Is Aortic Atherothrombotic Disease Detected Using Multidetector-Row CT Associated With an Increased Risk of Early Ischemic Lesion Recurrence After Acute Ischemic Stroke?

Youngchai Ko, MD; Wook-Joo Kim, MD; Myung Suk Jang; Mi Hwa Yang; Jung Hyun Park, MD; Sang Il Choi, MD; Eun Ju Chun, MD; Soo Joo Lee, MD, PhD; Moon-Ku Han, MD, PhD; Hee-Joon Bae, MD, PhD

Background and Purpose—Multidetector-row CT (MDCT) is emerging as a new tool for diagnosing aortic atherothrombotic disease (AAD). We elucidated whether MDCT-detected AAD is associated with an increased risk of early ischemic lesion recurrence on diffusion-weighted MRI after ischemic stroke.

Methods—A consecutive series of patients with acute ischemic stroke confirmed using diffusion-weighted MRI who were hospitalized within 48 hours after symptom onset and underwent MDCT were identified in a prospective stroke registry database. AAD on MDCT was defined as the presence of plaque formation that was noncalcified and ≥4 mm thick, ulcerative, or soft and thrombosed (vulnerable) in the proximal aortic arch. Ischemic lesion recurrence on diffusion-weighted MRI was defined as the occurrence of any new lesion separate from the index lesion on follow-up diffusion-weighted MRI performed within 14 days after symptom onset.

Results—A total of 138 patients was selected. MDCT detected AAD in 24 of 138 (17.4%); ≥4 mm thickness in 17 of 138 (12.3%); ulcerated plaque in 20 of 138 (14.5%); and vulnerable plaque in 16 of 138 (11.6%). With respect to diffusion-weighted MRI lesion recurrence, the crude ORs (95% CIs) were as follows: AAD, 3.56 (1.43–8.89); vulnerable plaque, 3.21 (1.11–9.30); ulcerated plaque, 3.37 (1.27–8.95); and ≥4 mm thickness of the noncalcified plaque, 4.23 (1.11–16.19). These results remained significant after adjustments for potential confounders were made.

Conclusions—This study shows that AAD detected by MDCT increases the risk of early ischemic lesion recurrence after acute ischemic stroke, thus supporting the role of MDCT in diagnosing AAD and assessing its contribution to recurrence. (Stroke. 2012;43:764-769.)

Key Words: aortic arch ■ cerebral infarction ■ multidetector-row computed tomography ■ stroke ■ thromboembolism

Recurrent stroke is highly prevalent among stroke survivors and is a major cause of morbidity and mortality in these patients. Aortic atherothrombotic disease (AAD) with a plaque of ≥4 mm thickness located proximal to the ostium of the left subclavian artery is strongly associated with cerebral embolism. Moreover, the incidence of recurrent brain infarction in patients with aortic plaque thickness of ≥4 mm has been reported to be 9.1% to 11.9% per year, suggesting that AAD may be a significant risk factor for recurrence. However, AAD is not regarded as a potential source of embolic stroke in clinical practice or in classifying ischemic stroke subtypes, partly due to the fact that there is relatively little evidence to guide therapeutic decisions for preventing stroke recurrence in patients with AAD. Another important reason is that the diagnosis of AAD is difficult without the use of transesophageal echocardiography (TEE). However, TEE has several limitations as a diagnostic tool and is not always feasible in acute stroke settings.
The recently introduced 64-multidetector-row CT (MDCT) is a powerful tool that enables rapid, noninvasive, and specific diagnosis of aortic pathology.\textsuperscript{11,12} Recent studies show that MDCT is comparable to TEE in measuring plaque thickness, discovering ulceration, and evaluating plaque characteristics.\textsuperscript{13,14} However, the role of MDCT-detected AAD in stroke recurrence has not yet been investigated.

Studies have reported that early ischemic lesion recurrence on diffusion-weighted imaging (DWI) occurs in approximately 40\% of patients within 1 week after stroke onset and is a surrogate marker of late recurrence.\textsuperscript{1,15} Therefore, the purpose of this study was to determine whether AAD diagnosed by MDCT is associated with early ischemic lesion recurrence on DWI in patients with acute ischemic stroke.

Materials and Methods

Study Population
This was a retrospective study of patients with acute ischemic stroke admitted to Seoul National University Bundang Hospital between May 2007 and April 2008. Patients with ischemic stroke who were admitted within 48 hours of onset, who had relevant lesions on DWI, and who underwent MDCT were recruited from our prospectively collected stroke registry database. During the study period, MDCT was performed mainly for 2 purposes: (1) to identify the embolic source in patients with a clinical history or radiological findings suggestive of cardioembolic etiology but with no evident embolic source; or (2) to screen high-risk patients for coronary heart disease.

We excluded patients who did not undergo follow-up DWI or who had other neurointerventional procedures including conventional angiography that could provoke the recurrence of ischemic lesions on follow-up DWI. The demographics, vascular risk factors, and other clinical profiles including Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification\textsuperscript{7} were gathered directly from the prospective stroke registry database and by electronic medical record review. The Institutional Review Board approved this study.

Assessment of AAD Using MDCT
MDCT protocols were adopted from our previous study that suggests the etiologic role of AAD detected by MDCT in patients having possible embolic stroke.\textsuperscript{16} Patients with a heart rate of $>70$ beats per minute received 10 to 30 mg intravenous esmolol (Jeil Pharm Co Ltd, Seoul, Korea) before MDCT. Electrocardiography-gated MDCT was performed using a 64-slice MDCT scanner (Brilliance 64; Philips Medical Systems, Best, The Netherlands). A standard scanning protocol was applied with 64×0.625-mm section collimation, 420-ms rotation time, a tube voltage of 120 kV, and an effective tube current of 800 mA. All scans were performed using electrocardiography-gated dose modulation. An 80-mL bolus of iomeprol (Iomeron 400; Bracco, Milan, Italy) was intravenously injected (4 mL/s) followed by a 50-mL saline chaser. To identify aortic atheroma, we additionally performed delayed nongated scanning from the upper border of the aortic arch to the descending thoracic aorta, including the entire heart.

AAD was diagnosed if the aortic plaque met at least 1 of the following criteria associated with the development of ischemic stroke probably involving an embolic mechanism: (1) $\geq 4$-mm-thick noncalcified plaque adjacent to the aortic wall with a transverse projection\textsuperscript{17,18}; (2) ulcerated plaque\textsuperscript{19}; or (3) vulnerable plaque.\textsuperscript{3} Ulcerated plaque in the aortic arch was defined as extension of the contrast medium beyond the vascular lumen into the surrounding plaque with a wide orifice ($>3$ mm).\textsuperscript{20,21} These were adopted from TEE criteria because MDCT-based criteria have not yet been established.\textsuperscript{2,3} Using a cutoff of 180 Hounsfield units, plaques were classified as either calcified or noncalcified for analysis purposes. Calcified aortic plaques (which are less lipid-laden) have been reported to have a lower risk of plaque rupture, thrombus formation, and embolization.\textsuperscript{14,18} Vulnerable plaque was defined as a protruding atheroma with a clearly visualized area of hypodensity ($<80$ Hounsfield units) that would be mainly composed of a soft or thrombotic mass.\textsuperscript{17,18} The typical MDCT findings of AAD are shown in the Figure. Because plaques in the ascending aorta and proximal arch are more likely to be a source of cerebral embolism than plaques in other regions, we focused on these 2 areas of the thoracic aorta.

Two experienced cardiovascular radiologists (S.I.C. and E.J.C.), who were blinded to the clinical information, independently reviewed all of the MDCT images using a 3-dimensional workstation (Brilliance; Philips Medical Systems). After independent evaluations, a consensus was reached to obtain a final MDCT diagnosis. Interobserver agreement for diagnosing AAD was excellent (Cohen $k=0.89$).

MRI Protocols and Assessments of Ischemic Lesion Recurrence by DWI
According to the institution’s standard protocols, all eligible patients with acute ischemic stroke underwent a MRI scan at presentation and a follow-up scan within 1 week of hospitalization. Ischemic lesion recurrence on DWI (DWI-LR) was defined as the presence of a newly developed ischemic lesion on the follow-up DWI located outside of the index lesions on the initial DWI. Enlargement of the initial ischemic lesion was not considered a new lesion. New lesions were determined by slice-to-slice comparisons between the initial and follow-up scans. Two neurologists (W.-J.K. and Y.K.), who were blinded to the clinical information, reviewed all of the MRI scans that were obtained within 14 days after stroke onset. After independent evaluation for the presence of DWI-LR, any discrepancies were resolved by consensus ($k=0.86$).

Clinical Outcome Assessment
Patients were contacted at 3 months and 1 year after stroke onset by telephone interview as a part of our institution’s quality-of-care
monitoring program for hospitalized patients with stroke. An experienced stroke nurse (M.H.Y.), who was blinded to the presence or absence of AAD, was responsible for assessing stroke recurrence and/or death using a structured questionnaire. Deaths were verified by obtaining information from a national death certificate system.

### Statistical Analysis

Continuous variables are expressed as mean±SD, whereas categorical variables are presented as absolute values and percentages. Patients with and without AAD were compared to identify potential clinical correlates for stroke recurrence. We used Student t test or the Mann-Whitney U test to compare means, Pearson χ² test or Fisher exact test to compare proportions, and Mantel extension test to verify the existence of a linear trend. To express the association of AAD with DWI-LR, ORs and their 95% CIs were calculated using multiple logistic regression analysis. Variables identified in bivariate analyses as showing a possible association (P<0.2) with the presence of AAD were selected for adjustment. The dose–response relationship between plaque thickness and DWI-LR was examined using a likelihood ratio test for trends. Time to stroke recurrence and mortality after discharge were estimated using the Kaplan-Meier product-limit method and were compared for patients with and without AAD using log-rank tests. Probability values <0.05 were considered statistically significant.

### Results

During the study period, 470 patients with acute ischemic stroke were admitted to our hospital within 48 hours after onset: 458 (97.4%) underwent DWI at presentation, whereas 392 (83.4%) had relevant ischemic lesions on DWI. Of these 392 patients, 235 (59.9%) received MDCT for identification of embolic sources or screening for coronary disease. Baseline characteristics were not significantly different between the MDCT and non-MDCT groups (Supplemental Table I; http://stroke.ahajournals.org) except for undetermined cause of stroke (23.4% versus 14.6%) and age (66.3±13.3 years versus 69.1±13.2 years). Forty-three patients (18.3%) with no follow-up DWI and 54 (23.0%) who had neurointerventional procedures were excluded from the study. A total of 138 patients was ultimately enrolled in this study.

The overall prevalence of AAD was 17.4% (24 of 138). The clinical characteristics of patients with and without AAD are presented in Table 1. Patients with AAD were significantly older (71.8 versus 66.8 years, P=0.025) and also more frequently had strokes of undetermined etiology (45.8% versus 22.8%, P=0.028) compared with those without AAD. However, the proportions of stroke having cardioembolic sources and the regimens of acute treatment (antithrombotic drugs administered on admission) were not significantly different. The median interval of performing MDCT from the index event was identical (ie, 2 days [interquartile range, 1–4]) in both groups. No difference in laboratory findings (white blood cell counts, C-reactive protein, low-density lipoprotein cholesterol) was noted.

Follow-up DWI revealed ischemic lesion recurrence in 26.8% (37 of 138) of patients with the median interval from the initial DWI to the follow-up scan being 5 days (interquartile range, 4–6 days) in patients with DWI-LR. Among those 37 DWI-LR cases, 6 (16.2%) were associated with neurological deterioration.

The incidence of DWI-LR was significantly higher in patients with AAD than in those without AAD (50.0% versus 21.9%, P<0.01; Table 2). The incidence of symptomatic AAD indicates aortic atherothrombotic disease; NIHSS, National Institutes of Health Stroke Scale; CE, cardioembolic sources; PFO, patent foramen ovale; TOAST, Trial of ORG 10172 in Acute Stroke Treatment; tPA, tissue plasminogen activator; DWI, diffusion-weighted magnetic resonance imaging; MDCT, multidetector-row CT; SBP, systolic blood pressure; LDL, low-density lipoprotein; WBC, white blood cells.


c ^*P values were calculated using Student t test or the Mann-Whitney U test for comparison of means and by Pearson χ² test or Fisher exact test for comparison of proportions where appropriate.

DWI-LR was also higher in the AAD group than in the non-AAD group (12.5% versus 2.7%, P=0.03).

Regarding plaque thickness, there was no significant linear trend with the incidence of DWI-LR (P=0.19 on Mantel-Whitney U test or the Mann-Whitney U test for comparison of means and by Pearson χ² test or Fisher exact test for comparison of proportions where appropriate.}

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### Table 1. Baseline Characteristics of Patients With and Without AAD

<table>
<thead>
<tr>
<th></th>
<th>AAD</th>
<th>No</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male</strong></td>
<td>16 (66.7)</td>
<td>67 (58.8)</td>
<td>0.47</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td>71.8±10.1</td>
<td>66.8±13.3</td>
<td>0.025</td>
</tr>
<tr>
<td><strong>Initial NIHSS</strong></td>
<td>3.5 (1.3–11.8)</td>
<td>3 (2–6)</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>16 (66.7)</td>
<td>59 (51.8)</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td>7 (29.2)</td>
<td>31 (27.2)</td>
<td>0.84</td>
</tr>
<tr>
<td><strong>Hyperlipidemia</strong></td>
<td>4 (16.7)</td>
<td>14 (12.3)</td>
<td>0.56</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>11 (45.8)</td>
<td>40 (35.1)</td>
<td>0.32</td>
</tr>
<tr>
<td><strong>Stroke history</strong></td>
<td>5 (20.8)</td>
<td>16 (14.0)</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>High risk for CE</strong></td>
<td>7 (29.2)</td>
<td>26 (22.8)</td>
<td>0.65</td>
</tr>
<tr>
<td><strong>Atrial fibrillation</strong></td>
<td>5 (20.8)</td>
<td>23 (20.2)</td>
<td>0.94</td>
</tr>
<tr>
<td><strong>Medium risk for CE</strong></td>
<td>1 (4.2)</td>
<td>10 (8.8)</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>PF0</strong></td>
<td>1 (4.2)</td>
<td>6 (5.3)</td>
<td>0.82</td>
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<tr>
<td><strong>TOAST classification</strong></td>
<td></td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Large artery disease</td>
<td>4 (16.7)</td>
<td>36 (31.6)</td>
<td></td>
</tr>
<tr>
<td>Lacunar</td>
<td>3 (12.5)</td>
<td>20 (17.5)</td>
<td></td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>5 (20.8)</td>
<td>32 (28.1)</td>
<td></td>
</tr>
<tr>
<td>Other causes</td>
<td>1 (4.2)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Undetermined cause</td>
<td>11 (45.8)</td>
<td>26 (22.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Acute treatment</strong></td>
<td></td>
<td></td>
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<tr>
<td>Heparin</td>
<td>4 (16.9)</td>
<td>17 (14.9)</td>
<td>0.83</td>
</tr>
<tr>
<td>Aspirin+clopidogrel</td>
<td>8 (33.3)</td>
<td>26 (22.8)</td>
<td>0.28</td>
</tr>
<tr>
<td>Warfarin</td>
<td>5 (20.8)</td>
<td>26 (22.8)</td>
<td>0.83</td>
</tr>
<tr>
<td><strong>Onset to follow-up DWI, d</strong></td>
<td>5 (4–6)</td>
<td>5 (4–6)</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>Onset to MDCT, d</strong></td>
<td>2 (1–4)</td>
<td>2 (1–4)</td>
<td>0.77</td>
</tr>
<tr>
<td><strong>Initial SBP, mm Hg</strong></td>
<td>154.9±29.3</td>
<td>157.6±30.0</td>
<td>0.61</td>
</tr>
<tr>
<td><strong>Total cholesterol, mmol/L</strong></td>
<td>4.8±0.9</td>
<td>5.2±1.7</td>
<td>0.21</td>
</tr>
<tr>
<td><strong>LDL cholesterol, mmol/L</strong></td>
<td>2.99±0.73</td>
<td>3.46±1.64</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>WBC counts, ×10³/mm³</strong></td>
<td>8.50±3.19</td>
<td>7.62±2.69</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>C-reactive protein</strong></td>
<td>0.35 (0.12–3.76)</td>
<td>0.23 (0.11–1.00)</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Initial glucose, mmol/L</strong></td>
<td>7.6±4.0</td>
<td>8.0±3.8</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Continuous variables are presented as mean±SD or median (interquartile range), whereas categorical variables are presented as no. of patients (%).

*P values were calculated using Student t test or the Mann-Whitney U test for comparison of means and by Pearson χ² test or Fisher exact test for comparison of proportions where appropriate.
Calcification was reported to be a surrogate marker for stable
ness compared with the calcified plaque (Tables 2 and 3).

Haenszel $\chi^2$ test for trend; Table 2), and both crude and
adjusted ORs included the null value (Table 3). However,
when we separated noncalcified plaques from calcified ones
and adopted the calcified plaque as a reference, the incidence
of DWI-LR increased significantly by the increase of thick-
ness in the noncalcified plaque ($P=0.01$); the risk of DWI-LR
was >4-fold in the noncalcified plaque with ≥4 mm thickness
compared with the calcified plaque (Tables 2 and 3).
Calcification was reported to be a surrogate marker for stable
plaque with a low risk of cerebral embolism.19

The presence of vulnerable or ulcerated plaques was also
significantly associated with DWI-LR. The crude ORs were
3.56 (95% CI, 1.43–8.89) for AAD, 3.21 (1.11–9.30) for
vulnerable plaque, and 3.21 (1.11–9.30) for ulcerated plaque
(Table 3). The association with DWI-LR remained significant
after adjustment for age, hypertension, stroke subtypes, and
total cholesterol.

Information about stroke recurrence and death was avail-
able for 136 patients (98.6%). Stroke recurred in 3 of 24 with
AAD versus 3 of 112 without AAD (12.5% versus 2.7%,$P=0.04$ using the log-rank test). Four of 24 with AAD died
within 1 year versus 8 of 112 without AAD (23.6% versus
7.1%, $P=0.15$).

### Discussion

Our study shows that AAD identified using MDCT is
associated not only with ischemic lesion recurrence captured
by DWI within several days after the onset of ischemic
stroke, but also with clinical recurrence. Its association with
stroke recurrence was not remarkable, partly due to the small
sample size and that with mortality rate within 1 year after
onset was not significant. Using an alternate method for
diagnosing AAD and stroke recurrence than those of previous
TEE studies,5,6 this study proved the significance of AAD as
a potential risk factor for stroke recurrence.

According to the Stop Stroke Study TOAST (SSS-
TOAST) system,22 which was recently developed for the
purpose of improving TOAST,7 AAD is now regarded as an
embolic source with a low or uncertain risk. Our study
revealed that a large proportion of patients who were catego-
rized as undetermined etiology by TOAST criteria7 had AAD
(11 of 37 [29.7%]; Table 1). We previously showed that AAD
may be a potential risk factor for embolic stroke, particularly
in patients without evident embolic sources.19 From these
results, the presence of AAD should be considered in patients
with ischemic lesion recurrence who have no relevant arterial
pathology or embolic sources.

Ischemic lesion recurrence on diffusion-weighted MRI has
an important clinical implication; it can serve as a useful
surrogate end point in clinical trials evaluating stroke prevention
therapies.1 Although most recurrent ischemic lesions on
MRI are clinically silent, they are assumed to have the same pathophysiology as clinical recurrence. In our study, the recurrence was identified by follow-up DWI irrespective of the development of new neurological symptoms that were mostly asymptomatic (31 of 37 [83.8%]).

Although it is well known that the presence of aortic plaques with ≥4 mm thickness is a strong risk factor for embolic stroke, the association between plaque thickness and DWI-LR was not statistically significant on $\chi^2$ test for trend (Table 2). However, after distinguishing calcified plaques from noncalcified ones and then using calcified plaques as a reference group, an independent dose-dependent relationship with DWI-LR by trend analysis was evident (Tables 2 and 3), and we demonstrated that composition and thickness play important roles in plaque stability. This finding agrees with the findings of the French Study of Aortic Plaques in Stroke.

Although MDCT has some advantages in evaluating AAD, which could be attributable to its ability to reconstruct high-quality multidimensional images and enable retrospective review with the same quality of reproducibility, high doses of radiation exposure and contrast medium are the most serious obstacles when using MDCT for patients with possible embolic stroke. Furthermore, MDCT is a static imaging modality that cannot evaluate plaque mobility, a factor that is highly suggestive of thrombus and also important in risk stratification. Newer-generation MDCT systems with submillimeter collimation could provide improved image quality and more reliably differentiate thrombi from soft plaques.

Cardiac MRI has several advantages: it provides contrast between different tissue types thereby revealing morphological components of the atherosclerotic plaque (ie, calcification, fibrocellular tissue, lipid, and thrombus) as well as hemodynamic information. However, compared with CT, MRI has a longer scan time, which makes monitoring patients during scans more difficult. Therefore, cardiac MRI may not be suitable for patients who are critically ill. Moreover, patients who have ferromagnetic implants, particles, pacemakers, and claustrophobia cannot undergo MRI. For these reasons as well as cost, cardiac MRI has limitations for use as a standard tool for evaluating cardioembolic sources in acute stroke.

Identification of AAD by MDCT would be helpful for making therapeutic decisions to prevent stroke recurrence. Because AAD induces intravascular embolization of thrombi, anticoagulation therapy was initially used to prevent recurrence in patients with severe aortic plaques. Studies have demonstrated that warfarin is not harmful and may be useful in preventing cerebral embolism in patients with AAD. However, a recent study reported that randomization of warfarin and aspirin did not affect stroke recurrence or death in patients with AAD. Further research is warranted before anticoagulation may be accepted as standard treatment for preventing embolism in AAD. We also expect that the new generation of anticoagulants such as dabigatran may help prevent stroke in patients with AAD. Statins can also provide another therapeutic option. There has been no randomized trial to date in this area, but in an observational study of 519 patients with severe aortic plaques, statins were used to prevent recurrence.

A prospective randomized clinical trial is ongoing in patients with atherothrombosis of the aortic arch and a recent cerebral or peripheral embolic event (Aortic Arch Related Cerebral Hazard Trial [ARCH]). This study aims to compare the efficacy and tolerance of 2 antithrombotic strategies, 75 mg clopidogrel +75 mg aspirin versus warfarin (international normalized ratio, 2–3). We hope that the ARCH trial or a similarly designed future trial may provide new evidence in treating high-risk AAD.

This study has a few limitations. First, it was a single hospital-based retrospective study with a relatively short follow-up period and a small sample size. Second, we selected patients for MDCT with the goal of evaluating coronary disease or embolic sources. The risk of selection bias was inevitable, which may have contributed to the relatively high prevalence of AAD in this study. Third, the lack of validity of the AAD criteria should be noted; due to a lack of published MDCT criteria for AAD, we used TEE criteria in this study.

Conclusions

To the best of our knowledge, this is the first study to report an association between AAD and DWI-LR, a surrogate marker of stroke recurrence. Our results suggest that MDCT is a useful tool to diagnose AAD in patients suspected to be at risk of embolic stroke. Comprehensive efforts to evaluate stroke mechanisms can reduce the uncertainty and improve the accuracy of assessing the risk of stroke recurrence.

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Disclosures

None.

References


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### Supplemental Table

Baseline characteristics of patients with and without performing Multidetector-row computed tomography (MDCT)

<table>
<thead>
<tr>
<th></th>
<th>MDCT</th>
<th>P values*</th>
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<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>(N=235, 59.9%)</td>
<td>(N=157, 40.1%)</td>
</tr>
<tr>
<td>Male</td>
<td>137 (58.3)</td>
<td>91 (58.0)</td>
</tr>
<tr>
<td>Age (mean±SD, years)</td>
<td>66.3 ±12.6</td>
<td>69.1 ±13.2</td>
</tr>
<tr>
<td>Initial NIHSS (median and IQR)</td>
<td>4 (2 to 8)</td>
<td>4 (2 to 9)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>131 (55.7)</td>
<td>100 (63.7)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>61 (26.0)</td>
<td>52 (33.1)</td>
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<tr>
<td>Hyperlipidemia</td>
<td>36 (15.3)</td>
<td>26 (16.6)</td>
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<td>Smoking</td>
<td>84 (35.7)</td>
<td>62 (39.5)</td>
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<tr>
<td>Previous stroke history</td>
<td>42 (17.9)</td>
<td>33 (21.0)</td>
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<td>TOAST classification</td>
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<tr>
<td>Large artery disease</td>
<td>81 (34.5)</td>
<td>58 (38.2)</td>
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<tr>
<td>Lacunae</td>
<td>35 (14.9)</td>
<td>42 (28.3)</td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>59 (25.1)</td>
<td>30 (19.7)</td>
</tr>
<tr>
<td>Other causes</td>
<td>5 (2.1)</td>
<td>3 (2.0)</td>
</tr>
<tr>
<td>Undetermined causes</td>
<td>55 (23.4)</td>
<td>23 (14.6)</td>
</tr>
<tr>
<td>Systolic blood pressure (mean±SD, mmHg)</td>
<td>151.2±28.9</td>
<td>156.0±25.2</td>
</tr>
<tr>
<td>Total cholesterol (mean±SD, mmol/L)</td>
<td>5.1 ±1.0</td>
<td>5.3 ±1.1</td>
</tr>
<tr>
<td>Initial glucose (mean±SD, mmol/L)</td>
<td>7.8 ±3.4</td>
<td>8.5 ±3.9</td>
</tr>
</tbody>
</table>

*Continuous variables are presented as mean±SD or median (interquartile range), and categorical variables are presented as number of patients (%).

SD, standard deviation; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; TOAST, Trial of Org 10172 in Acute Stroke Treatment

*P values were calculated by student t-test or Mann-Whitney U test for comparison of means, and by Pearson’s chi-square test, or Fisher exact test for comparison of proportions, where appropriate.
脳動脈瘤を有する虚血性脳卒中患者における静脈内血栓溶解療法の安全性 — 症例シリーズおよび文献レビュー

The Safety of Intravenous Thrombolysis for Ischemic Stroke in Patients With Pre-Existing Cerebral Aneurysms — A Case Series and Review of the Literature

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背景および目的: 未破裂脳動脈瘤は現在、急性虚血性脳卒中治療のための静脈内組織プラスミノゲン活性化因子投与の禁忌とされている。これは、動脈瘤破裂からの出血リスクが理論上増大するためであるが、このリスクが重大なものであるかどうかは不明である。我々は、既存の動脈瘤患者コホートにおける静脈内組織プラスミノゲン活性化因子投与の安全性の検討を試みた。

方法: 2つの大学病院関連施設で11年間に組織プラスミノゲン活性化因子による急性虚血性脳卒中の治療を受けた患者の記録を調査した。血栓溶解療法前の血管画像で未破裂脳動脈瘤が認められた患者を同定した。対象とした転帰はすべての頭蓋内出血、症候性頭蓋内出血、および髄膜下出血である。Fisherの直接確率検定を用いて、動脈瘤のある患者と動脈瘤のない患者の出血率を比較した。

結果: 236例の適格な患者を同定し、うち22例に未破裂脳動脈瘤が認められた。動脈瘤患者の頭蓋内出血の発生率(14%, 95% CI: 3 ~ 35%)は、動脈瘤のない患者の発生率(19%, 95% CI: 14 ~ 25%)と有意差がなかった。動脈瘤患者で症候性頭蓋内出血が発生した患者はいなかった(0%, 95% CI: 0 ~ 15%)、動脈瘤のない患者214例のうち10例に症候性頭蓋内出血が発生した(5%, 95% CI: 2 ~ 8%)。髄膜下出血が発生した患者的割合は同程度であった(5%, 95% CI: 0 ~ 23% 対 6%, 95% CI: 3 ~ 10%)。

結論: 動脈瘤破裂および症候性頭蓋内出血のリスクは低いため、既存の脳動脈瘤を有する患者に対して急性虚血性脳卒中治療のための組織プラスミノゲン活性化因子を静脈内投与しても安全であることが、本研究の結果から示唆される。

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表2 既存の動脈瘤の有無別にみた頭蓋内出血発生率

<table>
<thead>
<tr>
<th>動脈瘤患者</th>
<th>動脈瘤のない患者</th>
</tr>
</thead>
<tbody>
<tr>
<td>すべてのICH</td>
<td>3 (13.6%)</td>
</tr>
<tr>
<td>症候性ICH</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>SAH</td>
<td>1 (4.5%)</td>
</tr>
</tbody>
</table>

ICH: 頭蓋内出血, SAH: 髄膜下出血。

表3 以前に報告された症例全体の静脈内血栓溶解療法の転帰

<table>
<thead>
<tr>
<th>研究</th>
<th>患者数</th>
<th>最大動脈瘤のサイズ</th>
<th>動脈瘤の部位</th>
<th>ICH</th>
<th>SAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al.</td>
<td>7*</td>
<td>8 mm</td>
<td>7つのうち4つが前方循環系</td>
<td>患者7例中3例</td>
<td>なし</td>
</tr>
<tr>
<td>D’Ollhaberriague et al.</td>
<td>2</td>
<td>&gt; 5 mm</td>
<td>ICA, A. comm</td>
<td>なし</td>
<td>なし</td>
</tr>
<tr>
<td>Matsuzaki et al.</td>
<td>1</td>
<td>6 mm</td>
<td>L MCA</td>
<td>なし</td>
<td>なし</td>
</tr>
<tr>
<td>Yoneda et al.</td>
<td>1</td>
<td>7 mm</td>
<td>A. comm</td>
<td>なし</td>
<td>なし</td>
</tr>
<tr>
<td>Desai et al.</td>
<td>1</td>
<td>16 mm</td>
<td>ICA 海綿静脈洞</td>
<td>なし</td>
<td>なし</td>
</tr>
</tbody>
</table>

* 8例が報告され、1例を除くした(動脈瘤ではなく偽動脈瘤)。

正確なサイズは報告されていない。
다혈관산화단층촬영(Multidetector-Row CT)을 이용하여 진단된 대동맥 족상혈전질환이 급성 혈전성뇌졸중 후에 초기 혈전성 병변 재발 위험도의 증가와 연관성이 있는가?

Is Aortic Atherothrombotic Disease Detected Using Multidetector-Row CT Associated With an Increased Risk of Early Ischemic Lesion Recurrence After Acute Ischemic Stroke?

Youngchai Ko, MD; Wook-Joo Kim, MD; Myung Suk Jang; Mi Hwa Yang; Jung Hyun Park, MD; Sang Il Choi, MD; Eun Ju Chun, MD; Soo Joo Lee, MD, PhD; Moon-Ku Han, MD, PhD; Hee-Joon Bae, MD, PhD

(Stroke. 2012;43:764-769.)

Key Words: aortic arch □ cerebral infarction □ multidetector-row computed tomography □ stroke □ thromboembolism

배경과 목적
다혈관산화단층촬영(multidetector-row CT)은 대동맥 족상혈전질환(aortic atherothrombotic disease, AAD)을 진단하기 위해 발전하고 있는 새로운 기술이다. 우리는 이러한 다혈관산화단층촬영에 의한 진단된 대동맥 족상혈전질환이 혈전성뇌졸중 후 확산강조 자기공명영상(diffusion-weighted MRI)에서 초기 혈전성 병변의 재발 위험도의 증가와 연관성이 있는지를 평가하였다.

방법
증상발생 후 48시간 안에 입원하여 확산강조 자기공명영상을 통해 급성 혈전성뇌졸중으로 진단받고 다혈관산화단층촬영을 활용한 일정 기간의 모든 환자들이 정상적인 뇌졸중 등록 데이터베이스로부터 추출되었다. 다혈관산화단층촬영영상에서 보이는 근위 대동맥공의 족상혈전질환이 4 mm 이상의 혈전화 족상관, 경막성 족상관, 또는 부드러우나 혈전이 형성된 불안정성 족상관의 존재로 정의되었다. 확산강조영상에서 혈전성 병변의 재발은 증상 발생 후 14일 내에 시행된 추적 확산강조영에서 처음 병변과 구분된 새로운 병변의 발생으로 정의되었다.

결과
총 138명의 환자들이 선택되었다. 다혈관산화단층촬영에서 족상혈전질환이 138명 중 24명(17.4%)에서 발견되었고, 그중 4 mm 이상의 족상관이 138명 중 17명(12.3%)에서, 경막성 족상관이 20명(14.5%)에서, 불안정한 족상관이 16명(11.6%)에서 발견되었다. 확산강조영상에서 병변의 재발과 관련하여 각 지표의 교차비(95% 신뢰구간)는 족상혈전질환에서는 3.56 (1.43~8.89), 불안정한 족상관에서는 3.21 (1.11~9.30), 경막성 족상관에서는 3.37 (1.27~8.95), 4 mm 이상의 비색화 족상관에서는 4.23 (1.11~16.19)이었다. 이러한 결과들은 다른 가능한 재관변수를 보정한 후에도 의미가 있었다.

결론
이 연구는 다혈관산화단층촬영을 이용하여 진단된 대동맥 족상혈전질환이 초기 혈전성 병변의 재발 위험도를 증가시킨다는 것을 보임으로써 대동맥 족상혈전질환을 진단하고 병변의 재발을 예측하는 데 다혈관산화단층촬영의 필요성을 제안한다.