Amplitude of Tissue Oxygenation Index Change Predicts Cerebral Hyperperfusion Syndrome During Carotid Artery Stenting

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■ OBJECTIVE: **Hyperperfusion syndrome (HPS) after carotid artery stenting (CAS) is a rare but serious complication. HPS is associated with preoperative hemodynamic impairment as the result of poor collateral flow and intraoperative cerebral ischemia. Filter-type embolic protection devices maintain anterograde carotid flow during CAS and prevent HPS somewhat. The early treatment of patients undergoing CAS and at risk for HPS is essential. Near-infrared spectroscopy allows noninvasive, real-time measurement of frontal lobe regional cerebral O_2 saturation (TOI; tissue oxygenation index).**

■ METHODS: **The perioperative amplitude of TOI was monitored in 130 patients undergoing CAS while using a filter-type embolic protection device. Patients were divided retrospectively into good ($n = 110$) and poor/no crossflow groups ($n = 20$), and we compared the amplitude of the TOI change, correlation with ipsilateral regional cerebral blood flow, and clinical results.**

■ RESULTS: **The incidence of HPS was significantly greater in the poor/no crossflow group ($P = 0.019$). In 2 patients with HPS, the amplitude of the TOI change was V-shaped, with a decrease after postdilatation and an increase above baseline 5 minutes after reperfusion. The TOI/baseline ratio was significantly decreased after internal carotid artery occlusion for postdilatation in the ipsilateral hemisphere in the poor/no crossflow group ($P < 0.05$). Significant linear correlations were observed between TOI/baseline ratio changes and preoperative cerebrovascular reactivity and the postoperative asymmetry index ($r = -0.346$, $P = 0.002$, $r = 0.613$, $P < 0.001$, respectively).**

■ CONCLUSIONS: **The amplitude of the TOI change measured by near-infrared spectroscopy was an excellent predictor of cerebral HPS after CAS.**

INTRODUCTION

Hyperperfusion syndrome (HPS) after carotid artery stenting (CAS) and carotid endoarterectomy (CEA) is a life-threatening complication that occurs in approximately 3%–5% of patients after treatment.[1] When not recognized in a timely manner and not treated adequately, HPS can lead to intracerebral hemorrhage, the most feared complication, which is associated with a mortality of 40%.[2] Furthermore, a recent study suggested that HPS occurs significantly earlier after CAS than after CEA.[3] Therefore, prediction and early treatment of patients undergoing CAS who are at risk for HPS is essential.

Key words
- Carotid artery stenting
- Hyperperfusion syndrome
- Near-infrared spectroscopy

Abbreviations and Acronyms
ACZ: Acetazolamide
AI: Asymmetry index
CAS: Carotid artery stenting
CBF: Cerebral blood flow
CEA: Carotid endoarterectomy
CVR: Cerebrovascular reactivity
EPDs: Embolic protection devices
HPS: Hyperperfusion syndrome
ICA: Internal carotid artery
IMP: N-isopropyl-p-[^{123}I]iodoamphetamine
MCA: Middle cerebral artery
MRI: Magnetic resonance imaging
NIRS: Near-infrared spectroscopy
PTA: Percutaneous transluminal angioplasty
rCBF: Regional CBF
rSO_2: Regional cerebral oxygen saturation
SPECT: Single-photon emission computed tomography
TOI: Tissue oxygenation index

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A recent study suggested that development of HPS after CAS is associated with both preoperative hemodynamic impairment due to poor collateral flow supply and intraoperative cerebral ischemia.[4] CAS currently is performed widely as a less-invasive alternative to CEA, and a recent randomized trial showed no differences in stroke, myocardial infarction, or death between CAS and CEA; however, patients undergoing CAS had a greater incidence of periprocedural stroke.[5] Embolic protection devices (EPDs) provide a theoretical mechanism to reduce periprocedural strokes, and filter-type EPDs are available widely and easy to use.[6] Filter-type EPDs allow maintenance of anterograde carotid flow during the procedure and can reduce the incidence of HPS because they shorten the ischemic time in the ipsilateral hemisphere during CAS. HPS still occurs, however, and the development of HPS after CAS is not completely preventable.

Single-photon emission computed tomography (SPECT) scanning is useful for predicting HPS after CAS and CEA[7]; however, SPECT is expensive, complicated, and time-consuming and cannot be performed during CAS. Currently, near-infrared spectroscopy (NIRS) often is used to monitor the frontal lobe regional cerebral O_2 saturation after CAS and CEA. This technique is a promising alternative cerebral monitoring technique, because it is easy to use, allows noninvasive, continuous real-time detection, and can be used in all patients.[8,9] The NIRO-200NX (Hamamatsu Photonics, Hamamatsu City, Japan) provides continuous measurement, such as hemoglobin concentration changes and the tissue oxygen index (TOI), during perioperative stages.[10,11] A recent report suggested that the TOI reflects cerebral oxygenation with a high degree of sensitivity and specificity during carotid surgery.[10] The possibility that the amplitude of TOI changes during CAS while using filter-type EPDs, however, can predict postoperative HPS has not been investigated fully.

The aim of the present study was to evaluate whether the amplitude of the TOI change assessed with continuous NIRS monitoring during CAS while using filter-type EPDs can predict postoperative HPS and to investigate whether the amplitude of the TOI change is influenced by collateral flow or preoperative hemodynamic impairment.

PATIENTS AND METHODS

Inclusion Criteria of Patients

Between January 2010 and February 2015, 130 consecutive patients who underwent CAS for carotid artery stenosis at Nara Medical University were enrolled in the present study. The criteria for CAS included stenosis >80% for asymptomatic lesions or stenosis >50% for symptomatic lesions, and patients with a high risk for CEA in accordance with the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) criteria.[12] All procedures were performed under local anesthesia with a filter protection device. Dual-channel NIRS also was used to measure the cerebral oxygen saturation during and after the CAS procedure.

All cases were classified retrospectively into 2 groups, the good crossflow group and the poor crossflow group, according to previous studies.[13,14] The degree of crossflow was classified as follows. Good crossflow was defined as visualization of an established anatomical segment of A1-4 for the anterior cerebral artery and M1-4 for the middle cerebral artery (MCA) by the Matas or Allcock maneuver, and no crossflow was diagnosed as no visualization of one or both arteries as diagnosed by preoperative digital subtraction angiography. All patients were analyzed for a correlation between the amplitude of TOI changes and cerebrovascular reactivity (CVR) before CAS and the asymmetry index (AI) after CAS, as assessed with continuous NIRS monitoring and SPECT performed before and after the CAS procedure. All patients were provided with an informed consent document that explained all of the CAS procedures. All patients signed a written authorization allowing access to their medical records for research purposes, and our institutional review board approved the research protocol.

Near-Infrared Spectroscopy

A transcranial cerebral oximeter (NIRO-200NX; Hamamatsu Photonics) was used to monitor several oxygen parameters (oxygenated hemoglobin change, deoxygenated hemoglobin change, total hemoglobin change, normalized tissue hemoglobin index, and TOI). After thorough cleaning of the patient's skin, the sensors were bilaterally and symmetrically placed over the forehead, according to the manufacturer's instructions. The oximeter uses a method that combines the multidistance measurements of optical attenuation. The underlying mathematical model is based on spatially resolved spectroscopy and the modified Beer-Lambert law. The NIRO-200NX generates 3 wavelengths of infrared light (735, 810, 850 nm) that are produced by a light-emitting diode. Using 1 emitting laser diode and 2 detecting photodiodes, we were able to measure the ratio of oxygenated to total tissue hemoglobin, which is considered to be the TOI.

Calculation of the TOI depends on spatially resolved spectroscopy. During the CAS procedure, the bifrontal TOI was monitored by NIRS, recorded at 0.5-second intervals, and stored for analysis. The following data points were recorded for the side ipsilateral to the CAS procedure: the baseline TOI value before the CAS procedure, the value immediately after postdilatation balloon percutaneous transluminal angioplasty (PTA), and the value 5 minutes after postdilatation balloon PTA. We also calculated the ratio at each time point from the baseline TOI value. The TOI/baseline ratio is calculated as (TOI/baseline value 5 minutes after postdilatation balloon PTA − TOI/baseline value in postdilatation balloon PTA)/TOI/baseline.

Single-Photon Emission Computed Tomography

All patients underwent SPECT via a rotating 3-head gamma camera (GCA-9300A; Toshiba Medical Systems, Tochigi, Japan) before and after the procedure as perioperative management for HPS. Cerebral blood flow (CBF) in the cerebral hemisphere was quantified with ^{123}I-SPECT before and immediately after the procedure. The details of the IMP (N-isopropyl-p-[^{123}I]iodoamphetamine) SPECT study with acetazolamide (ACZ) challenge have been reported.[15,16] The absolute relative CBF values were quantified with the microsphere method. An irregular, mirror-shaped region of interest was placed bilaterally in the entire cerebral cortex at the level of the parietal lobe, excluding any infarcts, and in the corresponding contralateral region. Resting regional CBF (rCBF), CVR following the ACZ challenge, and AI were measured quantitatively for the hemodynamic reserve.

The control value for resting rCBF that was obtained from 20 healthy volunteers (18 men and 2 women; aged 65–85 years old; mean age, 76.3 years old) was 30.6 ± 2.9 mL/100 g/min. A resting rCBF value that was lower than the mean + 2 SD (i.e., 24.8 mL/100 g/min) was defined as a decrease in resting rCBF. The CVR (%) was calculated as follows: (ACZ challenged rCBF in the affected cerebral hemisphere − resting rCBF in the affected territory)/ resting rCBF in the affected territory × 100%. The control CVR value that was obtained from the same 20 healthy volunteers described above was 50.4% ±13.3. A CVR value that was lower than the mean + 2 SD (i.e., 23.8%) was defined as reduced CVR.

The AI (%) was calculated as the measure of blood flow between the 2 cortical hemispheres by calculating the ratio of rCBF of the affected to unaffected hemisphere excluding any ischemic/ infarcted areas (rCBF in the affected cerebral hemisphere/rCBF in the mirror territory) × 100. The control AI value obtained from 20 healthy volunteers (11 men and 9 women; aged 68–80 years old; mean age, 76.7 years old) was 102.1% ± 0.85. An AI value that was greater than the mean + 3 SD (i.e., 104.6%) was defined as an increase in AI. In the present study, hyperperfusion after CAS was defined as an increase in rCBF >4.6% compared with that on the normal side.

CAS Procedure

All patients were given 2 of the following 3 antiplatelet agents, clopidogrel 75 mg/d (Plavix; Sanofi-Aventis Co. Ltd., Tokyo, Japan), aspirin 100 mg/d (Bayaspirin; Bayer Yakuhin Co. Ltd., Osaka, Japan), or cilostazol 200 mg/d (Pletaal: Otsuka Pharmaceutical Co. Ltd., Tokushima, Japan), starting at more than 4 weeks before the CAS. Under local anesthesia, transfemoral catheterization was performed, and an 8-French guide catheter was delivered to the common carotid artery. Systemic anticoagulation was provided by intravenous administration of a bolus of heparin (100 U/kg; 6000 U maximum infusion) to maintain an activated clotting time >275 seconds. A 3- to 3.5-mm balloon catheter was used to cross and predilate the stenosis while a filter protection device was used (Angioguard Xp; Cordis Endovascular, Miami Lakes, Florida, USA or Filterwire EZ; Boston Scientific, Natick, Massachusetts, USA) for passage of the stent-mounted catheter. The stenting device (Carotid Wallstent; Boston Scientific or Precise; Johnson & Johnson, Miami Lakes, Florida, USA or Protégé; EV3, Plymouth, Minnesota, USA) was deployed, and conservative postdilation balloon PTA was performed with a controlled-compliant balloon dilation catheter. Conservative postdilation was performed with an angioplasty balloon with a diameter no greater than approximately 80% of the normal luminal diameter distal to the stenosis, as determined by intravascular sonography (Eagle Eye Gold; Volcano Corporation, San Diego, California, USA). At the end of the procedure, the EPD was removed. An aspiration catheter was used to perform multiple aspirations of the column of the blood proximal to the filter when a slow flow or no-flow phenomenon was observed.

After CAS, a systolic blood pressure was maintained less than 140 mm Hg for 7 days after the procedure. In case of HPS after CAS, sedation and strict systolic blood pressure management less than 120 mm Hg were introduced under continuous monitoring until relieving hyperperfusion phenomenon. During patient follow-up, we recorded all symptomatic ischemic events, hemorrhagic events within 30 days, and any diffusion-weighted magnetic resonance imaging (MRI) abnormalities that occurred.

Clinical Diagnosis of Cerebral HPS

A diagnosis of HPS required the following: 1) Occurrence of headache, seizure, confusion, deterioration of consciousness level, and/or development of focal neurological signs such as motor weakness; 2) absence of any additional ischemic lesion on MRI performed the first postoperative day; and 3) postoperative increase in rCBF in the ipsilateral hemisphere exceeding the flow in the contralateral hemisphere as measured using SPECT.

Data Analysis and Statistics

Measurements for each group are expressed as means ± standard deviation. Comparisons between the 2 groups were assessed with the Mann-Whitney U test, Fisher exact test, analysis of variance test, and Pearson correlation test. Differences were deemed statistically significance if $P < 0.05$.

RESULTS

Study Population

We enrolled and evaluated a total of 130 patients (109 male and 21 female; mean age, 74 years old, age range; 53–89 years old). Table 1 presents the clinical characteristics of the patients from the 2 different groups. For the good crossflow group (110 patients), the mean age was 74 years old (range, 53–89 years old), and for the poor/no crossflow group (20 patients), the mean age was 74 years old (range, 59–86 years old). The lesion characteristics including the average degree of stenosis according to NASCET, the rate of symptomatic lesions, and the rate of vulnerable plaques were similar among the 2 different study groups. The incidence of a decrease in the ipsilateral rCBF value as determined with ^{123}I-IMP SPECT, however, was significantly greater in the poor/no crossflow group than the good crossflow group ($P = 0.002$) (Table 1).

CAS was performed successfully in all 130 patients. No significant differences were observed for the patients between the 2 groups in terms of the stent design, or bright lesions on diffusion-weighted imaging 1 day after CAS (Table 2). HPS was observed in 2 cases presenting with headache and confusion after CAS; however, intracranial hemorrhage did not occur because of postoperative sedation and strict blood pressure control immediately after suspicion of HPS. These 2 patients were discharged from our hospital without any neurologic deficits.

Typical TOI, SPECT, and angiographic findings for a patient with HPS are shown in Figure 1A–H. This 84-year-old man presented with severe, symptomatic left internal carotid artery (ICA) stenosis. Preoperative digital subtraction angiography showed no crossflow through the anterior communicating and posterior communicating arteries, and preoperative ^{123}I-IMP SPECT in the resting state demonstrated that rCBF in the ipsilateral hemisphere was reduced in comparison with that in the contralateral hemisphere (Figure 1F).

He underwent CAS on the left side under local anesthesia with continuous NIRS monitoring (Figure 1A–C). During the CAS procedure, the amplitude of the TOI with NIRS monitoring suddenly decreased just after balloon inflation for postdilatation

Table 1. Patient and Lesion Characteristics

Variable	No. Patients (%) Good Crossflow Group ($n = 110$)	Poor/No CrossflowGroup ($n = 20$)	*P* Value
General characteristics			
Mean age, years (range)	72 (58–89)	74 (59–86)	0.826
Females	8 (15.1%)	7 (12.5%)	0.134
Lesion characteristics			
Symptomatic	17 (36.2%)	24 (45.3%)	0.418
Vulnerable plaque	19 (40.4%)	28 (52.8%)	0.235
Degree of stenosis (%)	80.9 ± 11.5	82.1 ± 10.2	0.720
Decrease in resting rCBF	29 (26%)	13 (65%)	0.002*

rCBF, regional cerebral blood flow value measured by single photon emission computed tomography.
*$P < 0.05$.

and immediately increased after reperfusion above the baseline TOI value (Figure 1D). One day after the CAS, he suffered from a headache and confusion. ^{123}I-IMP SPECT in the resting state demonstrated that the ipsilateral hemisphere rCBF was increased dramatically and exceeded the flow in the contralateral hemisphere (Figure 1G). MRI showed the absence of any additional ischemic lesions, and hence, he was diagnosed with postoperative HPS. We strictly controlled his systolic blood pressure between 100 and 120 mm Hg and induced sedation with dexmedetomidine. As TOI laterality (left TOI/right TOI) recovered 5 days after CAS (Figure 1E), sedation and strict blood pressure management was terminated. He recovered from the symptoms, and then ipsilateral hemisphere rCBF in the resting state demonstrated normalization on the 1-week follow-up ^{123}I-IMP SPECT (Figure 1H). He was discharged without any neurological deficits.

Table 2. Treatment and Clinical Results

Variable	No. Patients (%) Good Crossflow Group ($n = 110$)	Poor/No Crossflow Group ($n = 20$)	*P* Value
Treatment			
Filter protection	110 (100%)	20 (100%)	1.000
Closed cell stent	93 (84%)	16 (80%)	0.859
Clinical results			
DWI positive	15 (14%)	3 (15%)	0.850
Ischemic events	0 (0%)	0 (0%)	1.000
Hemorrhagic events	0 (0%)	0 (0%)	1.000
Hyperperfusion syndrome	0 (0%)	2 (10%)	0.019*

DWI, diffusion-weighted imaging.
*$P < 0.05$.

TOI/Baseline Ratio Changes and the Relationship with CVR

The course of the TOI/baseline ratio of all 130 cases during the CAS procedure is illustrated in Figure 2A. The TOI/baseline ratio decreased just after ICA occlusion by the postdilatation balloon PTA. At reperfusion 5 minutes after the balloon PTA, the ratio increased above the baseline value. Patients with HPS after CAS in particular showed this V-shaped pattern (dotted lines in Figure 2A). In fact, patients with HPS after CAS demonstrated highest TOI/baseline ratio change compared with patients without HPS. The TOI/baseline ratio was related strongly to the status of the collateral flow. The TOI/baseline ratio was significantly decreased in the ipsilateral hemisphere in the poor/no crossflow group (Figure 2B; $P < 0.05$). Furthermore, the TOI/baseline ratio increased above the baseline 5 minutes after postdilatation balloon PTA in the ipsilateral hemisphere in the poor/no crossflow group (without a significant difference). We found no differences in the TOI/baseline ratio in the contralateral hemisphere in the poor/no crossflow group and good crossflow group (Figure 2B).

Figure 3A shows the relationship between preoperative CVR and the TOI/baseline ratio changes in the ipsilateral hemisphere in all patients. A significant linear correlation was observed between these parameters ($r = -0.346$, $P = 0.002$) (Figure 3A). Furthermore, we observed a significant linear correlation between the postoperative AI and the TOI/baseline ratio changes in the ipsilateral hemisphere in all patients ($r = 0.613$, $P < 0.001$) (Figure 3B). In fact, preoperative ipsilateral CVR was 3.4% and 5.5% in patients with HPS and 42.1 ± 17.3% in patients without HPS, which seems remarkable difference between patients with and without HPS.

DISCUSSION

In the present study, we demonstrated that the amplitude of TOI changes from baseline as measured by NIRS was strongly related to the status of collateral flow. The incidence of HPS was significantly greater in the poor/no crossflow group ($P = 0.019$). A typical V-shaped pattern was observed in 2 cases with HPS after CAS. Furthermore, we demonstrated significant linear correlations between the TOI/baseline ratio changes and preoperative CVR and postoperative AI. Therefore, the amplitude of the TOI change as measured by NIRS was an excellent predictor of cerebral HPS after CAS.

Cerebral HPS is rare but is a severe complication that can lead to intracranial hemorrhage. The incidence of HPS after CEA or CAS is 0.2% to 18.9%.[1,9] Recent reports have indicated that HPS develops soon after the procedure of CAS, within 12 hours, which is sooner than HPS after CEA.[3] Therefore, prediction and early treatment of patients at risk for HPS are essential. Recognizing HPS in real time during the perioperative period of the CAS procedure is necessary. The efficacy of SPECT for diagnosing postoperative HPS after CEA has been reported in the literature.

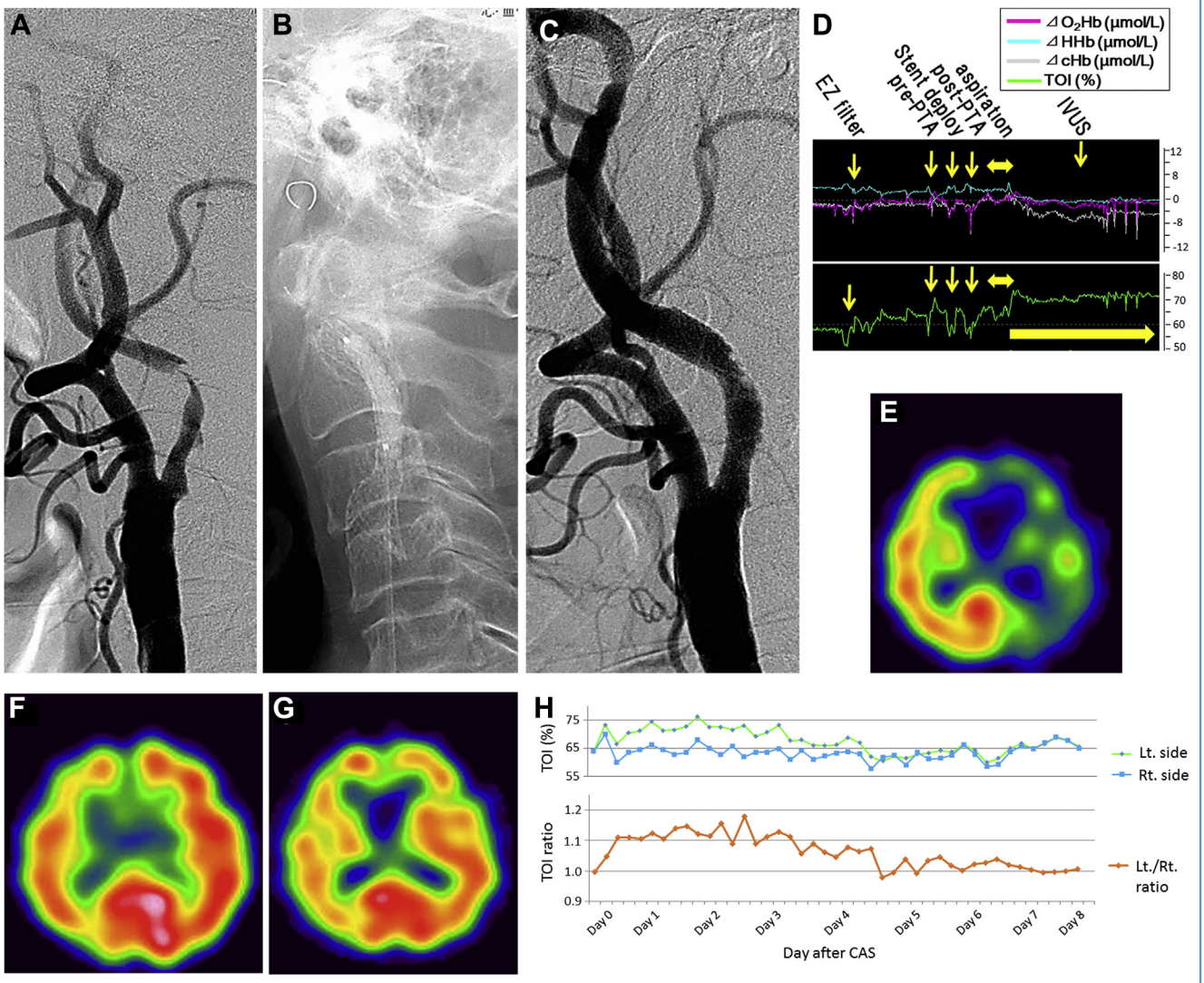

Figure 1. Typical images for a patient (84-year-old man) with cerebral hyperperfusion syndrome after the carotid artery stenting (CAS) procedure. (**A**) Left common carotid angiography showed severe stenosis in the left internal carotid artery. (**B**) Balloon angioplasty for postdilatation was performed after stent placement while using filter protection. (**C**) Left common carotid angiography after CAS confirmed stent patency. Continuous near-infrared spectroscopy monitoring of tissue oxygenation index (TOI) changes during the CAS procedure. The measured TOI value during monitoring decreased immediately after several procedures. (**D**) Just after the CAS, the TOI value increased from the preoperative baseline. (**E**) Left-side TOI and left TOI/right TOI ratio increased after CAS and recovered 5 days after CAS. (**F**) Preoperative -isopropyl-p-[^{123}I] iodoamphetamine single-photon emission computed tomography in the resting state showed a decrease in regional cerebral blood flow in the left hemisphere. (**G**). One day after CAS, hyperperfusion was seen in the ipsilateral hemisphere. (**H**). One week after CAS, hyperperfusion in the ipsilateral hemisphere had normalized. ΔO_2Hb, oxygenated hemoglobin change; ΔHHb deoxygenated hemoglobin change; ΔcHb, total hemoglobin change; PTA, percutaneous transluminal angioplasty.

Ogasawara et al.[17] demonstrated that preoperative measurement of ACZ-induced changes in rCBF, which is performed using SPECT scanning, can be used to identify patients at risk for hyperperfusion after CEA. In addition, post-CEA monitoring of rCBF performed using SPECT scanning results in timely and reliable identification of patients at risk for HPS. Although SPECT or positron emission tomography studies can accurately measure rCBF, they are complicated, time-consuming, and cannot be performed during CAS. Several studies have demonstrated the value of non-invasive transcranial Doppler sonography to predict the occurrence of HPS. Iwata et al.[18] reported that transcranial color-coded sonography is useful for predicting HPS, that a pre-CAS predictor of HPS is the MCA mean blood flow velocity, and that an immediate post-CAS predictor of HPS is the MCA mean blood flow velocity ratio. However, transcranial Doppler sonography is not easy to perform, because it requires training of medical personnel and is difficult to record continuously. NIRS is a noninvasive, safe, and simple application for measurement of

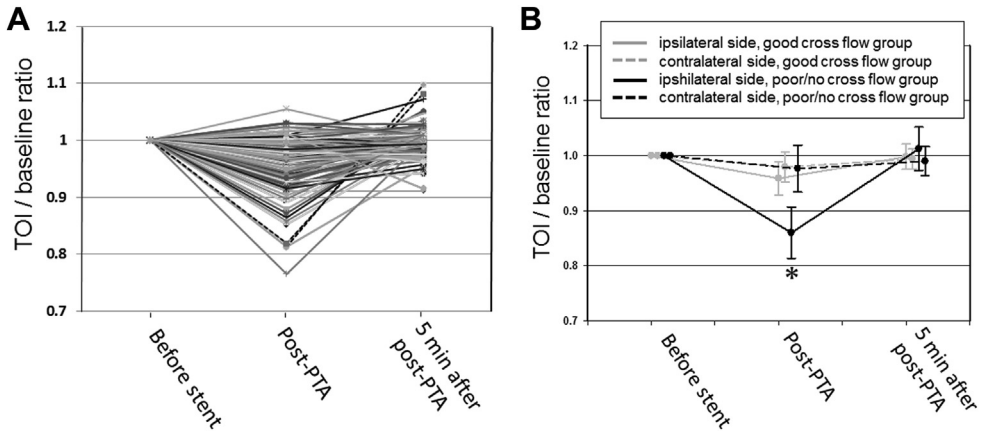

Figure 2. (**A**) The course of the tissue oxygenation index (TOI)/baseline ratio of all cases during the carotid artery stenting procedure. The amplitude of the TOI change showed a typical V-shaped pattern, with a decrease just after postdilatation and an increase above the baseline value 5 minutes after reperfusion in cases of hyperperfusion syndrome (*dotted line* in A). (**B**) The TOI/baseline ratio was significantly decreased just after postdilatation in the ipsilateral hemisphere in the poor/no crossflow group. *$P < 0.05$. PTA, percutaneous transluminal angioplasty.

tissue oxygenation, and has the advantage that it can be used to evaluate continuous, real-time changes in regional cerebral hemodynamic values.[10,19] Various monitoring techniques have been described previously for NIRS, but their accuracy remains controversial because of physiological and anatomical variations. The NIRO-200NX, which we used in this study, involves spatially resolved spectroscopy, and the calculated values reflect cerebral oxygenation with a high degree of sensitivity and specificity.[10]

In the present study, the amplitude of TOI changes from baseline as measured by NIRS was significantly decreased just after ICA occlusion for postdilatation in the ipsilateral hemisphere in the poor/no crossflow group ($P < 0.05$), and the incidence of HPS was significantly higher in the poor/no crossflow group ($P = 0.019$). Kluytmans et al.[14] investigated the relationship between collateral flow and the cerebral hemodynamic status in patients with ICA stenosis or occlusion. They demonstrated that in patients with unilateral ICA occlusion, collateral pathways have a significant influence on the cerebral hemodynamic status, and collateral circulation via the anterior communication artery or via both the anterior and posterior communicating arteries is a sign of a well-compensated hemodynamic status. A recent study using a computational model of the cerebral circulation suggested that the diameters of the cerebral communicating arteries and the severity of carotid artery stenosis both significantly influence the post-CAS cerebral hyperperfusion rates.[20] These results are consistent with our present results.

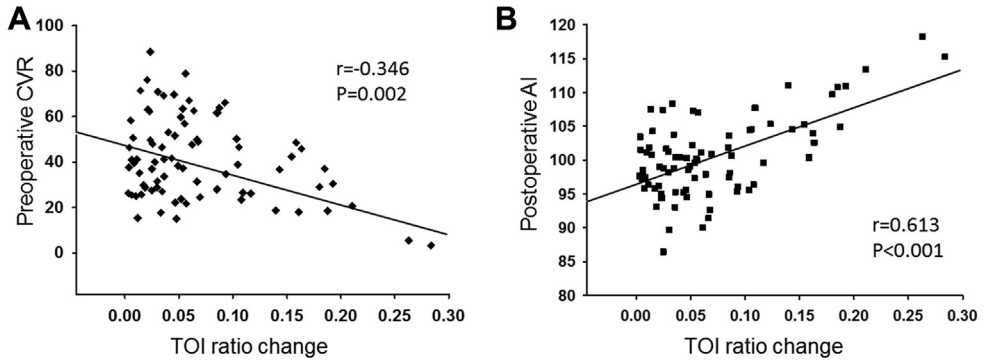

Figure 3. (**A**) The relationship between preoperative cerebrovascular reactivity (CVR) and tissue oxygenation index (TOI)/baseline ratio changes in the ipsilateral hemisphere. A significant linear correlation was observed between these parameters. (**B**) The relationship between postoperative asymmetry index (AI) and TOI/baseline ratio changes in the ipsilateral hemisphere. We observed a significant linear correlation between postoperative AI and TOI/baseline ratio changes in the ipsilateral hemisphere.

The development of HPS after carotid artery revascularization is associated with not only preoperative hemodynamic impairment but also intraoperative cerebral ischemia.[4] In the present study, however, all patients were treated with filter-type EPDs, which allow maintenance of anterograde carotid flow during the procedure and can reduce the incidence of HPS because of a shorter ischemic time in the ipsilateral hemisphere during CAS. Therefore, preoperative hemodynamic impairment that results from poor collateral flow supply may be the most important factor for predicting HPS after CAS while using filter-type EPDs.

On the other hand, the amplitude of the TOI/baseline ratio of 2 postoperative HPS cases in the present study showed a sudden decrease just after ICA occlusion by the post-dilatation balloon PTA, and then dramatically increased above baseline during reperfusion 5 minutes after the balloon PTA (dotted lines in **Figure 2A**). A previous study predicting postoperative HPS after CEA using NIRS demonstrated that regional cerebral oxygen saturation (rSO_2) increased after declamping of the ICA in all patients with post-CEA hyperperfusion and that postdeclamping rSO_2 values were more than 105% of preclamping values; these values increased to more than 110% by the end of the procedure.[21]

Furthermore, a recent study that assessed post-CAS HPS using NIRS showed that postreperfusion rSO_2 values increased >24% from baseline until 3 minutes after reperfusion in patients with HPS after CAS.[8] These results from previous studies are consistent with our present results. Therefore, we emphasize that a typical V-shaped TOI pattern, a decrease in short ICA occlusion, and an increase above baseline after reperfusion, as shown by the dotted line in **Figure 2A**, are useful for predicting postoperative HPS after CAS while using filter-type EPDs.

Previous studies have reported that patients with reduced preoperative CVR to ACZ have a high risk of developing post-CEA hyperperfusion.[3,7] Suga et al.[22] observed post-CEA hyperperfusion in 12 (52%) of 23 patients with reduced preoperative CVR to ACZ but in none of the patients with normal preoperative CVR ($n = 67$). Buczek et al.[23] reported that more patients with postoperative HPS had impaired CVR before the procedure compared with patients without postoperative HPS (63.6 vs. 26.5%), and the sensitivity and specificity of CVR for HPS were 63.6 and 73.5%, respectively. A recent positron emission tomography study demonstrated that the AI for rCBF in the resting state increases 2–7 days after CAS.[24] In the present study, significant linear correlations were observed between TOI/baseline ratio changes and preoperative CVR or postoperative AI ($r = -0.346$, $P = 0.002$, $r = 0.613$, $P < 0.001$, respectively) (**Figure 3A–B**). Our results are consistent with previous studies. We believe that the amplitude of the TOI change as measured by NIRS is an excellent predictor of cerebral HPS after CAS in the filter-type EPDs era. A randomized controlled study including a large number of patients is required to establish the efficacy of the TOI change as measured by NIRS for predicting HPS.

Limitations

Our study has several limitations. The coverage area of the NIRO-200NX was limited to the cortical region of the frontal lobe because of the placement of oximeter sensors over the forehead. Furthermore, extracranial contamination such as extracranial blood flow, cerebral metabolism, arterial saturation, and the hematocrit influence on cerebral oxygen by NIRS may have occurred. It is unlikely, however, that extracranial contamination had any significant effects on TOI measurements during and after CAS.[10] In addition, because each patient's wavelength of infrared light cannot be measured, we need to compare them by substituting a mean light length. However, this equipment may reflect relative hemodynamic changes. This study design was a nonrandomized retrospective study, and the small sample size may have introduced biases regarding patient and data collection. In addition, it is difficult to draw a strong conclusion about the predictive ability of the amplitude of TOI changes as measured by NIRS because only 2 patients presented with HPS. Well-designed randomized controlled trials involving a large number of patients are required to confirm these results.

CONCLUSIONS

The amplitude of TOI changes as measured by NIRS indicated a strong relationship with the status of collateral flow and showed a typical V-shaped pattern in patients presenting with HPS after CAS. Furthermore, significant linear correlations were observed between TOI/baseline ratio changes and preoperative CVR or postoperative AI. Therefore, the amplitude of the TOI change as measured by NIRS in patients with poor collateral flow may be an excellent predictor of cerebral HPS after CAS.

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