Selection of patients for extra-intracranial arterial bypass surgery based on rCBF measurements

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Extracranial intracranial arterial anastomosis is gaining acceptance as a form of treatment in selected cases with ischemic cerebrovascular disease. To establish indications for this operation and to provide an objective assessment of postoperative results, regional cerebral blood flow (rCBF) studies were performed in 110 patients with cerebrovascular insufficiency considered for extra-intracranial bypass surgery. The $^{133}$Xe intracarotid injection method with 16 externally placed detectors was used for measuring rCBF. Postoperatively, rCBF was measured in 40 patients. From these results our present criteria for surgery have evolved. The probability of a good postoperative result is best in patients who showed focal cerebral ischemia or a moderate general reduction of CBF with an additional ischemic focus. The operation is contraindicated in patients with either normal or severely reduced CBF values (less than 60% of normal).

Key Words: extra-intracranial arterial bypass • cerebral ischemia • regional cerebral blood flow • transient cerebral ischemic attacks

Development of the extra-intracranial arterial bypass procedure (EIAB) by Donaghy, and Yaşargil, et al., in 1967 has resulted in a new surgical treatment of ischemic cerebrovascular disease. The results reported to date have not only shown that the operation is technically feasible with a patency rate above 80% but also suggest the value of this operation in the prevention of stroke. Until now, selection of appropriate candidates and assessment of postoperative results have been based on clinical grounds and on findings from cerebral angiography. The natural history in cerebrovascular insufficiency is unpredictable, making evaluation of surgery difficult in individual cases.

In order to obtain objective data to determine which patients may benefit from EIAB, 167 regional cerebral blood flow (rCBF) studies were performed pre- and postoperatively on 110 patients over a 5-year period.

Methods and Clinical Material

Technique

Regional cerebral blood flow was mea-
sured simultaneously over 16 regions of one hemisphere by the $^{133}$Xe intracarotid injection method. The common carotid artery was punctured, and a Teflon catheter inserted into the internal carotid artery. Correct placement of the catheter was confirmed when an injection of saline showed blanching limited to the supraorbital region. In patients with unilateral occlusion of the internal carotid artery, the contralateral internal artery was injected, thus, the CBF was able to be measured over both hemispheres which provided an interhemispheric comparison of flow. After surgery, the external carotid artery was injected to evaluate the new anastomosis. Approximately 2 mCi of $^{133}$Xe dissolved in 3 to 5 cc saline were rapidly injected into the catheterized vessel. The uptake and subsequent clearance of the radioactivity was monitored by 16 small scintillation detectors arranged over the appropriate hemisphere. The signals from the detectors were stored on magnetic tape for a 2-minute recording period and were then logarithmically displayed on a chart recorder for further analysis. For calculation of flow values the initial slope index (ISI) method was used. A value of 50 ml/100 gm/min, plus or minus 10% was considered to represent normal flow. Generally, the rCBF measurements were performed with the patient at rest and alert, with CO₂ inhalation and with hyperventilation. The autoregulatory capacity of the cerebral vasculature was studied in selected cases by increasing the systemic blood pressure with a controlled intravenous infusion of angiotensin. Samples of arterial blood for determination of pCO₂ were taken through the carotid catheter at the start of each measurement. Arterial blood pressure was monitored by the same route. After completion of the entire study, which lasted from 60 to 80 minutes depending on the number of isotope injections, the position of three detectors was marked with small pieces of lead for localization of the counting fields. The same catheter was then used to perform cerebral angiography.

Clinical Material

This series included 110 patients who presented with symptoms of cerebrovascular disease. There were 75 men and 35 women from 19 to 73 years of age with an average of 50 years. The clinical diagnosis ranged from transient cerebral ischemic attacks (TIA) to completed strokes (Table 1). All patients were admitted to the hospital where they underwent general physical, laboratory, and neurological examinations as well as cerebral angiography and rCBF studies.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>transient cerebral ischemic attacks (TIA)</td>
<td>17</td>
</tr>
<tr>
<td>prolonged reversible intermittent neurological deficits (PRIND)</td>
<td>23</td>
</tr>
<tr>
<td>strokes in evolution</td>
<td>6</td>
</tr>
<tr>
<td>completed strokes</td>
<td>64</td>
</tr>
</tbody>
</table>

Results

rCBF Measurements

The results of the rCBF measurements were divided into six groups (Fig. 1). Severe general reduction of CBF (Group 1) is defined as flow less than 60% of normal. All patients in this group had a clearly subnormal flow increase when the study was repeated during CO₂ inhalation. Moderate general reduction of CBF was defined as 60% to 80% of normal flow (Group 2). Patients defined as having relative focal reduction of CBF (Group 3), had a moderately decreased mean hemispheric blood flow with a specific ischemic focus. Focal reduction of CBF was considered to be present when the hemispheric blood flow was normal except for a specific ischemic focus (Group 4). Due to its impaired vascular reactivity, the ischemic focus is more easily delineated when the study is repeated during inhalation of CO₂, as the difference between the flow of the ischemic and the normal regions becomes even more pronounced. Acute disorders of flow (Group 5) are seen in patients studied within a few days after an attack of cerebral ischemia. The rCBF study

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*Cerebrograph was manufactured by Meditronic A/S, Hadsund, Denmark.
†Hypertensin was manufactured by Ciba-Geigy AG, Wehr/Baden, West Germany.
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Fig. 1. Classification of rCBF findings in ischemic cerebrovascular disease: Group 1 = severe general reduction; Group 2 = moderate general reduction; Group 3 = relative focal reduction; Group 4 = focal reduction; Group 5 = acute disorders (asterisks indicate areas with hyperemic flow values); Group 6 = normal CBF. For group definitions see text. All measurements were performed under resting conditions with the arterial pressure CO₂ ranging from 37 to 40 mm Hg.
TABLE 2

Grouping by initial rCBF measurements
in 104 patients

<table>
<thead>
<tr>
<th>Findings</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 : severe general reduction</td>
<td>14</td>
</tr>
<tr>
<td>Group 2 : moderate general reduction</td>
<td>11</td>
</tr>
<tr>
<td>Group 3 : relative focal reduction</td>
<td>26</td>
</tr>
<tr>
<td>Group 4 : focal reduction</td>
<td>33</td>
</tr>
<tr>
<td>Group 5 : acute disorders</td>
<td>9</td>
</tr>
<tr>
<td>Group 6 : normal</td>
<td>11</td>
</tr>
</tbody>
</table>

* Six patients had only postoperative rCBF measurements. rCBF = regional cerebral blood flow.

TABLE 3

rCBF studies performed on 53 EIAB patients

<table>
<thead>
<tr>
<th>rCBF Studies</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>preoperative studies</td>
<td>47</td>
</tr>
<tr>
<td>postoperative studies</td>
<td>40</td>
</tr>
<tr>
<td>pre- and postoperative studies</td>
<td>33</td>
</tr>
<tr>
<td>follow-up studies</td>
<td>15</td>
</tr>
</tbody>
</table>

* rCBF = regional cerebral blood flow; EIAB = extra-intracranial arterial bypass.

TABLE 4

Results of preoperative rCBF studies in 47 patients

<table>
<thead>
<tr>
<th>Findings</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1: severe general reduction</td>
<td>4</td>
</tr>
<tr>
<td>Group 2: moderate general reduction</td>
<td>4</td>
</tr>
<tr>
<td>Group 3: relative focal reduction</td>
<td>21</td>
</tr>
<tr>
<td>Group 4: focal reduction</td>
<td>18</td>
</tr>
<tr>
<td>Group 5: acute disorders</td>
<td>0</td>
</tr>
<tr>
<td>Group 6: normal</td>
<td>0</td>
</tr>
</tbody>
</table>

* rCBF = regional cerebral blood flow.

may reveal a relative hyperemic region during resting state or paradoxical reactions during CO₂ inhalation or focal or global loss of autoregulation in response to an increase of the systemic blood pressure. A flow of 50 ml/100 gm/min, plus or minus 10% is considered a normal rCBF (Group 6).

Of the 110 patients examined with the rCBF technique (Table 2), 53 patients were selected for the EIAB. These are included in a series of 65 patients reported on after EIAB.¹⁰ The remaining patients either had a standard carotid endarterectomy or surgery was contraindicated because of rCBF findings, complicating medical illnesses, or refusal for surgery by the patients. Of the 53 patients who were selected for EIAB, rCBF measurements were performed in 47 patients preoperatively, and in 40 patients postoperatively; in 15 patients two postoperative measurements were obtained (Table 3). The rCBF findings obtained preoperatively in 47 patients are presented in Table 4.

Postoperatively, rCBF was measured in 40 patients (Table 5). In 33 patients the postoperative study was performed within 1 week, and in the remaining seven patients the study was performed at an average of 6.5 months after surgery. In 22 patients the external carotid artery was injected selectively, which allowed the isotope to reach the brain by way of the extra-intracranial anastomosis. The internal carotid artery was used in 18 patients for the injection of the isotope which allowed a direct comparison of the pre- and postoperative rCBF results. Of the 22 patients with postoperative external carotid artery studies, two showed no evidence for bypass function as demonstrated by the absence of a CBF pattern. In the other 20 patients the function of the anastomosis could be clearly established (Fig. 2). The CO₂ inhalation test was used routinely in all postoperative studies as an additional measure for the evaluation of the bypass. During hypercarbia, blood flow in the extracerebral compartment remained relatively constant, whereas blood flow increased significantly in the area supplied by the anastomosis revealing the cerebro-specific flow response to an elevated arterial pCO₂. A comparison of external cerebral flow studies with external carotid angiography revealed a good correlation of the area supplied by the anastomosis.

Postoperatively, the internal carotid artery was used for injection of the isotope in 18 patients. In all cases an improvement of cerebral hemodynamics could be demonstrated. In seven patients postoperative rCBF studies disclosed a relatively small area, not more than three counting fields of improved blood supply as compared to the preoperative rCBF studies. In 11 patients blood flow improved over an extended area, that is, in more than three adjacent detector fields following the EIAB operation (Fig. 3). Only a 15% change in flow was considered significant.

In 15 patients an additional measurement was obtained later in the postoperative
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### TABLE 5

*Results of postoperative rCBF studies in 40 patients*

<table>
<thead>
<tr>
<th>Findings</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>no function of bypass</td>
<td>2</td>
</tr>
<tr>
<td>secondary occlusion of bypass</td>
<td>3</td>
</tr>
<tr>
<td>function of bypass established</td>
<td>20</td>
</tr>
<tr>
<td>improvement of rCBF:</td>
<td>18</td>
</tr>
<tr>
<td>within small area</td>
<td>7</td>
</tr>
<tr>
<td>within extended area</td>
<td>11</td>
</tr>
</tbody>
</table>

* rCBF = regional cerebral blood flow.

The time interval between the two postoperative studies varied from 2 to 28 months, averaging 11 months. A secondary occlusion of the bypass was found in three patients in whom the earlier postoperative study had demonstrated bypass function. In six patients, the two postoperative measurements revealed identical results. In the remaining six patients further improvement of CBF could be demonstrated (Fig. 4) as compared to the earlier postoperative study.

**Discussion**

The main risk associated with the intra-arterial $^{133}$Xe injection method used to obtain rCBF measurements is the necessity of arterial puncture. In a recent report, based on the experience of close to 4000 rCBF studies performed in 18 clinical centers, the rate of complications was found to be 1.3%. In our own series of 285 studies in patients with cerebrovascular disease, only two patients (0.7%) experienced transient neurological symptoms following rCBF studies. The risk of performing rCBF studies is limited to the arterial puncture. There are no complications associated with the injection of the radioactive material. As angiography is generally performed in the evaluation of cerebrovascular ischemia, the two procedures may conveniently be combined, thus, only one arterial puncture is required. To eliminate any effects of angiography on rCBF, the flow study is performed first.

Non-invasive rCBF techniques, such as reported by Austin, et al., who used the intravenous $^{133}$Xe bolus technique, or the inhalation method for CBF measurement, reported by Obrist, et al., have certain limitations which make them less suitable for evaluating this group of patients. Calculation of the rCBF values is more complicated with these methods because of extracerebral contamination and recirculation of the isotope. More importantly, due to the considerably lower count efficiency, the non-
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FIG. 3. Preoperative (upper) and postoperative (lower) internal rCBF study in the same patient. In the area that was ischemic preoperatively, rCBF considerably improved after extra-intracranial bypass surgery. The arterial pressure CO₂ was 39 mm Hg preoperatively and 37 mm Hg postoperatively.

Invasive methods do not allow reliable quantitative blood flow measurements over multiple small regions of the brain. Since revascularization microneurosurgery offers the treatment of a specific ischemic focus, the method of rCBF measurement must be able to detect flow differences within one hemisphere. Therefore, the intracarotid injection method with the multidetector equipment must be considered the method of choice. Although a 16-channel apparatus was employed for this study, the use of eight to 10 probes is probably sufficient.

The clearance curve recorded by a regional detector is determined by geometrical factors that result in some overlapping of measuring fields as well as by a considerable Compton scatter from surrounding tissue due to the low energy spectrum of ¹³¹Xe. Therefore, information on minor flow changes within the brain is rather crude. Nevertheless, the sensitivity of the rCBF method is sufficiently high to establish the extent of an ischemic area, as seen in three cases with completed strokes. It was striking to find a pale area of apparent ischemia on the exposed cortex at operation, exactly where it had been predicted from preoperative rCBF studies.

The reason the initial slope index is used for calculation of flow is that this analytical method requires only a 2-minute period for data collection, which guarantees fairly stable conditions during the recording phase. This method also allows reliable measurements during functional studies as it is possible to control pCO₂ and arterial blood pressure for this short time period.

By analyzing the pre- and postoperative rCBF measurements and correlating them with the clinical results, we have established guidelines for the selection of patients most likely to benefit from the EIAB.

Group 1. In patients in whom the rCBF measurement revealed a severe general reduction of CBF, the surgical results have been poor. These patients are likely to suffer from small vessel disease that involves the whole brain and therefore, cannot be expected to benefit from a measure directed at improving CBF regionally such as the extra-intracranial bypass procedure. Thus, patients in Group 1 are no longer considered for surgery.

Group 2. In patients with moderate general ischemia as diagnosed by rCBF measurements, the operative results have been also poor, and these patients are no longer considered candidates for surgery. This rCBF pattern is characteristic of an old cerebrovascular accident.

Groups 3 and 4. The patients with relative focal reduction and focal reduction alone of CBF have shown the best clinical results from extra-intracranial bypass surgery. This appears logical as the EIAB offers a collateral blood supply which is regional in character, thus compensating the ischemic focus discovered and defined by rCBF measurement.

Group 5. The patients with acute disorders of rCBF, clinically those with a recent cerebrovascular accident, do not benefit from an EIAB, and in fact the surgery may worsen
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their clinical condition. Three of our early patients operated on with an acute cerebrovascular accident, died soon after the operation from massive brain swelling. This group of patients remains the subject of intense study in order to determine a time period during which surgical means may safely be employed to minimize or prevent the neurological sequelae of cerebrovascular accidents.

**Group 6.** We do not perform EIAB procedure on patients with normal rCBF results, as it seems superfluous to add additional collateral blood supply to a normally perfused cortex. The clinical symptoms in this group of patients are probably due to lesions deep within the brain, as, for instance, occlusion of the lenticulostriate arteries.

In the 40 patients studied postoperatively, there were five occlusions, of which two were early in the postoperative period and three were discovered later during the second postoperative study. None of these patients belonged to the two groups (Groups 3 and 4) with a specific focal reduction of CBF and thus would no longer be candidates for surgery according to our present criteria. An explanation of the poor patency rate of the anastomosis seen in patients with moderate or severe general reduction of CBF (Groups 1 and 2) may be due to the fact that in these cases the low rCBF is secondary to the decreased metabolic demand of the brain rather than to hemodynamic compromise. In these patients, the perfusion pressure of the middle cerebral artery is near normal, offering an insufficient pressure gradient between the extracranial and the intracranial circulation. Therefore, the flow through the bypass is sufficiently low to lead to occlusion in certain cases. On the other hand pressure gradient between the extracranial and the intracranial vessels in patients with focal cerebral flow defects is high, and results in a high patency rate of the anastomosis with actual dilatation of the anastomotic vessels as seen by serial postoperative follow-up angiography (Fig. 5). In all 18 patients with a preoperative focal cerebral flow defect, the postoperative rCBF measurements showed an improvement. A second postoperative rCBF measurement performed in 12 of these 18 patients revealed no change in the improved postoperative CBF in six patients, whereas in the other six patients there was further improvement of the CBF as compared to the first postoperative CBF examination. These patients with further improvement of the rCBF all showed a concomitant increase of the anastomosis on angiography. From these late follow-up results it becomes apparent that the final assessment of the operative procedure cannot be established from an early postoperative examination (rCBF or angiography) but must await at least a 3-month period postoperatively.

**Conclusion**

Measurement of rCBF allows the clinician for the first time to assess the objective flow...
abnormalities present in a patient with ischemic cerebrovascular disease. From the results of these measurements, an intelligent decision may be rendered on the advisability of surgical intervention. The rCBF results not only allow a classification of patients, with selection of those most likely to benefit from surgery, but this method also localizes the cortical ischemic area into which extracranial vessel should be anastomosed.

Our present criteria evolved over the initial 3-year period of our 5-year study. For the past 2 years, we have relied on rCBF measurements as the final criteria for patient selection. During this period, 32 patients in Groups 3 and 4 (the only groups operated on) received an extra-intracranial anastomosis. There were no postoperative occlusions in these patients. There were no recurrences of TIA’s in those patients who presented preoperatively with TIA’s, and no patient suffered a completed stroke postoperatively. A detailed analysis of the clinical material is reported elsewhere.10 It has been shown that patients with focal or relatively focal reduction of CBF (Groups 3 and 4) appear to benefit from the EIAB as demonstrated clinically as well as with postoperative rCBF and angiographic studies. On the other hand, patients presenting with generalized reduction of CBF (Groups 1 and 2), who show no clinical improvement and a high occlusion rate of the bypass, do not appear to benefit from the EIAB. As neither angiography nor clinical presentation can assess the presence of the various CBF patterns, rCBF measurements offer a unique and essential parameter in the establishment of criteria for extra-intracranial bypass surgery.

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