An Additional Monitoring of Regional Cerebral Oxygen Saturation to HMPAO SPECT Study During Balloon Test Occlusion

Makio Kaminogo, MD; Makoto Ochi, MD; Masanari Onizuka, MD; Hideaki Takahata, MD; Shobu Shibata, MD

Background and Purpose—To increase the reliability of 99mTc–hexamethyl propyleneamine oxime (HMPAO) single photon emission computed tomography (SPECT) study in the evaluation of hemodynamic change with balloon test occlusion (BTO) of the internal carotid artery, we attempted to clarify the usefulness of additional monitoring of regional oxygen saturation of the brain (rSO2).

Methods—During BTO, rSO2 monitoring with transcranial near infrared spectroscopy was performed 17 times on 16 patients. Asymmetrical distribution of the tracer was classified visually as follows: group 1, little or no asymmetry, and group 2, moderate or severe asymmetry. Seven regions of interest (ROI) were defined in the middle cerebral artery area of each hemisphere, and the asymmetry index (AI) = 200 × (Cnon − Coccl)/(Cnon + Coccl), where Cnon = mean counts on the nonoccluded side, and Coccl = mean counts on the occluded side were also calculated. Then, mean AI (MAI) was obtained from AI of 7 ROIs for each study.

Results—Of the 17 procedures, 10 BTOs were in group 1 and 5 BTOs were in group 2. Two patients did not undergo SPECT study because of the immediate appearance of a neurological deficit with BTO; they were defined as group 3. The MAI in group 1 was 2.6 ± 3.3%, which was significantly smaller than the MAI in group 2 (25.6 ± 5.0%, P < 0.02). The ΔrSO2 (baseline rSO2−rSO2 during ICA occlusion) with BTO in group 1 was 1.5 ± 1.4% (n = 10), which was statistically smaller than that in group 2 (5.5 ± 1.3%, n = 4, P < 0.05). The ΔrSO2 in group 3 was 9.0 ± 0.0% (n = 2). In group 1, however, rSO2 began to decline when the stump pressure fell to 45 mm Hg and always declined when the stump pressure fell below 40 mm Hg. Furthermore, in group 1, a significant correlation was observed between the ΔrSO2 and stump pressure (r = 0.85, P < 0.0001).

Conclusions—This preliminary study reveals that an obvious asymmetrical SPECT pattern always accompanies a profound decrease in rSO2 and that rSO2 parallels a severe reduction in stump pressure in cases exhibiting a symmetrical SPECT pattern. Thus, the cerebral oximetry sensitively reflects the cerebral oxygenation, and simultaneous measurements of rSO2 and stump pressure with 99mTc-HMPAO SPECT study apparently are useful in evaluating hemodynamic integrity with BTO. (Stroke. 1999;30:407-413.)

Key Words: balloon dilatation ■ cerebral arteries ■ oximetry ■ tomography, emission computed

Temporary or permanent occlusion of the internal carotid artery (ICA) is often required in the surgical treatment of patients with cerebral aneurysms, skull base tumors, or cervical tumors. Measurement of cerebral blood flow (CBF) during balloon test occlusion (BTO) has been used increasingly to raise the procedure’s reliability to predict high-risk patients. Among several methods of CBF study, 99mTc–hexamethyl propyleneamine oxime (HMPAO) SPECT is used widely in clinical BTO because it is readily available and simple. Because 99mTc-HMPAO rapidly distributes in the brain tissue and is kept constant for a long time after intravenous injection, the CBF pattern during transient ICA occlusion can be evaluated by intravenous injection of 99mTc-HMPAO during BTO, followed by SPECT study after the completion of all BTO procedures. 99mTc-HMPAO SPECT provides fair tomographic resolution of CBF and detects focal flow defects or asymmetrical CBF distribution during BTO. However, because 99mTc-HMPAO SPECT reveals only relative CBF distribution, CBF changes with BTO compared with the baseline have not been evaluated using this method.

During skull base surgery and carotid endarterectomy, regional oxygen saturation of the brain (rSO2) monitoring with transcranial near infrared spectroscopy (NIRS) has been

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407
Summary of Patient Characteristics and Data

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SB tumor indicates skull base tumor; NC, not calculated; and poor, poor recording.

*Patient 13 means BTO reexamined 7 mo later.

used and proven to provide reliable information about changes in cerebral perfusion during these procedures.\(^{13,14}\) Therefore, even with a bilateral symmetrical decrease of CBF, rSO2 monitoring can detect the relative CBF changes with BTO compared with baseline. In this study, we evaluated the feasibility and usefulness of additional rSO2 monitoring during BTO with \(^{99m}\)Tc-HMPAO SPECT to estimate the hemodynamic changes with ICA occlusion.

**Subjects and Methods**

Prior to ICA manipulation or ICA ligation, 16 patients (7 with cervical tumors, 5 with skull base tumors, and 4 with inaccessible aneurysms of the ICA) were examined with BTO of the ICA under \(^{99m}\)Tc-HMPAO SPECT (Table). Informed consent was obtained from the patients or their guardians. In these patients, \(^{99m}\)Tc-HMPAO SPECT study was also attempted after balloon occlusion. However, if any neurological symptoms or signs developed after inflation, the balloon was immediately deflated to restore blood flow without SPECT study.

**BTO**

All procedures were performed under local anesthesia with the patients in a fully awake state. After a neurological examination and 3- or 4-vessel angiogram, cross-filling via the communicating arteries was examined by contralateral carotid angiogram or vertebral angiogram under manual compression of the objective carotid artery. Then, a 7F balloon catheter was introduced into the carotid artery and placed at the C1 or C2 level. Systemic heparinization (5000 IU) was routinely used. In principle, a trial BTO was first performed for 5 minutes to obtain an outline of symptomatic changes in the arterial pulse wave. After the trial BTO, patients were transferred from the angiography suite to radioisotope suite with the balloon deflated but still in place. In the radioisotope suite, mean systemic pressure was reduced by approximately 20% with the continuous intravenous infusion of trimetaphan camsilate, a ganglion blocking agent.\(^{15}\) The balloon was inflated after stabilization of the systemic blood pressure. Neurological status, stump pressure, and rSO2 were evaluated every 30 seconds. Five minutes after inflation, 740 MBq of \(^{99m}\)Tc-HMPAO was injected intravenously. After the tracer injection, the ICA occlusion was maintained for an additional 15 minutes. Finally, protamine sulfate was used to reverse the effect of heparin.

**SPECT Studies**

SPECT imaging was performed after removal of the catheter and stabilization of the patients, usually 30 to 60 minutes after injection. SPECT was performed using a triple-headed gamma camera (PRISM 3000; Picker International, Cleveland, OH) equipped with a low-energy high-resolution fan beam collimator. A 20% window was centered on the 140 keV photopeak of \(^{99m}\)Tc. One hundred twenty 30-second frames were acquired using the elliptical contour rotation mode into a 128×128 image matrix. The images were prefiltered using a Butterworth filter (cutoff frequency=0.266 to 0.302 cycles/cm, order=8.1). The attenuation correction was set at 0.09. The reconstructed slice thicknesses were 3.91 mm for the transaxial planes and 7.81 mm for coronal and sagittal planes.

The SPECT images were analyzed both visually and semiquantitatively. For visual analysis, 3 experienced neurosurgeons (coauthors of this manuscript) ranked the asymmetrical distribution of the tracer as little or none or moderate or severe based on the color codes of the computer and the defined group 1 (Figure 1) or group 2 (Figure 2), respectively. Relative quantification by means of region of interest (ROI) analysis was performed retrospectively. A total of 7 ROIs were defined on each side of the middle cerebral artery (MCA) area in 2 transaxial slices parallel to the orbitomeatal line (Figure 3). The slices were selected by 2 observers and were at the level of the temporal and caudoputaminal region, and the mid-parietal region. The round-shaped ROI consisting of 55 to 60 pixels was used, and poor recording.

ΔrSO2 with BTO was calculated. The degree of side-to-side asymmetry (AI) in the MCA territory was then obtained using the equation AI=200×(C\text{non}-C\text{occl})/(C\text{non}+C\text{occl}), where C\text{non} is the mean tracer count on the nonoccluded side and C\text{occl} is the mean tracer count on
Monitoring of rSO₂, Systemic Blood Pressure, and Stump Pressure

Using a cerebral oximeter (INVOS 3100; Somanetics Corp), rSO₂ was continuously monitored on the forehead of the occluded side. Continuous monitoring of the arterial pressure was performed with the sheath introducer placed in the femoral artery and the balloon catheter placed in the ICA. In principle, the rSO₂, systemic blood pressure and stump pressure at 5 minutes of ICA occlusion when the tracer was injected were used for analysis.

Statistical Analysis

Values are expressed as mean±SD. The statistical differences of MAI, stump pressure, and ΔrSO₂ (baseline rSO₂−rSO₂ during ICA occlusion) between the groups were evaluated using the Mann-Whitney test. Correlation between the stump pressure and ΔrSO₂ was evaluated by a simple regression analysis. A significant difference in the statistical results was defined as P<0.05.

Results

Asymmetry in SPECT Images

Two patients exhibited right hemiparesis and aphasia immediately after left ICA occlusion; SPECT study could not be performed in these patients, and they were classified as group 3. Therefore, for those patients, the rSO₂ and blood pressure just before the deflation of the balloon were used in the following studies. In the remaining 14 patients, 15 BTOs were performed without the appearance of focal neurological deficits and the occlusions examined with SPECT study. These 15 SPECT studies during BTO consisted of 10 from group 1 and 5 from group 2. An AI could not be obtained from 2 of the BTOs in group 1 because raw data were not recorded for these 2 patients. The mean MAI in group 1 was 2.6±3.3% (n=8), which was significantly lower than that in group 2 (25.6±5.0%, n=5, P<0.02). No patient in group 1 had a MAI exceeding 10%, whereas all MAIs in group 2 reached above 19%. A resting SPECT study was performed in 7 patients. The MAI in the resting SPECT ranged from −3.1% to 4.2%. The mean absolute value of the resting MAI was 2.3±1.5%, which was not statistically different from the MAI in group 1 but was statistically smaller than the MAI in group 2 (P<0.01).

Stump Pressure and Asymmetry Index

The mean stump pressures in group 1, group 2, and group 3 were 41.4±9.8, 31.2±15.3, and 29.0±9.9 mm Hg, respec-
tively. However, there was no statistical difference between them. The mean stump pressure and MAI did not have a significant correlation ($r = 0.497$, $P = 0.0844$, Figure 4).

**Monitoring of rSO\(_2\)**

Although the rSO\(_2\) was monitored in all 17 BTO procedures, the rSO\(_2\) level was unstable during BTO in only 1 patient from group 2, which was then excluded from the subsequent studies. The $\Delta$rSO\(_2\) in group 1 was $1.5 \pm 1.4\%$ (n=10), in group 2 $5.5 \pm 1.3\%$ (n=4); this difference was statistically significant ($P<0.05$). The $\Delta$rSO\(_2\) in group 3 ($9.0 \pm 0.0\%$, n=2) was also greater than that in group 1 or group 2. Group 3, however, was too small to evaluate statistical significance.

In 8 of 10 patients in group 1, the SPECT study with rSO\(_2\) monitoring was performed under induced hypotension. In these patients, the preceding 5-minute test occlusion of the ICA with rSO\(_2\) monitoring was also performed under no hypotensive provocation in the angiography suite. The rSO\(_2\) monitoring in the 18 BTO procedures indicated that even in group 1, the rSO\(_2\) started to decrease if the stump pressure fell to 45 mm Hg, and the rSO\(_2\) always decreased when the stump pressure fell below 40 mm Hg (Figure 5). Furthermore, a significant linear correlation existed in group 1 between the $\Delta$rSO\(_2\)$ and the stump pressure during BTO ($r=0.85$, $P<0.0001$).

**Discussion**

Among several methods used to determine CBF distribution in BTO, $^{99m}$Tc-HMPAO SPECT is used most frequently because of its wide availability. Reportedly, $^{99m}$Tc-HMPAO SPECT is very useful in detecting unilateral asymmetrical distribution of CBF with BTO.\(^{5-9}\) It is generally accepted that areas of diminished perfusion are abnormal when the inter-hemispheric differential activity is greater than 10%.$^{5,16}$ In the present study, visual classification of CBF distribution corresponded well with relative quantitative analysis; no MAI in group 1 exceeded 10%, and all MAIs in group 2 were higher than 19%. The present study also supports the feasibility and usefulness of $^{99m}$Tc-HMPAO SPECT in high-risk patients because in the present study 5 of 15 BTOs showed significant asymmetry (group 2) without the appearance of neurological symptoms. Furthermore, significant asymmetry on $^{99m}$Tc-HMPAO distribution was also observed in 1 patient, despite a fairly high level of stump pressure (Figure 2, left). How-

![Figure 2. HMPAO SPECT images for group 2. Left, Moderate asymmetry during balloon occlusion of the right ICA was revealed on a 73-year-old man. Stump pressure was kept higher at 52 mm Hg; however, MAI reached 25.1%. Right, Severely asymmetrical distribution was depicted when stump pressure fell to 22 mm Hg, and rSO\(_2\) decreased by 7% with right ICA occlusion on 63-year-old woman.](http://stroke.ahajournals.org/)

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ever, symmetrical distribution of 99mTc-HMPAO does not always indicate negative hemodynamic changes during BTO. Well-developed collateral circulation through the anterior communicating artery or posterior communicating artery possibly leads to a bilateral reduction of CBF with the occlusion of 1 carotid artery. A qualitative CBF study with a stable xenon CT scan indicated that a symmetrical decrease in CBF was frequently observed. Indeed, a stable xenon CT scan is very useful for the quantitative evaluation of CBF; however, balloon inflation must be performed on the CT table, and inhalation of xenon-mixed gas for several minutes affects the neurological observation during BTO. Furthermore, the stump pressure is not always stable during BTO, especially under provocative hypotension, and the duration of several minutes for a xenon CBF study possibly affects the evaluation of CBF values. Yet, 99mTc-HMPAO is taken up rapidly by the brain with little redistribution, allowing a snapshot of the brain perfusion at the time of injection. CBF imaging during the balloon inflation, thus, can be obtained simply by venous injection of 99mTc-HMPAO during ICA occlusion and scanning, after all the BTO procedures have been completed. Furthermore, it provides a fairly good spatial resolution of CBF compared with a xenon CT study. The timing of the tracer injection may significantly affect the development of perfusion abnormalities. A previous experimental study, in which changes in CBF and tissue oxygen tension with transorbital MCA occlusion were continuously monitored in the MCA area of rabbits, indicated that collateral circulation developed promptly within 5 minutes after the start of ischemia; the tracer was thus injected at 5 minutes after the start of BTO in the present study.

**Figure 3.** Two transaxial slices with placement of ROIs. Seven ROIs (red circle) were placed symmetrically on the MCA territory.

**Figure 4.** The relationship between mean stump pressure and MAI during BTO. An open circle indicates group 1, and a closed circle, group 2. There was no significant correlation between them ($r=0.497$, $P=0.0844$).

**Figure 5.** The relationship between mean stump pressure and $\Delta rSO_2$ during BTO in group 1. An open circle indicates BTO without induced hypotension ($n=10$); closed circle, BTO with induced hypotension ($n=8$). A significant linear correlation was indicated between mean stump pressure and $\Delta rSO_2$ ($r=0.85$, $P<0.0001$).
As a simple yet reliable technique for monitoring altered CBF or oxygenation of the brain, rSO2 monitoring by measurement of NIRS with the INVOS 3100[3,14,20] or other instruments[31] has been used during skull base surgery, removal of a cervical tumor involving the carotid artery, and carotid endarterectomy. The sensor for the INVS 3100 consists of a flexible pad (8.8×4.4 cm) with 1 light source and 2 photodetectors. The distances between the light source and 2 photodetectors were set at 30 and 40 mm to eliminate the interference of blood oxygen saturation from all extrace- rebral components. The cerebral oximetry used in this experiment reflects the change of cerebral oxygen saturation between the light source and the 40-mm distant photodetector.[22] The rSO2 recording became stable within a few minutes except in 1 case, and it could be monitored continuously in 16 of 17 BTOs. Repeated carotid occlusion during a series of tests to verify the reproducibility was not performed in this study. However, 2 sets of BTOs were carried out within a 7-month period in patient 13. The rSO2 decreased by 6% in the first BTO and 7% in the second BTO. The mean stump pressure and MAI were 15 mm Hg and 23.5% in the first BTO and 22 mm Hg and 32.4% in the second BTO. These results might support the good reproducibility in the rSO2 monitoring in the present study.

A critical rSO2 level or ΔrSO2 to induce neurological deficit has not been well established. In the present study, we monitored rSO2 in addition to performing 99mTc-HMPAO SPECT to evaluate the change of cerebral perfusion on the occluded hemisphere with BTO. Carlin et al[13] reported cases of awake carotid endarterectomy in which the mean ΔrSO2 by carotid cross-clamp in patients without the appearance of neurological deficit was 7.2%. Dujovny et al[14] reported on 2 patients who exhibited neurological deteriorations with a fall in rSO2 of more than 10% after BTO. Our present results indicate that rSO2 dropped by 9% immediately after balloon occlusion of the left ICA in 2 patients who experienced right hemiparesis and aphasia, whereas rSO2 decreased by 4% to 7% without the appearance of a neurological deficit in patients in group 2. Our previous study on the simultaneous measurement of rSO2 and CBF indicated that 1000 mg acetazolamide increased CBF by 44.4% and rSO2 from 64.2% to 69.6%,[23] Holzschuh et al[24] also demonstrated similar results. In the present study, ΔrSO2 was 5.5±2.1% (n=4) in group 2, which was significantly higher than the ΔrSO2 in group 1 (1.5±1.4%, n=10). ΔrSO2 in group 3 was 9.0±0.0% (n=2), which was also higher than the ΔrSO2 in group 1; however, no statistical difference could be found because group 3 was too small. Although the relationship between rSO2 and CBF is not simply linear but is determined by Fick’s equation, the prominent fall of rSO2 in groups 2 and 3 suggests that a fairly profound reduction in CBF develops with BTO in these cases. Furthermore, even in group 1, if stump pressure fell to 45 mm Hg, then rSO2 started to decline, and rSO2 always decreased when stump pressure fell below 40 mm Hg. These results indicate that deterioration of cerebral perfusion develops even in the case of group 1 when the stump pressure falls below 40 mm Hg. The relation between asymmetrical CBF distribution and stump pressure during BTO is still controversial,[25,26] and the present study did not determine a significant correlation between them. In our study, stump pressure fell below 40 mm Hg in 9 BTOs. Of these 9 BTOs, a focal neurological deficit appeared immediately in 2 BTOs, and asymmetrical distribution of CBF was observed in 3 BTOs, whereas 99mTc-HMPAO SPECT in the remaining 4 BTOs exhibited symmetrical rather than asymmetrical CBF distribution. Our results concerning the relation between ΔrSO2, stump pressure, and asymmetrical CBF distribution in SPECT study indicate that a lower stump pressure does not always signify asymmetrical CBF distribution; however, a stump pressure less than 40 mm Hg always accompanies a perfusion disturbance to affect the rSO2 level. Furthermore, in group 1, which exhibited little or no asymmetry with BTO, a significant linear correlation between ΔrSO2 and stump pressure was demonstrated (r=0.85, P<0.0001). Lorberboym et al[16] reported that 4 of 18 patients in whom 99mTc-HMPAO SPECT study during BTO revealed symmetrical distribution subsequently suffered from cerebral ischemia after the permanent sacrifice of the carotid artery. Although the etiology of their ischemic event was not clearly identified and stump pressure during BTO was not evaluated in these patients, the possible involvement of hemodynamic factors is suggested in their report.

Among the patients in the present study, the following surgical procedures were performed: common carotid ligation in 2, permanent occlusion of the ICA in 1, transient occlusion of the ICA in 1, and resection followed by reconstruction of the common carotid artery in 1. Thromboembolic complications were observed in 1 patient in group 1 after permanent ICA occlusion. Although in the present study we were not able to reveal definitive criteria to predict hemodynamic complication with permanent ICA occlusion, our preliminary study indicates that obvious asymmetrical CBF distribution without the appearance of a neurological deficit always accompanies a profound decrease in rSO2, suggesting the development of a prominent reduction of CBF. Furthermore, even in patients with symmetrical CBF distribution during BTO, a decrease in mean stump pressure below 40 mm Hg always accompanies a decrease in rSO2, and rSO2 parallels a severe reduction in stump pressure in cases in which a symmetrical SPECT pattern is exhibited.

Thus, we verified in this study that rSO2 monitoring is a simple and easily applicable but very sensitive indicator of the cerebral oxygenation, and we deduce that the simultaneous measurement of rSO2 and stump pressure with SPECT study is useful in the evaluation of hemodynamic integrity after BTO. Furthermore, rSO2 monitoring is now applied for intraoperative monitoring in skull base surgery, carotid endarterectomy, and neck surgery involving the carotid artery. It provides useful information for the operative manipulation of carotid artery under rSO2 monitoring to correlate ΔrSO2 following BTO with stump pressure and SPECT imaging preoperatively.

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