Beneficial Effect of Carotid Artery Stenting on Cerebral Hemodynamic Impairment and Cognitive Function

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Abstract

The aim of this study was to evaluate the effects of the carotid artery stenting (CAS) procedure on cerebral hemodynamics and cognitive performance in patients with internal carotid artery stenosis. In this prospective observational study, 16 consecutive patients in a single institute were treated with CAS from 2010 to 2011 (71.7 ± 7.3 years old, 12 males, and six left-sided procedures). Before and after the CAS procedure, all patients were evaluated with single photon emission computed tomography using 123I-iodoamphetamine and acetazolamide as well as the Weschler Adult Intelligent Scale (WAIS) to assess three intelligent quotients and four indexes. Patients with decreased preprocedural cerebral blood flow (CBF) and cerebrovascular reserve (CVR) experienced significant increases in CBF and CVR (P = 0.01 and 0.03). Twelve (75%) patients experienced a significant increase in one or more WAIS scores, while two (13%) showed a significant decrease. The most frequently improved scores were the Working Memory Index and Processing Speed Index (seven patients/44%). Preprocedural CBF was significantly correlated with the Full-scale and Performance Intelligent Quotients (r = 0.51–0.56, P = 0.02–0.04), and patients who experienced a significant increase in these scores had larger increases in CVR than patients with unchanged scores (P = 0.0097–0.019). These results indicate that the CAS procedure improved impaired cerebral hemodynamics and might benefit the cognitive function of patients with internal carotid artery stenosis related to impaired cerebral hemodynamics.

Key words: carotid artery stenosis, carotid artery stenting, cerebrovascular reserve, cognitive dysfunction, surgical outcome

Introduction

Carotid artery stenting (CAS) became the standard care for patients with symptomatic and asymptomatic internal carotid artery stenosis (ICAS) after it was shown to exert a protective effect against ischemic stroke.1,2 In Japan, CAS has been covered by insurance since April 2008. ICAS increases the risk of cognitive dysfunction3 as well as ischemic stroke, and low cognitive performance is a risk factor for death, even in asymptomatic ICAS patients.4 However, whether CAS benefits patients with ICAS in terms of cerebral hemodynamic impairment and cognitive function remains controversial. The aim of this study was to evaluate how CAS affects cerebral hemodynamics and cognitive performance in patients with ICAS and evaluate the factors related cognitive function improvement.

Materials and Methods

Study protocol

This study was approved by the ethics committee of our institute, and informed consent was obtained from all participants. From April 2010, the time at which the CAS procedure became possible in our institute, to September 2011, all consecutive patients with ICAS treated with CAS in our institute were included in this study. The indication for CAS was symptomatic ICAS patients with >50% stenosis or asymptomatic patients with >80% stenosis with good preprocedural activity of daily living (modified Rankin Scale ≥2), which was decided after the patients were evaluated by angiography with arterial catheterization. The degree of ICAS was measured according to the method of the North American Symptomatic Carotid Endarterectomy Trial. If the patient carried some high-risk factor for carotid...
endarterectomy (CEA), we recommended that the patients receive CAS instead of CEA. Otherwise, patients were provided with detailed information on CAS and CEA and allowed to choose which procedure was performed.

Before the procedure, all patients were evaluated with $^{123}$I-iodoamphetamine (IMP) single photon emission computed tomography (SPECT) and the Weschler Adult Intelligent Scale (WAIS). Preoperative magnetic resonance imaging (MRI) with T2-weighted imaging (T2WI; repetition time (TR) = 4.5 s, echo time (TE) = 91 ms, flip angle (FA) = 160°, slice thickness = 5 mm, slice gap = 1 mm, slice number = 24) and fluid attenuation inversion recovery (FLAIR; TR = 2.6 s, TE = 91 ms, FA = 170°, slice thickness = 5 mm, slice gap = 1 mm, slice number = 24) imaging was performed before the operation to assess the degree of white matter hyperintensity using the Fazekas grading system and the presence of brain atrophy with a 1.5-T unit (Aera, Siemens Healthcare GmbH, Forchheim, Germany). A Fazekas grade of 3 was defined as strong white matter hyperintensity. Six weeks after CAS, patients were evaluated with SPECT, and six months after the procedure, patients were evaluated with WAIS, as determined in reference to the initial protocol of the Japan Extracranial-intracranial bypass Trial (JET) study.

**CAS procedure**

Carotid artery stenting was performed via a femoral approach using a biplane flat-panel detector angiographic system (AXIOM Artis, Siemens Healthcare GmbH, Forchheim, Germany) and an appropriately sized balloon and stent and a distal protection device (Precise and Angioguard Xp, Cordis, Doublin, OH, USA) in all patients except for the last one patient treated with a Carotid Wallstent (Boston Scientific, Natick, MA, USA). All procedures were performed by a single neurosurgeon who was a board-certified member of The Japanese Society for Neuroendovascular Therapy (M.S.). One week before the procedure, patients were treated with oral aspirin (81 mg/day) and clopidogrel (75 mg/day). Local anesthesia was applied unless the patient was unable to stay still during the angiography, in which case we performed the CAS procedure under general anesthesia. During the procedure, changes in oxyhemoglobin that correlated with cerebral blood volume were monitored using near-infrared time-resolved spectroscopy. If the patient did not show symptoms or signs suggesting periprocedural embolism, we did not perform MRI immediately after the procedure. One month after the procedure, MRI with diffusion-weighted images (TR = 5.0 s, TE = 76 ms, FA = 90°, slice thickness = 5 mm, slice gap = 1 mm, slice number = 24), T2WI and FLAIR was performed to detect any brain embolism caused by the procedure using the same 1.5 T scanner before the operation. Aspirin and clopidogrel were continued for at least 3 months after successful intervention.

**Quantitative cerebral blood flow measurement using IMP-SPECT**

The SPECT protocol was performed using the standardized method described in the JET studies and the dual table autoradiography method described elsewhere. A three-headed camera and a parallel collimator (PRISM-IRIX and LEHR Parallel Collimator, Shimazu Medical Systems, Tokyo, Japan) were used under an energy range centered at 159 keV with a width of 20% ±10%. Two-minute rotation was performed 14 times in continuous mode after each intravenous administration of $^{123}$I-IMP (167 MBq) before and after acetazolamide (17 mg/kg) injection. The matrix size was 64 × 64 pixels. Acquired images were reconstructed, and cerebral blood flow (CBF) quantitation was performed using the QSPECT image reconstruction package (Nihon Medi-Physics Co. Ltd., Tokyo, Japan). Cerebrovascular reserve (CVR) was automatically calculated as ([CBF after acetazolamide challenge – CBF at rest]/CBF at rest) × 100. The regional values of middle cerebral artery territories were calculated from manually drawn regions of interest by a single experienced researcher who participated in the JET and JET-2 trials (M.S.); the average value of cortical regional values in three consecutive slices, as the bottom slice to be set at the level of the foramen of Monro, was recorded. Decreased CBF and decreased CVR were defined as <34 mL/min/100 g and <30%, respectively, in accordance with the JET study.

**Cognitive test**

Neuropsychologists in our institute evaluated patients using the WAIS-III (except for the first patient, who was evaluated with the WAIS-R because this was the standardized version used at that time). In symptomatic patients, a cognitive examination was performed more than 1 month after the ischemic episode. The WAIS-III provides three intelligent quotients, including one for overall intellectual ability (Full-scale Intelligence Quotient, IQ), one for overall verbal ability (Verbal IQ), and one for overall nonverbal performance ability (Performance IQ), as well as four index scores that reflect language and verbal ability (Verbal Comprehension Index), the ability to organize nonverbal visual stimuli (Perceptual Organization Index), auditory attention and mental manipulation (Working Memory Index) and visual-motor speed (Processing Speed Index).
The scores had an average of 100 and a standard deviation of 15 when adjusted for each age group. The WAIS test manual provides the practice effect and 90% confidence interval (CI) of each score that was recorded during the Japanese standardization\(^{11,12}\) and should be considered when the same person is evaluated with WAIS within 1 year. When the same person is evaluated with consecutive WAIS tests within 1 year, the difference is regarded as significant if it exceeds the practice effect and/or 90% CI. The 90% CI is broader than the practice effect in all age groups.

### Statistical analysis

A significant change (improvement or decline) in each person's IQ and indexes was defined as changes beyond the practice effect and/or 90% CI, as recommended in the WAIS technical manual.\(^{12}\)

A paired t-test was performed to compare the preoperative and postoperative values of SPECT and WAIS. Pearson's correlation coefficient (r) between preprocedural CBF/CVR and preprocedural WAIS scores was calculated and tested for significance. The preprocedural WAIS scores and the percentages of patients who experienced a significant increase in WAIS scores were compared between patients who underwent right and left CAS, between symptomatic and asymptomatic patients, and between patients with strong white matter hyperintensity or brain atrophy using unpaired t-tests and Chi-squared tests, as appropriate. \(P<0.05\) was regarded as statistically significant. Except where stated otherwise, the data are presented as the mean ± standard deviation.

### Results

A representative case is described in Fig. 1. Of the 19 patients recruited in this study, 16 completed preoperative and postoperative evaluations and were included in the analysis; two patients refused postoperative SPECT studies, and we could not schedule a preoperative evaluation in one patient who required arterial valve surgery as soon as possible after the CAS procedure. During this study period, no other patients received CEA in our institute. The backgrounds of the analyzed patients are summarized in Table 1. Three patients carried high-risk

![Image](image_url)

Fig. 1 A representative case of an 80-year-old male patient (No. 15) who developed sudden-onset mild left hemiparesis and was subsequently diagnosed with a small new infarction of the left corona radiata by magnetic resonance imaging 3 months before the procedure. A detailed workup at our institute revealed 80% stenosis of the right internal carotid artery (Rt. IC, left upper panel), decreased cerebral blood flow (CBF), and markedly reduced cerebrovascular reserve (CVR) in the right hemisphere (right upper panels). After a successful carotid artery stenting procedure (left lower panel), the CBF and CVR increased in the right hemisphere, and the laterality diminished (right lower panels). Compared with his preoperative scores, the patient's postoperative Full-scale Intelligence Quotient (IQ) improved from 63 to 72 (+9), and his Performance IQ improved from 63 to 78 (+15); both of these results exceeded the 90% confidence interval of the scores and were therefore regarded as significant.
Table 1  Patient backgrounds. The lowest column shows the average ± standard deviation or \( N \) (%).

| No. | Age (years) | Sex | Degree of stenosis (%) | Symptomatic or asymptomatic | Location of infarction | Fazekas grade (Rt/Lt) | Brain atrophy | Procedure | Contralateral stenosis (%) | Past medical histories | Improved cognition |
|-----|-------------|-----|-------------------------|----------------------------|------------------------|-----------------------|---------------|-----------|---------------------------|-----------------------|-------------------|
| 1   | 73          | M   | 84.0                    | S                          | Lt O, Bil BG           | 3/3                   | 3/3           | Yes       | Rt                        | Yes                   | Yes               |
| 2   | 78          | M   | 82.4                    | S                          | -                      | 1/1                   | 2/2           | Yes       | Rt                        | Laryngeal cancer (removed after XRT) | Yes               |
| 3   | 68          | M   | 80.7                    | A                          | -                      | 1/1                   | 2/1           | Lt        | Yes                      | SAH (post coiling to rt. IC-PC An), HU | Yes               |
| 4   | 72          | F   | 86.4                    | S                          | Rt F + P               | 1/1                   | 1/1           | Rt        | Unruptured Acom An        | Cerebral infarction (brainstem) | Yes               |
| 5   | 83          | M   | 62.6                    | S                          | Rt F                   | 2/2                   | 2/2           | Rt        | 70.0                     | Yes                   | Yes               |
| 6   | 61          | F   | 83.9                    | S                          | Rt F                   | 2/2                   | 2/1           | Rt        | 66.0                     | Rickets               | Yes               |
| 7   | 68          | M   | 70.6                    | A                          | -                      | 1/1                   | 1/1           | Rt        | Yes                      | Cerebral infarction (brainstem) | Yes               |
| 8   | 64          | M   | 72.5                    | S                          | Lt F + P, Rt BG        | 2/2                   | 1/1           | Lt        | Previous Lt, STA–MCA bypass | Gastric tumor (removed) | Yes               |
| 9   | 74          | M   | 87.2                    | A                          | Rt F + P               | 2/2                   | 1/2           | Rt        | 100                      | Previous Rt. CEA | Yes               |
| 10  | 67          | F   | 63.5                    | A                          | Lt BG                  | 1/1                   | 1/1           | Lt        | 40.0                     | Yes                   | Yes               |
| 11  | 61          | M   | 60.7                    | S                          | -                      | 1/1                   | 2/2           | Rt        | Yes                      | Gastric tumor (removed) | Yes               |
| 12  | 65          | M   | 52.0                    | S                          | Bil BG                 | 3/3                   | 3/3           | Lt        | Yes                      | Rt. MCA stenosis | Yes               |
| 13  | 72          | M   | 54.7                    | S                          | Lt P                   | 2/2                   | 2/2           | Lt        | Yes                      | HU                   | Yes               |
| 14  | 75          | F   | 93.4                    | S                          | Rt F + P               | 2/2                   | 1/1           | Rt        | Yes                      | Yes                  | Yes               |
| 15  | 80          | M   | 77.1                    | S                          | Rt F, Rt BG            | 1/1                   | 1/1           | Yes       | Rt                        | Yes                  | Yes               |
| 16  | 86          | M   | 79.7                    | A                          | -                      | 2/2                   | 2/2           | Yes       | Lt                        | Prostate cancer (removed) | Yes               |
|     | 71.7 ± 7.3  | M = 12 | 74.5 ± 12.1 | 11 (69%)                  | Grade 3 = 2            | 3 (18%)              | 4 (25%)       | 11 (69%)  | 6 (25%)                  | 2 (13%)               | 12 (75%)          |

A, asymptomatic; Acom, anterior communicating artery; An, aneurysm; Bil, bilateral; BG, basal ganglia; CAD, coronary artery disease; CEA, carotid endarterectomy; DLP, dyslipidemia; DM, diabetes mellitus; F, female; F, frontal; HTN, hypertension; HU, hyperuricemia; IC-PC; internal carotid artery and posterior cerebral artery; Lt, left; M, male; MCA, middle cerebral artery; O, occipital; P, parietal; Rt, right; S, symptomatic; SAH, subarachnoid hemorrhage; SSS, sick sinus syndrome; STA, superficial temporal artery; XRT, radiation therapy.
Surgical Outcome of CAS

Factors for CEA (No. 1, 2 and 9), and four patients had contralateral ICAS. Two patients showed strong white matter hyperintensity (Fazekas grade 3), and three patients exhibited diffuse brain atrophy on preoperative MRI.

One patient required general anesthesia during the CAS procedure (No. 15). During the CAS procedure, seven patients (44%) experienced hypotension during the procedure and required transient infusion of dobutamine and/or transient discontinuation of antihypertensive drugs. Due to preoperative bradycardia, one patient (No. 1) required the insertion of a temporary pacemaker during the procedure. No patient experienced other periprocedural complications, showed new signs or symptoms, or developed symptomatic stroke or any other symptoms during the 6-month follow-up period. An asymptomatic brain embolism was detected in one patient by MRI 1 month after the procedure (No. 4).

CAS effect on CBF and CVR

The SPECT studies were carried out 28.2 ± 34.5 days before CAS and 41.6 ± 10.5 days after CAS. Analysis of all the patients together showed no significant difference between preoperative and postoperative CBF/CVR (Fig. 2). However, patients with decreased preoperative CBF/CVR showed significant improvement in postoperative CBF/CVR (CBF, 27.7 ± 4.5 mL/min/100 g vs. 31.0 ± 5.4 mL/min/100 g; and CVR, 14.6 ± 10.5% vs. 32.6 ± 18.4%).

Effect of CAS on cognitive function

Patients were assessed on the WAIS 15.3 ± 9.6 days before CAS and 183.6 ± 5.8 days after CAS. Among the patients, 12 (seven symptomatic patients and seven patients treated with a right-sided procedure) showed a significant postoperative improvement in one or more scores that exceeded the practice effect and/or the 90% CI (Fig. 2). The most frequently improved scores were the Working Memory Index and Processing Speed Index (seven patients/44%), followed by Verbal IQ (six patients/38%). Paired t-tests evaluating all patients revealed that there were significant postoperative improvements in Verbal IQ, the Verbal Comprehension Index and the Processing Speed Index.

Two patients (13%) experienced a significant decline in some scores. One of these patients (No. 8) had symptomatic left IC stenosis and showed reductions in Full-scale IQ (−6) and the Perceptual Organization Index (−14). The other had symptomatic right IC stenosis (No. 14) and showed reductions in Performance IQ (−7) and the Perceptual Organization Index (−12) but a significant increase in the Processing Speed Index (+14) from the preoperative to postoperative evaluation. Four patients (25%, three symptomatic patients treated with a right-sided procedure and one asymptomatic patient treated with a left-sided procedure) had no significant change in any IQs or indexes.

All three patients who experienced a significant increase in the Verbal Comprehension Index had contralateral IC stenosis and were treated with a right-side procedure (No. 5, 6, 9), while all four patients with contralateral IC stenosis showed significant improvement in one or more scores. When we compared the patients who received right CAS to those who received left CAS and the asymptomatic patients to the asymptomatic patients, no significant differences were observed between preprocedural and postprocedural IQs and indexes (P = 0.29–0.69) or in the percentages of patients who experienced a significant improvement in each IQ or index (P = 0.21–1.00). Neither the presence of strong white matter intensity nor brain atrophy showed a significant correlation with preprocedural and postprocedural scores (P = 0.15–0.93 and 0.17–0.97, respectively) or the presence of improved cognitive function (P = 0.94 and 0.57, respectively). One patient who had asymptomatic embolic stroke did not show improved cognitive function (No. 4).

Preprocedural Full-scale IQ and Performance IQ were significantly correlated with preprocedural CBF at rest (Table 2). Patients who experienced a significant improvement in Full-scale IQ and Performance IQ had larger postoperative increases in CVR than patients without significant improvements in these scores (Table 3).

Discussion

In this prospective study, we evaluated consecutive patients treated by the CAS procedure in a single institute and found that CAS improved hemodynamic impairment in patients with decreased CBF/ CVR and some aspects of cognitive function in the majority of patients.

Our study showed that the majority of ICAS patients treated with the CAS procedure experienced a significant increase in some aspects of cognitive function regardless of the laterality of the procedure or whether they were symptomatic. Many studies have evaluated and compared the effects of the CAS procedure on cognitive function in ICAS patients1,13–18; however, conclusions have varied among studies, possibly because different studies used different neuropsychological batteries. Studies that used WAIS scores13,14,16 evaluated their results using paired t-tests and rarely focused on
whether each patient showed a significant change. Using neuropsychologically appropriate methods based on the WAIS test manual, we demonstrated that the most frequent improvement observed after CAS was in the Working Memory Index and Processing Speed Index. The disruption of white matter integrity by ischemic damage has been associated with a decline in performance on cognitive tests related to working memory and processing speed\(^{19,20}\) and some studies have also reported a significant increase in processing speed after the CAS procedure.\(^{14}\) If the CAS procedure improves impaired cerebral hemodynamics, it might also improve white matter integrity, thereby improving these cognitive aspects. However, we did not find a direct correlation between the Working Memory

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**Fig. 2** Postoperative changes in cerebral blood flow (CBF), cerebrovascular reserve (CVR) and cognitive function in all cases. In the upper panels, *solid lines* show decreases in preprocedural CBF/CVR, and *dotted lines* indicate no decrease in preprocedural CBF/CVR. In the middle and bottom columns, *solid lines* show that the score changes exceeded the 90% confidence interval (CI) and were therefore regarded as significant. *Dashed lines* indicate that the changes exceeded the practice effect but were within the 90% CI. *Dotted lines* indicate changes that were within the 90% CI.
to the reported improvement in verbal functions in patients with bilateral ICAS\(^{18}\) and our patients treated with a right-sided procedure.

We found that preprocedural CBF was significantly correlated with Full-scale IQ and Performance IQ and that patients who showed a significant increase in these scores also showed greater postprocedural increases in CVR. These observations suggest that patients with severe impairment of cerebral hemodynamics could cognitively benefit more from the CAS procedure than patients with less impairment in cerebral hemodynamics. Studies that have focused on cognitive performance after carotid endarterectomy have shown that the normalization of increases in hypoxic tissues\(^ {26}\) and decreases in cortical benzodiazepine receptors\(^ {27}\) was associated with improved cognition after the procedure. Although preoperative CBF at rest but not CVR correlated with cognitive function, the patients who experienced improved cognition showed a greater increase in CVR, but not CBF at rest. The discrepancy might suggest that decreased CBF in some patients resulted from low CBF demand as a consequence of irreversible low neuronal function and that the postoperative increase in CVR was indicative of a reversal in neuronal function at risk of neuronal death and suppressed function before the procedure. Considering that longstanding hemodynamic impairment subsequently leads to the progression of cortical neuronal loss\(^ {28}\), early intervention would be preferred in patients with ICAS to improve cognitive function, as well as stroke prevention.

Limitations of our study include the small sample size and heterogeneous backgrounds of our patients and the lack of a medically treated control population.\(^ {18}\) The observed improvement in cognitive function might be associated with

| Table 2 Correlation between preprocedural (pre) cerebral hemodynamics and cognitive function |
|---------------------------------|-----------------|-----------------|
|                                | CBF at rest (Pre) | CVR (Pre) |
| Full-scale IQ (Pre)            | \(0.51 \ (0.04^*)\) | 0.20 (0.45) |
| Verbal IQ (Pre)                | 0.45 (0.08)       | 0.23 (0.39)    |
| Performance IQ (Pre)           | \(0.56 \ (0.02^*)\) | 0.18 (0.50)    |
| Verbal Comprehension Index (Pre) | 0.51 (0.06)       | 0.28 (0.33)    |
| Perceptual Organization Index (Pre) | 0.49 (0.07)       | 0.01 (0.98)    |
| Working Memory Index (Pre)     | 0.35 (0.22)       | 0.26 (0.37)    |
| Processing Speed Index (Pre)   | 0.52 (0.07)       | 0.25 (0.42)    |

\(^*P<0.05.\) CBF, cerebral blood flow; CVR, cerebrovascular reserve; IQ, Intelligence Quotient.

| Table 3 Comparison of the CBF and CVR difference (\(\Delta\)) before and after the procedure (post-pre) in patients with improved cognition (improved) and unchanged cognition (unchanged) |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| \(\Delta\)CBF at rest (Post-Pre, mL/min/100 g) | \(\Delta\)CVR (Post-Pre, %) |
| Improved scores | Unchanged scores | \(P\)-value | Improved scores | Unchanged scores | \(P\)-value |
| Full scale IQ   | \(-0.9 \pm 4.4\) | 3.5 \(\pm 3.4\) | 0.14 | \(29.2 \pm 22.5\) | \(-3.8 \pm 14.3\) | 0.0097* |
| Verbal IQ       | 1.0 \(\pm 5.5\) | 2.7 \(\pm 3.1\) | 0.42 | 16.3 \(\pm 9.0\) | 3.7 \(\pm 23.3\) | 0.30 |
| Performance IQ  | 0.5 \(\pm 3.7\) | 2.7 \(\pm 4.4\) | 0.69 | \(34.4 \pm 22.5\) | 0.2 \(\pm 16.7\) | 0.019* |
| Verbal Comprehension Index | 4.0 \(\pm 1.7\) | 1.4 \(\pm 4.8\) | 0.39 | 0.1 \(\pm 5.0\) | 7.3 \(\pm 24.6\) | 0.63 |
| Perceptual Organization Index | 2.3 \(\pm 4.6\) | 1.8 \(\pm 4.5\) | 0.85 | 13.0 \(\pm 30.4\) | 1.7 \(\pm 16.3\) | 0.38 |
| Working Memory Index | 1.3 \(\pm 4.4\) | 2.7 \(\pm 4.5\) | 0.57 | 11.0 \(\pm 25.8\) | 0.5 \(\pm 17.5\) | 0.39 |
| Processing Speed Index | 2.0 \(\pm 4.4\) | 2.0 \(\pm 4.7\) | 0.99 | 0.8 \(\pm 21.9\) | 10.7 \(\pm 22.4\) | 0.42 |

\(^*P<0.05.\) CBF, cerebral blood flow; CVR, cerebrovascular reserve; IQ, Intelligence Quotient.
improvement in anxiety and/or depression,\textsuperscript{29} which we did not measure using depressive scales in this study; however, other studies have reported that depressive scales were unchanged after the CAS procedure.\textsuperscript{15,16} The result of long-term follow-up was unclear; however, some studies have reported observing sustained improvement in cognition at 60 months after the CAS procedure.\textsuperscript{16} No patient experienced new symptoms during the postoperative SPECT and WAIS evaluation, but we cannot confirm that the hemodynamic status was the same during the interval. Postoperative MRI might have failed to detect ischemic microemboli due to the gap between the procedure and imaging; therefore, how microemboli may have affected cognitive function remains unclear. Because we only obtained standard MRI images and did not use a volumetric approach, we are unable to deny the possibility that preoperative cognitive function or its improvement was affected by preexisting white matter hyperintensity\textsuperscript{30} and/or brain atrophy,\textsuperscript{31} especially in elderly patients who might have had a dual pathology of mild cognitive impairment or Alzheimer’s disease. Despite these limitations, our study showed that an uncomplicated CAS procedure is safe and might be beneficial in ICAS patients in terms of its effects on cerebral hemodynamics and cognitive function. 

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Conflicts of Interest Disclosure

All authors declare they have no conflicts of interest, are members of the Japan Neurosurgical Society, and registered online Self-reported COI Disclosure Statement Forms through the website.

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