Stepwise Revascularization for Prevention of Postoperative Hyperperfusion

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Abstract

Abrupt normalization of cerebral blood flow (CBF) after surgical procedures to improve excessive cerebral hypoperfusion can cause irreversible brain parenchymal damage. Such hyperperfusion, which is caused by inflow at normal blood pressure into maximally dilated fine vessels, is an important complication following carotid endarterectomy (CEA). Strict control of blood pressure in the perioperative period can prevent this complication except in a few patients, who have severe cerebral hypoperfusion and poor cerebrovascular reserve due to extremely severe stenosis of the ipsilateral or the bilateral carotid arteries, for which CEA is indicated. The requirement for improved CBF and the risk of postoperative hyperperfusion conflict in the pathogenesis of these patients. We tried to prevent abrupt improvement in perfusion by attempting gradual restoration of CBF. Superficial temporal artery-middle cerebral artery anastomosis was first performed to improve the poor cerebrovascular reserve by allowing insufficient blood flow. A few weeks later, CEA was performed to completely restore CBF. This surgical approach obtained good results without postoperative problems in four patients. The indications of this surgical management and efficacy of stepwise restoration of CBF to prevent postoperative hyperperfusion depend on careful preoperative evaluation of perfusion studies.

Key words: bypass, carotid endarterectomy, hyperperfusion, stepwise revascularization

Introduction

Hyperperfusion syndrome is one of the most serious complications of carotid endarterectomy (CEA) and may also occur after superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis, as well as in a few patients following revascularization surgery. Preoperatively, patients with a high risk of postoperative hyperperfusion can be identified based on preoperative perfusion data such as severe hypoperfusion and poor cerebrovascular reserve (CVR) below 10%, and intraoperative stump pressure below 40 mmHg. In such patients, blood pressure should be strictly controlled immediately following the restoration of cerebral blood flow (CBF) by revascularization surgery. Despite intensive management, postoperative perfusion study has rarely demonstrated ipsilateral hyperperfusion. Postoperative cerebral hemorrhage or seizure induced by hyperperfusion is very rare. However, the critical value for perfusion separating the asymptomatic and symptomatic states, leading to irreversible cerebral damage, remains undefined in patients with hyperperfusion. Such postoperative hyperperfusion should be avoided to decrease the associated morbidity and mortality.

High risk patients with extremely low preoperative perfusion may suffer further ischemic attacks during the preoperative period. In such severe cases, the fine cerebral vessels are maximally dilated and the CVR more reduced because of the closeness to the critical level of ischemia. Such patients can more easily suffer postoperative hyperperfusion than ordinary high risk patients despite strict control of blood pressure and should be distinguished as a group with higher risk of postoperative hyperperfusion.

Hyperperfusion may be considered to result from abrupt restoration of CBF with normal perfusion pressure in the injured fine vessels with dysautoregulation. The best strategy to restore CBF without inducing hyperperfusion in the higher risk group may be gradual rather than sudden complete restoration of CBF.

The present study investigated the effect of...
Table 1 Preoperative cerebral blood flow (CBF) and cerebrovascular reserve (CVR) in four patients treated by stepwise revascularization

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Pre-bypass ipsilateral CBF (ml/100 g/min)</th>
<th>Pre-bypass ipsilateral CVR (%)</th>
<th>Pre-CEA ipsilateral CBF (ml/100 g/min)</th>
<th>Pre-CEA ipsilateral CVR (%)</th>
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CEA: carotid endarterectomy.

stepwise revascularization consisting of STA-MCA double anastomosis followed by CEA to gradually restore CBF in the higher risk group.

Subjects and Methods

This study included four of 51 patients treated by CEA since 2001 who were considered to have high risk of hyperperfusion. Patients in the higher risk group basically have severe misery perfusion with poor CVR. Our policy is strict control of the blood pressure of patients with risk of hyperperfusion during the postoperative course. However, hyperperfusion cannot be prevented by only control of blood pressure in such higher risk patients, resulting in problems during the postoperative management. These patients were considered candidates for stepwise revascularization. The specific indications were as follows: extreme misery perfusion with poor CVR due to severe unilateral cervical carotid artery stenosis or occlusion, particularly associated with crescendo transient ischemic attacks (TIAs) in the acute phase, considered to indicate impending cerebral stroke; and severe bilateral stenosis or occlusion with misery perfusion.

Patients with severe unilateral cervical carotid artery stenosis or occlusion suffered from frequent ischemic events induced by severe misery perfusion despite treatment with anti-platelet or fibrinolytic agents since the first episode. Their preoperative perfusion state was considered to approach the critical level, with the risk of ischemia in the interval prior to CBF stabilization. This interval could not be prolonged in patients with impending cerebral stroke, but these patients already had high risk of hyperperfusion or hemorrhage if ischemia had already developed.

Patients with severe bilateral carotid artery stenosis or occlusion had the risk of ischemic event on the contralateral side after postoperative decrease in blood pressure for prevention of hyperperfusion following unilateral CEA. The postoperative blood pressure level is difficult to balance between the ipsilateral hyperperfusion and the contralateral ischemic event. Therefore, the CBF on the ipsilateral side was incompletely increased by performing almost double STA-MCA anastomosis, followed by CEA after an interval of a few weeks.

This strategy was adopted for four patients. Table 1 shows the pre-bypass CBF and CVR, and pre-CEA CBF and CVR. CBF was measured with single photon emission computed tomography (SPECT) (HEADTOME SET-031; Shimadzu, Osaka) with xenon-133 (133Xe) inhalation in Cases 1 and 2, and SPECT (Millennium VG; GE, Tokyo) with N-isopropyl-p-[123I]iodoamphetamine in Cases 3 and 4.

Representative Cases

Case 1: A 68-year-old male presented with occipital headache. Neurological examination found no abnormalities. Magnetic resonance (MR) imaging showed only old lacunar infarct in the left corona radiata. Cervical MR angiography and left cervical carotid angiography showed severe stenosis (Fig. 1A). SPECT with 133Xe inhalation showed hypoperfusion as 29 ml/100 g/min on the left against 35 ml/100 g/min on the right at rest, and low CVR of 7% on the left against 26% on the right after administration of acetazolamide (Fig. 1B, C).

The surgical indication was CEA. However, he was suspected to have a high risk of postoperative hyperperfusion. CEA was planned with postoperative intensive care for hyperperfusion, but he experienced right transient hemiparesis for a few minutes on the day before the operation. Hexamethylpropyleneamine oxime (HM-PAO) SPECT revealed deterioration in misery perfusion (Fig. 2A). Therefore, the surgical procedure was changed to STA-MCA anastomosis followed by CEA.

The frontal and parietal branches of the STA were individually anastomosed to the frontal and temporal branches of the MCA. HM-PAO SPECT taken immediately after the surgery showed no hyperperfusion in the left hemisphere compared with the right hemisphere (Fig. 2B). Two weeks later 133Xe SPECT showed restoration of CBF to 35 ml/100 g/min on the left against 35 ml/100 g/min on the right at rest and improvement of CVR to 14% on the left against 28% on the right (Fig. 2C, D). CEA was then performed on the left (Fig. 3A). The patient suffered no hyperperfusion after CEA and showed no neurological deficits (Fig. 3B).

Case 2: A 70-year-old male experienced transient...
Stepwise Revascularization

Fig. 1 Case 1. A: Left carotid angiogram showing severe stenosis of the cervical bifurcation with ulcer formation. B, C: Single photon emission computed tomography (SPECT) scans taken on the day before surgery indicating deterioration of left hypoperfusion at rest (B) and poor cerebrovascular reserve after acetazolamide administration (C).

Fig. 2 Case 1. A, B: Hexamethylpropyleneamine oxime single photon emission computed tomography (SPECT) scans taken on the day before surgery indicating deterioration of left hypoperfusion (A), and after superficial temporal artery-middle cerebral artery anastomosis showing similar cerebral blood flow to the contralateral side (B). C, D: SPECT scans with xenon-133 inhalation taken a few weeks after the first operation showing mild hypoperfusion compared to the contralateral side at rest (C) and slightly poor cerebrovascular reserve, but better than the previous findings (D).

Fig. 3 Case 1. A: Postoperative left carotid angiogram showing improvement of the severe stenosis. B: Hexamethylpropyleneamine oxime single photon emission computed tomography scans taken immediately after carotid endarterectomy showing no abnormalities.

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weakness in the left upper and lower extremities immediately after taking anti-hypertensive medication. The same event had occurred 5 years ago. He consulted our hospital. The diagnosis was TIA induced by mild hypotension. Neurological examination and MR imaging showed no abnormalities. Carotid angiography showed severe stenosis of the bilateral cervical portions and moderate stenosis of the right MCA, and poor development of the collateral circulation (Fig. 4). $^{133}$Xe SPECT showed severe bilateral hypoperfusion of 22 ml/100 g/min on the right and 24 ml/100 g/min on the left. Acetazolamide administration showed low CVR of 12% on the right and 13% on the left (Fig. 5A, B). We suspected a high risk of hyperperfusion and difficult postoperative intensive management of blood pressure. Therefore, stepwise revascularization surgery was planned.

First, STA-MCA anastomosis was performed on the right (Fig. 5C). Postoperative SPECT showed that the preoperative ipsilateral hypoperfusion was sufficiently improved by the single bypass (Fig. 5D). The postoperative course was uneventful. Therefore, CEA was performed on the left 3 weeks later to improve the collateral flow. The distal pressure through the internal shunt tube was 54 mmHg. Postoperative control of blood pressure was strictly performed to avoid hyperperfusion. HM-PAO SPECT showed improved hypoperfusion on the left (Fig. 6A). However, the temporary decrease in blood pressure to 120 mmHg had induced left hemiparesis and mild deterioration of consciousness. These
symptoms disappeared immediately after the blood pressure was increased, and MR imaging also showed no new lesions. The patient finally underwent ipsilateral CEA. No neurological events occurred in the postoperative course. Postoperative SPECT showed bilateral improvement in hypoperfusion (Fig. 6B).

Discussion

Cerebral vessels that are exposed to severe ischemia for a particular period are maximally dilated. This condition is similar to that observed in the acute phase of ischemic events. The dilated vessels can occasionally induce fatal bleeding or cerebral edema even after the restoration of normal CBF perfusion. However, this phenomenon is fundamentally different from the pathogenesis of hemorrhagic infarction, which is caused by the restoration of blood flow into the necrotic vessels and rupture of new vessels. SPECT shows normal CBF perfusion as hyperperfusion in the maximally dilated vessels. Fatal damage due to hyperperfusion results from normal pressure perfusion breakthrough (NPPB) as applied to intracranial bleeding following the removal of arteriovenous malformation (AVM).

The cerebral tissue surrounding the AVM is chronically exposed to ischemic stress and the regional vessels are extremely dilated. The duration or severity of ischemia is related to the degree of dilation of the fine vessels, which is important in the induction of NPPB in the area of severe hypoperfusion.

The treatment for severe carotid artery stenosis involves only the restoration of CBF by removing the lesion with a procedure like CEA. A better indication for cerebrovascular revascularization, e.g., CEA or bypass surgery against ischemic lesion, has a higher risk of inducing postoperative hyperperfusion. To prevent postoperative deterioration caused by hyperperfusion as far as possible, we should first select patients with a risk of hyperperfusion and strictly control the postoperative blood pressure within the range of approximately 80–90% of the preoperative value.
Previously, we reported the importance of the preoperative evaluation of CBF and CVR.\textsuperscript{10} Patients showing misery perfusion or poor CVR below 10% were considered to have high risk of postoperative hyperperfusion. Furthermore, the pressure measured at the distal portion of the ipsilateral carotid artery (distal pressure) appeared to be closely related to the postoperative hyperperfusion in such high risk patients.\textsuperscript{11} The distal pressure indicating the development of collateral flow revealed chronic exposure to hypoperfusion in one patient with severe stenosis. Patients with distal pressure below 40 mmHg or high delta pressure might have higher risk of hyperperfusion. The postoperative blood pressure of the selected patients was intensively controlled immediately following the insertion of the internal shunt tube. However, postoperative reduction of the blood pressure in patients with severe stenosis of the bilateral carotid arteries was extremely dangerous due to progression of the contralateral ischemia. Therefore, we conducted perfusion studies for at least 3 weeks following the initial ischemic attack to stabilize cerebral perfusion and evaluate the correct state. Patients who exhibited impending cerebral stroke manifesting as crescendo TIAs were deemed to be close to the critical line of ischemia and to have higher risk of hyperperfusion.

We performed stepwise revascularization to gradually increase CBF in patients with high risk of hyperperfusion. The improvement in CBF provided by STA-MCA anastomosis is apparently insufficient in comparison with that provided by CEA. However, the slight improvement is important to suppress postoperative hyperperfusion if poor CVR can be improved. A follow-up study of STA-MCA bypass reported improved CVR rather than restoration of CBF.\textsuperscript{8} Stepwise revascularization in all our four patients revealed improvement of poor CVR by SPECT after the first operation (Table 1) and no patient suffered postoperative hyperperfusion. Normalization of CVR is probably very important to prevent hyperperfusion.

The stepwise strategy is more invasive to the patients because of the greater number of surgeries, and may carry the risks of deteriorating hypoperfusion caused by intraoperative hypotension or inadequate CBF after the first surgery. Preoperative perfusion studies must be thoroughly evaluated to carefully select the patients for this strategy.

References


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Commentary

Dr. Fujimoto and coauthors have pointed out an important problem for patients with severe ischemia. In high risk patients with extremely low preoperative perfusion, the fine cerebral vessels are maximally dilated and the cerebrovascular reserve (CVR) more reduced. Such patients can more easily suffer from postoperative hyperperfusion despite strict control of blood pressure (BP). The authors indicated a strategy to prevent the postoperative hyperperfusion by stepwise revascularization method. I agree with the author’s idea and we had several similar cases. The authors could add some more details to the cases to explain the following.

1. Criteria of patient selection to decide whether carotid endarterectomy (CEA) with severe postoperative BP control, or preventive superficial temporal artery-middle cerebral artery (STA-MCA) bypass followed by CEA and BP control should be performed.
2. The necessary interval period between the first STA-MCA bypass and second CEA procedure, that is, how many days to recover CVR.
3. The technical points of CEA in patients with preventive STA-MCA bypass surgery, for example, do not float the debris to the external carotid artery.
4. Comparison of the risk between only CEA and CEA with preventive bypass surgery.

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This is a clever and scholarly article that attempts to improve the outcome of high-risk carotid surgery in critical carotid stenosis patients by preventing hyperperfusion hemorrhage. The authors have developed a set of criteria that they feel predicts this complication, and have in four patients employed a “bridging” strategy of STA-MCA bypass to improve ipsilateral cerebral reserve, followed several weeks later by definitive CEA. They had no complications in these four patients; of course we will never know whether they would have had such complications with CEA without previous bypass; the surgical strategy most of us would have employed in such cases.

The authors feel that several factors predict hyperperfusion syndrome following CEA, and have shown this in their previous works. These factors are “misery” perfusion, reduced or abolished cerebral reserve, and low “stump” pressure in the isolated ICA at the time of carotid cross-clamping. Of course, the stump pressure is of no value in predicting the need for bypass since it can only be measured at the time of CEA exposure (by then it is too late).

In this series of 4 patients selected from a larger group of 51 CEA patients in their practice, the authors chose to perform pre-CEA bypass for extreme misery perfusion with poor CVR for unilateral disease patients, and for misery perfusion in patients with bilateral severe carotid stenosis. Patients with crescendo TIAs were felt to be at the highest risk.

It is clear from Table 1 that the pre-CEA bypass strategy is effective in improving CBF and CVR, although they do not return to normal values. The authors did not provide a table of CBF and CVR values post-CEA; this would be very interesting data to see in a future report.

As mentioned, the clinical outcomes in all 4 patients were excellent, indicating that pre-CEA bypass certainly did not harm these patients, and may well have protected them against hyperperfusion at the time of delayed CEA.

Finally I am curious about the long-term patency rate of these STA-MCA bypasses once CEA has been performed. Classical wisdom dictates that an unneeded bypass will close spontaneously. I would like to know if these bypasses remained open long-term, or did they close, and were there any problems with bypass flow at the time of common carotid artery cross-clamping for the CEA, when external carotid flow would be reduced or eliminated.

This is an excellent, beautifully documented, scholarly article that advances our knowledge, and I commend the authors for their novel and innovative work.

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Hyperperfusion syndrome is a rare but serious complication after carotid endarterectomy and carotid stenting for patients with severe carotid stenosis, low cerebral perfusion and poor cerebral vascular reactivity. To avoid a drastic increase of cerebral blood flow after carotid endarterectomy, Yoshimoto et al. performed superficial temporal artery-middle cerebral artery (STA-MCA) bypass surgery to stepwise increase cerebral blood flow prior to a definite revascularization procedure. Their results revealed that cerebral vascular reactivity of all four patients improved after the bypass surgery, with no hyperperfusion syndrome in any of the patients. Therefore, they concluded that STA-MCA bypass prior to carotid endarterectomy restores cerebrovascular reactivity in patients with low cerebral perfusion and minimizes the risk of postoperative hyperperfusion.

However, the authors fail to provide a clear criterion for selecting patients for this stepwise revas-
cularization procedure. Yoshimoto et al. choose to define all patients with a vascular reactivity of less than 10% as those at risk for hyperperfusion syndrome. (In this study, of the four patients selected, one even presented with a vascular reactivity at 12%, above the stated criterion.) In our institution, out of 200 patients receiving carotid endarterectomy, at least 10 patients displayed a vascular reactivity of less than 10%, but only one patient exhibited hyperperfusion syndrome. Thus, in selecting for patients with a vascular reactivity lower than 10%, Yoshimoto et al. inadvertently widened their patient population to include those who would not have been at risk for hyperperfusion syndrome.

In my opinion, routinely performing these procedures on patients with low cerebral vascular reactivity cannot be justified. The ischemic insult resulting from temporary occlusion of recipient vessel during anastomosis on a hemisphere with hypoperfusion enhances the perioperative risk of this prophylactic therapy. Furthermore, the increased possibility of inducing an embolism from the external carotid artery into the intracranial vessel via the STA-MCA anastomosis also puts the patients at an unnecessary risk of perioperative stroke. Without providing more detailed requirements for patient selection, the potential benefits from this stepwise revascularization procedure do not justify its use in every patient with low profusion and poor vascular reactivity.

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