Clinical Significance of Fluid-Attenuated Inversion Recovery Vascular Hyperintensities in Transient Ischemic Attack

Junpei Kobayashi, MD; Toshiyuki Uehara, MD; Kazunori Toyoda, MD; Kaoru Endo, MD; Tomoyuki Ohara, MD; Jun Fujinami, MD; Kazuyuki Nagatsuka, MD; Kazuo Minematsu, MD

Background and Purpose—Fluid-attenuated inversion recovery vascular hyperintensity (FVH) is often identified in patients with acute ischemic stroke. The purpose of this study was to determine the clinical significance of FVH in patients with transient ischemic attack (TIA).

Methods—Consecutive inpatients with TIA who underwent MRI within 24 hours of symptom onset were studied. The frequency, relative factors, and time course of FVH were determined.

Results—Of the 202 patients who were enrolled (76 women, mean age, 69.0±13.2 years), FVH was identified in 41 patients (20%). Multivariate analysis showed that atrial fibrillation (odds ratio, 7.14; 95% confidence interval [CI], 2.69–18.1), arterial occlusive lesion (odds ratio, 4.89; 95% CI, 3.03–12.2), and hemiparesis (odds ratio, 2.81; 95% CI, 1.17–7.48) was independently associated with FVH. Of 23 recurrence-free patients with FVH positive undergoing follow-up MRI within a median of 7 days after the onset, FVH was no longer positive in 15 patients (65%). Atrial fibrillation was more common (P=0.027) and arterial occlusive lesion was less common (P<0.001) in patients with transient FVH compared with those with persistent FVH. Within 90 days after the onset, 13 patients developed recurrent TIA or ischemic stroke. After Cox proportional hazard analysis, FVH (hazard ratio, 3.65; 95% CI, 1.09–12.7), arterial occlusive lesion (hazard ratio, 4.15; 95% CI, 1.18–17.1), and coexistence of FVH and arterial occlusive lesion (hazard ratio, 13.9; 95% CI, 3.36–71.0) were significantly associated with recurrent TIA or ischemic stroke.

Conclusions—The presence of FVH early after symptom onset may help to diagnose TIA, to identify the potential mechanisms of TIA and to predict recurrence risk after a TIA. (Stroke. 2013;44:1635-1640.)

Key Words: acute stroke ■ atrial fibrillation ■ fluid-attenuated inversion recovery ■ magnetic resonance angiography ■ transient ischemic attack

High signal intensity within blood vessels on fluid-attenuated inversion recovery vascular hyperintensity (FLAIR), otherwise known as FLAIR vascular hyperintensity (FVH), is often observed in patients with acute ischemic stroke. The purpose of this study was to determine the clinical significance of FVH in patients with transient ischemic attack (TIA).

Methods—Consecutive inpatients with TIA who underwent MRI within 24 hours of symptom onset were studied. The frequency, relative factors, and time course of FVH were determined.

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Key Words: acute stroke ■ atrial fibrillation ■ fluid-attenuated inversion recovery ■ magnetic resonance angiography ■ transient ischemic attack

From a database of patients admitted to our department between January 2005 and December 2011, consecutive inpatients with TIA who underwent MRI and MRA within 24 hours of symptom onset were retrospectively selected. The diagnosis of TIA was made by neurologists if clinical symptoms lasted <24 hours regardless of imaging findings (such as DWI positivity) according to the third edition of Cerebrovascular Disease Classification by the National Institute of Neurological Disorders and Stroke. Patients who underwent thrombolysis or endovascular therapy were excluded.

Received January 11, 2013; final revision received March 8, 2013; accepted March 12, 2013.
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Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.111.000787
from the study. In our institute, patients who arrived within 24 hours after TIA onset were principally treated during hospitalization. Basically, patients with TIA having mechanisms of cardioembolic stroke underwent anticoagulant therapy, whereas the other patients were treated with antiplatelet agent. The hospital’s ethics committee approved this series of clinical studies on the basis of the database of our stroke/TIA inpatients.

MRI Methods and Analysis
MRI, including DWI, FLAIR imaging, and time-of-flight MRA, was performed at 1.5 T (Magnetom Sonata or Magnetom Vision; Siemens Medical Solutions, Erlangen, Germany). DWI was performed using the following parameters for the Magnetom Sonata (parameters for the Magnetom Vision were the same as those for the Magnetom Sonata, unless noted in parentheses): repetition time, 3000 ms (4000 ms); echo time, 72 ms (100 ms); matrix, 128×128; field of view, 23 cm; section thickness, 4 mm; intersection gap, 2 mm; and b values, 0 and 1000 s/mm². FLAIR images were as follows: repetition time, 9000 ms; echo time, 119 ms (105 ms); inversion time, 2500 ms (2400 ms); matrix, 182×256; field of view, 23 cm; flip angle, 150° (180°); section thickness, 5 mm (4 mm); and intersection gap, 1 mm (2 mm). Time-of-flight MRA was obtained using the following parameters: repetition time, 37 ms (35 ms); echo time, 7.15 ms (7.6 ms); flip angle, 25° (20°); field of view, 200 mm; matrix, 230×512 (224×512); and slice thickness, 0.6 mm.

The criterion for FVH was either dotted hyperintensity identified in the subarachnoid space on 2 or more axial slices (Figure 1B) or serpentine hyperintensity on 1 or more axial slices (Figure 1B). FLAIR images were independently estimated by 2 board-certified neurologists (J.K. and K.E.), who were informed about the patients’ symptoms and neurological signs. They re-evaluated all FLAIR images after 1 month. When the judgment of the 2 neurologists was inconsistent, a decision was made by discussion without considering the information other than FLAIR imaging.

MRA and carotid ultrasound were performed for all patients, and digital subtraction angiography was performed for some. Assessments of extracranial internal carotid arteries on digital subtraction angiography, MRA, and carotid echography were made by North American Symptomatic Carotid Endarterectomy Trial (NASCET)-based methodology. Stenosis in major intracranial arteries on digital subtraction angiography and MRA was evaluated by Warfarin Aspirin Symptomatic Intracranial Disease (WASID)-style methodology. An AOL was defined as >50% stenosis, or as occlusion of extra- and intracranial large arteries assessed by MRA or digital subtraction angiography without recanalization on the follow-up examination. Vascular imaging was repeated for patients initially exhibiting steno-occlusive findings.

To assess whether FVH was persistent or transient, some of the patients with FVH positive underwent follow-up MRI and MRA around the seventh hospital day.

Clinical Characteristics
The patients’ clinical background characteristics, including sex, age, cardiovascular risk factors, history of TIA or stroke, blood pressure levels on arrival, clinical symptoms of TIA, symptom duration, and presence or absence of symptoms on arrival were collected from medical charts. Individual ABCD² scores, which use a simple scoring system to predict the risk of stroke after TIA, were calculated. ECG and 24-hour electrocardiographic monitoring were performed in all patients. Atrial fibrillation (AF) was diagnosed on the basis of either documentation of the examinations or a confirmed history.

Cardiovascular Event After a TIA
Patients were routinely reassessed at 90 days by attending stroke neurologists in outpatient clinic, and the timing of the occurrence of stroke, TIA, acute coronary syndrome, undergoing vascular intervention, and death within 90 days was recorded. If the patient could not visit the clinic for follow-up, follow-up was performed by telephone interview or by a mail-in survey. We assessed recurrent stroke on the basis of the neurological examination and the new DWI-positive lesions on brain MRI.

Statistical Analysis
Continuous variables were expressed as the mean±SD (age and blood pressure), and as the median and interquartile range (ABCD² score and symptom duration). Categorical data were summarized as percentages. Differences between groups were analyzed using the Student t test and Mann–Whitney U test for continuous values and Pearson χ² test and Fisher exact test for categorical variables as appropriate. Multivariate analyses were performed to find predictors for the presence of FVH on the basis of the variables listed in Table 1. A backward selection procedure was performed using P>0.10 for the likelihood ratio test for exclusion. Factors that were independently associated with TIA or IS recurrence were determined using the Cox proportional hazard model on the basis of the ABCD² score, sex, AF, DWI positivity, FVH, and AOL (forced-entry method). A P value of <0.05 was considered statistically significant. Cohen κ values were calculated to quantify the level of agreement regarding the presence of FVH to determine inter- and intraobserver variability. All statistical analyses were conducted using JMP 9.0.2 statistical software (SAS Institute, Inc, Cary, NC).

Results
Two hundred seventy patients with TIA were admitted to our hospital during this investigation period. Of these, 12 patients were excluded because of contraindication for MRI by implanted cardiac devices, 54 were excluded because the initial MRI was performed >24 hours after symptom onset, and 2 were excluded because of lack of carotid imaging. No patients received thrombolysis or endovascular therapy. As a result, a total of 202 patients (76 women, mean age, 69.0±13.2 years) were enrolled in this study.

FVH was identified in 41 patients (20%). The κ coefficients for intraobserver agreement of FVH by the 2 examiners were
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FLAIR Vascular Hyperintensity in TIA

Factors Related to FVH
Baseline characteristics of the patients are shown in Table 1. AF (P<0.001), a DWI lesion (P=0.020), and AOL (P=0.004) were more common and the duration of symptoms was shorter (P=0.013) in the FVH-positive group than in the FVH-negative group. Multivariate logistic regression analysis showed that AF (odds ratio, 7.14; 95% confidence interval [CI], 2.69–18.1), AOL (odds ratio, 4.89; 95% CI, 3.03–12.2), and hemiparesis (odds ratio, 2.81; 95% CI, 1.17–7.48) were independently associated with FVH (Table 2).

Time Course of FVH According to Follow-up MRI
Of 41 patients with FVH positive, 23 patients received follow-up MRI during their acute hospitalization (median, 7 days; interquartile range, 6–11 days) without episodes of recurrent TIA or IS before the follow-up MRI. There were no significant differences in patient characteristics shown in Table 1 between patients having the follow-up MRI or not.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients (n=202)</th>
<th>Positive FVH (n=41)</th>
<th>Negative FVH (n=161)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women, n (%)</td>
<td>76 (38%)</td>
<td>15 (37%)</td>
<td>61 (38%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Age, y (mean±SD)</td>
<td>69.0±13.2</td>
<td>70.9±12.3</td>
<td>68.5±13.4</td>
<td>0.287</td>
</tr>
<tr>
<td>Risk factor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>35 (17%)</td>
<td>7 (17%)</td>
<td>28 (17%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>150 (74%)</td>
<td>35 (85%)</td>
<td>115 (71%)</td>
<td>0.075</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>99 (49%)</td>
<td>17 (41%)</td>
<td>82 (51%)</td>
<td>0.299</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>51 (25%)</td>
<td>20 (49%)</td>
<td>31 (19%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous stroke or TIA, n (%)</td>
<td>58 (29%)</td>
<td>17(41%)</td>
<td>41(25%)</td>
<td>0.053</td>
</tr>
<tr>
<td>SBP on arrival, mm Hg (mean±SD)</td>
<td>152±27</td>
<td>151±28</td>
<td>152±27</td>
<td>0.830</td>
</tr>
<tr>
<td>DBP on arrival, mm Hg (mean±SD)</td>
<td>83±16</td>
<td>85±16</td>
<td>83±16</td>
<td>0.423</td>
</tr>
</tbody>
</table>

Characteristics of TIA

| Clinical features, n (%) | | | | |
|--------------------------|---------------------|----------------------|---------|
| Unilateral weakness      | 136 (67%)           | 33 (80%)             | 103 (64%)| 0.152   |
| Isolated speech disturbance | 18 (9%)           | 2 (5%)               | 16 (10%) |         |
| Other symptoms           | 48 (24%)            | 6 (15%)              | 42 (26%) |         |
| Symptom duration, median (IQR), min | 60 (20–275)  | 20 (10–300)          | 90 (30–273) | 0.013   |
| Presence of symptoms on arrival, n (%) | 68 (34%)        | 10 (24%)             | 58 (36%) | 0.196   |
| ABCD2 score, median (IQR) | 5 (4–5)          | 5 (4–5)              | 5 (4–5)  | 1.000   |
| DWI lesion, n (%)        | 36 (18%)            | 13 (32%)             | 23 (14%) | 0.020   |
| AOL, n (%)               | 60 (30%)            | 20 (49%)             | 40 (25%) | 0.004   |
| AOL at the initial examination, n (%) | 73 (36%)        | 30 (73%)             | 43 (27%) | <0.001  |
| Recanalization, n (%)    | 13 (18%)            | 10 (33%)             | 3 (7%)   | 0.005   |

AOL indicates arterial occlusive lesion; DBP, diastolic blood pressure; DWI, diffusion-weighted imaging; FVH, fluid-attenuated inversion recovery vascular hyperintensity; IQR, interquartile range; SBP, systolic blood pressure; and TIA, transient ischemic attack.

FVH was no longer positive in 15 patients (65%; transient FVH). In the transient FVH group, AF was more common (67% versus 13%; P=0.027) and AOL was less common (0% versus 88%; P<0.001) than in the 8 patients with persistent FVH. Particularly in the 9 patients with FVH positive without a DWI lesion or AOL at the initial assessment, all FVHs completely resolved, and DWI revealed hyperintense lesions that were compatible with the initial symptom of TIA in 4 of these 9 patients (Figure 2).

Recurrent TIA/Stroke and FVH
One hundred eighty-one patients (90%) had catamnestic follow-up at 90 days. Nine patients developed recurrent TIA, 4 developed IS, 1 developed hemorrhagic stroke, and none...
developed acute coronary syndrome, received vascular intervention, or died within 90 days. Figure 3A shows the cumulative rate of recurrent TIA or IS. In the FVH-positive group, 3 patients developed recurrent TIA and 4 patients developed IS on the ipsilateral side of FVH; 5 of these 7 patients developed these events within the initial week. In the FVH-negative group, 1 patient developed recurrent TIA and 5 patients developed IS; 5 of these 6 patients developed these events within the initial week. Cox proportional hazard analysis showed that FVH (hazard ratio, 3.64; 95% CI, 1.08–12.6) and AOL (hazard ratio, 3.82; 95% CI, 1.07–15.8) were independently associated with the events (Table 3, Model A). Because a significant association was found between FVH and AOL in this study, the analysis was repeated using 4 subgroups divided according to FVH and AOL: 20 patients with both FVH and AOL, 40 patients with only AOL, 21 patients with only FVH, and 100 patients without FVH or AOL. Patients having both FVH and AOL were independently associated with the events (hazard ratio, 12.8; 95% CI, 3.09–64.4; Table 3, Model B; Figure 3B).

Discussion
This is the first study to determine the frequency and clinical significance of FVH, and the association between FVH and recurrence of TIA or IS in patients with TIA. The first major finding of this study was that FVH was identified in 20% of patients with TIA on the clinically relevant side. The second major finding was that AF and AOL were independently associated with FVH; AF was especially associated with transient FVH and AOL with persistent FVH. Third, AOL and FVH were predictive of recurrence of TIA or IS within 90 days.

Patients with AIS often have FVH associated with large-vessel stenosis or occlusion. In patients with AIS receiving intravenous thrombolysis within 3 hours from symptom onset, the frequency of FVH was 57% at baseline, 44% at 2 hours, and 25% at 24 hours; large artery occlusion was identified in 91% of the patients with FVH positive and 63% of the patients with FVH negative at baseline. In another study, FVH was detected in 45% of patients within 24 hours after AIS onset, and all patients with FVH had large-vessel occlusion or severe stenosis. In a study on TIA patients, FVH was identified in 33%, and again had a strong association with large-vessel occlusion or severe stenosis. In contrast, only a report of a patient with AIS indicated that AF caused transient FVH without large AOLs. In our series, FVH was identified only in 20% of the present patients within 24 hours after TIA onset, and only 49% of patients with FVH showed AOL. The incidence of FVH and large artery occlusive lesions in this study was obviously lower than those in the studies on AIS.
In conclusion, FVH could be interpreted as a marker of altered hemodynamics in patients with TIA and AF and in those with AOL. The results of this study suggest that the presence of FVH early after symptom onset may help to differentiate TIA from stroke mimic, to identify the potential mechanisms of TIA, and to predict recurrence risk after a TIA.

Acknowledgments

The authors thank Dr. Naomi Morita of the Department of Radiology at the National Cerebral and Cardiovascular Center for her valuable advice. The authors thank Akiko Kada for advice on the statistical analyses.

Sources of Funding

This study was supported by Grant-in-Aid (H21-Jyunkanki-Ippan-017, H24-Jyunkanki-Ippan-011) from the Ministry of Health, Labor and Welfare, Japan (MHLW-Japan) and JSPS KAKENHI Grant Number 24591309.

Disclosures

None.

References


Table 3. Cox Proportional Hazard Analysis for Factors Associated With Recurrent TIA and Ischemic Stroke Within 90 Days

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Model A</th>
<th></th>
<th></th>
<th>Model B</th>
<th></th>
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<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>P Value</td>
<td>HR</td>
<td>95% CI</td>
<td>P Value</td>
</tr>
<tr>
<td>Sex</td>
<td>1.18</td>
<td>0.33–3.86</td>
<td>0.785</td>
<td>1.16</td>
<td>0.33–3.77</td>
<td>0.812</td>
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<tr>
<td>ABCD²</td>
<td>1.00</td>
<td>0.65–1.60</td>
<td>0.998</td>
<td>1.00</td>
<td>0.65–1.60</td>
<td>0.997</td>
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<tr>
<td>DWI positivity</td>
<td>1.06</td>
<td>0.26–3.75</td>
<td>0.926</td>
<td>1.03</td>
<td>0.25–3.67</td>
<td>0.964</td>
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<tr>
<td>AF</td>
<td>0.73</td>
<td>0.14–2.89</td>
<td>0.664</td>
<td>0.79</td>
<td>0.16–3.05</td>
<td>0.743</td>
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<tr>
<td>FVH</td>
<td>3.64</td>
<td>1.08–12.6</td>
<td>0.037</td>
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<tr>
<td>AOL</td>
<td>3.82</td>
<td>1.07–15.8</td>
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<td>FVH(−) AOL(−)</td>
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<td>...</td>
<td>...</td>
<td>1.00</td>
<td>(Reference)</td>
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<td>...</td>
<td>1.97</td>
<td>0.10–17.3</td>
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<td>...</td>
<td>2.80</td>
<td>0.50–15.7</td>
<td>0.232</td>
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<tr>
<td>FVH(+) AOL(+)</td>
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<td>...</td>
<td>12.8</td>
<td>3.09–64.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; AOL, arterial occlusive lesion; CI, confidence interval; DWI, diffusion-weighted imaging; FVH, fluid-attenuated inversion recovery vascular hyperintensity; HR, hazard ratio; and TIA, transient ischemic attack.


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*Stroke*. 2013;44:1635-1640; originally published online May 7, 2013;
doi: 10.1161/STROKEAHA.111.000787

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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