Hemodynamic Instability Increases New Ischemic Brain Lesions on Diffusion-Weighted Imaging After Carotid Artery Stenting

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Abstract

Hemodynamic instability (HI) may impair the washout of debris during distal intracranial circulation and increase the risk of clinically evident cerebral ischemia. However, the interaction between HI and new ischemic brain lesions detected on diffusion-weighted imaging (DWI) has not been examined. This study evaluated whether HI was significantly associated with the incidence of new ischemic brain lesions on DWI. Data on 128 patients who underwent carotid artery stenting (CAS) with the same devices and procedures between January 2005 and May 2010 were retrospectively analyzed. HI was noted in 31 (24.2%) patients. New ischemic brain lesions were detected on DWI in 25 (19.5%) patients. Ten of 31 (32.2%) patients with HI showed new ischemic brain lesions on DWI. Fifteen of 97 (15.5%) patients without HI showed new lesions. Univariate analysis showed that patients with HI had a significantly higher incidence of new ischemic brain lesions than patients without HI (p = 0.04). A multivariable model showed that age and HI were significantly associated with the incidence of new ischemic brain lesions. In patients with carotid artery stenosis, decreased blood pressure produced no active vascular response, but reduced the cerebral blood volume and velocity due to impaired dynamic cerebral autoregulation. The results of this study suggest that HI with CAS induces impaired clearance of microembolisms and causes an increased number of new ischemic brain lesions detected on DWI.

Key words: hemodynamic instability, new ischemic brain lesion, diffusion-weighted magnetic resonance imaging, carotid artery stenting, postdilation

Introduction

Carotid artery stenting (CAS) has been more frequently used for the treatment of selected patients with extracranial carotid artery stenosis, because of the perceived advantages of reduced invasiveness and less procedure-related discomfort. However, a recent randomized clinical trial showed that CAS is associated with a higher risk of periprocedural ischemic stroke compared to carotid endarterectomy (CEA).5

Periprocedural ischemic stroke is associated with factors such as stent type, use of embolic protection devices (EPDs), and morphological features of the carotid plaque.4,17,21 Hemodynamic instability (HI), such as hypotension or bradycardia, is often observed with CAS. HI can occur in CAS as a result of stretching of the carotid sinus baroreceptors by the balloon and the stent. HI increases the risk of major periprocedural adverse clinical events, defined as myocardial infarction and cerebrovascular events.8 However, the interaction between HI and new ischemic brain lesions on diffusion-weighted imaging (DWI) has not yet been examined.

CAS can be achieved using a variety of available stents and EPDs. Furthermore, the procedure, especially in terms of the use of stents and EPDs, varies among surgeons.12,18 This study involved a retrospective assessment of the association between HI and new ischemic brain lesions detected on DWI. We have consistently performed CAS without postdilation using a closed-cell type self-expanding stent. The findings add to our understanding of the association between HI and new ischemic brain lesions.
Patients and Methods

This study retrospectively analyzed data collected by trained staff at our institution between January 2005 and May 2010 using a registry of 139 consecutive patients who underwent CAS. Information regarding the following factors was collected for each patient by reviewing their medical records: age, sex, history of coronary artery disease (angina pectoris or myocardial infarction), hypertension, diabetes mellitus, hyperlipidemia, radiological imaging, and reports of periprocedural complications. CAS was indicated by the presence of angiographically documented carotid artery stenosis of >70% in symptomatic patients and >60% in asymptomatic patients, according to the North American Symptomatic Carotid Endarterectomy Trial criteria.3) Data of 11 (8.6%) patients were excluded; these cases included CAS with postdilation due to insufficient predilation (n = 6), CAS without predilation due to floating thrombus (n = 1), unsuccessful CAS due to severe calcification (n = 1), and lack of post-procedural magnetic resonance imaging (MRI) due to the presence of temporary pacemakers (n = 3). HI was defined as a fall of >20 mmHg in systolic blood pressure from the baseline level (hypotension) and a decrease of >10 beats/min in heart rate from the baseline level (bradycardia). Atropine was not administered prophylactically. Patients with <80 mmHg in systolic blood pressure who required continuous vasopressor infusion after the procedure were considered to have persistent HI.

All patients underwent diagnostic angiography before the intervention to document the length and degree of the lesion, anatomical variations, stenosis at the origin of the great vessels, severely diseased aortic arches, intracranial pathology, and presence of any posterior circulatory problems. Three days before the procedure, all patients received antiplatelet therapy with two of the following four drugs: aspirin (100 mg/day), ticlopidine (200 mg/day), clopidogrel (75 mg/day), or cilostazol (200 mg/day). Patients with hypertension received their usual medication before the procedure. Furthermore, all patients received routine fluids throughout the procedure under general anesthesia. CAS in all the cases was initiated through transfemoral access. After placement of an 8-F sheath, every patient received intravenous heparin to achieve an activated coagulation time of 250–300 seconds. An 8-F introducing catheter was then guided to the ipsilateral common carotid artery proximal to the carotid artery stenosis. A distal EPD (PercuSurge GuardWire; Medtronic, Minneapolis, Minnesota, USA) was placed at the internal carotid artery distal to the stenosis using roadmap technique. After temporary occlusion of the internal carotid artery, the stenosis lesion was dilated for 20 seconds using an angioplasty balloon with a size difference of 1 mm compared to that of the internal carotid artery distal to the stenosis. Next, a closed-cell type self-expanding stent (Wallstent RP; Stryker Neurovascular, Mahwah, New Jersey, USA) was applied. The selected stent was larger than the common carotid artery by 2–3 mm. In each case, 20 ml of blood was aspirated three times through the catheter to collect debris. The temporary occlusion was deflated after the aspiration. Heparin effects were not reversed after the procedure, and were allowed to spontaneously disappear. Heart rate and oxygen saturation were continuously monitored during the entire procedure. Blood pressure was measured in the left upper arm by using automated cuff inflation at 2.5-minute intervals. After the procedure, the patients were transferred to the inpatient ward, and their heart rate, oxygen saturation, and blood pressure were continuously monitored for 24 hours.

MRI scanners and parameters, and axial DWI with echo planar methods used in this study are listed in Table 1. Postprocedural MRI was performed 1
day after CAS. The incidence of new ischemic brain lesions on DWI was checked by two neurosurgeons unaware of the clinical details. The inter-observer reliability of new ischemic brain lesions on DWI was excellent ($\kappa = 0.92$). Disagreement was resolved by consensus. This study was approved by the Institutional Ethics Committee at our institution.

Continuous data are expressed as mean ± standard deviation, and discrete data are presented as counts and percentages. Differences between groups were assessed using the Pearson’s chi-square and Fisher exact tests for discrete data, and the Mann-Whitney U test for continuous data. Binomial logistic regression analysis was used to calculate the risk factors for new ischemic brain lesions on DWI. The inter-observer reliability was determined with the $\kappa$ statistic. SPSS statistics software version 17.0 (SPSS Inc., Chicago, Illinois, USA) was used for all analyses. A p value of $<0.05$ was considered as the threshold for significance.

Results

Of the 128 patients studied, 112 (87.5%) patients were men and 16 (12.5%) were women. The mean age of the patient population was 70.9 ± 7.7 years (median 72 years). Seventy-four (57.8%) patients showed symptomatic stenosis, and 54 (42.2%) patients were asymptomatic. Among the symptomatic patients, 8 (10.8%) patients presented with hemispherical transient ischemic attack, 58 (78.4%) with minor stroke, 4 (5.4%) with moderate stroke, and 4 (5.4%) with amaurosis fugax. Mean degree of stenosis was 77.7 ± 11.1% (median 80%). Mean degree of stenosis after stent placement was 18.2 ± 12.6% (median 16.2%). Concomitant disease states were recorded in many patients, including in 90 (70.3%) patients with hypertension, 48 (37.5%) with diabetes mellitus, 31 (24.2%) with hyperlipidemia, and 31 (24.2%) with coronary artery disease.

HI was noted in 31 (24.2%) patients. Bradycardia occurred in 23 (18.0%) patients, and hypotension in 23 (18.0%) patients. Bradycardia without hypotension occurred in eight (6.3%) patients. Hypotension without bradycardia occurred in eight (6.3%) patients. Persistent HI was noted in nine (7.0%) patients and was detected during the procedure in six patients and after the procedure in three patients. The baseline characteristics of patients with and without HI and the results of the univariate analyses are summarized in Table 2. None of the clinical baseline characteristics were associated with HI. None of the patients developed cardiovascular diseases.

New ischemic brain lesions were detected on DWI in 25 of 128 (19.5%) patients. Two (1.6%) patients showed symptomatic minor cerebral infarction, and neither had HI. The baseline characteristics of patients with and without new ischemic brain lesions and the results of the univariate analyses are summarized in Table 2. Patients with new ischemic brain lesions were older than patients without these lesions (74.4 ± 7.3 vs. 70.1 ± 7.6 years, p = 0.004). Ten 31 (32.2%) patients with HI showed new ischemic brain lesions on DWI. Fifteen of 97 (15.5%) patients without HI showed new lesions. Univariate analysis showed that patients with HI had a significantly higher incidence of new ischemic brain lesions than patients without HI (p = 0.04). Multivariable modeling showed that age and HI were significantly associated with the incidence of new ischemic brain lesions (Table 4). Three of 9 (33.3%) patients with persistent HI showed new ischemic brain lesions on DWI. Twenty-two of 119 (18.5%) patients without persistent HI showed new lesions. Univariate analysis showed no significant difference.

The frequency of new ischemic brain lesions on
Table 3 Baseline characteristics of patients with and without new ischemic brain lesions

<table>
<thead>
<tr>
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<th>New ischemic brain lesions on diffusion-weighted imaging</th>
<th>p Value</th>
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<tbody>
<tr>
<td></td>
<td>Yes (n = 25)</td>
<td>No (n = 103)</td>
</tr>
<tr>
<td>Age (mean ± SD; median), years</td>
<td>74.4 ± 7.3; 77</td>
<td>70.1 ± 7.6; 71</td>
</tr>
<tr>
<td>Male</td>
<td>24 (96.0%)</td>
<td>88 (85.4%)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>13 (52.0%)</td>
<td>61 (59.2%)</td>
</tr>
<tr>
<td>Degree of stenosis (mean ± SD; median), %</td>
<td>77.2 ± 12.6; 82</td>
<td>77.8 ± 10.8; 80</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17 (68.0%)</td>
<td>73 (70.9%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6 (24.0%)</td>
<td>42 (40.8%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5 (20.0%)</td>
<td>26 (25.2%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>5 (20.0%)</td>
<td>26 (25.2%)</td>
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SD: standard deviation.

Table 4 Binominal logistic regression analysis to predict new ischemic brain lesions on diffusion-weighted imaging

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.113</td>
<td>1.037–1.189</td>
<td>0.006</td>
</tr>
<tr>
<td>Hemodynamic instability</td>
<td>3.510</td>
<td>2.499–4.521</td>
<td>0.015</td>
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CI: confidence interval.

Discussion

HI with CAS increases the risk of major perioperative adverse clinical events, such as myocardial infarction, stroke, and death. Hypotension may impair the washout of debris in distal intracranial circulation and increase the risk of clinically evident cerebral ischemia. Low blood flow velocity in the middle cerebral artery is correlated with the development of DWI-characterized postoperative ischemic brain lesions associated with microembolization during CEA. However, to the best of our knowledge, no study has indicated that HI with CAS is associated with the development of new ischemic brain lesions detected on DWI.

After CAS, age is reported to be one of the major risk factors of new ischemic brain lesions detected on DWI. This study assessed the association of age and HI with new ischemic brain lesions using a binominal logistic regression analysis, and showed that both age and HI were significantly associated with the development of new ischemic brain lesions. Previous reports have shown that almost all patients with CAS showed microembolic signals on transcranial Doppler sonography. However, there is no established relationship between the number of microembolic signals and the incidence of new ischemic brain lesions detected on DWI. Almost all microembolisms produced during CAS are thought to be washed out, as previously proposed. In patients with carotid artery stenosis of more than 50%, a decrease in blood pressure would not produce an active vascular response, but would reduce cerebral blood volume and velocity due to impairment of dynamic cerebral autoregulation.

Therefore, in patients with carotid artery stenosis, HI may impair clearance of microembolisms and cause an increase in the number of new ischemic brain lesions detected on DWI.

Reported frequencies of bradycardia, hypotension, and persistent hypotension in previous studies of CAS were 13–27%, 14–27%, and 11–17%, respectively; however, the definitions of bradycardia and hypotension and the prophylactic use of atropine varied in each study. The results of our study are not significantly different from those of the previous studies. Both diameter and length of the balloon and stent were shown to affect HI. Balloons are generally selected to be 3–4 mm in diameter and 15–40 mm in length at predilation, and 4.5–6 mm in diameter and 15–30 mm in length at postdilation. The main difference between our study and others may be that a large predilation balloon was used for dilation in our institute.

The frequency of new ischemic brain lesions detected on DWI was 19.5% in this study, which was less than the 39.4–55.0% cited in previous reports. This difference may be due to the procedure employed in this study. Previous studies on microembolic signals using transcranial Doppler sonography showed that stent deployment and postdilation were...
associated with higher embolization risk. In our institute, patients undergo CAS without postdilation, as using a closed-cell type self-expanding stent can provide scaffolding and lead the fractured plaque and thrombogenic material away from the circulation. This stent also allows easy removal of the EPD because it does not have the fine split of a stent strut. Therefore, postdilation may have been prevented by the use of the closed-cell type self-expanding stent in the procedure. CAS without postdilation may be one of the reasons reducing the incidence of new ischemic brain lesions detected on DWI.

None of the patients with carotid artery stenosis underwent CEA at our institute. In this study, CAS was performed using the same devices and procedures in all patients. Previous reports have shown that the frequencies of HI and new ischemic brain lesions detected on DWI differ depending on the type of EPD and stent employed. The procedure, especially the use of stents and EPDs, varies among surgeons. This study is highly credible because both devices and procedures were constant. One limitation of this study was the use of a different matrix in the multi-MRI instrument. Therefore, the imaging protocol was unified. Every MRI scanner was 1.5 Tesla, and DWI was acquired with the echo planar methods and b-values 1000 sec/mm² in this study.

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Conflicts of Interest Disclosure

The authors have no commercial, proprietary, or financial interest in any products or companies described in this article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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