Continuous monitoring of regional cerebral blood flow during temporary arterial occlusion in aneurysm surgery

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Object. Temporary arterial occlusion (TAO) during aneurysm surgery carries the risk of ischemic sequelae. Because monitoring of regional cerebral blood flow (rCBF) may limit neurological damage, the authors evaluated a novel thermal diffusion (TD) microprobe for use in the continuous and quantitative assessment of rCBF during TAO.

Methods. Following subcortical implantation of the device at a depth of 20 mm in the middle cerebral artery or anterior cerebral artery territory, rCBF was continuously monitored by TD microprobe (TD-rCBF) throughout surgery in 20 patients harboring anterior circulation aneurysms; 46 occlusive episodes were recorded. Postoperative radiographic evidence of new infarction was used as the threshold for failure of occlusion tolerance.

The mean subcortical TD-rCBF decreased from 27.8 ± 8.4 ml/100 g/min at baseline to 13.7 ± 11.1 ml/100 g/min (p < 0.0001) during TAO. The TD microprobe showed an immediate exponential decline of TD-rCBF on clip placement. On average, 50% of the total decrease was reached after 12 seconds, thus rapidly indicating the severity of hypoperfusion. Following clip removal, TD-rCBF returned to baseline levels after an average interval of 32 seconds, and subsequently demonstrated a transient hyperperfusion to 41.4 ± 18.3 ml/100 g/min (p < 0.001). The occurrence of postoperative infarction (15%) and the extent of postischemic hyperperfusion correlated with the depth of occlusion-induced ischemia.

Conclusions. The new TD microprobe provides a sensitive, continuous, and real-time assessment of intraoperative rCBF during TAO. Occlusion-induced ischemia is reliably detected within the 1st minute after clip application. In the future, this may enable the surgeon to alter the surgical strategy early after TAO to prevent ischemic brain injury.

KEY WORDS • cerebral blood flow • aneurysm • cerebral ischemia • thermal diffusion flowmetry • intraoperative monitoring • temporary arterial occlusion

TEMPORARY arterial occlusion of a parent vessel is an integral component of aneurysm surgery.3,31,33,38,42,43,45,47,51,52 Its use facilitates dissection and proper clipping of the aneurysm neck by reducing the pressure and the size of the lesion. Temporary occlusion, however, induces regional hypoperfusion in the corresponding vascular territory and therefore carries the risk of ischemic neurological sequelae. Whether this hypoperfusion actually causes neuronal damage and consequently neurological deficits, depends on the depth and the duration of ischemia. The reduction of rCBF resulting from TAO varies widely among patients due to individual differences in collateral circulation.45,52 Attempts to define empirically the maximal safe time limit for TAO as approximately 15 minutes33,44,47,51 have proven unsuccessful; iatrogenic ischemic damage has not been prevented using this time limit.

Although several monitoring techniques have been introduced into the operating room, no method has been proven to limit surgery-induced ischemic injury.52 Electrophysiological monitoring constitutes an accepted method for detecting cerebral ischemia during TAO.4,33,38,39,48,51 The time delay of pathological changes,3,38 the insensitivity to subcortical ischemia,2 and the anatomical limitations,38,48,51,52 however, still render the tolerance for TAO in individual patients unpredictable.4,52 Neurochemical monitoring by multisensor probes15,24,26,30,36 or by microdialysis1,29,30,37 to monitor brain tissue gases and pH has also been applied to cerebrovascular surgery. Both electrophysiological and neurochemical monitoring are used to estimate the downstream consequences of ischemia and are characterized by a variable latency in potentially detecting insufficient blood supply to the brain. Monitoring of TAO, however, requires a procedure with which to identify critical hypoperfusion rapidly, at best immediately after application of the temporary clip. This would enable the surgeon to change the surgical strategy prospectively. Therefore, several authors have attempted to quantify CBF directly in the corresponding vascular territory. Two methods primarily have been applied intraoperatively for continuous CBF monitoring: LDF12,14,17 and cortical TDF7,9,13,42,43,45 The clin-
ical use of these procedures has remained limited so far. In the case of LDF, this is because it can be used to assess CBF only by relative means. Because the reliability of the absolute CBF values has also been questioned in the case of cortical TDF, in addition to practical difficulties in its use, no sufficiently reliable monitoring technique has been discovered for TAO to date.

Recently, we have experimentally and clinically validated a novel TD microprobe for the continuous, minimally invasive, and real-time monitoring of cerebral perfusion at the bedside. This microprobe is implanted intraparenchymally and accurately assesses subcortical rCBF in absolute flow values with a high temporal sensitivity. In the present study, we further evaluate this microprobe for the continuous assessment of rCBF during TAO in aneurysm surgery.

Clinical Material and Methods

Patient Population

This study was approved by the local research ethics committee. A total of 20 patients older than 18 years of age who had an intracranial aneurysm were enrolled in the study. The aneurysms were all located in the anterior cerebral circulation and they were judged preoperatively to be likely to require TAO due to the angiographically observed size or morphological features of the lesions. Nineteen patients suffered an SAH and one patient presented with an unruptured aneurysm. Fifteen patients underwent surgery within 72 hours of SAH, whereas in four surgery was delayed due to late referral.

Surgical Protocol

The management of the patients followed a standardized protocol. Aneurysm clipping was performed after induction of anesthesia with propofol and fentanyl, in conjunction with atracurium-induced muscle relaxation. All patients received a bolus of 250 ml mannitol immediately before the craniotomy and were maintained in a normothermic and normotensive state throughout surgery. A standard pterional approach was used. Cerebrospinal fluid was drained through a ventriculostomy catheter in patients with high-grade SAH.

Proximal TAO was used in 18 patients based on the necessity judged intraoperatively by the surgeon. Occlusion was achieved by placement of a Yaşargil temporary titanium clip (Aesculap, Tuttingen, Germany) on the parent artery. If prolonged TAO was anticipated, the inspired oxygen fraction was elevated to 100% before application of the temporary clip.

Probe Implantation

The TD microprobe (diameter 0.9 mm: QFLOW200 Perfusion Monitoring System; Thermal Technologies, Inc., Cambridge, MA) was inserted through either the pterional craniotomy or a one-way bolt (DID Medical, Simbach am Inn, Germany) that had been implanted through a separate 3.2-mm coronal burr hole. The probe was placed subcortically at a depth of 20 mm, and was secured either by fixing it at the rim of the craniotomy or by tightening the bolt. The implantation site of the bolt was chosen according to the vascular territory of interest parasagittally, either 2 cm lateral to the midline for aneurysms of the ACA or 6 cm lateral to the midline for aneurysms of the MCA or ICA.

Thermal Diffusion Flowmetry

Quantification of tissue perfusion by TD microprobe relies on the tissue’s ability to transport heat, which can be divided into the intrinsic conductive properties of the tissue and the convective effects caused by tissue blood flow. The characteristics of the TD microprobe used in this study have been described in detail previously. Because calibration algorithms determine the individual conductivity constant of the monitored tissue, the TD microprobe reliably yields the tissue perfusion values in milliliters per 100 grams per minute at a sampling rate of 1 Hz. The calibration procedure is conducted before each measurement phase and it takes approximately 2 minutes before reliable continuous TD-rCBF values are obtained. A system version without correction algorithms for temperature variations occurring after the calibration period was used to avoid an adverse effect of intraoperative temperature changes on the accuracy of TD microprobe rCBF monitoring.

Measurement Protocol

After dural opening, the TD-rCBF was continuously monitored throughout the surgical procedure. Previous studies have shown that no equilibration phase is needed. Monitoring was only interrupted by calibration at 30-minute intervals, except during TAO, and in cases of temperature fluctuations, to ensure reliable absolute values.

Postoperative Evaluation

Postoperatively, a CT scan was obtained in all patients 24 hours after surgery, with at least one additional scan performed thereafter, depending on the patients’ clinical course. The primary parameter of outcome evaluated in our study was the development of any new hypodensity in the vascular territory supplied by the temporarily occluded artery. This radiographic evidence of cerebral infarction was used as the threshold for failure of occlusion tolerance, regardless of its correlation with neurological deficits. Cerebral angiography was routinely performed postoperatively to check on occlusion of the aneurysm and to rule out accidental permanent vessel occlusion.

Data Handling and Statistical Analysis

Physiological parameters, arterial blood gases, and TD-rCBF values are given as the means ± SD. The rCBF measured using the TD microprobe is expressed in absolute flow values (milliliters per 100 grams per minute).

Data summed for the 2-minute period immediately before clip placement (baseline) were compared with the lowest value during TAO and the highest value during posts ischemic reperfusion (hyperperfusion), and data were summed for the subsequent 2-minute period starting 200 seconds after clip release (post-TAO). To identify possibly deleterious and thus clinically relevant occlusion-induced hypoperfusion, the reduction of TD-rCBF to less than 50% of baseline was defined as potentially indicating sig-
significant ischemia. With no previous data on intraoperative subcortical rCBF, this threshold was chosen because less marked hypoperfusion should be safely tolerated. For statistical analysis, the occlusive episodes were therefore grouped into two categories, as follows: decrease of average TD-rCBF during TAO to more than 50% of baseline (Group I: nonischemic), and decrease of average TD-rCBF during TAO to less than 50% of baseline (Group II: ischemic).

For intraoperative monitoring to influence the surgical strategy prospectively, the information on vascular compromise has to be available early after clip application. Therefore, to illustrate the response time of the TD microprobe to TAO, the TD-measured decrease in rCBF caused by clip application and the TD-measured increase in rCBF following clip removal are expressed as percentages of the total decline (baseline - minimum TD-rCBF during TAO). Episodes lacking a significant decline in TD-rCBF (decrease of average TD-rCBF during TAO by < 10% of baseline) were excluded from this analysis.

For statistical comparison of occlusive episodes, compromise of brain perfusion during TAO had to be objectively quantified. Because the extent of ischemia is indirectly proportional to rCBF and directly proportional to the duration of ischemia, a hypoperfusion index was calculated for each occlusive episode as follows: hypoperfusion index = 1/TD-rCBF * time (g * min²/ml).

Comparisons of independent and dependent variables were tested using the unpaired and paired Student t-tests, respectively. Correlations were assessed using univariate linear regression analysis. Probability values less than 0.05 and 0.01 were considered to be significant and highly significant, respectively.

Results

Forty-six occlusive episodes were monitored in 18 patients. In two patients TAO was not considered necessary by the surgeon. The mean duration of TAO was 5.6 ± 7.2 minutes. Total occlusion time per patient was 12.9 ± 12.9 minutes and correlated with the size of the aneurysm (r = 0.55, p = 0.02). Patient characteristics are summarized in Table 1. The mean arterial blood pressure was kept above 80 mm Hg in all patients and arterial blood gases were within physiological limits, except for the hyperoxygenation induced in several cases (Table 2). In 17 patients—13 with aneurysms of the MCA, two with lesions in the ICA, and two with posterior communicating artery aneurysms—the probe was implanted through a bolt or craniotomy in the MCA territory. Measurements were obtained through the bolt in the ACA territory in three patients who harbored aneurysms of the ACoA (Table 3).

Probe Implantation and Data Quality

Probe-related complications after implantation, such as intracerebral hemorrhage, were not observed. Probe dislocation requiring repositioning occurred at the beginning of our series due to inappropriate fixation of the probe at the rim of the craniotomy in two patients monitored via the surgical approach. The TD readings for rCBF after implantation were stable and reliable, with a mean value of 28.4 ± 8.4 ml/100 g/min. Because surgical manipulations were found to influence TD-rCBF, we attempted to keep brain retraction unaltered during TAO. The hypoperfusion phase following clip application could be monitored reliably in all cases. Irrigation, however, caused a marked temperature variation at the end of three occlusive episodes, requiring a 2-minute recalibration. Therefore, the reperfusion phase could not be monitored in these instances.

Illustrative Case

This 58-year-old man suffered an SAH (Hunt & Hess 28)

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**Table 1**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (range)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (yrs)</td>
<td>55 ± 10 (32–73)</td>
</tr>
<tr>
<td>female/male</td>
<td>13:7</td>
</tr>
<tr>
<td>aneurysm size (mm)</td>
<td>8.8 ± 4.5 (4–20)</td>
</tr>
<tr>
<td>unruptured status</td>
<td>5% (1 of 20)</td>
</tr>
<tr>
<td>multiple aneurysms</td>
<td>15% (3 of 20)</td>
</tr>
<tr>
<td>no. of occlusive episodes</td>
<td>2.3 ± 1.6 (0–5)</td>
</tr>
<tr>
<td>occlusion time (mins)</td>
<td>5.6 ± 7.2 (0.5–29.4)</td>
</tr>
<tr>
<td>total occlusion time (mins)</td>
<td>12.9 ± 12.9 (0–46.2)</td>
</tr>
<tr>
<td>duration of surgery (mins)</td>
<td>178 ± 50 (85–295)</td>
</tr>
<tr>
<td>timing of surgery (hrs post-SAH)</td>
<td>80 ± 104 (8–336)</td>
</tr>
<tr>
<td>SAH grade†</td>
<td>5% (1 of 20)</td>
</tr>
<tr>
<td>0</td>
<td>5% (1 of 20)</td>
</tr>
<tr>
<td>I</td>
<td>40% (8 of 20)</td>
</tr>
<tr>
<td>II</td>
<td>25% (5 of 20)</td>
</tr>
<tr>
<td>III</td>
<td>25% (5 of 20)</td>
</tr>
<tr>
<td>IV</td>
<td>15% (3 of 20)</td>
</tr>
<tr>
<td>Fisher grade</td>
<td>5% (1 of 20)</td>
</tr>
<tr>
<td>1</td>
<td>35% (7 of 20)</td>
</tr>
<tr>
<td>2</td>
<td>45% (9 of 20)</td>
</tr>
<tr>
<td>3</td>
<td>45% (9 of 20)</td>
</tr>
<tr>
<td>4</td>
<td>45% (9 of 20)</td>
</tr>
</tbody>
</table>

* Values other than percentages are expressed as the means ± SD.
† According to the Hunt and Hess scale.

**Table 2**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (range)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MABP (mm Hg)</td>
<td>93.1 ± 6.7 (81.3–103.3)</td>
</tr>
<tr>
<td>arterial pH</td>
<td>7.42 ± 0.04 (7.29–7.48)</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>37.5 ± 2.7 (34.3–43.0)</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>209.3 ± 95.2 (82.0–415.8)</td>
</tr>
<tr>
<td>inspired O₂ fraction</td>
<td>0.70 ± 0.25 (0.4–1.0)</td>
</tr>
</tbody>
</table>

* Values are expressed as the means ± SD.)

**Table 3**

<table>
<thead>
<tr>
<th>Aneurysm Location</th>
<th>Measurement Site</th>
<th>No. of Patients</th>
<th>No. of Occlusive Episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACoA</td>
<td>ACA</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>MCA</td>
<td>MCA</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>ICA</td>
<td>MCA</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>PCoA</td>
<td>MCA</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>total</td>
<td></td>
<td>20</td>
<td>17</td>
</tr>
</tbody>
</table>

* NA = not applicable; PCoA = posterior communicating artery.
Cerebral blood flow monitoring during temporary arterial occlusion

Grade IV, Fisher Grade 3) from a small (4-mm) aneurysm of the ACoA. Following CT scanning to establish the diagnosis, the patient was referred to our department 23 hours after the insult. After ventriculostomy catheter placement and cerebral panangiography, surgery was performed 38 hours posthemorrhage via a right-sided pterional approach. After draping, the TD microprobe was implanted subcortically in the right parasagittal frontal lobe through a coronal bolt. The TD-rCBF was monitored throughout the surgery in the ACA territory. During dissection of the aneurysm neck, the ICA and the bilateral A1 segments were temporarily occluded for 31 and 278 seconds, respectively. Figure 1 depicts the original recording. Contralateral A1 occlusion did not cause significant hypoperfusion.

Measurement of rCBF With TD During TAO

The mean subcortical TD-rCBF decreased exponentially, from 27.8 ± 8.4 ml/100 g/min at baseline to a mean of 16.4 ± 11 ml/100 g/min during TAO (−42 ± 32.5%, p < 0.0001). The lowest TD-rCBF value, 13.7 ± 11.1 ml/100 g/min (−51.9 ± 33.6%, p < 0.0001), was mostly observed just before clip release. Following reopening of the artery, TD-rCBF demonstrated a transient hyperperfusion, to 41.4 ± 18.3 ml/100 g/min (51.2 ± 68.5%, p < 0.001) before reaching a plateau of 34.6 ± 11.4 ml/100 g/min (24.5 ± 41%, p < 0.001; Fig. 2).

Dynamics of TD-rCBF Changes

Intraparenchymal TDF indicated an immediate decline of TD-rCBF within seconds after TAO. On average, 12 seconds after clip application, 50% of the total decline was reached (Fig. 3A). Following clip release, a comparably rapid recovery of TD-rCBF was observed during reperfusion. Preocclusion levels were passed after an average interval of 32 seconds. Marked differences in the time delay to maximum hyperperfusion, however, caused a pronounced variability, as indicated by the high SDs in Fig. 3B.

Extent of Ischemia

The extent of ischemia was highly variable. The TD-rCBF did not fall below an average of 90% of baseline during TAO, indicating a lack of significant hypoperfusion in 12 episodes (26%). These 12, in addition to 18 episodes (39%) that showed a decrease of TD-rCBF to a level between 50% and 90% of baseline, were classified as nonischemic (Group I). Sixteen episodes (35%) caused marked hyperperfusion by decreasing to less than 50% of baseline, and were thus classified as ischemic (Group II). Forty seconds after clip application, TD-rCBF had decreased to less than 50% of baseline in 15 of 16 ischemic episodes. Consequently, an ischemic episode was already correctly classified within the 1st minute of TAO in 94% of cases. The TD-rCBF value 1 minute after clip placement was tightly correlated with the minimum TD-rCBF value during TAO, indicating a lack of significant hypoperfusion early during TAO.

Induced TAO in Group II was followed by a rapid hyperperfusion to a maximum of 55.3 ± 22.1 ml/100 g/min (114.6 ± 93%, p < 0.001 compared with baseline), which was reached after 128 ± 94 seconds. In Group I, only mild hyperperfusion to a maximum value of 35.5 ± 12.9 ml/100 g/min (24.4 ± 28.1%) was present after a time interval of 133 ± 98 seconds (p < 0.001 compared with baseline, p < 0.0001 compared with Group II). In Fig. 5 we compare both the time course and the maximum value of TD-rCBF between the groups after clip release. The degree of hyperperfusion correlated with the severity of the preceding occlusion-induced hypoperfusion (maximum TD-rCBF after TAO compared with minimum TD-rCBF during TAO: r = 0.62; p < 0.0001).

Comparison of patient characteristics between the two groups revealed a significantly older population in Group II (p < 0.05); however, there were no significant differences concerning timing of surgery, SAH grade, occlusion time, or other parameters (Table 4).

Outcome of TAO

New areas of hypodensity were present on postoperative CT scans in three patients (15%). One of these har
bored an ICA aneurysm, and TAO of the ICA for 14 minutes and 38 seconds at a mean TD-rCBF of 0.6 ml/100 g/min was obviously responsible for a complete infarction of the MCA territory. The other two patients underwent surgery for MCA aneurysms; TAO of the ICA (four episodes) resulted in only mild hypoperfusion. The most relevant episodes of MCA occlusion according to degree and duration of hypoperfusion, however, showed a marked reduction of mean TD-rCBF to 0.5 ml/100 g/min for 13 minutes and 58 seconds, and to 3.7 ml/100 g/min for 27 minutes and 44 seconds. Small infarcts were located in the dorsal part of the internal capsule and in the angular region with subcortical involvement. Projection of the microprobe’s implantation site on the postoperative CT scans revealed that the probe had not been positioned within these two infarcted regions, but next to them at a distance of approximately 2 cm. Graphic presentation of the relationship among the mean TD-rCBF during TAO, occlusion time, and postoperative evidence of infarction illustrates the dependence of irreversible ischemic injury on the duration and depth of ischemia (Fig. 6).

The hypoperfusion index of all occlusive episodes amounted to 186 /5.10^{-6} 540 g * min^{-2}/ml. In patients with multiple occlusive events, the episode yielding the highest hypoperfusion index was correlated with outcome; the other episodes caused only minimal hypoperfusion in our series (17 ± 22 g * min^{-2}/ml) and thus were not considered clinically relevant. Analysis of the data revealed a hypoperfusion index of 145 ± 168 g * min^{-2}/ml (range 5–557 g * min^{-2}/ml) in patients without changes demonstrated on CT scans and of 1971 ± 1083 g * min^{-2}/ml (range 747–2803 g * min^{-2}/ml) in patients with a new hypodensity on CT scans (p < 0.0001; Fig. 7). This indicates an ischemic threshold for TAO of approximately 600 g * min^{-2}/ml.

**Occluded Artery**

The depth of ischemia was most variable during TAO of the ICA. No significant decrease of TD-rCBF (< 10% of baseline) could be detected in seven occlusive episodes of the ICA, whereas seven episodes were classified as ischemic. Only three episodes showed moderate hypoperfusion (TD-rCBF 50–90% of baseline). A TAO of the
ACA did not cause hypoperfusion levels of less than 10 ml/100 g/min in our series, even though the occlusion time was significantly prolonged in aneurysm surgery of the ACA complex \((p < 0.05)\). No further differences were present, however, in operative features and TD-rCBF among the different occluded arteries (Table 5).

Statistical analysis revealed no significant difference in occlusion-induced changes with respect to early compared with late surgery, SAH grade according to the Hunt & Hess scale, Fisher grade, probe implantation in the ACA compared with the MCA territory, or sex of the patient.

**Discussion**

In our study, a novel TD-based microprobe was prospectively evaluated for use in the assessment of subcortical rCBF during TAO in aneurysm surgery. Cerebral perfusion was continuously monitored in absolute flow values reliably in all occlusive episodes, thus yielding the exact time course of TD-rCBF during hypoperfusion and reperfusion in a series of temporary occlusions. The probe’s high temporal sensitivity at a sampling rate of 1 Hz allowed identification of potentially ischemic episodes of TAO within the 1st minute after clip placement. Occlusion-induced reduction of TD-rCBF demonstrated a clear relationship to the occurrence of postoperative infarction.

**Temporary Arterial Occlusion**

Temporary occlusion of the parent artery is being used with increasing frequency in the management of intracranial aneurysms.\(^{44-47}\) Attempts to define clinically the safe limits of occlusion time have failed to limit ischemic injury due to the vast individual variability of collateral circulation and the variety of surgical protocols used for brain protection. Samson, et al.,\(^{47}\) and Lavine, et al.,\(^{33}\) demonstrated that patients routinely tolerated 14 and 13.6 minutes of TAO, respectively. For the MCA, maximum occlusion times of 8,\(^{11,15}\) 10,\(^{15,20}\) 20,\(^{34,43,45}\) as well as 40 minutes\(^{41}\) have been reported. These impressive differences are even more pronounced for different cerebral arteries.\(^{11,31,33,45,47,52}\) In short, a surgeon still has no means to predict which patient is going to tolerate occlusion of a basal artery.\(^{47}\) Regardless of this situation, some authors advocate a safely tolerated occlusion interval of 15 minutes.\(^{33,44,47}\) Several investigators have attempted additionally to consider other potentially important factors, like age, SAH grade, or timing of surgery, that may play a role in the conversion of transient iatrogenic ischemia to permanent infarction.\(^{34,47}\)

Using current protocols, the infarction rate varies, with a mean of 15 to 20%.\(^{3,11,33,44,47,52}\) Regardless of recent advances in cerebrovascular surgery, there is a need to increase the safety of TAO.

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**TABLE 4**

Comparison of characteristics of patients with nonischemic and ischemic occlusive episodes*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nonischemic (Group I)</th>
<th>Ischemic (Group II)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of occlusive episodes</td>
<td>30</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>age (yrs)</td>
<td>52.1 ± 10.3</td>
<td>58.9 ± 9.8</td>
<td>0.037</td>
</tr>
<tr>
<td>timing of surgery (hrs post-SAH)</td>
<td>83.3 ± 96.1</td>
<td>61.4 ± 72.7</td>
<td>0.471</td>
</tr>
<tr>
<td>Hunt &amp; Hess grade</td>
<td>2.7 ± 1.0</td>
<td>2.8 ± 1.3</td>
<td>0.651</td>
</tr>
<tr>
<td>occlusion time (mins)</td>
<td>4.7 ± 7.0</td>
<td>7.7 ± 7.3</td>
<td>0.174</td>
</tr>
</tbody>
</table>

* Patients were classified into Group I or II according to the severity of occlusion-induced hypoperfusion. Reduction of the mean TD-rCBF to less than 50% of baseline was defined as a potentially ischemic episode.

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**Fig. 6.** Scatterplot showing the relationship among mean residual TD-rCBF during TAO, occlusion time, and postoperative evidence of infarction. Occlusive episodes in patients with no changes demonstrated on CT scans (open circles) are compared with occlusive episodes in patients with radiological evidence of infarction (filled circles). Two patients harboring MCA aneurysms demonstrated postoperative infarction: TAO of the ICA did not cause significant hypoperfusion in these cases (short arrows). Each of the three patients with postoperative evidence of infarction had suffered one long-lasting and severely ischemic occlusive episode (long arrows). According to these data, the degree of hypoperfusion and its duration determine the occurrence of irreversible ischemic injury.

**Fig. 7.** Scatterplot showing a comparison of hypoperfusion index between patients without changes (open circles) and patients with new hypodensities (filled circles) on postoperative CT scans. The hypoperfusion index was defined for occlusive episodes as the product of the occlusion time and the reciprocal of TD-rCBF, attempting a quantification of ischemia. In patients with multiple occlusive episodes, the episode yielding the highest hypoperfusion index was used for this outcome analysis.
Monitoring Techniques During TAO

Electrophysiological Monitoring. Because a failure of electrical activity precedes the deterioration of ionic homeostasis, electrophysiological monitoring, for example, of SSEPs, can potentially detect insufficient blood supply to the brain tissue, and thus constitutes an accepted method of intraoperative monitoring.2,3,8,39,46,48,51,52 The information derived from SSEP monitoring, however, is restricted to the functional status of the tissue, so that conclusions concerning the integrity and viability of the cells cannot be reliably drawn.52 Importantly, the application of the technique is limited to defined brain regions.38,46,51,52 In a recent article, Holland27 doubted the usefulness of SSEP monitoring during TAO because of its insensitivity for the detection of subcortical ischemia. In addition to the non-specific indication of cerebral ischemia, changes in SSEPs can alert the surgeon after a significant time delay of several minutes following temporary clip application.3,38,39,46,51,52 The information on the rapid dynamics of changes caused by TAO has precluded its clinical use.4 The same is true for the intraoperative application of ultrasonic19,23 or electromagnetic41 flow probes, as well as imaging methods like single-photon emission CT.35 In fact, TDF is currently the only procedure that allows a continuous and quantitative assessment of regional tissue perfusion.32 Carter and Atkinson3 were the first investigators to present quantitative rCBF data obtained with a cortical thermal sensor. Modifications of this flow probe have been applied both intraoperatively6,9,13,22,42,43,45,53 and chronically10,12,20,32,49,50 in neurosurgical patients. The probe can be positioned on the cortical surface via the surgical approach, thus enabling assessment of cortical CBF without invading the brain tissue. Ogawa, et al.,43 reported a relationship between CBF and electroencephalographic changes, as well as a correlation between the postoperative neurological deficit and the degree and duration of residual CBF during TAO. Several intraoperative registrations of cortical CBF have demonstrated the capability of this method to detect rapid changes in cerebral perfusion.7,9,22,42,45 A statistical analysis of the time course of CBF during a series of temporary occlusions, however, is still lacking. Additionally, the reliability of the absolute values of cortical TDF has been questioned,30,42,49 so that some investigators only used relative CBF data.15,42 Other disadvantages of cortical TDF monitoring of TAO include the potential loss of direct cortical contact due to surgical maneuvers or release of cerebrospinal fluid, the instability of the thermal field as a result of contact with air or irrigation fluid, and the accessibility of regions distant to the craniotomy (for example, the ACA territory).12 For the aforementioned reasons, Ogata, et al.,42 could obtain valid data in only half of their patients. Even though these difficulties may be less significant in experienced hands, they have so far precluded the method from being used in routine clinical practice.

Monitoring of CBF With the Novel TD Microprobe

Our study demonstrated that the novel TD microprobe reliably measured subcortical rCBF intraoperatively in both the MCA and ACA territories during TAO. The probe allows for continuous, minimally invasive, and real-time assessment of cerebral perfusion in absolute flow values. The method’s high temporal sensitivity has been evaluated experimentally by comparing it with LDF during a series of standardized CBF variations.34 Previously, our group has validated the subcortical TD-rCBF val-
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ues obtained in patients in the intensive care unit (34.8 ± 9.8 ml/100 g/min) by using the stable xenon-CT procedure. The baseline levels of 28.4 ± 8.4 ml/100 g/min in the operating room correspond well to the data obtained in the intensive care unit, if depth of anesthesia and surgical manipulations, for example brain retraction, are taken into account. Introduction of the probe into routine intraoperative monitoring should be practicable, because its diameter of less than 1 mm is comparable with other minimally invasive microprobes already used in a clinical setting, such as intraparenchymal intracranial pressure sensors, tissue O2 sensors, or microdialysis catheters. Like these, the microprobe can be implanted into the parenchyma at any depth and can thus assess rCBF in either white, mixed subcortical, or deep gray matter. Compared with epicortical TDF monitoring, the intraparenchymal placement ensures a more stable thermal environment and avoids failure caused by loss of direct cortical contact.

Limitations of the Procedure

This procedure is not suitable for reliable assessment of CBF in cortical gray matter. Like other intraparenchymal monitoring devices, the microprobe invades the brain tissue to a minimal extent, thus potentially causing tissue damage. Fluctuations of the thermal field constitute a significant problem for TDF. Even though intraparenchymal placement minimizes the method’s susceptibility to external temperature variations, reperfusion could not be monitored in three episodes in our series. Recalibration also had to be performed in several instances because of surgical maneuvers or irrigation not coinciding with TAO. One important concern associated with intraoperative monitoring with this procedure is the need not to use correction algorithms for temperature fluctuations. This is especially important because such algorithms are incorporated into updated versions of the device and sensitively take fluctuations in the thermal microenvironment into account to ensure maximum data quality at the bedside. Intraoperatively, however, temperature variability can be significant due to the open skull, irrigation, or surgical manipulation, so that the correction algorithms meant for bedside use are not optimal.

Dynamics of TD-rCBF Changes

In our series, changes in TD-rCBF were rapidly detected because of the high temporal sensitivity of the method. A rather precise estimation of the depth of ischemia was possible within the 1st minute after clip application, in contrast with data obtained by electrophysiological or neurochemical monitoring. Based on the results of this evaluation study, future use of the TD microprobe could alter the surgical strategy early during TAO. Its use can also provide guidance for positioning of the permanent aneurysm clip. In three patients in our series, reduced TD-rCBF after clipping of the aneurysm neck indicated vascular compromise of the parent artery. Normal perfusion was quickly restored by repositioning the clip.

Deep White Matter and Perforating Vessel Ischemia

In previous studies it has been suggested that perforating branches of major arteries may be highly sensitive to the effects of TAO, because as many as 50% of postoperative hypodensities on CT scans from TAO were located in the distribution of perforating arteries. This vulnerability of brain regions supplied by perforating vessels has been attributed to a very poor collateral blood supply, which is supported by experimental data demonstrating ischemic lesions predominantly in the subcortical structures after proximal MCA occlusion in rabbits. In aneurysm surgery, however, these low-density lesions could also be related to permanent injury to a perforating vessel. In our series, one infarct was located in the deep white matter in the territory of a lenticulostriate artery. Because surgical manipulation in this patient, who had an aneurysm of the MCA bifurcation, did not involve the proximal M1 segment except for positioning the temporary clip, permanent occlusion of the perforating vessel seems unlikely.

It is questionable whether focal assessment of subcortical CBF sufficiently detects deep white matter ischemia. Although the microprobe was not located exactly in the infarcted area, severe hypoperfusion was detected during TAO in one case of deep white matter infarction. According to single-photon emission CT data, TAO results in hypoperfusion of the entire corresponding vascular territory. Therefore, subcortical ischemia may reliably coincide with deep white matter ischemia during TAO.

Extent of Ischemia and Outcome

The occlusive episodes were classified according to the severity of hypoperfusion. A threshold level of 50% of baseline, which amounted to approximately 14 ml/100 g/min, was chosen to distinguish between potentially clinically relevant episodes and those that presumably are safe. Previous studies of CBF in gray matter have shown loss of neuronal function at approximately 20 ml/100 g/min and failure of neuronal metabolism and integrity at approximately 10 ml/100 g/min. For subcortical measurements, as in our series, lower thresholds have to be assumed.

The effects of TAO are known to be highly variable, which is supported by our data. Because most variability was seen in cases of ICA occlusion and no profound ischemia could be detected during ACA occlusion, this is most likely due to individual variations in collateral circulation. A reduction of collateral blood flow with increasing age, possibly as a result of progressive arteriosclerosis, may account for the significantly older population in Group II (patients with ischemic episodes). Not surprisingly, occlusion-induced ischemia correlated with reactive hyperemia, which is in accordance with experimental data.

Radiographic assessment of outcome revealed infarcts in three patients, which correlated with the depth and duration of residual TD-rCBF. Interestingly, two of these three patients had undergone occlusion durations of less than 15 minutes. A very preliminary threshold for irreversible ischemic injury can be drawn from our data, and a much larger data pool will be needed to validate and refine these results.

Conclusions

A novel, previously validated TD microprobe was pro-
spectively evaluated for use in the assessment of rCBF during TAO in aneurysm surgery. This method appears to detect occlusion-induced ischemia reliably within the 1st minute after clip application, thus enabling the surgeon to alter surgical strategy early after temporary occlusion. This contrasts with other monitoring procedures, which are tainted with a marked delay in indicating ischemia. Further studies are needed to refine the ischemic thresholds of subcortical TD-rCBF in aneurysm surgery.

Disclosure
None of the authors has a financial interest in the TD microprobe or Thermal Technologies, Inc.

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