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HEAD AND NECK

FLAIR vascular hyperintensity in acute stroke is associated with collateralization and functional outcome

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Abstract

Purpose Fluid-attenuated inversion recovery vascular hyperintensity (FVH) is frequently found in stroke patients after intracranial arterial occlusion, but the prognostic value of FVH findings is unclear. We assessed whether FVH is associated with cerebral collateral status and functional outcome in patients with acute stroke patients receiving endovascular therapy.

Methods FVH score, American Society of Interventional and Therapeutic Neuroradiology (ASITN) grade, the functional outcome at 3 months (modified Rankin Scale (mRS)), and other clinical data were collected for 37 acute stroke patients with large vessel occlusion (LVO) receiving MRI before and after endovascular therapy. Statistical analysis was performed to predict functional outcome after stroke.

Results The good functional outcome group ($n = 16$) had a higher FVH_1 (FVH before therapy) score (4.63 ± 1.20 vs 3.14 ± 1.15; $p = 0.001$) and ASITN grade (3.31 ± 0.48 vs 2.00 ± 1.22; $p < 0.001$) and a lower FVH_2 (FVH after therapy) score than the poor functional outcome group ($n = 21$; 0.125 ± 0.50 vs 1.44 ± 2.16; $p = 0.030$). mRS at 3 months was negatively correlated with FVH_1 ($r = -0.525$, $p = 0.001$) and the ASITN grade ($r = -0.478$, $p = 0.003$) and positively correlated with FVH_2 ($r = 0.376$, $p = 0.034$). FVH_1 (OR, 0.085; 95% CI, 0.013–0.577; $p = 0.012$) and FVH_2 (OR, 2.724; 95% CI, 1.061–6.996; $p = 0.037$) were independently associated with functional outcome in multivariable logistic regression analysis.

Conclusions Assessing FVH before and after therapy in acute stroke patients with LVO might be useful for predicting functional outcome after stroke.

Key Points

- *Fluid-attenuated inversion recovery vascular hyperintensity is a circular or serpentine brightening in the brain parenchyma or cortical surface bordering the subarachnoid space on MR imaging.*
- *A prospective study showed that fluid-attenuated inversion recovery vascular hyperintensity is associated with cerebral collateral circulation and prognosis.*
- *Fluid-attenuated inversion recovery vascular hyperintensity helps clinicians to predict the prognosis of patients with acute stroke.*

Keywords Stroke · Magnetic resonance imaging · Angiography · Collateral circulation · Prognosis

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Abbreviations

ASITN	American Society of Interventional and Therapeutic Neuroradiology
ASPECTS	Alberta Stroke Program Early CT Score
CI	Confidence interval
CTA	Computed tomography angiography
DSA	Digital subtraction angiography
DWI	Diffusion-weighted imaging
FLAIR	Fluid-attenuated inversion recovery
FVH	Fluid-attenuated inversion recovery vascular hyperintensity

LVO	Large vessel occlusion
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
mRS	Modified Rankin Scale
mTICI	Modified Thrombolysis in Cerebral Ischemia
NIHSS	National Institutes of Health Stroke Scale

Introduction

Acute stroke is characterized by ischemic penumbra, which is tenuously perfused by collateral blood. Good collateral vessels can improve the odds for a larger volume of surviving brain tissue by sustaining the ischemic penumbra [1, 2]. Most cases of acute stroke with robust collaterals usually have better clinical outcomes [3]. Standard methods for evaluating collaterals in the acute setting include computed tomography angiography (CTA) [4], magnetic resonance angiography (MRA) [5], and digital subtraction angiography (DSA) [6]; however, the use of CTA and MRA to assess collaterals is insufficient and requires direct comparison with angiography—the gold standard for cerebral collateralization assessment [3, 7].

Fluid-attenuated inversion recovery vascular hyperintensity (FVH) is a circular or serpentine brightening in the brain parenchyma or cortical surface bordering the subarachnoid space [8]. FVH is frequently found in large vessel steno-occlusive disease due to atherosclerosis or other vasculopathies such as Moyamoya disease [9–11]. Notably, FVH is seen in 45–100% of patients with stroke after an intracranial arterial occlusion [12]. Most studies agree that FVH is associated with large vessel occlusion [12] and represents slow retrograde flow in leptomeningeal collaterals [13]. Although the pathophysiological interpretation of FVH is not entirely clear at present, FVH may provide prognostic information despite the inconsistent results. Some studies found that FVH is associated with poor functional outcome and represents insufficient collateralization [12, 14]. However, others have reported that FVH has good prognostic value and is indicative of sufficient collateralization [10, 15]. These discrepancies may be due to differences in populations, end points, or FVH classifications. Interestingly, FVH disappears in some but not all patients after endovascular therapy; however, currently available studies have reported only the association of FVH before endovascular therapy with functional outcome in patients with acute stroke. Whether the prognostic value of FVH after therapy is similar to that of FVH before therapy has not been reported.

Therefore, in this study, we hypothesized that FVH reflects collateral status and predicts functional outcome in acute stroke patients. We sought to assess whether FVH is associated with cerebral collateral status and functional outcome 3 months after acute stroke in patients who received endovascular therapy. Furthermore, whether FVH after therapy is associated with functional outcome was assessed.

Materials and methods

Subjects and clinical data

The hospital review board of Nanjing Medical University approved the study protocol. We prospectively evaluated consecutive acute stroke patients who were admitted to the Nanjing First Hospital from January 2017 to March 2018. Acute stroke was defined as acute clinical vascular syndrome with evidence of cerebral infarction on DWI. Intravenous thrombolysis (alteplase; rt-PA) was administered after CT scanning followed immediately by MRI. If large vessel occlusion (LVO) was found on MRA, a thrombectomy was performed immediately. LVO was defined as middle cerebral artery (MCA)-M1 or internal carotid artery (ICA) occlusion on MRA and underwent thrombectomy; non-LVO was defined as no large vessel (e.g., M1, ICA) occlusion on MRA and underwent only intravenous thrombolysis. Bridging therapy was defined as patients who received both intravenous thrombolysis and thrombectomy. A total of 116 patients were screened, 28 patients were excluded, and 88 patients were included. The patients included in the present study presented the following: (1) a first-ever acute anterior circulation stroke or a previous stroke with hemiplegia sequelae that did not affect the neurological score; (2) acute stroke patients ≤ 4.5 h of symptom onset; (3) pretreatment MRI with DWI, fluid-attenuated inversion recovery (FLAIR), and MRA; (4) intravenous thrombolysis and/or thrombectomy; and (5) a clinical follow-up of the modified Rankin Scale (mRS) at 3 months. The exclusion criteria were as follows: (1) cerebral hemorrhage, tumor or trauma detected by the CT scanner; (2) any contraindication for MRI; (3) any missing mRS at 3 months after stroke; (4) refusal of thrombolysis or thrombectomy; (5) any MRI or DSA that could not be evaluated due to a motion artifact; (6) patients did not receive thrombectomy due to chronic thrombosis occlusion during DSA examination or thrombus in large vessel still existed after thrombectomy; and (7) patients with MCA-M2, MCA-M3, or vertebrobasilar artery occlusion.

Age; sex; homocysteine; the National Institutes of Health Stroke Scale (NIHSS) score; history of hypertension, diabetes mellitus, hyperlipidemia, and atrial fibrillation; and hospital admission and discharge data were collected. Functional outcome at 3 months was assessed using the mRS. A good clinical outcome was defined as an mRS score ≤ 2 at 3 months. All patients in this study provided written informed consent before examination. The study was approved by the local ethics committee of the Nanjing Medical University.

MRI protocol

Pretreatment and follow-up MRI scans were performed using a 3.0 Tesla MRI scanner (Ingenia, Philips Medical Systems) with an eight-channel receiver array head coil. The MRI protocol included fluid-attenuated inversion recovery (FLAIR) axis sequencing, DWI axial scanning, and MRA. The scanning parameters were as follows: FLAIR (inverse recovery (IR) sequence, TR 7000 ms; TE 120 ms; acquisition matrix, 356 × 151; field of view (FOV), 230 mm × 230 mm; flip angle (FA), 90°; slices, 18; section thickness, 6 mm; and intersection gap, 1.3 mm) and DWI (spin echo (SE) sequence, TR, 2501 ms; TE, 98 ms; acquisition matrix, 152 × 122; 3 directions; FOV, 230 mm × 230 mm; FA, 90°; slices, 18; section thickness, 6 mm; and intersection gap, 1.3 mm. DWI was obtained with *b* values of 0 and 1000 s/mm^2. 3D-MRA scans were obtained using the fast field echo (FFE) sequence with the following parameters: TR, 4.9 ms; TE, 1.82 ms; acquisition matrix, 528 × 531; FOV, 330 mm × 330 mm; section thickness, 1.2 mm.

Image analysis

FVH was defined as focal, tubular, or serpentine hyperintensity present in the subarachnoid space relative to cerebrospinal fluid with a typical arterial course [8]. Two experienced neuroradiologists (YX and YM), blinded to the clinical data, assessed FVHs using the FVH score according to their spatial distribution in the Alberta Stroke Program Early CT Score (ASPECTS) cortical areas (insula, M1–M6) [16]. The FVH scores ranged from 0 (no FVH) to 7 (FVHs abutting all ASPECTS cortical areas) and were divided into low FVH score (0–3 score) and high FVH score (4–7 score). The FVH scores before and after therapy were defined as FVH_1 and FVH_2, respectively. In case of a discrepant score between the two readers, images were reviewed, and a consensus was established.

Two experienced interventional neuroradiologists who were blinded to the clinical information assessed the baseline angiography data of the endovascular therapy patients. Revascularization success was graded using the Modified Thrombolysis in Cerebral Ischemia (mTICI) score (0 = complete occlusion to 3 = complete revascularization). A good mTICI score was defined as mTICI 2b-3. The collateral grading score was evaluated using the American Society of Interventional and Therapeutic Neuroradiology (ASITN) scoring system (0 = no collaterals to 4 = complete and rapid collateral perfusion of ischemic territory) [17]. Good collateral status was defined by an ASITN grade of 3–4 [18].

Statistical analysis

Continuous data are shown as the mean ± SD, whereas categorical variables are presented as absolute and relative frequencies. We analyzed the differences between groups using the chi-squared test for categorical variables and an independent-samples *t* test or Fisher's exact test for continuous variables. $p < 0.05$ was considered to indicate statistically significance. The possible associations among FVH, ASITN grade, and functional outcome were analyzed by calculating Spearman's rank correlation coefficients. Logistic regression analysis of significantly associated variables ($p < 0.05$) was used to identify factors predictive of good functional outcome. Univariate and multivariate logistic regression analysis was performed using mRS at 3 months as the outcome variable, and the OR and 95% CI were obtained. All statistical analyses were conducted using commercially available software (SPSS for Windows, version 19.0; SPSS).

Results

During the study period, 116 patients underwent intravenous thrombolysis and/or thrombectomy. Twenty-eight patients were excluded (no pretreatment MRI, $n = 9$; severe artifacts on DWI or FLAIR, $n = 12$; no mRS at 3 months, $n = 7$), and 88 patients were included in the analysis (Table 1). Thirty-seven patients (41.57%) had LVO, 23 of whom received thrombectomy (62.16%) and 14 of whom received bridging therapy (37.84%); 51 patients (57.30%) with non-LVO were treated with intravenous thrombolysis. The patients did not differ with regard to sex ($p = 0.956$), age ($p = 0.533$), median time to onset ($p = 0.947$), or median time to MRI scan ($p = 0.094$). The presence of $FVH_1$was observed in 65 patients (73.03%). Interestingly, FVH_1 was found more frequently in patients with LVO (94.59%) compared with that in patients with non-LVO (58.82%). The FVH_1 and FVH_2 scores were significantly higher in patients with LVO than in patients with non-LVO ($p < 0.001$; $p = 0.029$, respectively). Although the NIHSS score at admission and discharge and the DWI volume in patients with LVO were significantly higher than those in patients with non-LVO, there was no significant difference in mRS at 3 months between the two groups ($p = 0.096$) (Table 1).

The analysis of 37 patients with LVO revealed that 16 of 37 patients (43.24%) had a good functional outcome (mRS at 3 months 0–2) and 21 (56.76%) had a poor functional outcome (mRS at 3 months 3–6). The good functional outcome group had a higher FVH_1 score (4.63 ± 1.20 vs 3.14 ± 1.15; $p = 0.001$), higher ASITN grade (3.31 ± 0.48 vs 2.00 ± 1.22; $p < 0.001$), and smaller DWI

Table 1 Comparison of patients with large vessel occlusion (LVO) and non-LVO

	Patients with LVO ($n = 37$)	Patients with non-LVO ($n = 51$)	*T* value	*p* value
Sex, male	23 (62.16%)	32 (62.75%)	0.003	0.956
Age (years)	69.41 ± 12.51	67.71 ± 12.60	0.626	0.533
Median time to onset (h)	2.03 ± 0.88	2.04 ± 1.11	− 0.066	0.947
Median time to MRI scan (h)	2.80 ± 0.85	3.15 ± 1.04	− 1.692	0.094
Smoking	6 (16.22%)	8 (15.69%)	0.005	0.947
Alcohol drinking	3 (8.11%)	3 (5.88%)	0.000	1.000
Diabetes mellitus	11 (29.73%)	14 (27.45%)	0.055	0.815
Hypertension	36 (97.30%)	48 (94.12%)	0.036	0.850
Atrial fibrillation	17 (45.95%)	16 (31.37%)	1.943	0.163
Hyperlipidemia	2 (5.41%)	4 (7.84%)	0.000	0.984
Homocysteine	3 (8.11%)	9 (17.65%)	1.657	0.198
NIHSS at admission	13.97 ± 5.26	6.96 ± 5.98	5.706	< 0.001*
FVH_1	35 (94.59%)	30 (58.82%)	14.213	< 0.001*
FVH_1 score	4.27 ± 1.73	1.51 ± 1.58	7.782	< 0.001*
FVH_2	8 (22.86%)[a]	7 (14.58%)[b]	0.936	0.393
FVH_2 score	0.91 ± 1.77[a]	0.19 ± 0.49[b]	− 2.277	0.029*
DWI volume	27.54 ± 34.98	11.52 ± 22.06	2.456	0.017*
NIHSS at discharge	8.30 ± 7.94	4.82 ± 6.78	2.206	0.030*
mRS at 3 months	2.73 ± 1.68	2.12 ± 1.69	1.681	0.096

LVO, large vessel occlusion; *NIHSS*, National Institutes of Health Stroke Scale; *FVH*, fluid-attenuated inversion recovery vascular hyperintensity; *FVH_1*, FVH before therapy; *FVH_2*, FVH after therapy; *DWI*, diffusion-weighted imaging; *mRS*, modified Rankin Scale

[a] Missing data for 3 patients

[b] Missing data for 3 patients

*$p < 0.05$

volume (14.78 ± 17.07 vs 37.27 ± 41.89; $p = 0.034$) than the poor functional outcome group (Figs. 1 and 2). The patients with a good functional outcome were more likely to have a lower NIHSS score at admission (11.75 ± 4.64 vs 15.67 ± 5.16; $p = 0.023$) and at discharge (1.25 ± 2.11 vs 13.67 ± 6.34; $p < 0.001$). There were no statistically significant differences in age, sex, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, or homocysteine levels between the two groups ($p > 0.05$). In addition, we compared FVH_2 among 34 patients (mRS 0–2: $n = 16$; mRS 3–6: $n = 18$) who underwent MRI after thrombectomy. In contrast to the FVH_1 score, the FVH_2 score in the good functional outcome group was lower than that in the poor functional outcome group (0.125 ± 0.50 vs 1.44 ± 2.16; $p = 0.030$) (Table 2, Fig. 3).

Our study showed no significant differences concerning age, sex, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, and homocysteine levels between patients with low FVH score and high FVH score. Patients with high FVH score had higher ASITN grade (3.16 ± 0.69 vs 1.94 ± 1.26; $p = 0.001$) and better functional outcome after 3 months (mRS 1.95 ± 1.35 vs 3.56 ± 1.62; $p = 0.002$) than patients with low FVH score. Although the FVH_2 score (1.06 ± 1.89 vs 0.78 ± 1.59) and DWI volume (38.00 ± 43.44 vs 17.64 ± 21.27) in the low FVH score group were higher than those in the high FVH score group, there were no significant differences ($p = 0.636$; $p = 0.085$) between the two groups (Table 3).

Spearman's rank correlation analysis revealed that FVH_1 ($r = -0.525$, $p = 0.001$; Fig. 4a) and ASITN grade ($r = -0.478$, $p = 0.003$; Fig. 4b) were negatively correlated with mRS at 3 months, while FVH_2 was positively correlated with mRS at 3 months ($r = 0.376$, $p = 0.034$; Fig. 4c). Furthermore, the Spearman rank correlation coefficients between FVH_1 and ASITN grade were significant ($r = 0.704$, $p < 0.001$; Fig. 4d).

Multivariable logistic regression analysis demonstrated that FVH_1 (OR, 0.085; 95% CI, 0.013–0.577; $p = 0.012$) and FVH_2 (OR, 2.724; 95% CI, 1.061–6.996; $p = 0.037$) were independently associated with functional outcome. However, exploratory multivariable logistic regression analysis did not show a statistically significant association between ASITN grade and functional outcome (OR, 0.137; 95% CI, 0.013–1.426; $p = 0.096$).

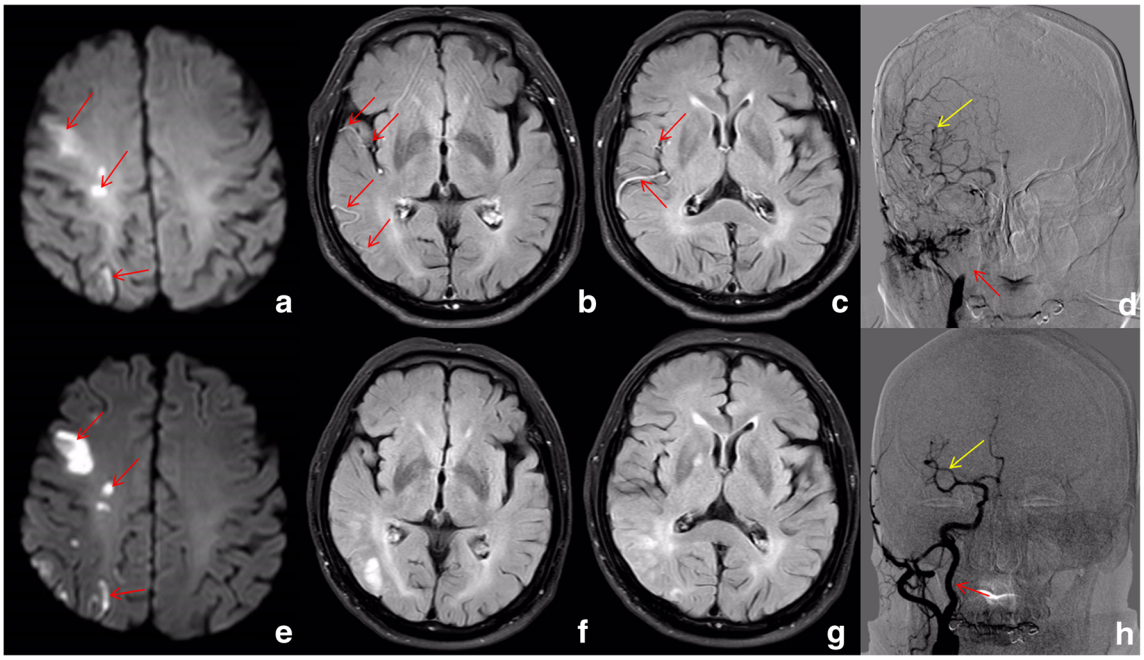

Fig. 1 A high FVH score before therapy is associated with good functional outcome (mRS at 3 months: 1 score) in acute stroke patients (**a** admission DWI image). **b**, **c** Admission FLAIR images, FVH visible in the insular cortex, M2, M3, M4, and M5 (red arrow); FVH score = 5. **d** DSA image showed showing occlusion of the right internal carotid artery C5 segment accompanied by thrombosis (red arrow). Collateralization was formed by the right external carotid artery-internal maxillary artery-anterior ethmoidal artery (yellow arrow); ASITN collateral grade = 3. **e** Follow-up DWI image. **f**, **g** Follow-up FLAIR images demonstrated FVH score = 0. **h** After thrombectomy, the right internal carotid artery C5 segment was recanalized (red arrow), and the right middle cerebral artery appeared after recanalization (yellow arrow)

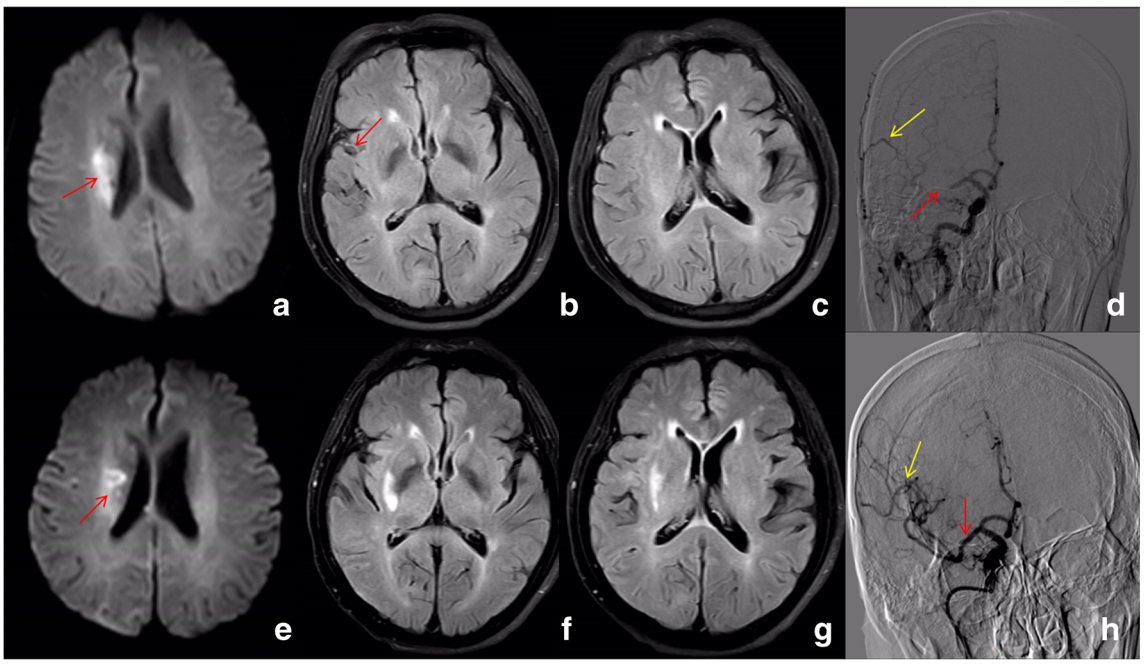

Fig. 2 A low FVH score before therapy is associated with poor functional outcome (mRS at 3 months: 3 score) in acute stroke patients (**a** admission DWI image). **b**, **c** Admission FLAIR images, FVH visible in the insular cortex and M2 (red arrow); FVH score = 2. **d** DSA image showing occlusion from the horizontal segment of the right middle cerebral artery to the lateral fissure trunk (red arrow). Mild collateralization was formed by right anterior cortical arteries (yellow arrow); ASITN collateral grade = 1. **e** Follow-up DWI image. **f**, **g** Follow-up FLAIR images demonstrated FVH score = 0. **h** After thrombectomy, the occluded artery was recanalized (red arrow), and a distant branch artery appeared after recanalization (yellow arrow)

Table 2 Comparison of mRS (0–2) and mRS (3–6) in 37 patients with large vessel occlusion

	mRS (0–2) ($n = 16$)	mRS (3–6) ($n = 21$)	T value	p value
Sex, male	11 (68.75%)	12 (57.14%)	0.520	0.471
Age (years)	65.19 ± 13.07	72.62 ± 11.34	− 1.849	0.073
Median time to onset (h)	1.88 ± 0.89	2.14 ± 0.88	− 0.914	0.367
Median time to MRI scan (h)	2.87 ± 1.03	2.74 ± 0.70	0.434	0.667
Median time to thrombectomy (h)	4.19 ± 1.47	4.20 ± 1.54	− 0.017	0.986
Location of occlusion				
Middle cerebral artery-M1	9 (56.25%)	12 (57.14%)	0.003	0.957
Internal carotid artery	3 (18.75%)	5 (23.81%)	0.000	1.000
Both	4 (25%)	4 (19.05%)	0.000	1.000
mTICI (2b-3)	15 (93.75%)	17 (80.95%)	0.413	0.520
ASITN	3.31 ± 0.48	2.00 ± 1.22	4.482	< 0.001*
Smoking	4 (25%)	2 (9.52%)	0.257	0.612
Alcohol drinking	3 (18.75%)	0 (0%)	2.138	0.144
Diabetes mellitus	3 (18.75%)	8 (38.10%)	0.833	0.362
Hypertension	15 (93.75%)	21 (100%)	0.019	0.890
Atrial fibrillation	8 (50%)	9 (42.86%)	0.187	0.666
Hyperlipidemia	1 (6.25%)	1 (4.76%)	0.000	1.000
Homocysteine	0 (0%)	3 (14.29%)	0.940	0.332
DWI volume	14.78 ± 17.07	37.27 ± 41.89	− 2.229	0.034*
NIHSS at admission	11.75 ± 4.64	15.67 ± 5.16	− 2.387	0.023*
NIHSS at discharge	1.25 ± 2.11	13.67 ± 6.34	− 8.390	< 0.001*
FVH_1 score	4.63 ± 1.20	3.14 ± 1.15	3.801	0.001*
FVH_2 score	0.125 ± 0.50	1.44 ± 2.16[a]	− 2.369	0.030*
mRS at 3 months	1.06 ± 0.77	4.00 ± 0.84	− 10.935	< 0.001*

mTICI, Modified Thrombolysis in Cerebral Ischemia; *ASITN*, American Society of Interventional and Therapeutic Neuroradiology; *DWI*, diffusion-weighted imaging; *NIHSS*, National Institutes of Health Stroke Scale; *FVH*, fluid-attenuated inversion recovery vascular hyperintensity; FVH_1, FVH before therapy; FVH_2, FVH after therapy; *mRS*, modified Rankin Scale

[a] Missing data for 3 patients

*$p < 0.05$

Discussion

From our analysis of patients with acute stroke, we found that FVH is more common in acute stroke patients with large arterial occlusion within 4.5 h after symptom onset. Moreover, FVH before therapy is associated with a better ASITN collateral grade and good functional outcome. In contrast to FVH before therapy, FVH after therapy is associated with poor functional outcome. FVHs before and after therapy were independently associated with functional outcome.

FVH is a common observation in acute stroke, although the mechanisms underlying this MRI sign and its clinical implications have been controversial. Some studies have shown via angiography that FVH most likely reflects slow arterial blood flow in leptomeningeal collateral circulation [13, 19], resulting in a loss of "flow void" and an increased signal in FLAIR sequences. Evidence for FVH representing impaired hemodynamics and retrograde collateral blood flow includes its presence in acute stroke due to a large arterial occlusion [8]. Our findings are more in accordance with other publications reporting that FVH was more frequently observed in acute stroke patients with LVO within 4.5 h after symptom onset. Mahdjoub et al [20] found FVH in most patients (99%) with an arterial occlusion, and like others, we found that 94.59% of patients with an arterial occlusion had FVH. Though 58.82% of patients [21] with non-LVO had FVH before therapy, the FVH score was very low (1.51 ± 1.58), compared with that in those with LVO (4.27 ± 1.73). Moreover, the presence of FVH was considered a reliable marker of arterial occlusion [20, 22, 23] and has mainly been proposed to serve as a sensitive marker of flow impairment [21, 24].

When an arterial occlusion occurs, the retrograde collateral flow reaches the cortical areas later than the anterograde flow during the venous angiographic phase. This sluggish flow likely explains FVH visibility [13]. As previously described, the FVH score reflects the number of leptomeningeal collateral vessels recruited during the acute disruption of blood flow in the middle cerebral artery [25]. In this study, the FVH score

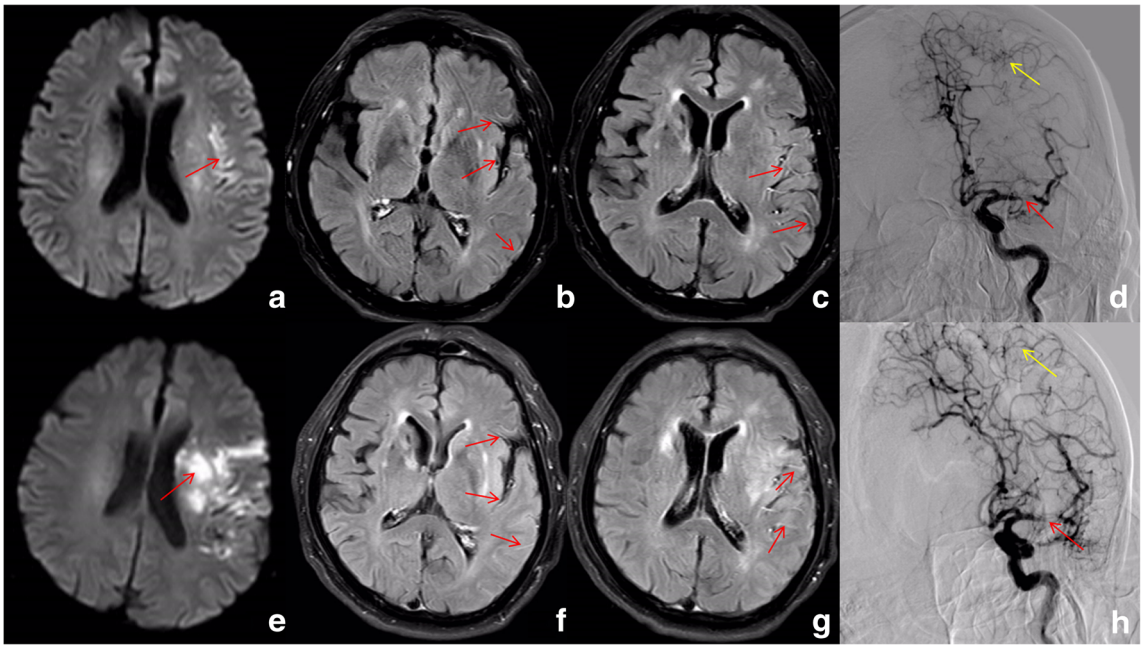

Fig. 3 A high FVH score after therapy is associated with poor functional outcome (mRS at 3 months: 3 score) in acute stroke patients (**a** admission DWI image). **b**, **c** Admission FLAIR images, FVH visible in the insular cortex, M1, M2, M3, and M5; FVH score = 5 (red arrow). **d** DSA image showing occlusion in the horizontal segment of the right middle cerebral artery accompanied by thrombosis (red arrow). Mild collateralization was formed by right anterior cortical arteries (yellow arrow); ASITN collateral grade = 1. **e** Follow-up DWI image. **f**, **g** Follow-up FLAIR images demonstrated that FVH still existed, and FVH score = 5. **h** After thrombectomy, the occluded artery was not completely recanalized (red arrow), while right anterior cortical arteries were more abundant (yellow arrow)

Table 3 Comparison of low FVH score and high FVH score in 37 patients with large vessel occlusion

	Low FVH score (FVH 0–3; $n = 18$)	High FVH score (FVH 4–7; $n = 19$)	T value	p value
Sex, male	9 (50.00%)	14 (73.68%)	2.204	0.138
Age (years)	69.78 ± 15.76	69.05 ± 8.84	0.171	0.865
Median time to onset (h)	2.00 ± 0.94	2.05 ± 0.85	− 0.179	0.859
Median time to MRI scan (h)	2.72 ± 0.69	2.87 ± 0.98	− 0.536	0.596
Median time to thrombectomy (h)	4.47 ± 1.73	3.93 ± 1.21	1.100	0.279
Location of occlusion				
Middle cerebral artery-M1	9 (50.00%)	12 (63.16%)	0.652	0.419
Internal carotid artery	5 (27.78%)	3 (15.79%)	0.236	0.627
Both	4 (22.22%)	4 (21.05%)	0.000	1.000
mTICI (2b-3)	14 (77.78%)	18 (94.74%)	1.055	0.304
ASITN	1.94 ± 1.26	3.16 ± 0.69	− 3.610	0.001*
Smoking	2 (11.11%)	4 (21.05%)	0.140	0.709
Alcohol drinking	1 (5.56%)	2 (10.53%)	2.138	0.144
Diabetes mellitus	6 (33.33%)	5 (26.32%)	0.833	0.362
Hypertension	17 (94.44%)	19 (100%)	0.019	0.890
Atrial fibrillation	7 (38.89%)	10 (52.63%)	0.187	0.666
Hyperlipidemia	1 (5.56%)	1 (5.26%)	0.000	1.000
Homocysteine	0 (0%)	3 (15.79%)	1.337	0.248
DWI volume	38.00 ± 43.44	17.64 ± 21.27	1.795	0.085
NIHSS at admission	16.00 ± 5.50	12.05 ± 4.33	2.434	0.020*
NIHSS at discharge	12.72 ± 8.21	4.11 ± 4.93	3.895	< 0.001*
FVH_1 score	2.67 ± 0.49	4.84 ± 1.07	0.003	< 0.001*
FVH_2 score	1.06 ± 1.89[a]	0.78 ± 1.59	0.477	0.636
mRS at 3 months	3.56 ± 1.62	1.95 ± 1.35	3.288	0.002*

mTICI, Modified Thrombolysis in Cerebral Ischemia; *ASITN*, American Society of Interventional and Therapeutic Neuroradiology; *DWI*, diffusion-weighted imaging; *NIHSS*, National Institutes of Health Stroke Scale; *FVH*, fluid-attenuated inversion recovery vascular hyperintensity; FVH_1, FVH before therapy; FVH_2, FVH after therapy; *mRS*, modified Rankin Scale

[a] Missing data for 3 patients

*$p < 0.05$

was quantified using the FVH-ASPECTS scoring system, and the collateral status was graded with the ASITN scoring system [26]. We found that FVH before therapy was positively correlated with the ASITN grade ($r = 0.704$; $p < 0.001$). The greater the FVH score before therapy, the greater the collateral status was, which is in accordance with other studies [15, 20]. FVH before therapy may prove to be a clinical decision-making parameter regarding the potential benefits of recanalization. Furthermore, numerous studies have been reported the prognostic value of FVH before therapy. Some studies found that FVH before therapy is a marker of good collateral status and favorable functional outcome [10, 27, 28]. Others have suggested that the presence of FVH before therapy was associated with worse functional recovery after stroke and have postulated that FVH represented insufficient collateralization [12, 14, 29]. Kufner et al [12] reported that FVH (> 4 score) before therapy was associated with a lager infarct growth and most likely indicated severe ischemia as a result of insufficient collateralization. Moreover, Hohenhaus et al [14] found that patients with FVH > 4 before therapy presented with more severe stroke and that a higher FVH might be a further surrogate marker for stroke severity. Our results showed that patients with an FVH of 4–7 before therapy had more sufficient collateralization and a better functional outcome after 3 months compared with patients with an FVH 0–3 before therapy. These studies were performed using nearly heterogeneous cohorts and clinical parameters or perfusion imaging to evaluate collateral status. In our study, we used DSA to evaluate collateral status, which is the gold standard for cerebral collateralization assessment. All samples were analyzed within 4.5 h after stroke. We found that both high FVH before therapy and good collateral status were associated with good functional outcome 3 months after stroke by Spearman's rank correlation analysis. While multivariable logistic regression analysis demonstrated that FVH before therapy was independently associated with functional outcome, collateral status (ASITN grade) did not show a statistically significant association with functional outcome. This finding is most likely explained by the fact that a high FVH score before therapy is regarded as a surrogate for good collateral status, and FVH before therapy might be useful for predicting functional outcome and developing clinical guidelines.

The strength of this study includes the investigation of the prognostic value of quantified FVH after therapy in terms of functional outcome at 3 months after stroke. FVH is generated by collateral flow through leptomeningeal collaterals on the cortical surface [13]. FVH is a temporary phenomenon that

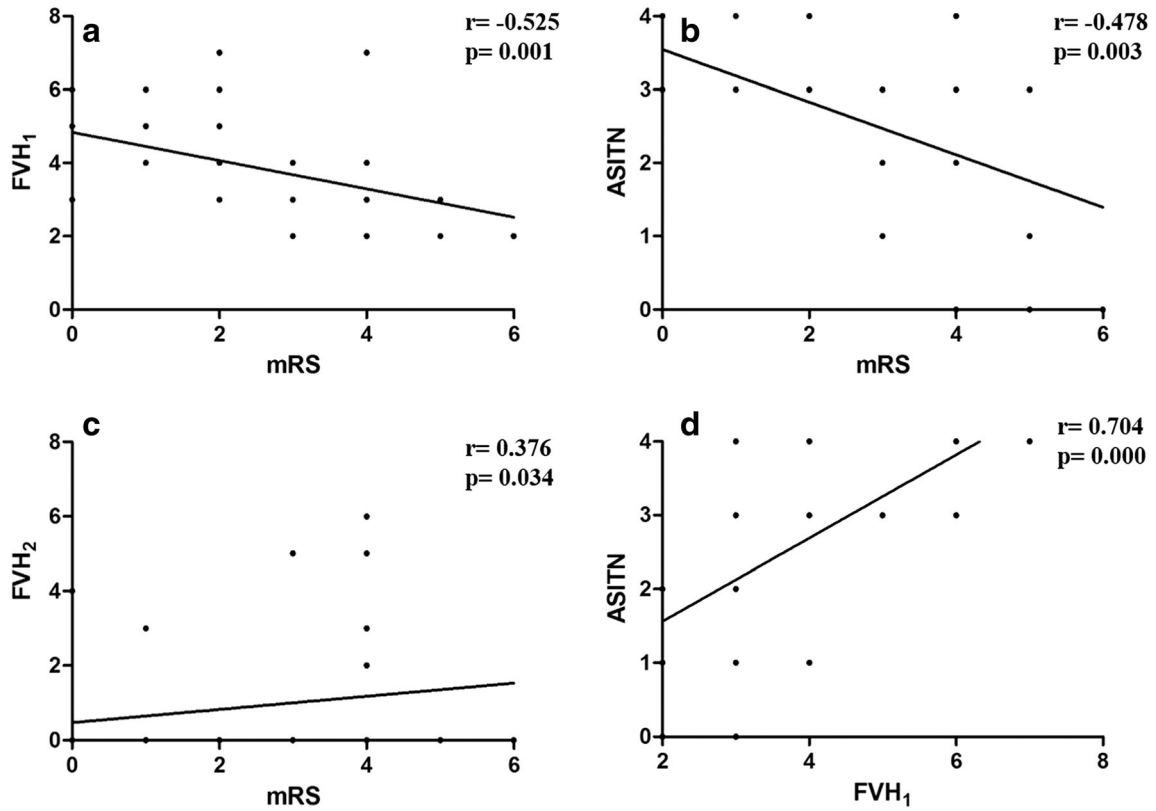

Fig. 4 Scatterplot representing correlations between FVH, ASITN, and mRS in patients with stroke. FVH_1 (**a**) and ASITN (**b**) were negatively correlated with mRS at 3 months, respectively, while FVH_2 (**c**) was positively correlated with mRS at 3 months. In addition, FVH_1 was positively correlated with ASITN (**d**). FVH_1: FVH before therapy; FVH_2: FVH after therapy; mRS: mRS at 3 months

commonly disappears within the first 24–36 h after onset. Sanossian et al [13] found persistence of FVH in patients with persistent vessel occlusions, which may reflect continued hemodynamic impairment. In our study, in contrast to the FVH score before therapy, the FVH score after therapy in the good functional outcome group was lower than that in the poor functional outcome group. Our findings of statistically significant association between FVH after therapy and functional outcome demonstrated that the presence of a high FVH score after therapy was associated with a poor functional outcome. Karadeli et al [30] thought that FVH before therapy indicated the status of leptomeningeal collateral perfusion available to the vulnerable brain tissue, rather than directly visualizing thrombus. Kobayashi et al [31] found that the persistence of FVH on follow-up MR images for acute stroke was associated with decreased or absent flow signal intensities on MRA, which suggested persistent vessel occlusion. Therefore, detection of FVH is also useful on follow-up MRI. If FVH still exists after thrombectomy, a poor functional outcome may be predicted.

Some limitations must be acknowledged. First, this study had a small sample size. This is a prospective study enrolled a large number of patients, but many heterogeneous cases were excluded after rigorous screening. Despite the small number of cases, we still found that FVH may have implications for clinical prognosis. Our further study will make the results more convincing or possibly reveal other meaningful findings by expanding the sample size. Second, 58.82% of patients with non-LVO had FVH in our study, but we did not explore the significance of the relationship between FVH and non-LVO. Moreover, due to ethical considerations, we performed the MRI scanning immediately after intravenous thrombolysis in patients who qualified for intravenous thrombolysis after CT scanning, without ruling out the effect of intravenous thrombolysis on the MRI. Finally, the patients included in our study all underwent successfully thrombus removal, and patients with poor revascularization (mTICI $\leq$ 2b) were not excluded. Future studies may increase the sample volume, explore the mechanism of FVH with non-LVO in acute stroke patients, and compare the differences in FVH between patients with intravenous thrombolysis and those without intravenous thrombolysis. We will also compare the difference in FVH between patients with poor revascularization (mTICI $\leq$ 2b) and good revascularization (mTICI > 2b). In fact, the functional outcome is determined by multiple confounding factors, and these factors should be considered for in the complex models of neuroimaging outcomes in stroke. Nevertheless, the association between FVH score and functional outcome, as seen in our study, most likely indicates that FVH may have implications for clinical prognosis.

Conclusions

A high FVH score before therapy is associated with good functional outcome, while a high FVH score after therapy is associated with poor functional outcome. Both FVH before therapy and FVH after therapy were independently associated with functional outcome. Assessments of FVH before and after therapy might be useful for predicting functional outcome after stroke.

Authors' contribution LJ and Y-C C designed the experiment, collected the data, performed the analysis, and wrote the paper. HZ, MP, HC, WG, and QX helped collect the data and perform the analysis. XY and YM contributed to the discussion and manuscript revision.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Xindao Yin.

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent All patients in this study have written informed consent before examined.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- prospective
- diagnostic or prognostic study
- performed at one institution

References

1. Siegler JE, Boehme AK, Kumar AD et al (2013) Identification of modifiable and nonmodifiable risk factors for neurologic deterioration after acute ischemic stroke. J Stroke Cerebrovasc Dis 22:e207–e213
2. Bang OY, Goyal M, Liebeskind DS (2015) Collateral circulation in ischemic stroke: assessment tools and therapeutic strategies. Stroke 46:3302–3309
3. McVerry F, Liebeskind DS, Muir KW (2012) Systematic review of methods for assessing leptomeningeal collateral flow. AJNR Am J Neuroradiol 33:576–582
4. Seker F, Potreck A, Möhlenbruch M, Bendszus M, Pham M (2016) Comparison of four different collateral scores in acute ischemic stroke by CT angiography. J Neurointerv Surg 8:1116–1118
5. Ichijo M, Iwasawa E, Numasawa Y et al (2015) Significance of development and reversion of collaterals on MRI in early

neurologic improvement and long-term functional outcome after intravenous thrombolysis for ischemic stroke. AJNR Am J Neuroradiol 36:1839–1845
6. Liebeskind DS (2005) Collaterals in acute stroke: beyond the clot. Neuroimaging Clin N Am 15:553–573 x
7. Martinon E, Lefevre PH, Thouant P, Osseby GV, Ricolfi F, Chavent A (2014) Collateral circulation in acute stroke: assessing methods and impact: a literature review. J Neuroradiol 41:97–107
8. Azizyan A, Sanossian N, Mogensen MA, Liebeskind DS (2011) Fluid-attenuated inversion recovery vascular hyperintensities: an important imaging marker for cerebrovascular disease. AJNR Am J Neuroradiol 32:1771–1775
9. Zhai DY, Zhu SG, Zhang W, Li X, Zhu YL (2017) Infarct morphology assessment in patients with carotid artery/middle cerebral artery occlusion using fast fluid-attenuated inversion recovery (FLAIR) vascular hyperintensity (FVH). PLoS One 12:e0188078
10. Liu D, Scalzo F, Rao NM et al (2016) Fluid-attenuated inversion recovery vascular hyperintensity topography, novel imaging marker for revascularization in middle cerebral artery occlusion. Stroke 47: 2763–2769
11. Hamano E, Kataoka H, Morita N et al (2017) Clinical implications of the cortical hyperintensity belt sign in fluid-attenuated inversion recovery images after bypass surgery for moyamoya disease. J Neurosurg 126:1–7
12. Kufner A, Galinovic I, Ambrosi V et al (2015) Hyperintense vessels on FLAIR: hemodynamic correlates and response to thrombolysis. AJNR Am J Neuroradiol 36:1426–1430
13. Sanossian N, Saver JL, Alger JR et al (2009) Angiography reveals that fluid-attenuated inversion recovery vascular hyperintensities are due to slow flow, not thrombus. AJNR Am J Neuroradiol 30: 564–568
14. Hohenhaus M, Schmidt WU, Brunecker P et al (2012) FLAIR vascular hyperintensities in acute ICA and MCA infarction: a marker for mismatch and stroke severity? Cerebrovasc Dis 34:63–69
15. Nave AH, Kufner A, Bücke P et al (2018) Hyperintense vessels, collateralization, and functional outcome in patients with stroke receiving endovascular treatment. Stroke 49:675–681
16. Legrand L, Tisserand M, Turc G et al (2015) Do FLAIR vascular hyperintensities beyond the DWI lesion represent the ischemic penumbra? AJNR Am J Neuroradiol 36:269–274
17. Higashida RT, Furlan AJ, Roberts H et al (2003) Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. Stroke 34:e109–e137
18. Singer OC, Berkefeld J, Nolte CH et al (2015) Collateral vessels in proximal middle cerebral artery occlusion: the ENDOSTROKE study. Radiology 274:851–858
19. Liu W, Xu G, Yue X et al (2011) Hyperintense vessels on FLAIR: a useful non-invasive method for assessing intracerebral collaterals. Eur J Radiol 80:786–791
20. Mahdjoub E, Turc G, Legrand L et al (2018) Do fluid-attenuated inversion recovery vascular hyperintensities represent good collaterals before reperfusion therapy? AJNR Am J Neuroradiol 39:77–83
21. Schellinger PD, Chalela JA, Kang DW, Latour LL, Warach S (2005) Diagnostic and prognostic value of early MR imaging vessel signs in hyperacute stroke patients imaged <3 hours and treated with recombinant tissue plasminogen activator. AJNR Am J Neuroradiol 26:618–624
22. Cheng B, Ebinger M, Kufner A et al (2012) Hyperintense vessels on acute stroke fluid-attenuated inversion recovery imaging: associations with clinical and other MRI findings. Stroke 43:2957–2961
23. Kono T, Naka H, Nomura E et al (2014) The association between hyperintense vessel sign and final ischemic lesion differ in its location. J Stroke Cerebrovasc Dis 23:1337–1343
24. Gawlitza M, Gragert J, Quaschling U, Hoffmann KT (2014) FLAIR-hyperintense vessel sign, diffusion-perfusion mismatch and infarct growth in acute ischemic stroke without vascular recanalisation therapy. J Neuroradiol 41:227–233
25. Noguchi K, Ogawa T, Inugami A et al (1997) MRI of acute cerebral infarction: a comparison of FLAIR and T2-weighted fast spin-echo imaging. Neuroradiology 39:406–410
26. Zaidat OO, Yoo AJ, Khatri P et al (2013) Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. Stroke 44:2650–2663
27. Lee KY, Latour LL, Luby M, Hsia AW, Merino JG, Warach S (2009) Distal hyperintense vessels on FLAIR: an MRI marker for collateral circulation in acute stroke? Neurology 72:1134–1139
28. Liu W, Yin Q, Yao L et al (2012) Decreased hyperintense vessels on FLAIR images after endovascular recanalization of symptomatic internal carotid artery occlusion. Eur J Radiol 81:1595–1600
29. Ebinger M, Kufner A, Galinovic I et al (2012) Fluid-attenuated inversion recovery images and stroke outcome after thrombolysis. Stroke 43:539–542
30. Karadeli HH, Giurgiutiu DV, Cloonan L et al (2016) FLAIR vascular hyperintensity is a surrogate of collateral flow and leukoaraiosis in patients with acute stroke due to proximal artery occlusion. J Neuroimaging 26:219–223
31. Kobayashi J, Uehara T, Toyoda K et al (2013) Clinical significance of fluid-attenuated inversion recovery vascular hyperintensities in transient ischemic attack. Stroke 44:1635–1640