ ), AF (OR = 5.83, 95% CI 2.24–9.46,  $p < 0.001$ ), and LASO (OR = 4.28, 95% CI 2.96–10.28,  $p < 0.001$ ) were independently associated with FVH positivity (Table 2).

Performance of FVH in Predicting Occlusion/Stenosis

Results for the performance of FVH in predicting LASO are listed in Table 3. Overall, the sensitivity and specificity of FVH for predicting LASO were 0.75 and 0.93, respectively, while the positive predictive value, negative predictive value, and accuracy were 0.71, 0.94, and 0.89, respectively. The ROC curve is shown in Figure 2. The area under the curve was 0.839.

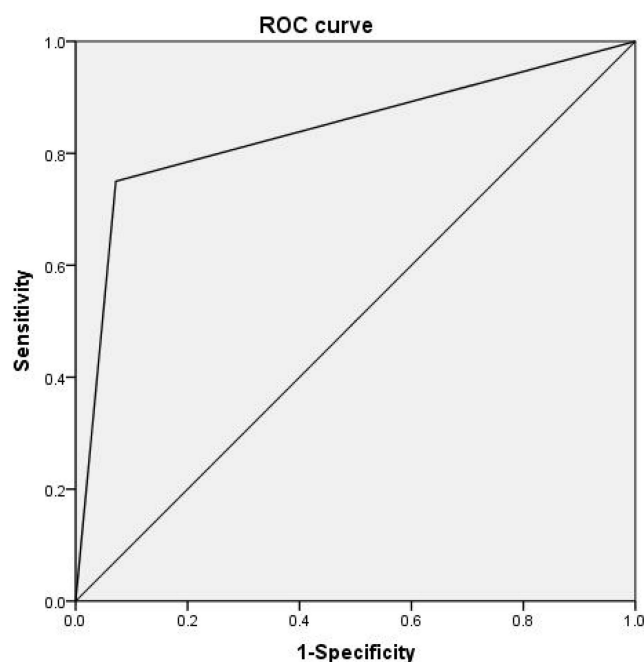
**Table 2** Multivariate Logistic Regression Analysis of Parameters Associated with FVH

	Odds Ratio	95% CI	p-value
History of TIA	2.74	0.95–5.81	0.547
Symptoms onset to MRI	0.82	0.76–0.97	0.042*
Previous stroke	2.95	1.58–6.74	0.002*
Atrial fibrillation	5.83	2.24–9.46	<0.001*
LASO	4.28	2.96–10.28	<0.001*

**Note:** \*There is significant difference between two groups.  
**Abbreviations:** FVH, FLAIR vascular hyperintensity; LASO, large artery severe stenosis or occlusion; CI, confidence interval.

**Table 3** Results of the Performances of FVH in Predicting LASO

	Patients with LASO (n=40)	Patients without LASO (n=167)
FVH-positive	30	12
FVH-negative	10	155



**Figure 2** Receiver operating characteristic analysis of FVH for the prediction of large-artery severe stenosis or occlusion. The area under the curve was 0.839.

## Results for FVH-Positive Patients with and without LASO

Table 4 lists detailed characteristics of FVH-positive TIA patients with and without LASO. Among the 42 FVH-positive TIA patients, LASO was confirmed in 30 cases and was absent in the remaining 12 cases. FVH-positive TIA patients with LASO had less AF (14 [46.7%] versus 11 [91.7%],  $p = 0.019$ ), longer times from symptom onset to MRI ( $6.8 \pm 2.8$  h versus  $4.8 \pm 1.3$  h,  $p = 0.004$ ), and a higher percentage rate of previous stroke (53.3% [16/30] versus 8.3% [1/12],  $p = 0.019$ ) than those without LASO.

**Table 4** Characteristics of the FVH-Positive TIA Patients with and without LASO

	Patients with LASO (n=30)	Patients without LASO (n=12)	p-value
Age (y)	57.8±6.6	60.1±7.3	0.327
Female sex	18(60.0%)	8(66.7%)	0.960
Characteristics of TIA			
History of TIA	14(46.7%)	3(25.0%)	0.345
Median ABCD <sup>2</sup> score	3.9±0.8	3.3±0.5	0.007*
Symptoms onset to MRI (hours)	6.8±2.8	4.8±1.3	0.004*
Duration of TIA (≥ 1 h)	9(30.0%)	3(25.0%)	1.000
Risk factor			
Previous stroke	16(53.3%)	1(8.3%)	0.019*
Hypertension	18(60.0%)	8(66.7%)	0.960
Diabetes mellitus	5(16.7%)	2(16.7%)	1.000
Hyperlipidemia	15(50.0%)	6(50.0%)	1.000
Current smoking	5(16.7%)	3(25.0%)	0.852
Atrial fibrillation	14(46.7%)	11(91.7%)	0.019*

**Note:** \*There is significant difference between two groups.

**Abbreviations:** LASO, large artery severe stenosis or occlusion; ABCD<sup>2</sup>, age, blood pressure, clinical features, duration of TIA, diabetes; FVH, FLAIR vascular hyperintensity; LASO, large artery severe stenosis or occlusion.

## Discussion

There are three main findings from the current study. Firstly, the presence of FVH was observed in 20.3% of TIA patients within 24 h, which is consistent with previous studies. Secondly, FVH demonstrated excellent diagnostic performance for the identification of LASO, and FVH-positive patients were significantly more likely to have severe stenosis or occlusion, higher percentage rates of AF, and shorter times from symptom onset to MRI than those without FVH. Thirdly, FVH-positive TIA patients with LASO had less AF and longer times from symptom onset to MRI than those without LASO.

According to previous reports,<sup>12–15</sup> the prevalence of FVH in TIA patients varied remarkably from 16% to 39.6% and was significantly lower than in acute ischemic stroke. When analyzing factors pertaining to FVH in our study, we found that a history of TIA, AF, and LASO were commoner in instances of FVH positivity, which is consistent with previous studies. Nam et al<sup>12</sup> reported that FVH was associated with early recurrence of ischemic lesions in patients with lesion-negative TIA. In our study, the percentages of patients with histories of TIA and previous stroke in the FVH-positive group were significantly higher in comparison with the FVH-negative group. The detection of FVH could be important for such patients.

The mechanism underlying FVH is still controversial, but the association of FVH in acute ischemic stroke with large-artery occlusion or stenosis is well established.<sup>16,17</sup> TIA is a common medical emergency and may precede ischemic stroke that causes permanent neurological deficits.<sup>3,18</sup> Patients presenting with transient neurological symptoms with evidence of LASO are at a higher risk of subsequent stroke. The early diagnosis and management of TIA with LASO is therefore a matter of clinical urgency to prevent possible stroke. In our study, 71.4% (30/42) of FVH-positive patients were identified as having LASO. Ding et al<sup>19</sup> reported that FVH was observed in up to 81.6% (31/38) of hospitalized TIA patients who had severe stenosis or occlusion. In the present study, FVH was detected in 75.0% (30/40) of patients with LASO. FVH may have utility in the evaluation of patients experiencing TIA, especially in patients in whom MRA is not performed.

Some FVHs in TIA patients were proved to be transient and were correlated with symptom resolution.<sup>20</sup> Two independent factors, namely, AF and arterial occlusion/stenosis, had significant and independent associations with FVH.<sup>17,21</sup> AF was thought to be associated with transient FVH, while arterial stenosis or occlusion was thought to be associated with persistent FVH.<sup>15</sup> Transient FVH with normal MRA findings was related to a mechanism of paroxysmal AF and early recanalization of emboli but was not associated with an increased risk of stroke. In contrast, persistent FVH was related to arterial occlusion and was associated with an increased risk of recurrent TIA and ischemic stroke. Kobayashi et al<sup>15</sup> reported that AF was commoner than arterial occlusive lesions in FVH-positive patients, but in our study the incidence of AF (59.5%) was lower than that of arterial occlusion (71.4%).

It is noted that the time from symptom onset to MRI in the FVH-positive group was significantly shorter in comparison with the FVH-negative group. On the other hand, in the FVH-positive group the time from symptom onset to MRI in patients without LASO was shorter in comparison with patients with LASO. We believe that the time from symptom onset may significantly influence the presence of FVHs. As previously reported, some FVHs are transient and may disappear when symptoms are relieved. Hence, we believe that some of the patients in the FVH-negative group had originally been FVH-positive. FVH-positive patients with LASO tended to be associated with persistent FVH, which did not resolve despite the longer duration of symptoms.

The current study had several limitations. Firstly, we investigated a relatively small, although relatively uniform, cohort of patients with TIA. The next step will be to repeat this type of investigation with a larger cohort of subjects. Secondly, follow-up MRI is needed to evaluate the persistence and prognostic value of FVH.

## Conclusions

The present study demonstrated that the presence of FVHs could be an important and convenient imaging marker for TIA patients. Many factors including LASO, AF, and time of symptoms onset to MRI are associated with the detection of FVHs. We are confident that this radiologic marker will provide a useful tool for future prevention and early intervention.

## Acknowledgments

The scientific guarantors of this publication are Mingguo Xie and Wenbin Wu. Authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article. The authors state that this work has not received any commercial funding.



## Funding

This research was funded by National Key R&D Program of China (2020YFC2003100, 2020YFC2003104) and the “Xing-lin Scholars” Project of Chengdu University of Traditional Chinese Medicine (Grant No. QNXZ2018004).

## Disclosure

The authors have no financial and/or non-financial conflicts of interest.

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