Evaluation of extracranial–intracranial arterial bypass function by using near-infrared spectroscopy

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Object. It has been reported that extracranial–intracranial (EC–IC) arterial bypass surgery can be useful in preventing stroke in patients with hemodynamic compromise. Little is yet known, however, regarding the extent to which the bypass contributes to maintaining adequate cerebral blood oxygenation (CBO) and its temporal changes following surgery. The authors evaluated bypass function repeatedly by using near-infrared spectroscopy (NIRS) after surgery.

Methods. The authors investigated 30 patients who had undergone EC–IC bypass surgery. Single-photon emission computerized tomography revealed a decrease in regional cerebral blood flow (rCBF) and a lowered rCBF response to acetazolamide. Changes in CBO were evaluated in the sensorimotor cortex during compression of the anastomosed superficial temporal artery (STA). When decreases in oxyhemoglobin (HbO2) and total hemoglobin (Hb) concentrations were observed, the bypass was considered to have maintained CBO in the sensorimotor cortex given that decreases in HbO2 and total Hb indicate cerebral ischemic changes. The bypass maintained CBO immediately after surgery in 36.7% of patients (Group I, 11 patients) and at some time after surgery, mostly within 1 year, in 43.3% of patients (Group II, 13 patients); however, it did not maintain it throughout the follow-up period in 20% of patients (Group III, six patients). Note that the preoperative rCBF in patients in Groups I and II was lower than that in patients in Group III (p < 0.004). In fact, the preoperative rCBF predicted whether a bypass would maintain CBO at a cutoff value of 24.5 to 25 ml/100 g/min. Among Groups I and II, 18 patients demonstrated an increase in deoxyhemoglobin during STA compression. The preoperative rCBF in these cases was lower than that in the six remaining patients (p < 0.006). Note that the preoperative rCBF predicted the postoperative deoxyhemoglobin response at a cutoff value of 22.2 to 24 ml/100 g/min.

Conclusions. The EC–IC bypass surgery can maintain CBO immediately after surgery or gradually within 1 year when the preoperative rCBF is below 24.5 to 25 ml/100 g/min. Furthermore, bypass flow plays a critical role in maintaining an adequate CBO when preoperative rCBF is below 22.2 to 24 ml/100 g/min.

Key Words • extracranial–intracranial arterial bypass • cerebral blood flow • stroke • near-infrared spectroscopy
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Clinical Material and Methods

Patient Population

We studied 30 patients (20 men and 10 women) ranging in age from 32 to 73 years (mean 53.3 ± 21.3 years). All patients had suffered multiple episodes of TIAIs due to hemodynamic compromise, which was in turn caused by occlusion of the ICA in 21 cases, occlusion of the MCA in four, and stenosis of the MCA in six. Magnetic resonance imaging results demonstrated watershed infarction in 12 cases and lacunar infarction in four. Table 1 summarizes the clinical profiles of the 30 patients.

All patients underwent EC–IC arterial bypass surgery (that is, anastomosis of the STA and MCA) during the period between 1997 and 1999. The clinical and scientific significance of this study was explained to all patients who underwent EC–IC bypass surgery during this period. The patients included in the study represent those who volunteered to participate. The study was approved by the Committee for Clinical Trials and Research on Humans. All patients gave informed consent for all procedures described herein. The ethics committee of the university hospital approved the study’s protocol.

In all patients, we measured rCBF at 3 weeks after the last TIA. Using the ethyl cysteinate dimer–resting and vascular reserve method and SPECT (PRISM 2000XP; Shimadzu Co., Kyoto, Japan), we estimated rCBF in patients at rest and 10 minutes after intravenous injection of acetazolamide (1 g) in the territory of the MCA ipsilateral to the site of surgery (Fig. 1). The %CVR to acetazolamide was calculated based on the following equation: %CVR = 100 × (rCBF_{ACZ} – rCBF_{rest})/rCBF_{rest}, where rCBF_{rest} and rCBF_{ACZ} represent rCBF before and after the injection of acetazolamide, respectively. Before surgery, all patients demonstrated an rCBF_{rest} of 30 ml/100 g/min or less and a %CVR of 10% or less. Table 2 lists preoperative rCBF values in each patient. During surgery, the STA flow was directly quantified by measuring the outflow of blood from the cut end of the STA (milliliters per minute).

Measurements Demonstrated on NIRS After EC–IC Bypass

We measured CBO with the aid of a spectrometer (NIRO-300; Hamamatsu Photonics K.K., Hamamatsu, Japan), as used in previous NIRS studies. The near-infrared light from four laser diodes was directed at the patient’s head through a fiberoptic bundle, and the reflected light was transmitted to a multisegment photodiode detector array. Absolute concentration changes in HbO₂, deoxyhemoglobin, and total Hb (the sum of HbO₂ and deoxyhemoglobin) were analyzed continuously and expressed in arbitrary units (if the differential pathlength factor of the adult head is assumed to be 5.9, one arbitrary unit equals 1 μM). (Note that the NIRO-300 is a spatially resolved spectrometer that permits one to determine the ratio of oxygenated to total tissue Hb [tissue O₂ index].) In the present study, we did not shave patient hair at the placement sites of the NIRS probes—which might obstruct light penetration into the skull—because we found that NIRS measurements of the...
CBO were easily possible when the probes were placed on the skull by separating the hair without shaving. Ultimately, however, we were unable to calculate the tissue oxygen index correctly in most cases because of hair that interfered with the detection of light in some of the photodiodes.

The NIRS probes were placed over the sensorimotor cortex on the side ipsilateral to the site of EC–IC bypass surgery. The method for measuring the CBO of the sensorimotor cortex is described in a previous NIRS activation study. Briefly, probes were placed over the sensorimotor cortex at a distance of 3 or 4 cm so that the axis of the probes could be superimposed on the central sulcus; the point 2 cm posterior to the midposition of the arc extends from nasion to inion, to the point 5 cm directly above the external auditory meatus. After performing the initial setting by this method, the position of the probes was adjusted so that the maximum responses of the HbO2 and total Hb were obtained during the motor task, which involved a repeated hand grasping task. Finally, magnetic resonance imaging with the aid of vitamin E capsules was used to confirm the location of the probes.

To evaluate EC–IC bypass function, digital compression was applied to the STA at the preauricular region for 30 to 100 seconds during the NIRS measurement. No patient revealed damage of the STA or any neurological symptoms during and after compression of the STA.

Following surgery all patients underwent periodic (one per month) neurological examinations performed by neurosurgeons in the outpatient department at our hospital; however, none revealed clear neurological deficits or behavioral abnormalities during the follow-up period. Near-infrared spectroscopy was performed every 3 months for 3 years, beginning 3 days after surgery. Postoperative cerebral angiography demonstrated the patency of the bypass in all patients. No patient suffered from a new episode of TIA during the entire follow-up period.

**Data Analysis**

We compared values of HbO2, deoxyhemoglobin, and total Hb during the 10-second period before compression of the STA with those obtained during the 10-second compression period in which maximum changes were observed. When a difference was detected at a probability value less than 0.01 by the paired t-test, the changes in these parameters were considered to be significant. In addition, we examined the relationships between NIRS-demonstrated responses to compression of the STA and preoperative rCBF, %CVR, and STA flow as well as frequency of TIA before surgery by calculating the unpaired t-test and chi-square test. We drew a receiver operating characteristic curve and configured cutoff values for preoperative rCBF. These values were calculated so that they gave preference to sensitivity over specificity to avert false-negative results as much as possible.
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Results

Responses to STA Compression Demonstrated on NIRS

In 24 (80%) of 30 patients, the concentrations of HbO_2 and total Hb decreased during STA compression and rapidly returned to baseline levels when compression was ceased (Fig. 2A and B). Decreases in HbO_2 and total Hb concentrations were observed immediately after surgery (within 3 days after surgery) in 11 patients (36.7%, Group I). In 13 patients (43.3%, Group II), the decreases in HbO_2 and total Hb occurred at some time after surgery, usually within 1 year (Fig. 3). Only two patients showed a decrease in HbO_2 and total Hb more than 1 year after surgery. In the remaining six patients (20%, Group III), STA compression elicited no significant change in concentrations of HbO_2 and total Hb during the entire follow-up period. There was no statistically significant difference in patient age and sex or distribution of vascular lesions among the three groups (Table 1).

In association with the decreases in the concentrations of HbO_2 and total Hb in Groups I and II, 18 patients demonstrated an increase in deoxyhemoglobin during STA compression throughout the follow-up period (Fig. 2A). The six remaining patients revealed a decrease in deoxyhemoglobin concentrations during STA compression (Fig. 2B). No significant change in the concentration of deoxyhemoglobin was observed in patients in Group III.

Relationship of NIRS-Demonstrated Responses to Preoperative rCBF, %CVR, TIA Frequency, and Blood Flow in the STA

Compared with that in Group III patients (25.3 ± 2.3 ml/100 g/min), preoperative rCBF values in Group I (21.2 ± 3.3 ml/100 g/min, p < 0.008) and Group II (21.4 ± 2.4 ml/100 g/min, p < 0.002) were significantly lower (Table 3).

The preoperative rCBF predicted the HbO_2 and total Hb response at a cutoff value of 24.5 to 25 ml/100 g/min (sensitivity 87.5%, specificity 66.7%; Fig. 4). Thus, concentrations of HbO_2 and total Hb decreased during STA compression in 21 (87.5%) of 24 patients when the preoperative rCBF was below this cutoff value. No significant difference existed between Groups I and II. There was no significant difference in either %CVR or STA flow between these groups (Table 3).

The deoxyhemoglobin responses in Groups I and II patients were clearly related to preoperative rCBF (Fig. 5). In fact, the preoperative rCBF in the 18 patients who experienced an increase in deoxyhemoglobin during STA compression (20.7 ± 2.3 ml/100 g/min) was significantly lower than that in the six patients who showed a decrease in deoxyhemoglobin (23.3 ± 2.3 ml/100 g/min; p < 0.00007) in

**TABLE 3**

Preoperative rCBF, %CVR, TIA frequency, and STA blood flow in 30 patients who suffered repeated TIA*s

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>rCBF (ml/100 g/min)</th>
<th>%CVR</th>
<th>TIA Frequency (times/yr)</th>
<th>Blood Flow in STA (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>21.2 ± 3.3†§</td>
<td>-0.91 ± 19.4</td>
<td>1.9 ± 0.5</td>
<td>34.6 ± 23.6</td>
</tr>
<tr>
<td>(11 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>21.4 ± 2.4†§</td>
<td>-4.75 ± 11.1</td>
<td>1.7 ± 0.3</td>
<td>29.9 ± 22.3</td>
</tr>
<tr>
<td>(13 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>25.3 ± 2.3</td>
<td>6.0 ± 6.9</td>
<td>1.8 ± 0.4</td>
<td>44.0 ± 24.0</td>
</tr>
<tr>
<td>(6 patients)</td>
<td></td>
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</tbody>
</table>

* All data are expressed as the means ± SD.
† p < 0.008, compared with Group III.
‡ p < 0.002, compared with Group III.
§ p < 0.004, Groups I and II compared with Group III.

**FIG. 3.** Graph demonstrating the appearance of the ischemic CBO response during STA compression following EC–IC bypass surgery. Near-infrared spectroscopy was performed 3 days after surgery and every 3 months during the follow up.

**FIG. 4.** Graph displaying a comparison of the NIRS-demonstrated responses and preoperative rCBF measured on SPECT. Groups I and II include patients who showed ischemic CBO changes immediately after surgery or at some time after surgery. Patients in Group III displayed no response on NIRS during the follow-up period. The gray zone indicates the cutoff value of 24.5 to 25 ml/100 g/min. n = number of patients.
association with decreases in HbO₂ and total Hb. Preoperative rCBF predicted the deoxyhemoglobin response at a cutoff value of 22.2 to 24 ml/100 g/min (sensitivity 94.0%; specificity 66.7%). Thus, the concentration of deoxyhemoglobin increased during STA compression in 17 (94.4%) of 18 patients when the preoperative CBF was below this cutoff value.

There was no significant difference between NIRS-demonstrated responses induced by STA compression in relation to preoperative %CVR, TIA frequency, or STA blood flow (Table 3).

**Discussion**

Near-infrared spectroscopy measures the concentrations of HbO₂ and deoxyhemoglobin within the illuminated area, which includes both intracranial and extracranial tissues when the probe is placed on the scalp. Changes in NIRS parameters in response to STA compression may therefore be caused by changes in the blood flow of the scalp.¹ The STA was removed from the skin and anastomosed to the MCA, however, so that the STA supplied blood to the intracranial tissues rather than the extracranial tissues. In addition, performance of the motor task (grasping) by the hand on the side contralateral to the site of surgery caused increases in HbO₂ and total Hb, indicating that NIRS measurements covered the sensorimotor cortex. It appears reasonable to assume therefore that the changes in NIRS parameters observed during STA compression reflected mostly changes in CBO.

Compression of the STA caused a decrease in the concentrations of HbO₂ and total Hb in 80% of the patients studied during the follow-up period. The decrease in the concentration of HbO₂ reflects a decrease in rCBF, and the decrease in the concentration of total Hb (sum of HbO₂ and deoxyhemoglobin) reflects a decrease in cerebral blood volume on both the arterial and venous sides.² These changes are consistent with previously reported changes in NIRS parameters caused by cerebral ischemia.¹⁶,⁷,⁹,¹¹–¹³,¹⁵,¹⁸,²⁷–²⁹,³¹,³²,⁴⁶,⁴⁷,⁵² In fact, the data indicate that in the studied patients, STA compression caused decreases in CBF and cerebral blood volume in the sensorimotor cortex. This implies that the bypass maintained CBO such that it contributed to the CBF of the territory of the MCA.

The results of repeated NIRS revealed that the bypass could maintain CBO immediately after surgery (Group I) and gradually within 1 year (Group II) in many patients. In the Group II patients, the STA flow appeared to increase gradually during certain periods after surgery. In agreement with this, an increase in the size of the anastomosed STA following EC–IC bypass surgery has been demonstrated on repeated cerebral angiography.²⁴ In addition, a progressive decrease in blood supply from the intracranial arteries may be involved in this phenomenon.

The STA compression caused no changes in HbO₂ and total Hb concentrations in 20% of the patients (Group III) during the follow-up period. The absence of NIRS-demonstrated responses was not due to problems with the surgical technique, given that postoperative cerebral angiography demonstrated the patency of the bypass. It appears that the bypass in Group III patients may have not played a role in maintaining CBO, suggesting that bypass may not be necessary in these patients. The mechanism of the disappearance of an ischemic attack in Group III patients following surgery remains unclear. Nonetheless, we speculate that the hemodynamic instability in Group III patients might have recovered as a result of medical treatments rather than the EC–IC bypass: all patients were subjected to medical treatments (that is, volume expansion and the administration of antiplatelet agents, anticoagulant agents, and so forth) in addition to bypass surgery. The relationship between preoperative CBF and NIRS-demonstrated responses indicates that EC–IC bypass may not be necessary in patients whose preoperative rCBF is in excess of 24.5 to 25 ml/100 g/min, which is the cutoff value in the present study (Fig. 4).

In experimental animals, an increase in the concentration of deoxyhemoglobin has been observed in severe ischemia, whereas a decrease in its concentration has been observed in mild ischemia.³⁰ Such an increased concentration in severe ischemia is consistent with an increased O₂ extraction from the limited flow. This indicates that the degree of the rCBF decrease caused by STA compression was greater in patients who experienced an increase in deoxyhemoglobin compared with those who showed a decrease in deoxyhemoglobin. In agreement with this, the present data reveal that the preoperative rCBF was significantly lower in the patients who experienced an increase in deoxyhemoglobin compared with those who experienced a decrease in deoxyhemoglobin. The cutoff value calculated in the present study indicates that the bypass becomes critical to maintaining an adequate CBO when the original flow of the MCA decreases below 22.2 to 24 ml/100 g/min.

**Conclusions**

The present findings indicate that a preoperative rCBF
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lower than approximately 24.5 to 25 ml/100 g/min predicts that the bypass will maintain CBO, and a preoperative rCBF lower than approximately 22.2 to 24 ml/100 g/min indicates that the bypass will play a vital role in maintaining an adequate CBO. Data in the present study failed to demonstrate that the %CVR has such a predictive value. Note, however, that the significance of the perfusion reserve may not be investigated properly in a resting hemodynamic status. Although noninvasive techniques, such as magnetic resonance angiography and ultrasonography, have been used to evaluate the bypass patency, these techniques do not provide us with information concerning the rCBF and CBO. Near-infrared spectroscopy is a useful diagnostic technique for evaluating the function of the EC–IC arterial bypass.

References


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