Rationale for graft selection in patients with complex internal carotid artery aneurysms treated with extracranial to intracranial high-flow bypass and therapeutic internal carotid artery occlusion

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OBJECTIVE After internal carotid artery (ICA) sacrifice without revascularization for complex aneurysms, ischemic complications can occur. In addition, hemodynamic alterations in the circle of Willis create conditions conducive to the formation of de novo aneurysms or the enlargement of existing untreated aneurysms. Therefore, the revascularization technique remains indispensable. Because vessel sizes and the development of collateral circulation are different in each patient, the ideal graft size to prevent low flow–related ischemic complications (LRICs) in external carotid artery (ECA)–middle cerebral artery (MCA) bypass with therapeutic ICA occlusion (ICAO) has not been well established. Authors of this study hypothesized that the adequate graft size could be calculated from the size of the sacrificed ICA and the values of MCA pressure (MCAP) and undertook an investigation in patients with complex ICA aneurysms treated with ECA-graft-MCA bypass and therapeutic ICAO.

METHODS In the period between July 2006 and January 2016, 80 patients with complex ICA aneurysms were treated with ECA-MCA bypass and therapeutic ICAO. Preoperative balloon test occlusion (BTO) was performed, and the BTO pressure ratio was defined as the mean stump pressure/mean preocclusion pressure. Low flow–related ischemic complications were defined as new postoperative neurological deficits and ipsilateral cerebral blood flow reduction. Initial MCAP (iMCAP), MCAP after clamping the ICA (cMCAP), and MCAP after releasing the graft (gMCAP) were intraoperatively monitored. The MCAP ratio was defined as gMCAP/iMCAP. Based on the Hagen-Poiseuille law, the expected MCAP ratio ([expected gMCAP]/iMCAP) was hypothesized as follows: (1 – cMCAP/iMCAP)(graft radius/ICA radius)² + (cMCAP/iMCAP). Correlations between the BTO pressure ratio and cMCAP/iMCAP, and between the actual and expected MCAP ratios, were evaluated. Risk factors for LRICs were also evaluated.

RESULTS The mean BTO pressure ratio was significantly correlated with the mean cMCAP/iMCAP (r = 0.68, p < 0.0001). The actual MCAP ratio correlated with the expected MCAP ratio (r = 0.43, p < 0.0001). If the expected MCAP ratio was set up using the BTO pressure ratio instead of cMCAP/iMCAP (BTO-expected MCAP ratio), the mean BTO-expected MCAP ratio significantly correlated with the expected MCAP ratio (r = 0.95, p < 0.0001). During a median follow-up period of 26.1 months, LRICs were observed in 9 patients (11%). An actual MCAP ratio < 0.80 (p = 0.003), expected MCAP ratio < 0.80 (p = 0.001), and (M² / radius)² < 0.49 (p = 0.002) were related to LRICs according to the Cox proportional-hazards model.

CONCLUSIONS Data in the present study indicated that it was important to use an adequate graft to achieve a sufficient MCAP ratio in order to avoid LRICs and that the adequate graft size could be evaluated based on a formula in patients with complex ICA aneurysms treated with ICAO.

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KEY WORDS complex aneurysm; formula; high-flow bypass; selection of the graft; vascular disorders
Treatment for complex internal carotid artery (ICA) aneurysms often requires permanent ICA occlusion (ICA0). Although most patients tolerate the loss of one ICA just after the operation, a significant percentage suffer either immediate or delayed neurological deficits related to poor collateral circulation. Preoperative balloon test occlusion (BTO) of the ICA is frequently performed to simulate the ischemic condition caused by ICAO; however, the test can sometimes produce false-negative findings, and ischemic surgical complications can subsequently develop. In fact, delayed ischemic complications can occur in 10% of patients who pass the BTO with hypotensive challenge. In addition, after ICAO without revascularization, hemodynamic alterations will occur in the circle of Willis with increased flow over the contralateral ICA. These hemodynamic changes create conditions conducive to the formation of de novo aneurysms or the enlargement of existing untreated aneurysms, exposing the patient to a risk of subarachnoid hemorrhage. Therefore, physicians implement cerebral revascularization strategies using the external carotid artery (ECA)-graft–middle cerebral artery (MCA) bypass when therapeutic ICAO is needed.

Because the vessel size of the sacrificed ICA and the development of collateral circulation are different in each patient, the ideal graft size to prevent low-flow–related ischemic complications (LRICs) in ECA-MCA bypass has not been well established. Our recent studies have shown that intraoperative MCA pressure (MCAP) can be used as a surrogate measure of regional cerebral perfusion pressure and that MCAPs have an impact on LRICs in complex ICA aneurysms treated with ECA-graft-MCA bypass and therapeutic ICAO.

We hypothesized that an adequate graft size could be calculated from the size of the sacrificed ICA and the MCAP values. This is the first study to investigate adequate graft size in patients with complex ICA aneurysms treated using the ECA-graft-MCA bypass and therapeutic ICAO.

Methods

This study is reported based on criteria from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. The study protocol was approved by our institutional ethics committees. Between July 2006 and January 2016, 81 patients underwent ECA-graft-MCA bypass with therapeutic ICAO for complex ICA aneurysms at our institutions. One patient was excluded because the MCAP could not be monitored. Thus, 80 patients participated in the present study. Collected data included age, sex, smoking history, past medical history (hypertension, hypercholesterolemia, and diabetes mellitus), preoperative symptoms, size of aneurysm, aneurysm location, operative side, thrombosis or calcification of aneurysm, vessel diameters, intraoperative MCAPs (initial, after ICAO, and after release of the graft bypass), graft type, temporary occlusion time during bypasses, postoperative diffusion-weighted imaging (DWI) findings, aneurysm recurrence, follow-up period, graft patency, and outcome. Taking into account back flow from the posterior communicating artery, the radius of the C2 portion of the ICA, which was proximal to the posterior communicating artery, was measured as the radius of the ICA. An Allen test was performed to confirm an intact palmar arch and adequate hand perfusion despite occlusion of the radial artery (RA). If an Allen test was negative, the saphenous vein (SV) was chosen as the high-flow graft.

Balloon Test Occlusion

After placing the patient in a biplane digital subtraction angiography scanner, we administered 5000 IU of intravenous heparin. A 6-Fr Flexor Shuttle guiding sheath (Cook Medical) and a 5.2-Fr Selecon MP balloon catheter (Terumo) were introduced in a coaxial fashion. To temporarily occlude the ICA, the balloon, which was positioned in the ICA between the artery’s origin and the first vertebral level, was gently inflated. Stump pressure was monitored, with an abrupt decrease in pressure signaling that occlusion was complete and that balloon inflation should stop. By injecting contrast medium through the guiding sheath, we confirmed occlusion. If any change in neurological status occurred, the balloon was immediately deflated and the procedure terminated. The BTO pressure ratio was defined as the mean stump pressure divided by the mean preocclusion pressure. To correct for the difference in systemic blood pressure, each pressure reading was divided by the mean systemic blood pressure measured before or during balloon occlusion.

Indication and Surgical Technique

The ECA-graft-MCA bypass with therapeutic ICAO was performed for complex ICA aneurysms with the following indications: aneurysms with a large and complex neck not suitable for clip reconstruction, blister aneurysms, dissecting aneurysms, aneurysms with an origin of branch vessel(s) from the aneurysm sac, calcification or atherosclerotic changes of the aneurysm neck, extensive thrombosis inside the aneurysm, and recurrent aneurysms that had failed endovascular or microsurgical treatment. The superficial temporal artery (STA)-MCA bypass was performed prior to the graft-MCA anastomosis to supply blood flow to the MCA territory during graft-MCA anastomosis as a protective bypass (although whether this bypass is also protective against the LRICs is unknown). The STA-MCA bypass was performed not only as a backup for clamping the graft-MCA anastomosis, but also as a means of monitoring the MCAPs. Continuous MCAP monitoring through this bypass was useful to check the patency of the graft after therapeutic ICAO.

The operative techniques for ECA-graft-MCA and STA-MCA bypasses and MCAP monitoring were recently published. The initial MCAP (iMCAP), MCAP after temporarily clamping the ICA (eMCAP), and MCAP after releasing the graft bypass (gMCAP) were monitored (Fig. 1). The MCAP ratio was defined as gMCAP divided by iMCAP. In calculating the actual MCAP ratio, each MCAP was divided by the mean systemic blood pressure measured at each MCAP reading to adjust for the difference in systemic blood pressure. After ECA-graft-MCA bypass was performed, the graft mean blood...
flow (ml/min) was measured using surgical flowmeters (Transonic Systems).

Expected MCAP Ratio

The senior author (R. Tanikawa) hypothesized that the cerebral blood flow rate is proportional to the square of the vessel radius per Hagen-Poiseuille’s law ($Q = \pi r^2 v$), where $Q$ is the volume flow rate, $r$ is the vessel radius, and $v$ is the average flow velocity. If velocity in both the ICA and the graft is the same, the expected gMCAP would be expressed as follows:

$$\text{Expected gMCAP} = \text{pressure by ICA blood flow} \times \left(\frac{r_{\text{graft}}}{r_{\text{ICA}}}\right)^2 + \text{pressure by total collateral flow}$$

where pressure by ICA blood flow = iMCAP – cMCAP and pressure by total collateral flow = cMCAP. Therefore, expected gMCAP

$$= (i\text{MCAP} - c\text{MCAP}) \left(\frac{r_{\text{graft}}}{r_{\text{ICA}}}\right)^2 + c\text{MCAP}.$$ 

Furthermore, (expected gMCAP)/iMCAP

$$= \frac{[(i\text{MCAP} - c\text{MCAP})/i\text{MCAP}] \left(\frac{r_{\text{graft}}}{r_{\text{ICA}}}\right)^2 + (c\text{MCAP}/i\text{MCAP})}{(i\text{MCAP})}$$

$$= (1 - c\text{MCAP}/i\text{MCAP}) \left(\frac{r_{\text{graft}}}{r_{\text{ICA}}}\right)^2 + c\text{MCAP}/i\text{MCAP}.$$ 

And if (expected gMCAP)/iMCAP is defined as expected MCAP ratio and cMCAP/iMCAP is defined as $k$ (and $k > 0$), then the expected MCAP ratio

$$= (1 - k) \left(\frac{r_{\text{graft}}}{r_{\text{ICA}}}\right)^2 + k.$$ 

In calculating expected MCAP ratio, each MCAP was divided by the mean systemic blood pressure measured at each MCAP reading to adjust for the difference in the systemic blood pressure.

To evaluate whether the recipient vessel was adequate...
for graft, \((r_{\text{graft}}/r_{\text{ICA}})^2\) was also calculated. The \(r_{\text{graft}}\), \(r_{\text{ICA}}\), and \(r_{\text{MC}}\) represent the radius of the graft, the \(C_2\) portion of the ICA, and the \(M_2\) portion of the MCA, respectively.

**Interrater Reliability**

Vessel diameters were measured, and the expected MCAP ratio in the 80 patients was calculated by 2 independent investigators. Interrater reliability was calculated using the intraclass correlation coefficient.

**Outcome**

Graft patency was confirmed using CT angiography (CTA). Postoperative DWI was performed to evaluate ischemic lesions. Low-flow–related ischemic complications were defined as follows: 1) new postoperative neurological deficits and 2) ipsilateral cerebral blood flow reduction on SPECT with and without new ischemic lesions in watershed territory on DWI. The LRICs were distinguished from aneurysm-related perforator infarction by the findings on DWI with SPECT. In aneurysm-related perforator infarctions, DWI showed no lesions in the watershed territory. The diagnosis of watershed infarction was made using the previously published template.\(^7\)\(^{12}\)\(^\text{62}\) A SPECT study was performed in patients with new postoperative neurological deficits. Clinical outcome was evaluated according to the modified Rankin Scale (mRS),\(^60\) either by telephone interviews (conducted by H.M., independent of the primary surgeon) with the patient or family members or by physical examination of patients who were able to visit our hospital. The mRS score was evaluated at admission, discharge, and at the 6-month follow-up examination or the last hospital visit.

**Statistical Analysis**

Statistical analysis was performed using SPSS for Mac (version 21.0, IBM Corp.). Variables are expressed as the mean ± standard deviation, the median (interquartile range 25th–75th percentile), or the number of patients (%), as appropriate. The chi-square test or Fisher exact test was applied for categorical variables, as appropriate. The \(\chi^2\)-test or Fisher exact test was performed in patients with new postoperative neurological deficits. The intraclass correlation coefficient for the expected MCAP ratio was 0.96 (95% CI 0.93–0.97, \(p < 0.0001\)).

**Results**

**Baseline Characteristics**

The 80 patients consisted of 66 women (82%) and 14 men (18%), with a mean age of 59 ± 15 years. Clinical presentations were minor headache in 32 patients (40%), double vision in 24 (30%), visual field and/or visual acuity abnormality in 11 (14%), postclipping or postcoiling aneurysm regrowth in 5 (6.2%), subarachnoid hemorrhage in 4 (5.0%), and mild hemiparesis in 2 (2.5%). When diagnostic imaging studies were performed, spontaneous cerebellar hemorrhage (1 patient) and cerebellar infarction (1 patient) were found. Median aneurysm size was 17 mm (range 11–24 mm). Aneurysms were located in the \(C_1\) (13 [16%]), \(C_2\) (18 [22%]), \(C_3\) (17 [21%]), and \(C_4\) (28 [35%]) segments of the ICA, and at the cervical ICA (dissecting aneurysm, 4 [5%]). There were 41 aneurysms (51%) on the left side and 39 (49%) on the right. Calcified aneurysms were seen in 38 cases (48%) and thrombosed aneurysms in 13 (16%).

**Interrater Reliability**

The intraclass correlation coefficient for the expected MCAP ratio comparison between the 2 independent observers was 0.96 (95% CI 0.93–0.97, \(p < 0.0001\)).

**Intraoperative and Postoperative Findings**

Mean diameters of the graft, STA, recipient \(M_2\), and \(C_4\) were 3.7 ± 0.82, 1.4 ± 0.44, 2.7 ± 0.42, and 4.0 ± 0.61 mm, respectively. The median value for \((r_{\text{graft}}/r_{\text{MC}})^2\) was 0.56 (0.42–0.70). Cervical ICA ligation was performed in 43 patients (54%) and aneurysm trapping was done in 37 (46%).

Mean BTO pressure ratio (0.45 ± 0.16) was significantly correlated to mean \(c\text{MCAP}/i\text{MCAP}\) (0.68 ± 0.22; \(r = 0.68\), \(p < 0.0001\)). A summary of values for MCAPs and MCAP ratios is shown in Table 1. The mean actual MCAP ratio was significantly correlated to the mean expected MCAP ratio (\(r = 0.43\), \(p < 0.0001\)). If expected MCAP ratio was set up by BTO pressure ratio instead of \(c\text{MCAP}/i\text{MCAP}\) (BTO-expected MCAP ratio), then mean BTO-expected MCAP ratio was 1.1 ± 0.36. Expected MCAP ratio was

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**Table 1. Summary of values of MCAPs and MCAP ratios**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Mean MCAP, mm Hg (SD)</th>
<th>Expected†</th>
<th>Expected‡</th>
<th>BTO-expected†</th>
<th>BTO-expected‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMCAP</td>
<td>71 (14)</td>
<td>1.0 (0.20)</td>
<td>1.0 (0.44)</td>
<td>1.1 (0.36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cMCAP</td>
<td>46 (14)</td>
<td>71 (12)</td>
<td>1.0 (0.44)</td>
<td>1.1 (0.36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>gMCAP</td>
<td>67 (12)</td>
<td>1.0 (0.20)</td>
<td>1.0 (0.44)</td>
<td>1.1 (0.36)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Actual MCAP ratio = gMCAP/iMCAP.
† Expected MCAP ratio = \((1 - k)(r_{\text{graft}}/r_{\text{ICA}})^2 + k\) (and \(k = c\text{MCAP}/i\text{MCAP}\) and \(k > 0\)).
‡ BTO-expected MCAP ratio = \((1 - k)(r_{\text{graft}}/r_{\text{ICA}})^2 + k′\) (and \(k′ = \text{stump pressure}/\text{[preocclusion pressure]}\)).

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Rationale for graft selection in EC-IC high-flow bypass

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± 3.8 minutes for the graft-M 2 anastomosis. were 18 ± 4.7 minutes for STA-MCA anastomosis and 20

cant difference between patients with and without LRICs. Other variables showed no signifi

ed with LRICs (Table 3). Other variables showed no signifi

cerbral infarction in 1. Of these patients, 4 (5%) had cogni -

tory distribution in 5, in the basal ganglia in 5, and in the

11 patients (14%)—in the anterior thalamoperforating ar -

revealed ischemia in the perforating artery distribution in

medical treatment during admission. Postoperative DWI

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rived well in these 4 patients, 1 had ischemic events due

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to SV graft occlusion.

Aneurysm regrowth occurred 162 days after the sur

gery in 1 patient (1.3%), a 70-year-old woman who had

had a giant aneurysm of the left cavernous portion along

with oculomotor nerve palsy. At first, she underwent ECA-

RA-M 2 bypass with cervical ICA ligation. After aneurysm

regrowth, she underwent aneurysm trapping.

Discussion

The present study demonstrated that a sufficient graft

size that can supply an adequate MCAP ratio can be cal-

culated using a formula to avoid LRICs in patients with

complex ICA aneurysms treated with therapeutic ICAO.

Indication for Cerebral Revascularization in Complex ICA

Aneurysm Surgery

Currently, there are 2 ways to avoid acute ischemic

complications after therapeutic ICAO. One is the selective

approach. Sufficient perfusion pressure appears to be pres-

ent in patients with well-developed collateral circulation; therefore, such patients will remain neurologically intact just after ICAO without high-flow bypass. Balloon test occlusion is used in the selective approach to determine whether bypass surgery should be performed; however, this test can produce false-negative findings in some pa-

patients, who could subsequently develop ischemic surgical

complications. In fact, 2%–22% of patients who pass the

BTO with hypotensive challenge can experience delayed ischemic complications. Moreover, current tech-
niques for predicting delayed ischemia after ICAO include transcranial Doppler ultrasonography, SPECT, xenon CT, perfusion CT, transcranial near-infrared spectroscopy, and perfusion MRI, although none has proved infallible. False-negative results leading to acute and
delayed ischemic complications have been reported. Furthermore, even when supplemented with cerebral blood flow studies, modern studies of ICA sacrifice after normal BTO show false-negative rates of up to

TABLE 2. Analysis of factors related to LRICs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Yes</th>
<th>No</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>9</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt;65 yrs</td>
<td>5 (56)</td>
<td>25 (35)</td>
<td>0.24</td>
</tr>
<tr>
<td>Female sex</td>
<td>8 (89)</td>
<td>58 (82)</td>
<td>0.59</td>
</tr>
<tr>
<td>Smoking</td>
<td>5 (56)</td>
<td>27 (38)</td>
<td>0.34</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7 (78)</td>
<td>32 (45)</td>
<td>0.065</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>3 (33)</td>
<td>9 (13)</td>
<td>0.12</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0</td>
<td>2 (2.8)</td>
<td>0.62</td>
</tr>
<tr>
<td>Radiological characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysm size &gt;15 mm</td>
<td>4 (44)</td>
<td>39 (55)</td>
<td>0.57</td>
</tr>
<tr>
<td>(r_M2/r_graft)&lt;0.49*</td>
<td>7 (78)</td>
<td>16 (22)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calcification of aneurysm</td>
<td>5 (56)</td>
<td>33 (46)</td>
<td>0.60</td>
</tr>
<tr>
<td>Thrombosed aneurysm</td>
<td>3 (33)</td>
<td>10 (14)</td>
<td>0.12</td>
</tr>
<tr>
<td>Period characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean graft flow &lt;120 ml/min</td>
<td>1 (11)</td>
<td>18 (25)</td>
<td>0.15</td>
</tr>
<tr>
<td>Actual MCAP ratio &lt;0.80*</td>
<td>3 (33)</td>
<td>2 (2.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Expected MCAP ratio &lt;0.80*</td>
<td>5 (56)</td>
<td>9 (13)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cervical ICA ligation*</td>
<td>2 (22)</td>
<td>41 (58)</td>
<td>0.049</td>
</tr>
<tr>
<td>Lt operative side</td>
<td>7 (78)</td>
<td>32 (45)</td>
<td>0.064</td>
</tr>
<tr>
<td>RA graft</td>
<td>8 (89)</td>
<td>51 (72)</td>
<td>0.28</td>
</tr>
<tr>
<td>Mean temporary occlusion time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STA-MCA &gt;18 min</td>
<td>4 (44)</td>
<td>20 (28)</td>
<td>0.29</td>
</tr>
<tr>
<td>Graft-MCA &gt;21 min</td>
<td>2 (22)</td>
<td>27 (38)</td>
<td>0.39</td>
</tr>
</tbody>
</table>

Data expressed as the number of patients (%).

* Variables significantly related to LRICs by the log-rank test.

significantly correlated to BTO-expected ratio (r = 0.95, p < 0.0001). Mean blood flow of the graft was 147 ± 52 ml/min, and it was significantly associated with gMCAP (r = 0.39, p = 0.006). The mean temporary occlusion times were 18 ± 4.7 minutes for STA-MCA anastomosis and 20 ± 3.8 minutes for the graft-M 2 anastomosis.

Low flow–related ischemic complications were observed in 9 patients (11%). Symptoms of motor aphasia and/or motor weakness occurred 1–7 days after the surgical procedures. These symptoms completely resolved with medical treatment during admission. Postoperative DWI revealed ischemia in the perforating artery distribution in 11 patients (14%)—in the anterior thalamoperforating artery distribution in 5, in the basal ganglia in 5, and in the internal capsule in 1. Of these patients, 4 (5%) had cognitive dysfunctions, 4 (5%) were asymptomatic, and 3 (3.8%) had hemiparesis and/or aphasia.

The results of an analysis of the factors related to LRICs are shown in Table 2. An actual MCAP ratio < 0.80, expected MCAP ratio < 0.80, (r_M2/r_graft)<0.49, and cervical ICA ligation were significantly associated with LRICs according to the log-rank test. Even in the multivariate analysis, actual MCAP ratio < 0.80, expected MCAP ratio < 0.80, and (r_M2/r_graft)<0.49 remained significantly associated with LRICs (Table 3). Other variables showed no significant difference between patients with and without LRICs.

TABLE 3. Multivariable analyses using the Cox proportional-hazards model for LRICs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted HR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual MCAP ratio &lt;0.8*</td>
<td>16</td>
<td>2.5–100</td>
<td>0.003</td>
</tr>
<tr>
<td>Expected MCAP ratio &lt;0.8*</td>
<td>17</td>
<td>3.0–94</td>
<td>0.001</td>
</tr>
<tr>
<td>(r_M2/r_graft)&lt;0.49*</td>
<td>64</td>
<td>4.7–85</td>
<td>0.002</td>
</tr>
<tr>
<td>Cervical ICA ligation</td>
<td>0.61</td>
<td>0.11–3.4</td>
<td>0.58</td>
</tr>
</tbody>
</table>

* Variables significantly related to LRICs.

Outcome and Follow-Up

No patient deaths were observed during the study pe-

riod. Preoperative, postoperative, and long-term outcomes by mRS score are shown in Fig. 3. During a median follow-up period of 26.1 months, all RA grafts remained patent on serial 3D CTA. Saphenous vein graft occlusion occurred at 5, 6, 8, and 11 months after the surgical procedure in 4 patients. Although the STA-MCA bypasses developed well in these 4 patients, 1 had ischemic events due to SV graft occlusion.

Aneurysm regrowth occurred 162 days after the sur-
gery in 1 patient (1.3%), a 70-year-old woman who had

had a giant aneurysm of the left cavernous portion along

with oculomotor nerve palsy. At first, she underwent ECA-

RA-M 2 bypass with cervical ICA ligation. After aneurysm

regrowth, she underwent aneurysm trapping.
rates aneurysm formation and the likelihood of rupture. A
dynamic burden increases wall shear stress and init-
ates the common carotid artery in rabbits. This increased he-
rysm growth, 11 and delayed hemorrhage. 20,43,45,46 Ibrahim et
cluded delayed ischemia, 5,52,58 symptoms of aneu-
These include delayed ischemia, 5,52,58 symptoms of aneu-
and death was observed in 3%–10% of patients who had
not experienced immediate neurological symptoms after
and death was observed in 3%–10% of patients who had
not experienced immediate neurological symptoms after
36
Another method of avoiding acute ischemic complica-
tions is the universal approach. In previous studies, neuro-
ological deterioration that could result in severe morbidity
and death was observed in 3%–10% of patients who had
not experienced immediate neurological symptoms after therapeu tic ICAO. 9,36 The short-term benefits of simple
ICAO are well recognized; however, several late complica-
tions can occur, even many years after the procedure. 9,8,10,33
These include delayed ischemia, 5,52,58 symptoms of aneu-
These include delayed ischemia, 5,52,58 symptoms of aneu-
graft-MCA bypass, especially one utilizing a sufficiently sized graft, is justified to avoid isch-
ic complications and hemodynamic stress in patients
with therapeutic ICAO. 21,22,31,35,44,45

**FIG. 3.** Preoperative, postoperative, and long-term outcomes by mRS
score. Proportions of patients with mRS Score 0–1 before operation,
the operation, if r graft shows 0, graft use turns out to be
adequate. 26

Taking into account only cerebral blood flow just after
the operation, if r graft shows 0, graft use turns out to be
redundant in this formula. Therefore, an adequate graft can be
calculated before the operation by using the following formula for expected MCAP ratio: 0.80.

\[
\text{Expected MCAP ratio} = \frac{1 - \text{BTO pressure ratio}}{r_{\text{graft}}/r_{\text{ICA}}} + \text{BTO pressure ratio} 
\]

Therefore,

\[
\left(\frac{r_{\text{graft}}/r_{\text{ICA}}}{1 - \text{BTO pressure ratio}}\right)\geq 0.80
\]

\[
(1 - \text{BTO pressure ratio})/(1 - \text{BTO pressure ratio}) 
\]

Therefore, 

\[
r_{\text{graft}} \geq \sqrt{\frac{(0.80 - \text{BTO pressure ratio})/(1 - \text{BTO pressure ratio})}{r_{\text{ICA}}}} 
\]

and \( r_{\text{graft}} \geq 0 \).

Taking into account only cerebral blood flow just after
the operation, if \( r_{\text{graft}} \) shows 0, graft use turns out to be
redundant in this formula. However, as stated above, ECA-
graft-MCA bypass may be needed to avoid delayed isch-
ic complications and hemodynamic stress in patients
with therapeutic ICAO. 21,22,31,35,44,45

**Rationale for Graft Selection**

Vessel sizes, including graft, recipient vessel, and sacrif-
iced ICA, vary from patient to patient. Therefore, there has
been no preoperative assurance about whether the RA or
SV can supply enough blood flow to compensate for the
sacrificed ICA. Thus, for the first time, we revealed that
the adequate graft size can be logically calculated using
a formula to obtain a sufficient MCAP ratio (\( > 0.80 \)).
The formula is based on the hypothesis that blood flow is
proportional to the square of the vessel radius, per Hagen-
Poiseuille’s law. 21,49 and that pressure by graft blood flow
be represented as (pressure by ICA blood flow)\( r_{\text{graft}}/r_{\text{ICA}} \). 21,49

Although significance was not very strong, the ex-
pected MCAP ratio was correlated to the actual MCAP
ratio. It may support the validity of the formula. Based on
the formula, small RA and SV grafts may be insufficient,
and a large STA may be a high-flow graft to a sacrificed
ICA. In addition, a BTO pressure ratio was correlated to
\( k \) value, and BTO-expected MCAP ratio was correlated to
expected MCAP ratio. Therefore, an adequate graft can be
calculated before the operation by using the following formula for expected MCAP ratio:

\[
(1 - \text{BTO pressure ratio})/(1 - \text{BTO pressure ratio}) 
\]

\[
\text{Expected MCAP ratio} = \frac{1 - \text{BTO pressure ratio}}{r_{\text{graft}}/r_{\text{ICA}}} + \text{BTO pressure ratio} 
\]

Therefore,

\[
\left(\frac{r_{\text{graft}}/r_{\text{ICA}}}{1 - \text{BTO pressure ratio}}\right)\geq 0.80
\]

\[
(1 - \text{BTO pressure ratio})/(1 - \text{BTO pressure ratio}) 
\]

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\text{Expected MCAP ratio} = \frac{1 - \text{BTO pressure ratio}}{r_{\text{graft}}/r_{\text{ICA}}} + \text{BTO pressure ratio} 
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Therefore,

\[
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\]

\[
(1 - \text{BTO pressure ratio})/(1 - \text{BTO pressure ratio}) 
\]
During the follow-up periods, all RA grafts were patent and the results were comparable or superior to those in previous studies. On the other hand, in 4 patients who were treated with an ECA-SV-M bypass, the SV grafts occluded in the chronic phase. We speculate that the possible mechanisms of SV graft failure were as follows: 1) the SV is not a vessel physiologically intended to convey arterial flow, and the lumen caliber more closely approximates that of the M1 portion, which is our usual recipient vessel; and 2) the SV has a uniform intimal wall that lacks the valves and varices of venous grafts. Therefore, if an Allen test is positive and an RA has a sufficient diameter, as evaluated using the formula, the RA may be a better candidate for the high-flow graft.

As regards recipient selection, the present study indicated that an inadequate recipient artery size, which caused LRICs due to a “narrowed bottleneck,” led to an insufficient blood supply, even if the graft was larger. Therefore, the MCA portion, which has a sufficient diameter, should be selected for the graft-MCA anastomosis.

Study Limitations

Some limitations of this study should be mentioned. First, because the number of patients and outcomes of interest (that is, LRICs) were small, the 95% confidence intervals of the odds ratios became large. Despite the small numbers, however, the association between the factors and LRICs was significant, even in the Cox proportional-hazards model.

Second, the MCAP measurement requires validation, considering that the territory supplied by the ECA-graft-MCA bypass may have different total vascular resistances depending on the anatomy. Inherent variations in the STA anatomy itself and possible vessel spasm during the procedure add additional variables that are time variant and not normalized or calibrated if one argues that there is intrapatient self-consistency of such physiology. However, the MCAP measurement could be continuously monitored and be a surrogate marker for LRICs, although graft blood flow measured by Transit flowmeter was not associated with the LRICs. In addition, if a sufficient MCAP ratio is not found intraoperatively, graft troubles such as kinking, twisting, and thrombosis should be suspected and graft revision should be performed. Actually, MCAP monitoring detected kinking or twisting of the graft in 7 patients (8.8%), which led to immediate revisions of the anastomosis during surgery. In this regard, we thought that the graft blood flow might have been influenced by the graft kinking and/or distortion, especially en route from the cranium to the neck, and that it might not reflect the accurate blood flow. If there are stenotic lesions, graft blood flow appears to be fast. On the other hand, gMCAP decreases, reflecting the lower graft blood volume. Because MCAP was measured distal to the graft-M1 anastomosis, it was more important for evaluating the cerebral perfusion given the difference in cerebral vascular resistance.

Third, the treatment strategy of ECA-graft-MCA bypass with MCAP monitoring for complex ICA aneurysms may be a complicated and rather impractical method. In addition, the time and risk associated with the construction of an STA-MCA bypass is a major limitation. However, the technique could be achieved by a combination of established neurosurgical techniques: sylvian fissure dissection and extracranial to intracranial bypass. Furthermore, continuous MCAP monitoring is easily performed and potentially useful because both neurosurgeons and anesthesiologists can respond quickly to a deterioration in hemodynamics during the anastomosis, dural closure, and bone flap fixation.

Fourth, it is unclear whether cerebral blood flow is proportional to the square of the vessel radius per Hagen-Poiseuille’s law or whether the velocity in both the ICA and the graft is the same. Given the limited number of patients with complex ICA aneurysms who needed to be treated with ECA-graft-MCA bypass and therapeutic ICAO, we were unable to prove the hypothesis.

Fifth, intraoperative evaluation of bypass patency can be performed in a variety of ways beyond simple visual inspection and palpation of pulse. These include routine intraoperative angiography, microvascular Doppler assessment, thermal diffusion flow probe, fluorescent dye (indocyanine green) angiography. However, these methods do not provide quantitative assessment of flow in the bypass and are therefore less definitive in confirming the adequacy of the revascularization strategy.

Sixth, there are other tests of flow dynamics that can be performed prior to the BTO (for example, MRI time-of-flight quantitative flow measurements) and acetazolamide challenges that can further increase the accuracy of the BTO. Charbel et al. demonstrated the efficacy of a novel simulation technique, the sector model, in the patient-specific prediction of clinical outcomes accompanying endovascular vessel occlusion. They showed that phase-contrast MR angiography measurements of flow and BTO predictions made using cerebral blood flow modeling were closely related to the clinical outcome of BTO with a hypotensive challenge. The advantages of flow measurements are that they are much simpler and do not require construction of an STA-MCA bypass to make the measurements. However, only 16 patients were included in that study, and even in their novel model, 1 (10%) of 10 patients who passed the BTO experienced ischemia ipsilateral to the occlusion and died several days after ICAO. Moreover, the authors evaluated only the immediate results and did not investigate long-term hemodynamic stress and de novo aneurysm formation.

Finally, although measurements of vessel diameter on the axial volume data of 3D CTA can differ from intraoperative measurements, the extent of the difference between radiological vessel diameters and actual vessel diameters remains unknown. Therefore, further studies are warranted to clarify results of the present study.

Conclusions

Data in the present study showed that it was important to select an adequate graft to achieve a sufficient MCAP ratio to avoid LRICs and that the adequate graft size could be determined using a formula consisting of MCAPs and the size of the sacrificed ICA. Because the development of collateral circulation and vessel sizes are variable from patient to patient, the formula may provide a rationale for graft selection in patients with complex ICA aneurysms who need therapeutic ICAO.


Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

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