Cerebral haemodynamics and long term prognosis after extracranial-intracranial bypass surgery

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Abstract

The effectiveness of extracranial-intracranial arterial (EC-IC) bypass surgery for haemodynamic stroke remains controversial. In this study correlation of presurgical and postsurgical cerebral haemodynamics with long term prognosis was evaluated.

Twenty eight patients (25 men, three women: mean age 61·4 (SD 8·2) years) with reduced cerebrovascular reserve due to steno-occlusive cerebral vascular disease formed the study group. Measurement of mean hemispheric cerebral blood flow (mCBF) and the cerebral vasodilatory capacity (% mCVR) with an intravenous acetazolamide injection were performed by a xenon-133 inhalation method and SPECT. Patients were treated with EC-IC bypass surgery and measurements of mCBF and % mCVR were made again about one month after surgery. The patients were then observed for a long period (range 27–115 months).

During the observation period, four patients experienced subsequent ischaemic strokes. The presurgical and the postsurgical resting mCBF for the affected hemisphere were significantly reduced in the patients with strokes during follow up compared with the values in patients without strokes during follow up (P < 0·03 and 0·01 respectively). The % mCVR of the affected hemisphere was significantly raised after surgery in all patients except one (P < 0·01). The postsurgical change in resting mCBF was not unidirectional.

In conclusion, resting mCBF was unchanged and % mCVR was improved after EC-IC bypass surgery in patients with reduced cerebrovascular reserve. The group of patients with a reduced presurgical and postsurgical resting mCBF continue to be a high risk group for subsequent ischaemic stroke seen after EC-IC bypass surgery.

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Several studies have reported that extracranial-intracranial (EC-IC) bypass surgery is potentially effective in a particular group of patients that presented with reduced haemodynamic reserve with respect to cerebral blood flow.[1–7] Cerebral perfusion reserve has been measured by PET,[8–12] SPECT, or xenon-CT with intravenous acetazolamide injection.[4 6 7 10–12]

There is less consistency however, as to whether EC-IC bypass surgery improves long term prognosis, particularly for those patients with a haemodynamic compromise.[4 6 9 12] There have been a few reports regarding postoperative cerebral haemodynamics and long term prognosis.[1 6]

We measured mean hemispheric cerebral blood flow (mCBF) by a xenon-133 inhalation method and SPECT. We also measured the cerebral vasodilatory capacity with an intravenous acetazolamide injection. These measurements enabled us to identify patients with reduced cerebrovascular reserve. We treated patients with reduced cerebrovascular reserve by EC-IC bypass surgery and repeated the CBF measurement after surgery. To explore the correlation of the presurgical and postsurgical cerebral perfusion with the long term prognosis, we studied these patients over a long period.

Materials and methods

PATIENTS

We studied 28 patients (25 men; three women) during the period 1988–90. Each had had symptoms or a stroke associated with reduced cerebrovascular reserve and was treated by EC-IC bypass surgery. The cerebral ischaemic attack was manifested as either a transient ischaemic attack, a reversible ischaemic neurological deficit, or a minor completed stroke. Those strokes occurred as a result of steno-occlusive lesions of major cerebral arteries in the anterior circulation, such as in the internal carotid artery and middle cerebral artery. The patients' ages ranged from 45 to 73 (mean; 61·4 (SD 8·2)). The initial symptoms were exhibited as transient ischaemic attack in 10 patients, reversible ischaemic neurological deficit in three. The other 15 had minor completed strokes. The first 13 patients were asymptomatic and the second 15 were symptomatic at the time of the presurgical CBF measurement. By means of the CBF measurement we confirmed that all of our patients had reduced cerebrovascular reserve in the hemisphere in which the initial ischaemic stroke had occurred (described later). Cerebral angiography involving three or four vessels disclosed a steno-occlusive vascular lesion, which appeared as an occlusion of the internal carotid artery in 12 patients, severe stenosis (⩾ 90%)

of the internal carotid artery in four, occlusion of the horizontal part of the middle cerebral artery in 10, and severe stenosis of this part of the middle cerebral artery in two. None of the subjects studied, when they were examined by CT or MRI, had a cerebral infarction, with the exception of a small infarction in the basal ganglia and deep white matter after the initial ischaemic episode.

All patients were treated by unilateral EC-IC bypass surgery using double to triple superficial to middle cerebral artery anastomoses. An EC-IC bypass was established to the hemisphere which had reduced cerebrovascular reserve. All bypasses were confirmed patent by cerebral angiography performed two to four weeks after surgery.

MEASUREMENT OF CBF

Mean hemispheric CBF (mCBF) was measured by a xenon-133 inhalation method and SPECT (HEADTOME SET-031; Shimazu Co, Kyoto, Japan). This tomograph acquires three slices with 24 mm thickness and an axial resolution of 20 mm (full width at half maximum). Each patient had two CBF measurements on the same day: the first at rest (resting mCBF) and the second 15 minutes after an intravenous injection of 10 mg acetazolamide/kg bodyweight (acetazolamide mCBF). The mCBF was calculated by the "sequential picture" method of Kanno and Lassen.[16] A region of interest was designed to cover each hemisphere on the slice 55 mm above the orbitomeatal line. This hemispheric region of interest included a perfusion territory of the internal carotid artery and the middle cerebral artery. Mean hemispheric cerebral vasoreactivity (% mCVR) to acetazolamide was calculated as follows:

% mCVR = (acetazolamide mCBF − resting mCBF)/resting mCBF × 100[4]

Normal control values of resting mCBF (mean (SD) 39·7 (5·2) ml/100 g brain/min) and % mCVR (21·5 (5·7)%) were obtained from 20 age matched normal volunteers with a mean age of 58·5 (8·9), range 45–78 years.

All of the presurgical mCBF measurements were performed at a time when the patients' neurological states were stable and no earlier than four weeks after the patients' initial ischaemic episode. We obtained a presurgical resting mCBF and % mCVR. The patients with significantly reduced mean hemispheric and/or regional cerebral vasoreactivity to acetazolamide (below mean −2 SD of normal) were diagnosed as having reduced cerebrovascular reserve, and were selected as candidates for EC-IC bypass surgery (three patients with normal % mCVR had regional reduction of cerebral vasoreactivity in a perfusion territory of the horizontal part of the middle cerebral artery (see figure)).[4] The postsurgical mCBF measurements were performed in a similar manner at about one month after the surgery.

LONG TERM OBSERVATION

All patients were observed for a long period. Patients with cerebral ischaemic episodes, manifested as either appearance or deterioration of neurological deficits, occurring during the observation period were considered as having subsequent ischaemic strokes. A progression of multi-infarct dementia, manifested as evidently exacerbated cognitive impairment with relatively abrupt onset, was also regarded as a subsequent ischaemic stroke. Slight perioperative ischaemic neurological deteriorations occurred in two patients and were transient. They were not considered as having subsequent ischaemic stroke.

STATISTICAL ANALYSIS

We compared the presurgical resting mCBF and % mCVR values for the affected hemisphere in which initial ischaemic stroke had occurred with the postsurgical values. We analysed the difference in those measures between the patients with and without strokes during follow up by Student's t test. We also analysed the change in these measures after EC-IC bypass surgery by paired t test. Differences between groups were considered significant when comparisons exceeded 95% confidence limits ($P < 0{\cdot}05$).

Results

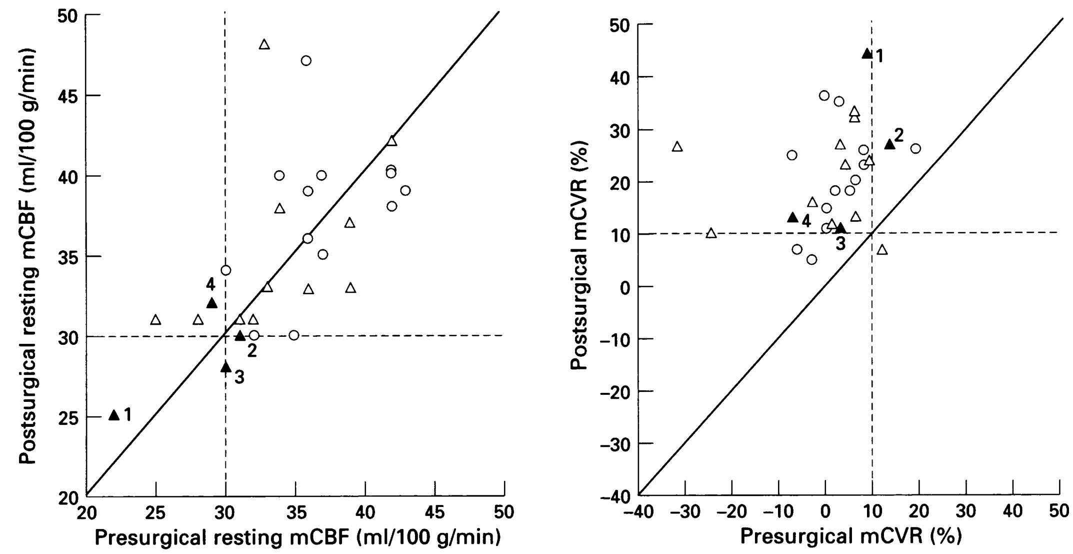
All 28 patients were studied during a period of 27 to 115 (mean; 48·9 (SD 17·4)) months. During this period, four patients had episodes of ischaemic strokes. Two of their original vascular lesions were located in the internal carotid artery, and the other two in the horizontal portion of the middle cerebral artery. Three strokes occurred on the side ipsilateral to the initial ischaemic episodes. The other one was manifested as the progression of multi-infarct dementia. Those strokes occurred two to 12 months (mean six months) after bypass surgery. The table summarises the clinical profiles of these four patients (patients 1–4). Three patients died during the observation period. Two deaths occurred in the patients without stroke during follow up, one from car-

Clinical profiles of the patients with subsequent ischemic stroke

Patient			*Initial stroke*		*Subsequent stroke*		
No	*Age (y)*	*Sex*	*Type*	*Vascular lesion*	*Type*	*Side**	*Period after surgery (months)*
1	51	M	Minor CS	ICA occlusion	Major CS	Ipsilateral	2
2	68	M	Minor CS	M1 occlusion	RIND	Ipsilateral	12
3	71	M	Minor CS	ICA stenosis	Progression of multi-infarct dementia	?	2
4	73	M	Minor CS	M1 occlusion	Minor CS	Ipsilateral	8

*Compared with the side of initial stroke; CS = completed stroke; RIND = reversible ischaemic neurological deficit; ICA = internal carotid artery; M1 = horizontal portion of middle cerebral artery.

Values of the presurgical and postsurgical resting mean hemispheric cerebral blood flow (mCBF) and mean hemispheric cerebral vasoreactivity (% mCVR) of the asymptomatic (○) and symptomatic patients (△). The values for the patients with stroke during follow up are denoted by closed symbols with the patient number displayed adjacent to their symbols. The dotted lines indicate the lower border of normal values (mean − 2 SD).



cinoma of the colon and one from general arteriosclerotic occlusive vascular disease. One patient with a stroke during follow up died at the age of 78 from ischaemic heart failure (patient 4). In total, the postoperative course was uneventful in 22 patients (79%).

The figure shows the values of the presurgical and postsurgical resting mCBF and % mCVR for each patient. Presurgical values were scaled to the *x* axis and postsurgical values to the *y* axis. Circles indicate values for the asymptomatic patients. Triangles indicate the values for the symptomatic patients. The values for the patients with stroke during follow up are denoted by closed symbols with the patient number displayed adjacent to their symbols. The dotted lines indicate the lower border of normal values (mean − 2 SD) from our age matched normal subjects. The diagonal line allows comparison of the presurgical with postsurgical measures. When symbols are located in the upper left of the diagonal line, it means that the measures were raised after surgery. When they are located in the lower right, the values were reduced after surgery.

RESTING mCBF

The presurgical and postsurgical resting mCBF in the patients with strokes during follow up was significantly reduced compared with the measures in the patients without strokes during follow up ($P < 0{\cdot}03$ and 0·01 respectively). In addition, the resting mCBF value in the symptomatic patients was reduced compared with the asymptomatic patients ($P < 0{\cdot}02$, presurgical; $P = 0{\cdot}05$, postsurgical). There was no unidirectional change in postsurgical resting mCBF values compared with the presurgical values. Eleven patients had raised mCBF values postsurgically, 12 had decreased values, and in four the values were unchanged. The values of the resting mCBF in the patients with strokes during follow up were below or near the lower border of the normal range in both the presurgical and postsurgical periods (figure, left panel).

% mCVR

Most of the presurgical measures were below the normal range. Although % mCVR was within the normal range in three patients, they had a distinct regional reduction in cerebrovascular reserve and underwent EC-IC bypass surgery. After the surgery, % mCVR was raised significantly for all the patients except one ($P < 0{\cdot}01$), and most of the postsurgical measures were within the normal range. In both the presurgical and postsurgical % mCVR, there was no significant difference between the patients with and without strokes during follow up, or between the symptomatic and asymptomatic patients (figure, right panel).

Discussion

Since the discouraging results from the EC-IC bypass group study,[17] some reports, but not all,[13,19] have discussed the correlation of abnormal cerebral haemodynamics with subsequent risk of stroke.[15,18] The effectiveness of EC-IC bypass surgery for treatment of haemodynamic ischaemia is still controversial. It has been shown to be effective in preventing subsequent ischaemic strokes for patients with haemodynamic compromise,[4,9] but not in all studies.[12,20]

The goal of this study was not to derive any advantage from EC-IC bypass surgery compared with medical treatment. We were exploring what, if any, limitations existed with EC-IC bypass surgery for the patients with reduced cerebrovascular reserve. Several CBF studies discussing EC-IC bypass surgery and postsurgical CBF were in agreement in that the EC-IC bypass surgery had helped restore the vascular reserve.[1,3-8,11] In most cases, however, EC-IC bypass surgery generally failed to raise the patient's CBF.[4-7] It was also reported that rCBF increased after EC-IC bypass surgery in patients who had severely reduced cerebrovascular reserve.[1,7,15] We judged that all our patients experienced strokes associated with reduced cerebrovascular reserve based on the result of CBF measurement. In accordance with the other published results, the vascular reserve in all of our patients except one was restored after surgery. Postsurgical changes for resting mCBF were not, however, unidirectional. Furthermore, postsurgical changes in mCBF did not correlate with the prognosis of the patients.

We noted that the presurgical and postsurgical resting mCBFs were significantly reduced in the patients with strokes during follow up compared with the patients without strokes during follow up. These findings are consistent with those of Yonas *et al*[15]—that is, among the patients with haemodynamic compromise, the group having a greater risk for stroke had a reduced baseline rCBF. In our patients with strokes during follow up, all individual values of the presurgical and postsurgical resting mCBF were below or near the lower border of the normal range. In both the presurgical and postsurgical % mCVR, on the other hand, no significant differences were observed between the patients with and without strokes during follow up.

Why are the patients with reduced resting mCBF at greater risk for further ischaemic strokes than the patients with normal resting mCBF? Resting mCBF is believed to represent the cerebral metabolism in the coupling state between the CBF and metabolism. In the instance when there is haemodynamic compromise, the vascular reserve is initially called on to keep the CBF normal. When reduction in CBF is more advanced, oxygen carriage reserve is called on to maintain the normal oxygen metabolism.[8] In our study, all of the patients with strokes during follow up, in fact, were symptomatic. None of the asymptomatic patients had further ischaemic strokes. In the symptomatic patients, the process of cerebral metabolism is supposed to be damaged to some degree. The cerebral tissues that have impaired metabolism do not recover after EC-IC bypass surgery.

Another factor influencing reduction of resting mCBF is the background arteriosclerosis in the small cerebral arteries. It is considered that one of the main causes of decline in resting rCBF is arteriosclerosis in the small cerebral arteries.[21] In our study, three of our patients with stroke during follow up were old (patients 2, 3, and 4) and, conceivably, these patients had advanced arteriosclerosis in the small cerebral arteries. In these patients, the EC-IC bypass surgery was successful in restoring their vascular reserve, and, therefore, was also successful in reducing the risk of further haemodynamic ischaemia. They, however, continued to be at greater risk of further ischaemic strokes consequent to arteriosclerotic or thromboembolic occlusion in small cerebral arteries. Indeed, our three older patients had subsequent ischaemic strokes which manifested as either reversible ischaemic neurological deficit, minor completed stroke, or progression of vascular dementia. These strokes seemed a consequence of the ischaemia in the territory of the cerebral small arteries. In the patient with a major completed stroke during follow up (case 1) on the other hand, the value of presurgical and postsurgical resting mCBF was the lowest of all our patients. In this case, even though % mCVR was restored postsurgically, CBF was reduced too far to maintain the oxygen metabolism after the further ischaemic compromise. The patient subsequently experienced the major completed stroke.

Our findings suggest the importance of measurement of resting CBF as well as the estimation of cerebrovascular reactivity for further randomised trials for EC-IC bypass surgery, especially when trials are considering older patients.

In conclusion, we found unchanged resting mCBF and improved % mCVR after EC-IC bypass surgery in patients with reduced cerebrovascular reserve. The group of the patients with a reduced presurgical and postsurgical resting mCBF, however, continue to be a high risk group for subsequent ischaemic stroke after EC-IC bypass surgery.

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