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Stroke 2001;32;1567-1573
Stroke is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0039-2499. Online ISSN: 1524-4628

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Background and Purpose—Hyperperfusion syndrome is a rare but potentially devastating complication after carotid endarterectomy (CEA). The aim of this study was to investigate whether preoperative measurement of cerebral vasoreactivity (CVR) and intraoperative measurement of internal carotid artery (ICA) flow could identify patients at risk for hyperperfusion after CEA.

Methods—For 26 patients with unilateral ICA stenosis ≥70%, cerebral blood flow (CBF) and CVR were investigated before and 1 month after CEA, with resting and acetazolamide-challenge single-photon emission CT. CBF on the first postoperative day was also measured. ICA flow was measured before and after reconstruction by electromagnetic flowmeter during surgery.

Results—Ipsilateral CBF on the first postoperative day significantly increased relatively (56.6±53.2%) as well as absolutely (37.9±8.8 to 57.7±18.0 mL/100 g per minute) in the reduced CVR group (CVR <12%) but not in the normal CVR group (CVR ≥12%) (10.3±15.5% and 40.6±7.9 to 43.9±5.7 mL/100 g per minute, respectively). One month later, this difference almost disappeared. Two patients showed ipsilateral CBF increase of ≥100%. A significant association of intracerebral steal with hyperperfusion (CBF increase ≥100%) on the first postoperative day was also observed. ICA flow increase after reconstruction significantly correlated with CBF increase on the first postoperative day in the reduced CVR group but not in the normal CVR group. The threshold of ICA flow increase for hyperperfusion was estimated to be 330 mL/min in the reduced CVR group.

Conclusions—Single-photon emission CT with acetazolamide challenge and ICA flow measurement during surgery could identify patients at risk for hyperperfusion after CEA, in whom careful monitoring and control of blood pressure should be initiated even intraoperatively. **(*Stroke*. 2001;32:1567-1573.)**

Key Words: blood flow ■ carotid endarterectomy ■ cerebral blood flow ■ tomography, emission computed ■ vasomotor reactivity

Most postoperative complications of carotid endarterectomy (CEA) are ischemic in nature, caused by embolization or inadequate cerebral protection in patients with poor collateral supply. In a small subset of patients, however, postoperative neurological deficit may also be related to hyperperfusion, which is defined as a major increase in ipsilateral cerebral blood flow (CBF) well above the metabolic demands of the brain tissue after removal of a high-grade carotid stenosis.[1,2] The patients with hyperperfusion may develop the classic clinical triad, which includes severe unilateral headache, face and eye pain, seizures, and intracerebral hemorrhage.[1–4] According to the literature, intracerebral hemorrhage is reported to occur in 0.4% to 1.8% of patients after CEA.[2,4–9] The largest series reported that intracerebral hemorrhage constituted approximately one fifth of perioperative strokes.[8] The prognosis for these patients is poor, with mortality rates of 36% to 63%, and survivors have significant morbidity. However, less florid manifestations of hyperperfusion are probably more common.[10]

Risk factors of this syndrome include long-standing hypertension, a high-grade stenosis, poor collateral blood flow, and contralateral carotid occlusion that often impairs cerebral hemodynamic reserve.[11] A rapid restoration of normal perfusion pressure after removal of a tight stenosis by CEA could cause a large increase of blood flow through the internal carotid artery (ICA) and hyperperfusion in a region of brain that had been chronically ischemic with autoregulatory vasoparalysis. In other words, hyperperfusion after CEA may be equivalent to normal perfusion pressure breakthrough to describe the cerebral edema and hemorrhage that sometimes

Received August 14, 2001; final revision received October 27, 2001; accepted February 21, 2001.

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occur after the resection of an arteriovenous malformation.[3,12] If this hypothesis is correct, the preoperative assessment of cerebral hemodynamic reserve and intraoperative measurement of ICA flow seem to be important in predicting this rare but potentially devastating complication. Many studies have reported the usefulness of single-photon emission CT (SPECT) with acetazolamide challenge for evaluation of cerebral hemodynamic reserve.[13–17] In addition, SPECT has been reported to show increased radionucleotide tracer uptake in patients with hyperperfusion after CEA,[18–20] even in the absence of CT findings.[21]

The purpose of this study was to investigate whether preoperative SPECT with acetazolamide challenge and intraoperative measurement of ICA flow could identify patients at risk for hyperperfusion after CEA.

Subjects and Methods

Between December 1998 and April 2000, 34 consecutive patients underwent CEA, 26 of whom fulfilled the following criteria and entered the present study. Inclusion criterion was unilateral ICA stenosis ≥70%. Exclusion criteria were bilateral carotid lesions, intracranial artery stenosis or occlusion, and/or major disabling stroke.

Twenty-two of the 26 patients were male, and 4 were female. Mean age was 69.5±6.8 years (mean±SD), ranging from 57 to 84 years. Twenty-one patients were hypertensive, and 8 had diabetes mellitus. Seventeen patients showed ipsilateral carotid territory symptoms. Transient ischemic attacks (TIAs) referring to the relevant carotid artery were the only symptoms for 5 patients. Three patients had suffered TIAs with subsequent strokes, and 9 patients had suffered strokes only. All stroke patients had made good functional recoveries. Nine patients exhibited asymptomatic ICA stenosis.

Preoperative CT and MRI demonstrated no signs of infarction in 11 patients. Infarctions were seen in the hemisphere ipsilateral to the side of ICA stenosis in 15 patients. Fourteen of them represented symptomatic infarctions correlating with clinical presentation of TIA or stroke. The final patient represented asymptomatic infarctions. Two patients had asymptomatic infarction in the contralateral hemisphere.

All patients underwent preoperative angiography. Overall average of the degree of ICA stenosis was 85.0±10.1%, with a range of 70% to 99%, according to the method of the North American Symptomatic Carotid Endarterectomy Trial.[22] There was no patient with ≥30% stenosis of contralateral ICA.

All patients underwent surgery under general anesthesia. Thirteen patients underwent surgery on the left side and 13 on the right side. An indwelling shunt (high-flow shunt) was routinely used.[23] We obtained informed consent from all patients or their next of kin.

Blood flow through the ICA was measured before and after reconstruction by a cuff probe of an electromagnetic flowmeter (Nihon Koden MFV-3200 FG) during CEA.

CBF Studies

The resting CBF was assessed by means of SPECT, with a rotating dual-headed gamma camera (GAMA View SPECT 2000 H-20, Hitachi) before CEA, 1 day after CEA, and 1 month after CEA. We also measured cerebral vasoreactivity (CVR) to the acetazolamide challenge for evaluation of cerebral hemodynamic reserve before and 1 month after CEA. Five to 7 days after resting SPECT, 1 g of acetazolamide was given intravenously; 20 minutes later, SPECT was repeated to investigate regional CVR (rCVR). The median time between the latest ipsilateral neurological event and preoperative SPECT study was 47.5 days (range, 18 to 178 days) for strokes and 30 days (range, 10 to 56 days) for TIAs. The median time between the preoperative SPECT studies and CEA was 15 days (range, 2 to 73 days).

We performed CBF measurement with *N*-isopropyl-*p*-[^{123}I]iodoamphetamine (IMP) combined with a modification of arterial input sampling.[17,24–26] The patient's head was immobilized with a holder, and bandages were placed across the forehead and fastened to the holder. An arterial line was placed in the radial artery and connected to an infusion pump. A dose of 111 MBq (3 mCi) of [^{123}I]IMP was injected into an arm vein. At the same time, the time-activity curve of the entire brain was monitored with a gamma camera in the anterior view until 15 minutes after injection. Arterial blood was withdrawn at a constant speed of 1.7 mL/min for 5 minutes immediately after injection. These arterial whole-blood samples were analyzed for true tracer activity with the use of octanol extraction. SPECT acquisition was started from 15 minutes after IMP injection and lasted for 35 minutes. Data were accumulated in 64 steps, and each step collected counts for 30 seconds. Data were collected in 64×64 matrices and were reconstructed in transaxial sections parallel to the orbitomeatal line with 8 mm thickness to allow the same area to be quantified between the preoperative and postoperative SPECT studies. After SPECT acquisition, the entire brain activity was obtained in the anterior view for 30 seconds. The attenuation correction technique was not used.

The equation for determining regional CBF (rCBF) is as follows:

$$F=\frac{(100\times R\times Cb)}{(N\times A)}$$

where F is rCBF (mL/100 g per minute), R is the constant withdrawal rate of arterial blood (mL/min), Cb is the brain activity (μCi/g), A is the total activity in the withdrawal arterial whole blood (μCi), and N is the fraction of A that is true tracer activity, which is determined by octanol extraction of arterial whole-blood activity.[26]

A cross-calibration factor between the rotating camera system and well counter was obtained with the use of a 20-cm-diameter cylindrical phantom filled with standard activity (0.35 μCi/mL). The factor was calculated by dividing the activity measured by well counter by reconstructed counts per pixel.

Reconstructed counts of tomographic images 30 minutes after injection, when the brain activity reached a plateau, were corrected to represent 5-minute reference values with the use of the monitored time-activity curve of the entire brain.

Cb values were calculated as follows:

$$Cb=(C5/C30)\times(\text{cross-calibration factor})\times(\text{reconstructed counts of tomographic images 30 min after injection})$$

$$C_{30}=\frac{(C_{15}+C_{50})}{2}$$

where C_5, C_{15}, and C_{30} represent counts at 5, 15, and 30 minutes on the time-activity curve of the entire brain, and C_{50} represents counts of the entire brain activity 50 minutes after injection. C_{30} was calculated as described above.

We measured rCBF by placing 6 to 10 regions of interest (each 16×16 mm) in bilaterally symmetrical regions of the middle cerebral artery territory on a SPECT image plane where the asymmetry of radioisotope uptake distribution was most prominent. The pairs that showed the largest difference in values were used. A region where infarction was seen on CT and/or MRI was carefully excluded from the evaluation.

The rCVR was calculated as follows:

$$rCVR\ (\%)=\frac{(\text{acetazolamide-challenge rCBF}-\text{resting rCBF})\times 100}{(\text{resting rCBF})}$$

Normal control values of rCBF (45.5±5.9 mL/100 g per minute) and rCVR (52.4±13.3%) in our hospital were obtained from 10 people who had no stenosis or occlusion of cervical or intracranial arteries. Eight of them were male, and 2 were female. Mean age was 65.9±10.3 years, ranging from 42 to 76 years. There was no

statistically significant difference in age and sex between the control and patient groups. When the values of cerebral vasoreactivity were less than the mean minus 3 SD, ie, 12%, they were rated as reduced CVR. When CBF decreased after acetazolamide challenge, it was defined as intracerebral steal.[27,28] Hyperperfusion after CEA was defined as CBF increase of ≥100% on the first postoperative day, according to Piepgras et al.[2]

Statistical Analysis

Descriptive statistics are presented as mean±SD. For comparison study, we used ANOVA in a repeated-measures design (independent variable: CVR status; within factors: side and time point; dependent variables: CBF or CBF increase [%]) and Student's *t* test. Fisher's exact test was used for proportion analysis. Values of $P<0.05$ are reported to be significant. A commercially available software package was used (Statview 5.0; Abacus Concepts and Statistica 4.1; StatSoft).

Results

The patients were divided into 2 groups on the basis of the preoperative status of cerebral vasoreactivity, ie, normal CVR (rCVR ≥12%; n=17) or reduced CVR (rCVR <12%; n=9). Six patients in the reduced CVR group demonstrated CBF decrease (−4.7±2.5%, ranging from −2.1% to −9.5%) after acetazolamide challenge, representing intracerebral steal (Figure 1, top row).

All patients recovered without new major neurological deficits after surgery. No patient exhibited postoperative intracerebral hemorrhage. In 2 patients, however, postoperative ipsilateral hyperperfusion (CBF increase of ≥100%) was clearly observed on SPECT on the first postoperative day (Figure 1, middle row), although postoperative CT scans were normal. Incidence of postoperative hyperperfusion was higher in the reduced CVR group (2/9; 22%) than in the normal CVR group (0/17; 0%), but there was no significant difference (Table). However, the incidence was significantly higher in the intracerebral steal group (2/6; 33%) than in the nonsteal group (0/20; 0%) ($P=0.046$) (Table). There was no significant association between hyperperfusion and clinical (age, hypertension, diabetes mellitus, and symptoms) or physiological (degree of stenosis) variables.

Changes of CBF Before and After CEA

Ipsilateral CBF significantly increased on the first postoperative day in the reduced CVR group (37.9±8.8 to 57.7±18.0 mL/100 g per minute; $P=0.00003$) but not in the normal CVR group (40.6±7.9 to 43.9±5.7 mL/100 g per minute) (Figure 2). As described above, ipsilateral hyperperfusion (CBF increase of ≥100%) on the first postoperative day was observed in 2 patients who had demonstrated intracerebral steal on the preoperative SPECT study (Figure 2, right panel, black arrows). The preoperative asymmetry of perfusion on both resting and acetazolamide-challenge SPECT was more severe and diffuse in the 2 patients than in other 4 patients with intracerebral steal (Figure 1, top row). These 2 patients suffered a unilateral headache and mild confusion for a couple of days after CEA but eventually fully recovered after strict control of blood pressure. Ipsilateral CBF significantly decreased 1 month after CEA compared with the values on the first postoperative day in the reduced CVR group, returning to the normal range (57.7±18.0 to 41.9±5.9 mL/100 g per minute; $P=0.0004$), but not in the normal CVR group (43.9±5.7 to 43.4±6.4 mL/100 g per minute) (Figure 2). No significant difference was observed between preoperative CBF and CBF 1 month after CEA in both groups (Figure 2). In some patients, however, preoperative hypoperfusion was remarkably improved (Figure 1, bottom row).

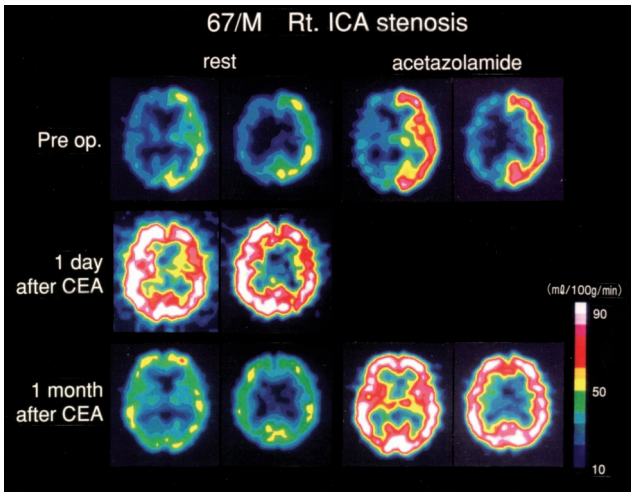

Figure 1. A case of hyperperfusion with severe right (Rt.) carotid stenosis. Top, Preoperative SPECT. Severe hypoperfusion is seen in the right ICA territory on resting SPECT. Almost no CBF response to acetazolamide is seen in the same territory, and intracerebral steal is seen in the right frontotemporal area (33.4 to 31.8 mL/100 g per minute, ie, −4.8% reduction). Middle, SPECT on the first postoperative day clearly demonstrates hyperperfusion (>90 mL/100 g per minute) in the right ICA territory. Moderate CBF increase is also seen in the left ICA territory. Bottom, SPECT 1 month after CEA. Preoperative hypoperfusion and CBF response to acetazolamide return to normal, with complete resolution of the lateralized hyperperfusion seen on SPECT on the first postoperative day. Rainbow displaying CBF from 0 to 90 mL/100 g per minute appears on the right.

Contralateral CBF increase was smaller but statistically significant on the first postoperative day in the reduced CVR group (43.5±9.1 to 51.0±14.7 mL/100 g per minute; $P=0.01$) but not in the normal CVR group (42.9±7.4 to 44.6±4.7 mL/100 g per minute) (Figure 3). Interestingly, a large increase of contralateral CBF on the first postoperative day was observed in the same 2 patients who demonstrated ipsilateral hyperperfusion (Figure 3, right panel, black arrows). Contralateral CBF significantly decreased 1 month after CEA compared with the values on the first postoperative day in the reduced CVR group, returning to the normal range

Relationship Between Cerebral Vasoreactivity and Hyperperfusion After CEA

	Hyperperfusion			
	+	−	Incidence	*P**
CVR status				
<12%	2	7	22%	NS (0.1)
≥12%	0	17	0%	
Steal				
+	2	4	33%	0.046
−	0	20	0%	

*Fisher's test.

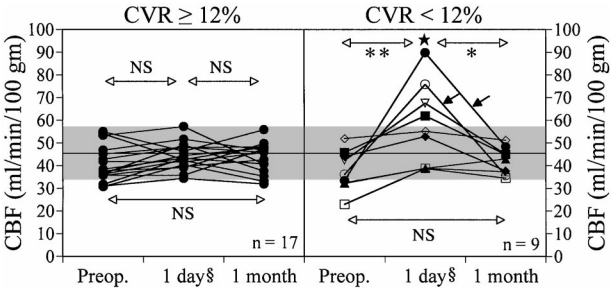

Figure 2. Preoperative and postoperative CBF on the side ipsilateral to CEA. Left, Normal CVR group. Right, Reduced CVR group. Shaded areas are mean±2 SDs of 10 normal controls in our center. Each symbol in Figure 2 right panel and Figure 3 right panel represents the same patient. Black arrows indicate 2 patients who demonstrated ipsilateral CBF increase of ≥100% on the first postoperative day. **,*Significant difference between each time point; §significant difference between normal and reduced CVR group; ★significant difference between ipsilateral and contralateral CBF (all $P<0.008$). See text for details.

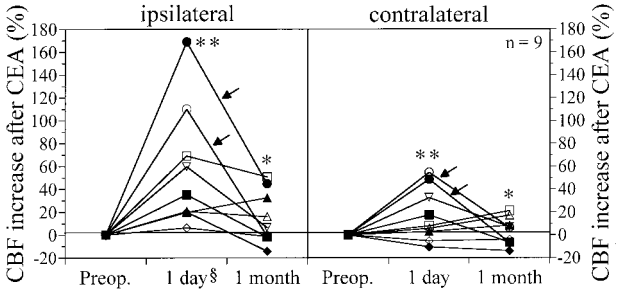

Figure 4. Postoperative CBF increase as a percentage of the preoperative CBF in the reduced CVR group. Left, Ipsilateral CBF increase. Right, Contralateral CBF increase. Each symbol in the right and left panels represents the same patient shown in Figures 2 and 3. Black arrows indicate 2 patients who demonstrated ipsilateral CBF increase of ≥100% on the first postoperative day. **,*Significant difference between ipsilateral and contralateral CBF increase; §significant difference between normal and reduced CVR group on the first postoperative day (all $P<0.02$). See text for details.

(51.0±14.7 to 44.2±6.7 mL/100 g per minute; $P=0.02$), but not in the normal CVR group (44.6±4.7 to 43.3±6.2 mL/100 g per minute) (Figure 3). No significant difference was observed between preoperative CBF and CBF 1 month after CEA in both groups (Figure 3).

Further analysis clearly demonstrated asymmetrical changes of CBF after CEA in the reduced CVR group but not in the normal CVR group. The ipsilateral CBF on the first postoperative day was significantly higher than the contralateral CBF in the reduced CVR group ($P=0.00022$), but it was not significantly higher in the normal CVR group (Figures 2 and 3). The ipsilateral CBF increase on the first postoperative day as a percentage of the preoperative CBF was significantly more pronounced compared with contralateral CBF increase in the reduced CVR group (56.6±53.2% and 16.9±23.2%, respectively; $P=0.0000081$) (Figure 4) but not in the normal CVR group (10.3±15.5% and 5.8±14.1%, respectively). In addition, CBF and its percent increase on the first postoperative day were significantly higher in the reduced CVR group than in the normal CVR group on the ipsilateral side ($P=0.0073$ and $P=0.0025$, respectively) but not on the contralateral side (Figures 2, 3, and 4). These results indicated a relative as well as absolute ipsilateral CBF increase only in the reduced CVR group. One month later this difference almost disappeared. However, a small but significant difference was still observed between percent increase of ipsilateral and contralateral CBF in the reduced CVR group ($P=0.015$) (Figure 4).

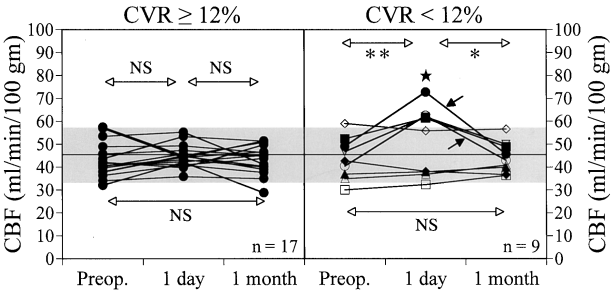

Figure 3. Preoperative and postoperative CBF on the side contralateral to CEA. Left, Normal CVR group. Right, Reduced CVR group. Shaded areas are mean±2 SDs of 10 normal controls in our center. Each symbol in Figure 2 right panel and Figure 3 right panel represents the same patient. Black arrows indicate 2 patients who demonstrated ipsilateral CBF increase of ≥100% on the first postoperative day. **,*Significant difference between each time point; ★significant difference between ipsilateral and contralateral CBF (all $P<0.03$). See text for details.

Relationship Among CVR, ICA Flow, and CBF Increase After CEA

The overall mean of ICA flow before and after reconstruction was 79.8±48.6 mL/min (range, 15 to 194 mL/min) and 192.2±80.7 mL/min (range, 75 to 400 mL/min), respectively. The average increase was 112.4±98.2 mL/min (range, −20 to 380 mL/min). The increase of ICA flow after CEA was significantly larger in the reduced CVR group than in the normal CVR group (204.7±102.5 and 63.5±50.0 mL/min, respectively; $P=0.00008$).

A significant linear correlation was observed between ICA flow increase after reconstruction and ipsilateral CBF increase on the first postoperative day as a percentage of the preoperative CBF, with the line defined by CBF increase (%)=−25.1+0.4×ICA flow increase (correlation coefficient $r=0.77$, $P=0.015$), in the reduced CVR group (Figure 5, right panel) but not in the normal CVR group (Figure 5, left panel). If the formula is reversed, the 95% CI associated with a predicted mean ICA flow increase for 100% CBF increase on the first postoperative day is 207 to 332 mL/min. Therefore, the threshold of ICA flow increase for hyperperfusion was estimated to be approximately 330 mL/min. In fact, CBF increase >100% was observed only in 2 patients with ICA flow increase >330 mL/min, who had demonstrated intracerebral steal on preoperative SPECT (Figure 5, right panel).

Discussion

The incidence of hyperperfusion, which is defined to be CBF increase of ≥100% after CEA, was reported to be 11.6%, according to Piepgras et al.[2] Of those with hyperperfusion, intracerebral hemorrhage developed in 3.3%. In contrast, only 0.24% of those with CBF increase <100% developed intra-

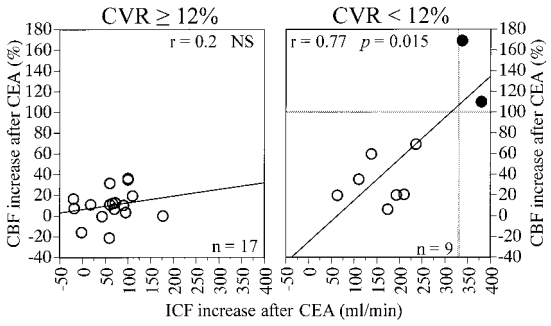

Figure 5. Left, No significant linear correlation was observed between ICA flow (ICF) increase after reconstruction and ipsilateral CBF increase on the first postoperative day as a percentage of the preoperative CBF in the normal CVR group. Right, A significant linear correlation was observed between ICA flow increase after CEA and ipsilateral CBF increase on the first postoperative day as a percentage of the preoperative CBF in the reduced CVR group (correlation coefficient r=0.77, P=0.015). Vertical shaded line indicates 330 mL/min increase of ICA flow, which seems to be the threshold for hyperperfusion. Horizontal shaded line indicates CBF increase of 100% as definition of hyperperfusion. ● indicates patients with hyperperfusion.

cerebral hemorrhage. Taken together, the risk of intracerebral hemorrhage in patients with hyperperfusion was >10 times that of patients without hyperperfusion. Therefore, detection of hyperperfusion after CEA is important in identifying patients at risk of intracerebral hemorrhage after CEA. Some previous studies suggested that patients with preoperative hemodynamic failure run a definite risk for hyperperfusion syndrome.[1,2,4,29] From these points of view, SPECT is very useful because it can quantitatively measure both CBF and hemodynamic reserve as cerebral vasoreactivity to acetazolamide challenge. The cerebral vasoreactivity to CO_2 or acetazolamide has been proposed as a test for cerebral hemodynamic reserve.[13–17] Acetazolamide is a carbonic anhydrase inhibitor that causes a disequilibrium of the CO_2 buffer system and results in vasodilation at least as effective as inhalation of 5% CO_2.[30] Administration of acetazolamide induces a rapid and marked increase in CBF, ranging from 20% to 80%,[14,27,31,32] which corresponds to the vasoreactivity of the controls in the present study. Recently, it has been demonstrated that transcranial Doppler ultrasonography (TCD) with acetazolamide challenge is also able to assess cerebral vasoreactivity.[33,34] However, TCD cannot measure CBF itself, in contrast to SPECT.

The present study demonstrated that a significant CBF increase on the first postoperative day was seen only in the reduced CVR group but not in the normal CVR group. Furthermore, CBF and its increase 1 day after CEA on the ipsilateral side were significantly higher than those on the contralateral side in the reduced CVR group but not in the normal CVR group. One month later this difference almost disappeared. This relative as well as absolute ipsilateral CBF increase is in accord with the previous study.[29] However, our results more clearly demonstrated a significant association of reduced CVR, which is directly measured on acetazolamide-challenge SPECT, with postoperative hyperperfusion. It is noteworthy that the CBF increase of >100% on the first postoperative day was only seen in 2 patients with intracerebral steal. Severe and diffuse asymmetry on preoperative SPECT of the 2 patients seems to be characteristic. A significant association of intracerebral steal with the hyperperfusion (CBF increase ≥100%) on the first postoperative day was also observed. These results suggest that the basic mechanism responsible for the hyperperfusion is massive vasodilatation due to loss of vasoconstriction because of chronic cerebral ischemia distal to the high-grade carotid stenosis. In this situation, the abrupt restoration of perfusion pressure after surgical correction of a tight ICA stenosis cannot be compensated for by vasoconstriction and may result in cerebral edema and even cerebral hemorrhage, as a consequence of a leaky capillary bed.[1–3,11] This is considered to be equivalent to the normal perfusion pressure breakthrough seen after the resection of some arteriovenous malformation.[3,12] In addition, autopsy studies of patients who died of intracerebral hemorrhage after CEA have demonstrated intracerebral arterial histological change resembling malignant hypertension, including swelling and hyperplasia of endothelial cells, extravasation of erythrocytes, and fibrinoid necrosis.[3,35] These findings are consistent with the cerebral hemodynamics hypothesis described above.

Recent studies have demonstrated that intraoperative TCD monitoring can also identify patients at risk for hyperperfusion.[7,36] The TCD criteria for hyperperfusion is >100% increase of ipsilateral peak blood flow velocity or pulsatility index of the middle cerebral artery, which seems to be analogous to hyperperfusion criteria in CBF measurement. Furthermore, repeated observations are more practical with TCD than SPECT. Results from the previous TCD study correlate well with results from the present study but also provide more information about the time course of recovery from hyperperfusion.[37] It has been reported, however, that symmetrically elevated velocities in both middle cerebral arteries were seen in a patient with ipsilateral hyperperfusion identified on SPECT.[21] In addition, TCD monitoring is not always possible for all patients because of a thick skull, resulting in a poor signal to noise ratio or no signal at all.[7,36] When the limitations of TCD are considered, SPECT may be the better method for identifying hyperperfusion after CEA, although it is more expensive. TCD is more suitable for repeated monitoring.

Previous studies with direct intraoperative measurements of ICA flow before and after reconstruction demonstrated results comparable to those reported here, with means of 80 to 130 and 160 to 210 mL/min, respectively.[29,38–40] In the present study ICA flow increase after reconstruction was significantly larger in the reduced CVR group than in the normal CVR group. In addition, ICA flow increase after reconstruction was significantly correlated with CBF increase on the first postoperative day in the reduced CVR group despite the 1-day interval between the measurement of ICA flow and CBF. This correlation was not observed in the normal CVR group. These results suggest that an extremely large increase of ICA flow after reconstruction occurs only in patients with severely impaired cerebral autoregulation. The 95% CI associated with a predicted mean ICA flow increase for 100% CBF increase on the first postoperative day suggests that the threshold of ICA flow increase for hyperperfusion is 330 mL/min in the reduced CVR group. Such a large

increase of ICA flow was observed only in 2 patients with intracerebral steal and resulted in hyperperfusion. During surgery, therefore, an ICA flow increase after reconstruction may be a good indicator of hyperperfusion after CEA.

Once hyperperfusion syndrome is established, it is difficult to control and treat.[9,34] Review of the literature suggests that the first few postoperative days are the high-risk period for intracerebral hemorrhage after CEA.[35] Therefore, it is important to diagnose patients as soon as possible to determine when to start preventative measures. The present results imply that severely reduced vasoreactivity (intracerebral steal) and an excessive increase in ICA flow after reconstruction (>330 mL/min) may help to identify patients at risk for developing cerebral hyperperfusion after CEA. Most authors recommend strict control of blood pressure in the postoperative period to prevent hyperperfusion syndrome.[1,4,11,35,36] According to the present results, it is possible to start strict control of blood pressure intraoperatively to prevent postoperative cerebral hyperperfusion if the patients demonstrate ICA flow increase of ≥330 mL/min. Because of the small number of cases in the present study, however, a larger number of cases would be required to establish the sensitivity and specificity of this value.

Conclusions

In the present study preoperative SPECT with acetazolamide challenge and ICA flow measurement during surgery seem to be sensitive methods to identify patients who are at risk for hyperperfusion after CEA. Intracerebral steal on SPECT enables us to select a small subset of patients among those clinically suspected to be at risk for hyperperfusion. ICA flow measurement may provide the opportunity to further distinguish patients at risk and to start careful monitoring and control of blood pressure intraoperatively to prevent postoperative hyperperfusion syndrome.

Acknowledgments

We want to express our gratitude to all members of the SPECT technical staff: Osamu Ueda, Yukihiro Otani, Toshiaki Yamaguchi, Masaru Ishihara, and Kenzo Sawada.

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