Perioperative Evaluation of Cerebral Blood Flow Using ¹²³I-labeled *N*-isopropyl-p-iodoamphetamine Single-Photon Emission Computed Tomography without Blood Sampling in Patients Who Underwent Carotid Artery Stenting

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Introduction

The evaluation of regional cerebral vascular reserve (rCVR) with single-photon emission computed tomography (SPECT) is useful for predicting cerebral hyperperfusion following carotid artery stenting (CAS) and carotid endarterectomy (CEA).[1] Quantitative SPECT dual table autoradiography (DTARG) is commonly used to evaluate regional cerebral blood flow (rCBF) and rCVR. However, this method requires arterial blood sampling, which is invasive and stressful for the patients.

The *N*-isopropyl-p-iodoamphetamine-rest and true acetazolamide images estimated method using dynamic acquisition (IMP-RAMDA) method is a noninvasive method with ¹²³I-labeled IMP which has the advantage of an excellent linearity of rCBF.[2] It measures rCBF at rest and after an acetazolamide (ACZ) challenge, thereby enabling rCVR to be evaluated without any blood sampling. The IMP-RAMDA method is used at many institutions in Japan. However, the perioperative usefulness has fewly been reported. The purpose of our retrospective study was to investigate the perioperative usefulness of the IMP-RAMDA method.

Case Report

Nine patients underwent CAS and one patient underwent CEA at our institution between August 2011 and March 2013. To conduct this study under similar conditions, we enrolled nine consecutive patients with carotid artery stenosis who underwent CAS. Pre- and post-operative rCBF and preoperative rCVR were evaluated in all patients using the IMP-RAMDA method. We performed CAS under local anesthesia at least 1 month after an ischemic event. Postoperative SPECT was performed on the 1st postoperative day. The mean age was 76.4 years (range: 72–84 years), and six patients were male. Six patients were symptomatic whereas three were asymptomatic. The average degree of stenosis was $83.2 \pm 6.3\%$ (mean ± standard deviation [SD], range: 70–90%), according to the North American Symptomatic Carotid Endarterectomy Trial criteria. We estimated resting rCBF and rCVR in the middle cerebral artery (MCA) areas. Cerebral hyperperfusion after CAS was defined as a CBF increase of ≥100%.[3] Reduced rCVR was defined as CVR <12%.[3] The following parameters were calculated:

- rCVR to ACZ: ([rCBF after ACZ challenge − rCBF at rest]/rCBF at rest) ×100%
- Asymmetry index: (rCBF at rest on the CAS side/rCBF at rest on the contralateral side) ×100%.

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Protocol of the *N*-isopropyl-p-iodoamphetamine-rest and true acetazolamide images estimated method using dynamic acquisition method and data analysis

The IMP-RAMDA method is a combination of Kawamura's method[4] and the graph plot method [Figure 1a].[5] SPECT study was performed using a two-head rotating gamma camera (E.cam, Toshiba Medical Systems Corporation, Tokyo, Japan) with a low-medium energy general purpose collimator. Data were obtained by continuous rotation in a 64 × 64 matrix. A dynamic scan was performed with the graph plot method[5] for 2 min after the first

administration of IMP (111 MBq) in a 1 min intravenous infusion. Sequential 5 min SPECT scans were initiated 5 min after the administration of IMP and were performed four times. ACZ (17 mg/kg) was administered 15 min after the first administration of IMP. IMP (111 MBq) was then administered 25 min after its first administration as a 1 min intravenous infusion. Sequential 5 min SPECT scans were started 5 min later and performed four times. Regions-of-interest (ROI) were selected on the spatial resolution-equalized and nonequalized CBF images both at rest and after an ACZ challenge, using an automatic ROI definition tool, Neuro Flexer (Nihon Medi-Physics, Tokyo, Japan). Anterior cerebral artery areas were susceptible to the effect of cross flow from the opposite side. Therefore, we selected MCA areas as the target region.
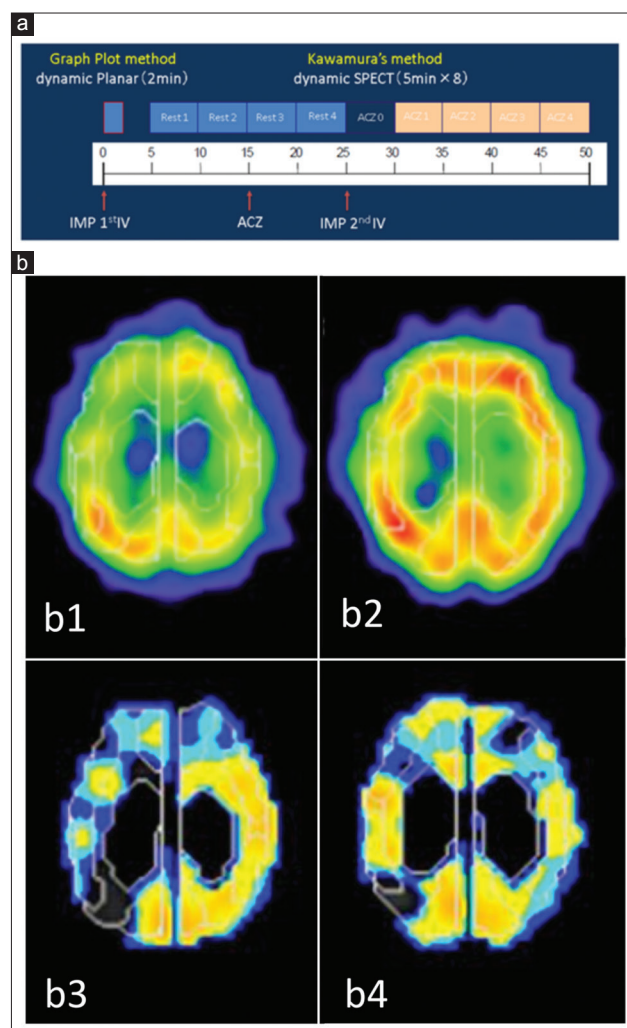
DISCUSSION

SPECT images (resting rCBF and rCVR) are shown in Figure 1b. CAS was successfully performed with no complications in all patients. The results of preoperative resting rCBF and rCVR are shown in Table 1, and the value of rCVR on the side of carotid artery stenosis was estimated to be 36.0 ± 14.7% (mean ± SD, range: 11.8–58.1%). On the other hand, the rCVR value on the contralateral side was 54.0 ± 14.4% (mean ± SD, range: 32.7–70.6%). These values are almost consistent with the previous ARG study.[6] The pretreatment asymmetry index was estimated at 94.3 ± 2.5% (mean ± SD, range: 90.2–97.9%) and was >75% in all patients. The ratio of postoperative resting rCBF to preoperative rCBF on the affected side was 104.2 ± 10.7% (mean ± SD, range: 79.0–112.0%). Furthermore, the ratio of postoperative resting rCBF on the affected side compared to that of the contralateral side was 98.8 ± 6.7% (mean ± SD, range: 90.6–112.6%). No patient developed cerebral hyperperfusion from the aspects of rCBF and clinical symptoms (e.g., headaches, seizures, and neurological deficits), and showed the significant laterality of postoperative rCBF.

The DTARG method quantitatively measures resting rCBF and rCVR within 1 h using arterial blood sampling. Arterial blood sampling is a painful procedure for patients and troublesome for hospital staff. We applied the IMP-RAMDA method to the perioperative evaluation of CAS for two purposes; (1) the postoperative detection and (2) the preoperative prediction of cerebral hyperperfusion.

The risk factors for postoperative cerebral hyperperfusion include (1) reduced CVR and (2) a pretreatment asymmetry index.[1] Kaku *et al.*[1] suggested that a pretreatment asymmetry index under 75% was a risk factor for cerebral hyperperfusion. In our study, no patient showed a reduction in CVR under 12%, except for one patient with a mild CVR reduction, and the pretreatment asymmetry index was over 75% in all patients. Therefore, all patients were considered to be of low risk for postoperative cerebral hyperperfusion. In our study, no patient showed cerebral hyperperfusion. These results indicate that the rCBF study with the IMP-RAMDA method correlated

Figure 1: (a) Protocol of the IMP-RAMDA method. (b) SPECT images in a 77-year-old man with stenosis of the right carotid artery. Preoperative cerebral blood flow in the resting state determined by SPECT (b1) and postoperative cerebral blood flow in the resting state determined by SPECT (b2). Preoperative image of cerebrovascular reactivity determined with IMP-RAMDA method (b3) and postoperative image of cerebrovascular reactivity determined with IMP-RAMDA method (b4). Preoperative SPECT showing low cerebrovascular reactivity in the right hemisphere and the value was 11.83 (b3). Postoperative SPECT revealed increased cerebrovascular reactivity on the side of carotid artery stenting and the value was 26.44 (b4). IMP: *N*-isopropyl-p-iodoamphetamine; RAMDA: Rest and true acetazolamide images estimated method using dynamic acquisition; SPECT: Single-photon emission computed tomography; ACZ: Acetazolamide.

Table 1: Results of perioperative rCBF and CVR with IMP-RAMDA method

Patients No.	Side of CAS				Contralateral side			
	rCBF (ml·100 g⁻¹·min⁻¹)			rCVR (%)	rCBF (ml·100 g⁻¹·min⁻¹)			rCVR (%)
	Before CAS	After CAS	P	Before CAS	Before CAS	After CAS	P	Before CAS
1	38.1	43.2	0.236	53.4	39.5	38.4	0.859	66.1
2	34.2	39.6		44.6	37.9	43.7		45.4
3	38.1	39.2		25.1	40.8	38.8		66.8
4	35.0	36.6		43.5	37.1	37.3		68.5
5	43.6	44.8		39.5	44.8	45.1		47.8
6	47.8	37.8		11.8	48.9	39.0		32.7
7	34.9	38.5		19.9	37.7	37.9		70.6
8	38.2	42.8		58.1	41.8	47.7		50.1
9	47.1	45.5		28.0	49.5	45.6		37.2

P values are derived from Wilcoxon signed rank test (IBM SPSS statistics version 22 procedure [IBM Corp., Armonk, NY, USA]). rCBF: Regional cerebral blood flow; CVR: Cerebral vascular reserve; IMP: *N*-isopropyl-p-iodoamphetamine; RAMDA: Rest and true acetazolamide images estimated method using dynamic acquisition; CAS: Carotid artery stenting.

well with the clinical manifestations and can be used to evaluate hemodynamic changes after CAS. To evaluate the detectability of cerebral hyperperfusion, we need to accumulate the data of patients who underwent perioperative evaluations with the IMP-RAMDA method.

Limitations

Our study is limited by its small sample size. Furthermore, no patient developed cerebral hyperperfusion; hence, the study is limited by inferring the predictability of CVR reductions with the IMP-RAMDA method for cerebral hyperperfusion. Our present study was also a retrospective study. Postoperative CVR was measured in only one patient [Figure 1] and perioperative hemodynamic changes were not evaluated in detail. Therefore, we need to accumulate data from more cases to establish the usefulness of the IMP-RAMDA method in predicting cerebral hyperperfusion and evaluating CVR changes.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Kaku Y, Yoshimura S, Kokuzawa J. Factors predictive of cerebral hyperperfusion after carotid angioplasty and stent placement. AJNR Am J Neuroradiol 2004;25:1403-8.
2. Iida H, Akutsu T, Endo K, Fukuda H, Inoue T, Ito H, *et al.* A multicenter validation of regional cerebral blood flow quantitation using [123I] iodoamphetamine and single photon emission computed tomography. J Cereb Blood Flow Metab 1996;16:781-93. doi: 10.109 7/00004647-199609000-00003.
3. Hosoda K, Kawaguchi T, Shibata Y, Kamei M, Kidoguchi K, Koyama J, *et al.* Cerebral vasoreactivity and internal carotid artery flow help to identify patients at risk for hyperperfusion after carotid endarterectomy. Stroke 2001;32:1567-73. doi: 10.1161/01. STR.32.7.1567.
4. Kawamura Y, Ashizaki M, Saida S, Sugimoto H. Usefulness of rate of increase in SPECT counts in one-day method of N-isopropyl-4-iodoamphetamine [123I] SPECT studies at rest and after acetazolamide challenge using a method for estimating time-dependent distribution at rest. Ann Nucl Med 2008;22:457-63. doi: 10.1007/s12149-008-0134-3.
5. Okamoto K, Ushijima Y, Okuyama C, Nakamura T, Nishimura T. Measurement of cerebral blood flow using graph plot analysis and I-123 iodoamphetamine. Clin Nucl Med 2002;27:191-6. doi: 10.1097 /00003072-200203000-00009.
6. Nakagawara J. Clinical neuroimaging of cerebral ischemia (In Japanese). No To Shinkei (Brain Nerve) 1999;51:502-13.