Intraoperative evaluation of local cerebral hemodynamic change by indocyanine green videoangiography: prediction of incidence and duration of postoperative transient neurological events in patients with moyamoya disease

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OBJECTIVE Transient neurological events (TNEs) occur frequently in the acute phase after direct bypass surgery for moyamoya disease (MMD), but there is currently no way to predict them. FlowInsight is a specialized software for analyzing indocyanine green (ICG) videoangiography taken with a surgical microscope. The purpose of this study was to investigate whether intraoperative evaluation of local hemodynamic changes around anastomotic sites using FlowInsight could predict the incidence and duration of TNEs.

METHODS From patients who were diagnosed with MMD in our hospital between August 2014 and March 2017 and who underwent superficial temporal artery–middle cerebral artery bypass surgery, we investigated 25 hemispheres (in 22 patients) in which intraoperative ICG analysis was performed using FlowInsight. To evaluate the local cerebral hemodynamics before and after anastomosis, regions of interest were set at 3 locations on the brain surface around the anastomotic site, and the mean cerebral blood flow (CBF), mean gradation (Grad), mean transit time (MTT), and mean time to peak (TTP) were calculated from the 3 regions of interest. Furthermore, the change rate in CBF (ΔCBF [%]) was calculated using the formula (postanastomosis mean CBF – preanastomosis mean CBF)/preanastomosis mean CBF. ΔGrad (%), ΔMTT (%), and ΔTTP (%) were similarly calculated.

RESULTS Postoperative stroke without TNE occurred in 2 of the 25 hemispheres. These 2 hemispheres (in 2 patients) were excluded from the study, and data from the remaining 23 hemispheres (in 20 patients) were analyzed. For each parameter (ΔCBF, ΔGrad, ΔMTT, and ΔTTP) calculated by FlowInsight, the difference between the groups with and without TNEs was significant. The median values for ΔCBF and ΔGrad were significantly higher in the TNE group than in the no-TNE group (ΔCBF 30.13 vs 3.54, p = 0.0106; ΔGrad 62.05 vs 10.78, p = 0.00435), whereas the median values for ΔMTT and ΔTTP were significantly lower in the TNE group (ΔMTT –16.90 vs –7.393, p = 0.023; ΔTTP –29.07 vs –7.02, p = 0.00342). Comparison of the area under the curve (AUC) for each parameter showed that ΔTTP had the highest AUC and was the parameter with the highest diagnostic accuracy (AUC 0.857). The Youden index revealed that the optimal cutoff value of ΔTTP was –11.61 (sensitivity 77.8%, specificity 71.4%) as a predictor of TNEs. In addition, Spearman’s rank correlation coefficients were calculated, and ΔCBF, ΔGrad, ΔMTT, and ΔTTP each showed a strong correlation with the duration of TNEs. The larger the change in each parameter, the longer the TNEs persisted.

CONCLUSIONS Intraoperative ICG videoangiography findings were correlated with the occurrence and duration of TNEs after direct bypass surgery for MMD. Screening for cases at high risk of TNEs can be achieved by ICG analysis using FlowInsight.

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KEYWORDS moyamoya disease; FlowInsight; indocyanine green; transient neurological events; cerebral blood flow; vascular disorders

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1
MOYAMOYA disease (MMD) is characterized by progressive stenosis/occlusion and abnormal collateral neovascularization at the terminal end of the bilateral internal carotid arteries, and its causes are unknown. Revascularization surgery typified by superficial temporal artery–middle cerebral artery (MCA) bypass improves cerebral ischemia and decreases the risk of future infarction and bleeding. On the other hand, transient neurological events (TNEs) such as numbness in the extremities, episodes of weakness, and severe headaches are experienced frequently in the acute phase after bypass surgery. Based on postoperative cerebral hemodynamic examinations, TNEs are thought to be due mainly to local hyperperfusion. However, local hypoperfusion, watershed shift, and inflammation have also been suggested to be involved. Thus, the physiological mechanism of TNEs remains unclear. TNEs occur in 14%–77% of patients after MMD bypass surgery, with the possibility of stroke and progression to irreversible sequelae. If occurrence of TNEs could be predicted, early intervention might reduce perioperative complications. Accordingly, elucidation of predictors of TNEs is desirable. In some reports, local and rapid hemodynamic change caused by bypass surgery was suggested to be a predictor of the occurrence of TNEs. In those studies, various devices were used to evaluate hemodynamic changes during surgery. However, reports to date have only examined the relationship between indirect parameters of hemodynamics and postoperative hyperperfusion syndrome. Therefore, it is difficult to claim that there is sufficient evidence to explain a causal relationship between hemodynamic changes and postoperative TNEs, and no predictor of TNEs has been identified.

FlowInsight (Infocom Corporation) is specialized software for analyzing indocyanine green (ICG) videoangiography performed with a surgical microscope. FlowInsight represents a new modality that can set a region of interest (ROI) for arbitrary shapes and sites and then calculate, for that ROI, direct parameters related to the local cerebral hemodynamics, such as cerebral blood flow (CBF), mean transit time (MTT), time to peak (TTP), and gradation (Grad; 5%–100% of maximum intensity/TTP), which cannot be determined with conventional software. We evaluated the hemodynamic changes around anastomotic sites from before to after bypass surgery using FlowInsight and examined whether the changes could predict the incidence and duration of TNEs.

Methods

Patients

In patients who were diagnosed with MMD in our hospital between August 2014 and March 2017 and who underwent STA-MCA bypass surgery, we investigated 25 hemispheres in which intraoperative ICG analysis had been performed using FlowInsight. All the patients were Japanese, and they all met the guidelines for diagnosis set by the Research Committee on Moyamoya Disease of the Ministry of Health, Labor, and Welfare of Japan. This study was approved by the institutional review board of Nagoya University Graduate School of Medicine. Informed consent was obtained from the study participants.

Surgical Procedures and Management

In all surgeries, the STA graft was anastomosed to the MCA (M4 segment) in an end-to-side manner after fronto-temporal craniotomy, and encephaloduromyopericranial synangiosis was performed.

Radiological Examinations

All patients underwent MRI, MR angiography (MRA), and single-photon emission CT (SPECT) 1 month before and 3 days after the operation to identify stroke events and bypass patency and to evaluate CBF. The nuclides used for CBF examination were 123I-N-isopropyl-p-iodoamphetamine for patients at least 13 years old and 99mTc-ethylcysteinate for patients younger than 13 years of age. In evaluation of SPECT results, marked CBF increases in local vascular territories were defined as local hyperemia.

FlowInsight Examination

ICG videoangiography was performed using a surgical microscope (Leica M525 OH4, Leica Microsystems). Patients were administered 2 ml of ICG solution (containing 5 mg of ICG) intravenously, followed immediately by a bolus of 20 ml of physiological saline. When the ICG videoangiography is incorporated into FlowInsight, a time-luminance curve for ICG in the ROI is generated within several seconds. By applying the principles of perfusion CT, cerebral blood volume (CBV) and MTT are calculated from the area surrounded by the time-luminance curve and the time, and CBF is calculated from CBV/MTT (Fig. 1). As shown in Fig. 2, two waves are seen in the ICG time-luminance curve, and this was consistent among the hemispheres studied. FlowInsight acquires measurements between the beginning of the first wave and the appearance of the second wave in the ROI. To evaluate the local cerebral hemodynamics before and after anastomosis, ROIs were set at 3 locations on the brain surface around the anastomotic site (Fig. 2). ROIs were created within the range of 2 gyri from the anastomotic site. The mean values of CBF, Grad, MTT, and TTP were calculated from 3 ROIs. Furthermore, for each of those parameters, the change from before to after anastomosis was calculated. That is, the percentage change in CBF (ΔCBF [%]) was calculated as (postanastomosis mean CBF – preanastomosis mean CBF)/preanastomosis mean CBF. ΔGrad (%), ΔMTT (%), and ΔTTP (%) were similarly calculated. Factors that might affect the change in the ICG time-luminance curve, including the timing of ICG administration, injection speed, microscope settings (magnification, range of the field of view, and focal length), and the intensity of illumination of the room, were strictly standardized before and after the anastomosis. The blood pressure and PaCO₂ were also kept constant during surgery.

Postoperative Evaluation

Each patient’s clinical records were evaluated retro-
spectively. The criteria for identifying postoperative TNEs were defined according to a previous report as follows: 1) reversible neurological deficits observed objectively (e.g., motor weakness, aphasia); 2) reversible neurological deficits recognized subjectively and reported by the patients (e.g., numbness of the extremities); 3) no sign of acute cerebral infarctions on radiological images; and 4) no sign of acute hemorrhage on radiological images. Mild headaches that were difficult to distinguish from postoperative pain were excluded.

Statistical Analysis

Because of the small sample, the Mann-Whitney U-test and Fisher’s exact test were used to identify differences between the 2 groups (with and without TNEs). The area under the receiver operating characteristic curve (AUC) was constructed to evaluate the diagnostic accuracy and to set the optimal cutoff point using the Youden index. Fisher’s exact test was used to examine the relationship between local hyperemia on postoperative SPECT and TNEs. Spearman’s rank correlation coefficient (rho) was calculated to assess the relationship between the duration of TNEs and parameters of FlowInsight. Statistical data were generated using EZR. Statistical significance was set at p < 0.05.

Results

A cerebral hemorrhage developed in one of the 25 investigated hemispheres after the surgery, and a cerebral infarction developed in another. Those events occurred immediately after and 3 days after the surgery without TNEs. Those 2 hemispheres were excluded, because no obvious TNEs preceding stroke were observed and the presence or absence of TNEs was unclear due to the symptoms of stroke. After exclusion of these 2 hemispheres, 23 hemispheres were available for inclusion in this study (5 hemispheres in 5 male patients and 18 hemispheres in 15 female patients; mean age 27.52 years, range 7–53 years). The patient group included 7 children (age < 18 years; with data from 10 hemispheres analyzed) and 13 adults (age ≥ 18 years; with data from 13 hemispheres analyzed). On the 3rd day after surgery, bypass patency was confirmed in all cases by MRA.

TNEs were identified as occurring in 9 (39.1%) of the 23 hemispheres after revascularization, with no TNEs in the remaining 14 hemispheres (60.9%). Numbness, aphasia, and severe headache occurred as symptoms of TNEs (Table 1). There were no significant differences between the 2 groups in regard to age, sex, or the operated side (Table 2). There were also no significant differences in the mean rate (%) of CBF reduction at the anastomotic site compared with the ipsilateral cerebellum in preoperative SPECT, Suzuki stage, or the conditions at the time of symptom onset. All TNEs were transient and disappeared without any residual symptoms. No particular adverse events due to the ICG administration were observed.

Relationships Between Parameters From FlowInsight and Incidence of TNEs

From before to after the bypass surgery, CBF and Grad increased significantly, whereas MTT and TTP decreased significantly (data not shown). All of the parameters (ΔCBF, ΔGrad, ΔMTT, and ΔTTP) calculated by FlowInsight showed significant differences between the patients.

\[
\begin{align*}
\text{Grad} &= \text{Peak} / \text{TTP} \\
\text{CBF} &= \text{CBV} / \text{MTT} \\
\text{CBV} &= \int_{\text{CutOFF}}^{\text{AT}} dt \cdot \text{ICG}_{\text{pre}}(t)
\end{align*}
\]
with and without TNEs. ΔCBF was significantly higher in patients with TNEs than in those without TNEs: median 30.13 (interquartile range [IQR] 22.04–77.94) and median 3.54 (IQR 0.16 to 28.29), respectively (p = 0.0106). ΔGrad was significantly higher in patients with TNEs than in those without TNEs: median 62.05 (IQR 37.96–118.00) and median 10.78 (IQR 5.52–43.37), respectively (p = 0.00435). On the other hand, ΔMTT was significantly lower in the patients with TNEs than in those without TNEs: median 16.90 (IQR –35.08 to –9.55) and median –7.393 (IQR –10.19 to –5.80), respectively (p = 0.023). ΔTTP was significantly lower in patients with TNEs than in those without TNEs: median –29.07 (IQR –38.07 to –11.61) and median –7.02 (IQR –11.52 to –4.91), respectively (p = 0.00342) (Fig. 3).

Receiver Operating Characteristic Curve Analysis for Developing TNEs

Using the Youden index from the receiver operating characteristic curve, we determined the optimal cutoff values as predictors for developing TNEs. The optimal cutoff value for ΔCBF was 7.916 (sensitivity 100%, specificity 64%), for ΔGrad it was 29.638 (sensitivity 100%, specificity 64.3%), for ΔMTT it was –8.325 (sensitivity 88.9%, specificity 64.3%), and for ΔTTP it was –11.610 (sensitivity 77.8%, specificity 71.4%). Furthermore, the AUC values were determined, and the diagnostic accuracy was verified. The AUC values of ΔCBF, ΔGrad, ΔMTT, and ΔTTP were 0.817, 0.849, 0.786, and 0.857, respectively. Therefore, ΔTTP was the parameter with the highest diagnostic accuracy.

Relationships Between Parameters From FlowInsight and Duration of TNEs

Associations between the duration of TNEs and parameters from FlowInsight were examined using Spearman’s rank correlation coefficient. All the parameters (ΔCBF, ΔGrad, ΔMTT, and ΔTTP) showed a strong correlation with the duration of TNEs. The Spearman’s rank correlation coefficients for ΔCBF, ΔGrad, ΔMTT, and ΔTTP were 0.548 (p = 0.0068), 0.640 (p = 0.000994), –0.518 (p = 0.0114), and –0.649 (p = 0.000789), respectively.
larger the change in each parameter, the longer the TNEs persisted (Fig. 4).

Relationships Between TNEs and SPECT

In 22 of the 23 analyzed hemispheres, SPECT was performed for CBF examination on the 3rd day after surgery. Local hyperemia was seen in postoperative SPECT in 4 of these 22 hemispheres. TNEs were detected in 3 (75%) of the 4 hemispheres in the group with local hyperemia. In contrast, TNEs were detected in 6 (33%) of the 18 hemispheres in the group with no local hyperemia. There was no significant difference between the incidence of postoperative TNEs and the detection of local hyperemia in SPECT (p = 0.264).

Discussion

Our analyses performed using ICG and FlowInsight showed that the parameters of cerebral hemodynamic change from before to after bypass surgery (i.e., ΔCBF, ΔGrad, ΔMTT, and ΔTTP) were predictive factors for the occurrence of postoperative TNEs. They were also correlated with the duration of TNEs.

Local hyperperfusion and hypoperfusion have been reported to occur when the local hemodynamic change caused by bypass surgery is excessively large. In those reports, it was discussed that moyamoya vessels are originally in a vasoparalytic state due to chronic ischemia, and excessive change due to bypass surgery acts as a stimulus that causes TNEs. Based on those reports, it could be inferred that TNEs are more likely to occur as the local hemodynamic change becomes larger, and that the TNEs will persist until becoming stable.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Operated Side</th>
<th>Local Hyperemia on SPECT</th>
<th>TNEs</th>
<th>TNE Duration (days)</th>
<th>Symptoms</th>
<th>ΔCBF (%)</th>
<th>ΔGrad (%)</th>
<th>ΔMTT (%)</th>
<th>ΔTTP (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>47, F</td>
<td>Lt</td>
<td>+</td>
<td>+</td>
<td>16</td>
<td>Aphasie, severe HA</td>
<td>191.002</td>
<td>183.456</td>
<td>−35.077</td>
<td>−41.199</td>
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<tr>
<td>2</td>
<td>10, F</td>
<td>Lt</td>
<td>−</td>
<td>+</td>
<td>13</td>
<td>Aphasie</td>
<td>71.771</td>
<td>170.013</td>
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<td>3</td>
<td>10, F</td>
<td>Rt</td>
<td>−</td>
<td>+</td>
<td>11</td>
<td>Numbness</td>
<td>7.916</td>
<td>113.318</td>
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<td>−38.468</td>
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<td>4</td>
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<td>Rt</td>
<td>−</td>
<td>+</td>
<td>10</td>
<td>Numbness</td>
<td>30.132</td>
<td>37.962</td>
<td>−8.325</td>
<td>−14.211</td>
</tr>
<tr>
<td>5</td>
<td>52, M</td>
<td>Rt</td>
<td>−</td>
<td>+</td>
<td>9</td>
<td>Severe HA, numbness</td>
<td>77.974</td>
<td>62.054</td>
<td>3.892</td>
<td>−7.047</td>
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<td>6</td>
<td>53, F</td>
<td>Rt</td>
<td>+</td>
<td>+</td>
<td>8</td>
<td>Severe HA</td>
<td>21.887</td>
<td>45.155</td>
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<tr>
<td>7</td>
<td>34, M</td>
<td>Lt</td>
<td>−</td>
<td>+</td>
<td>3</td>
<td>Aphasie, severe HA</td>
<td>25.478</td>
<td>35.988</td>
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<td>−9.123</td>
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<tr>
<td>8</td>
<td>44, F</td>
<td>Rt</td>
<td>+</td>
<td>+</td>
<td>2</td>
<td>Numbness</td>
<td>114.262</td>
<td>118.000</td>
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</tr>
<tr>
<td>9</td>
<td>13, F</td>
<td>Lt</td>
<td>−</td>
<td>+</td>
<td>2</td>
<td>Numbness</td>
<td>22.042</td>
<td>29.638</td>
<td>−9.551</td>
<td>−11.610</td>
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<td>10</td>
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<td>Rt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td></td>
<td>−27.304</td>
<td>−11.669</td>
<td>−10.204</td>
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<tr>
<td>11</td>
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<td>Lt</td>
<td>NA</td>
<td>−</td>
<td>0</td>
<td></td>
<td>25.458</td>
<td>22.828</td>
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<td>−11.111</td>
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<tr>
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<td>10, F</td>
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<td>−</td>
<td>0</td>
<td></td>
<td>54.664</td>
<td>50.341</td>
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<tr>
<td>13</td>
<td>40, M</td>
<td>Lt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td></td>
<td>−0.219</td>
<td>9.954</td>
<td>−10.151</td>
<td>−11.657</td>
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<tr>
<td>14</td>
<td>7, M</td>
<td>Lt</td>
<td>+</td>
<td>−</td>
<td>0</td>
<td></td>
<td>29.230</td>
<td>44.433</td>
<td>−12.569</td>
<td>−13.409</td>
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<td>15</td>
<td>11, M</td>
<td>Lt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td></td>
<td>6.727</td>
<td>61.101</td>
<td>−5.516</td>
<td>−7.321</td>
</tr>
<tr>
<td>16</td>
<td>10, F</td>
<td>Lt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td></td>
<td>86.685</td>
<td>79.493</td>
<td>3.740</td>
<td>10.740</td>
</tr>
<tr>
<td>17</td>
<td>13, F</td>
<td>Rt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td></td>
<td>2.747</td>
<td>8.692</td>
<td>−5.734</td>
<td>−4.839</td>
</tr>
<tr>
<td>18</td>
<td>11, F</td>
<td>Rt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td></td>
<td>4.338</td>
<td>11.581</td>
<td>−6.010</td>
<td>−6.436</td>
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<tr>
<td>19</td>
<td>32, F</td>
<td>Rt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td></td>
<td>0</td>
<td>8.513</td>
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<td>−8.645</td>
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<tr>
<td>20</td>
<td>38, F</td>
<td>Rt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td>−16.167</td>
<td>4.527</td>
<td>−19.253</td>
<td>−19.848</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>44, F</td>
<td>Rt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td>0.301</td>
<td>−0.348</td>
<td>−14.132</td>
<td>7.106</td>
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<tr>
<td>22</td>
<td>8, F</td>
<td>Lt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td>−13.982</td>
<td>−15.477</td>
<td>4.009</td>
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<tr>
<td>23</td>
<td>50, F</td>
<td>Rt</td>
<td>−</td>
<td>−</td>
<td>0</td>
<td>29.543</td>
<td>40.171</td>
<td>−6.406</td>
<td>−5.139</td>
<td></td>
</tr>
</tbody>
</table>

HA = headache; NA = not available; + = present; − = absent.
Three patients are represented by 2 cases (2 operations) each—cases 2 and 3, 9 and 17, and 16 and 18.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TNEs</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemisphere (total 23 sides)</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>Mean age (yrs)</td>
<td>32.00 ± 18.00</td>
<td>24.64 ± 17.08</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M (%)</td>
<td>2 (28.6)</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td>F (%)</td>
<td>7 (71.4)</td>
<td>11 (81.2)</td>
</tr>
<tr>
<td>Operated side</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rt (%)</td>
<td>5 (57.1)</td>
<td>7 (50)</td>
</tr>
<tr>
<td>Lt (%)</td>
<td>4 (42.9)</td>
<td>7 (50)</td>
</tr>
</tbody>
</table>

Values are numbers of patients or hemispheres unless otherwise indicated. Mean values are given with SDs.
In the event of a TNE, appropriate measures must be taken according to the individual patient’s cerebral hemodynamic needs, since a TNE may evolve into a stroke. Because the status of CBF after bypass surgery varies from case to case, depending on the degree of preoperative cerebral ischemia, bypass graft size, and blood pressure, CBF should be evaluated by hemodynamic examination, such as SPECT, followed by the management of TNEs. However, in many cases, hemodynamic examination in an emergency is difficult, and the number of examinations is limited. Because evaluation is performed only at a certain point during the first few days after surgery, when TNEs tend to occur, it is not possible to determine how CBF changes from minute to minute. Other problems may include the local spatial resolution for SPECT being too low or fluctuating results due to sedation or crying. In our series, the 9 hemispheres in which TNEs occurred, only 3 hemispheres showed abnormal SPECT findings. In other reports as well, TNEs and CBF were not correlated. Based on the above, it can be said that the response to TNEs will be insufficient if relying only on postoperative hemodynamic examination. Therefore, it is desirable to develop a modality for screening for patients at high risk for TNEs.

There are several reports on the prediction of TNEs based on evaluation of the local cerebral hemodynamics during bypass surgery. Various devices were used to evaluate hemodynamics: an electromagnetic flowmeter, micro-Doppler ultrasonography, infrared imaging, Photoshop software (Adobe), and thermal imaging. The measured parameters were the STA blood flow after anastomosis, the direction and speed of the MCA blood flow before and after anastomosis, the brain surface temperature, cortical venous redness, and tissue blood flow, respectively. However, measurement of these parameters is complicated and requires special equipment.

ICG videoangiography is commonly performed because it is a safe and simple method and can also judge the patency of the bypass. Furthermore, because the luminance of ICG correlates with CBF, ICG videoangiography is also attracting attention as a modality for local hemodynamic evaluation. In terms of analytical methods for ICG videoangiography, however, only indirect parameters have been previously used, including the peak time and blood flow index, the change in the scope of contrast on the brain surface, and the difference in contrast time between the artery and the vein. In contrast, FlowInsight is a new software developed to evaluate hemodynamics in tissues and blood vessels from ICG videoangiography by applying the principles of perfusion CT. With FlowInsight, it is possible to calculate direct hemodynamic parameters for an arbitrarily set ROI almost in real time after administration of ICG. We concluded that this is the best available method for establishing a predictor of TNEs, because it is easy and simple to evaluate. FlowInsight can perform virtual quantification by plotting an ROI in an artery and inputting actual measured values obtained with an electromagnetic blood flowmeter. However, the accuracy is poor because of great variation in the ICG luminance value due to individual differences in the thickness of blood vessel walls. Nevertheless, for our purpose, it is sufficient to just elucidate the rate of change.

In this study, ATTP was the parameter with the highest correlation coefficient among the parameters calculated by FlowInsight. However, because of their high sensitivity, ΔCBF and ΔGrad are also parameters that should be given attention. We use these parameters to try to identify patients at increased risk for postoperative TNEs and adjust the perioperative treatment accordingly. ICG analysis was performed using FlowInsight during the surgery, and we judge that TNEs are highly likely to occur postoperatively in patients with ΔTTP ≤ 12, ΔCBF ≥ 8, or ΔGrad ≥ 30. We manage such patients in an intensive care unit, protecting the brain by administering edaravone, maintaining body fluid balance carefully, and strictly maintaining the patient’s blood pressure within his or her regular baseline range (as measured in a relaxed state while at home); sedation may be continued to suppress brain metabolism in some cases. In all cases, SPECT is performed several days after surgery to assess patients’ postoperative cerebral hemodynamics, and the target value of blood pressure is reset accordingly. These management methods might reduce perioperative complications.

One patient who developed a postoperative cerebral infarction and another with a cerebral hemorrhage were excluded from this study, leaving 20 patients with 23 hemispheres. The FlowInsight results for those patients were −14.04 and −22.21 for ΔTTP, 31.23 and 64.92 for ΔCBF, and 40.78 and 79.38 for ΔGrad. Each of those parameters greatly exceeded the cutoff values for judging the patients to be at high risk for TNEs. The hemodynamics in these 2 cases remain unclear because they were not evaluated by

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**FIG. 3.** Relationship between each of the parameters calculated by FlowInsight and TNEs. All the parameters (ΔCBF, ΔGrad, ΔMTT, and ΔTTP) calculated by FlowInsight show a significant difference between the groups with and without TNEs. In the group with TNEs (compared with the group without TNEs), ΔCBF was significantly higher (median 30.13 vs 3.54, p = 0.0106) (A), and ΔGrad was also significantly higher (median 62.05 vs 10.78, p = 0.00435) (B). In contrast, ΔMTT was significantly lower (median −16.90 vs −7.393, p = 0.023) (C), and so was ΔTTP (median −29.07 vs −7.02, p = 0.00342) (D). The box-and-whisker plots indicate the median value (horizontal line within box) and the 25th (lower limit of box) and 75th (upper limit of box) percentiles. The error bars indicate the 10th and 90th percentiles. + = present; − = absent.
SPECT. However, the results of FlowInsight indicate that a situation of local hemodynamic instability existed, and we consider that stroke occurred due to a combination of factors, such as intraoperative bleeding, surgical invasion, and postoperative management. The perioperative complications of MMD are affected by patient care, and perioperative management should be strengthened for such cases. We intend to determine in the future whether treatment outcomes are improved by screening with FlowInsight and strengthening perioperative management.

Limitations

First, this was a retrospective study involving a small patient group. A prospective study involving a large patient group is needed to validate our results. In addition, ICG videoangiography was not performed for all patients, and we excluded 2 hemispheres in which stroke developed after surgery. Because this is not a complete series of patient samples, selection bias may have occurred. Preoperative cerebrovascular reserve capacity, anatomical vascular structures around the site of the anastomosis, degree of disruption, and subtle preoperative structural changes represented by an elevated apparent diffusion coefficient may affect TNEs. We have not taken these parameters into account here. The approximate values of ΔGrad and ΔTTP calculated by FlowInsight in this study can also be measured using another company’s ICG software. Therefore, an evaluation similar to that in this study could be performed. However, ΔCBF and ΔMTT cannot be calculated using software other than FlowInsight. For reasons of availability, this method has not been widely used and is limited. The usefulness of FlowInsight analysis as a function of the presence or absence of preoperative ischemia was not investigated in this study and remains unclear. This is a subject for future examination. In addition, postoperative assessment was based on subjective symptoms. Furthermore, TNEs tend to occur more readily in adults than in children, but this study evaluated all ages because the number of cases was small. However, despite the small number of cases, even when we analyzed adults and children separately, significant correlations were found between several FlowInsight parameters and TNEs (ΔCBF [p = 0.00816] and ΔGrad [p = 0.00466] in adults; ΔMTT [p = 0.0333] in children). Accordingly, if the number of cases increases in the future, those parameters could be evaluated in detail even if patients are stratified by age.

Conclusions

In this retrospective study, the intraoperative ICG find-
ings correlated with the occurrence and duration of TNEs after revascularization surgery for MMD. FlowInsight can be used to identify patients at high risk of TNE occurrence, allowing for adjustment of perioperative treatment. Combined use of FlowInsight and SPECT may reduce postoperative complications.

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