

Long-term changes in cerebral and ocular hemodynamics after carotid endarterectomy in symptomatic patients with unilateral carotid artery stenosis

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Abstract. – OBJECTIVE: The aim of the current study was to describe the alternation pattern of cerebral and ocular blood flow velocities (BFVs) in symptomatic patients with unilateral carotid stenosis after carotid endarterectomy.

PATIENTS AND METHODS: 20 symptomatic patients underwent carotid endarterectomy for $\geq 50\%$ unilateral carotid stenosis. Cerebral and ocular hemodynamics were evaluated by Transcranial Doppler (TCD) and Color Doppler imaging (CDI), respectively, first preoperatively, then during the following several days after carotid endarterectomy before discharge, and finally two to sixteen months later.

RESULTS: Statistically significant improvements in the BFVs were recorded in the ipsilateral anterior cerebral artery (ACA), middle cerebral artery (MCA) and short posterior ciliary artery (SPCA) during the following several days after carotid endarterectomy. Preoperative retrograde flows of the ipsilateral ophthalmic artery (OA) in two patients returned to antero-grade direction immediately following carotid endarterectomy. At the follow-up of two to sixteen months, the BFVs of the ipsilateral ACA, MCA and SPCA tended to decline and were no longer statistically significant from the preoperative values.

CONCLUSIONS: Carotid endarterectomy significantly increased the flow velocities of ipsilateral cerebral anterior circulation and OA branching artery in patients with unilateral carotid stenosis early after surgery. At the long-term follow-up, the flow velocities in the ipsilateral hemisphere had the tendency to reduce and approach the preoperative level.

Key Words:

Carotid endarterectomy, Cerebral hemodynamics, Ocular hemodynamics, Carotid stenosis, Blood flow velocity.

Introduction

The atheromatous plaque at the carotid bifurcation is a possible source of cerebral emboli and thus carotid stenosis is one of the most significant risk factors for stroke. Carotid endarterectomy (CEA) is an effective treatment for direct removal of carotid plaque in patients with moderate or severe carotid stenosis. Two large international clinical trials have demonstrated that CEA reduces the risk of embolic stroke in symptomatic patients with moderate or severe carotid stenosis^{1,2}. CEA may offer more advantages than the reduced stroke risk to symptomatic patients with carotid stenosis. The presence of carotid stenosis may be associated with an increased rate of cognitive deterioration due to an impaired cerebral hemodynamics status³⁻⁵. CEA removes carotid arterial narrowing, resolves chronic brain cortex hypoperfusion associated with the carotid stenosis, and thus improves cerebral cognitive performance⁶⁻⁸. The ophthalmic artery (OA) is the first branch of the internal carotid artery (ICA). Hemodynamically significant carotid stenosis results in decreased or reversed OA flow and displays chronic ocular ischemic syndrome⁹. CEA significantly increases the blood flow of OA, corrects the reversed OA flow, and improves or prevents the progress of chronic ocular ischemia¹⁰⁻¹².

There have been reports¹³⁻¹⁸ affirming that CEA significantly improves cerebral hemodynamics at different time-points postoperatively comprising within one week^{13,14}, one month^{15,16} and three months^{17,18} after surgery. Other investigations indicated that reduced OA blood flow velocity (BFV) in the carotid stenosis was corrected with

successful CEA within 48 hours¹⁰ and one week¹¹ after surgery. However, the changes in cerebral and ocular hemodynamics with the duration of the recovery after CEA have been less studied. The current study has investigated the cerebral and ocular hemodynamics at several days postoperatively before discharge and during a long-term follow-up and compared these outcomes with the preoperative measurement. Transcranial Doppler (TCD) and Color Doppler imaging (CDI) are the non-invasive and reproducible imaging techniques. TCD investigated the BFVs of the major intracranial cerebral arteries. CDI measured retrobulbar BFVs for the reliable assessment of ocular circulation.

Patients and Methods

Patients

From October 2013 to May 2016, 33 patients with symptomatic internal carotid artery stenosis underwent CEA in our surgical group. Of these, 7 patients were excluded from the analysis because 1 patient had the concurrent vertebral artery stenosis ($\geq 30\%$ diameter reduction) and 6 patients had the contralateral carotid occlusion. 6 patients were lost to follow-up. The remaining 20 patients (13 men and 7 women, aged 66.2 ± 7.2 years) who had unilateral carotid stenosis ($\geq 50\%$) with no or mild ($< 50\%$) stenosis on the contralateral side were finally enrolled into the study. The left 20 patients were symptomatic (6 patients had minor hemispheric stroke with mild disability, 14 patients had transient ischemic attacks including amaurosis fugax in 4 patients and 4 patients had ocular symptom). The degree of the ipsilateral carotid stenosis was $78.2\% \pm 14.7\%$, ranging from 55% to 95%. 9 patients were operated on the right side and 11 on the left side. The Ethics Committee of our hospital approved the study protocol.

The investigation of extracranial neck vessels was performed using color Duplex ultrasound scanning. The degree of carotid stenosis was calculated as the percentage of diameter reduction on the preoperative CT angiography (CTA) of the supra-aortic trunks. The patency of CEA was confirmed by means of carotid CTA on the approximately 4th postoperative day. TCD and CDI investigations were performed preoperatively and during the several days after CEA before discharge mostly on day three, four and five postoperatively, when the patients became ambulatory and hemodynamically stable. An additional late follow-up

investigation of TCD and CDI was performed after 2 to 16 months. The long-term patency of the operated ICA was also evaluated with color Duplex sonography at 2-16 months after CEA. Symptoms of hyperperfusion syndrome (HS) was explained as headache, seizures, confusion, neurologic deficit, and high blood pressure (systolic blood pressure > 150 mmHg/or diastolic blood pressure > 90 mmHg). We considered the occurrence of headache or hypertension during or after CEA as oligosymptomatic cases of HS, whereas a complete HS would show the rest of symptoms already mentioned. No patients suffered from the HS postoperatively.

Carotid Endarterectomy

All patients underwent successful CEA under general anesthesia at 3-6 weeks after the last neurologic event. The patients were artificially ventilated with an air-oxygen mixture and 0.4-1.0% inspired isoflurane. Routine monitoring during anesthesia was performed by using standard electrocardiography and placement of an intra-arterial catheter for direct arterial blood pressure and pulse oximetry. Blood pressure was kept stable in a range of $\pm 20\%$ of the preoperative level throughout the procedure by adjusting the depth of anesthesia. A longitudinal incision was made along anterior border of the sternocleidomastoid muscle to expose the carotid bifurcation. Heparin (5,000 IU) was given intravenously prior to cross-clamping. Vascular clumps were used to occlude common carotid artery (CCA), ICA and ECA. CCA and ICA were longitudinally opened along the anterior vessel walls. The atheromatous plaque and nearby intima were carefully removed from the carotid bifurcation. The arteriotomy was closed using a Dacron patch in all patients. An indwelling shunt was routinely used during the surgical procedure. The skin incision was eventually closed after ensuing vascular patency.

Transcranial Doppler

TCD investigation was performed by the same person to maintain a constant angle of insonation, with the patient lying in a comfortable supine position, with no visual or acoustic stimulation, in a quiet room. BFVs were measured by means of TCD in anterior cerebral arteries (ACA), middle cerebral arteries (MCA) and posterior cerebral arteries (PCA). Recording was made using commercially available equipment (DWL Elektronische Systeme GmbH, Sipplingen, Germany) with a 2-MHz pulsed Doppler probe was used. ACA, MCA and PCA were insonated through the tem-

poral window above the zygomatic arch at depths of 65-75, 50-60 and 60-75 mm, respectively.

If an intracranial vessel was not found, it was considered as a missing value, and was not included in the statistical analysis. BFV was expressed in cm/s as the peak value of the Doppler velocity spectrum outline (representing maximal flow velocity) over 4.5 s (V_{peak}). Blood pressure was measured at each examination using a regular cuff.

Color Doppler Imaging

All patients underwent BFV assessment of their OA, central retinal artery (CRA) and short posterior ciliary artery (SPCA) by means of CDI. The same experienced sonographer performed all retrobulbar CDI examinations by means of a color Doppler imaging device (General Electric, Tokyo, Japan) using a 7.5 Hz multifrequency linear transducer. During the examinations, patients were examined in the supine position with their heads inclined at about a 30-degree angle. The transducer was covered in gel and gently placed externally upon the eyelid, avoiding excessive pressure. The OA was identified as the vessel parallel to the nasal border of the optic nerve just after crossing it, the CRA as the vessel within the optic nerve and approximately 2-5 mm behind the globe, and the SPCA as the vessel on the temporal side of the optic nerve approximately 10-15 mm behind the globe. Peak systolic BFVs were recorded in OA, CRA and SPCA, and flow direction was noted. Negative values represent flow velocity in a reversed direction. The BFV was measured at the medial proximal point of the arteries using a wall filter of 100 Hz and sample volume of 0.12 mm. Doppler insonation angle was adjusted between 0 and 40 degrees to the vessels.

Statistical Analysis

Statistical analysis was done with SPSS version 11.5 software (SPSS, Chicago, IL, USA). Continuous data were presented as mean \pm standard deviation. Comparisons of the BFVs between

the different groups were made using two-tailed paired *t*-test. A *p*-value of < 0.05 was considered statistically significant.

Results

Changes in Cerebral Hemodynamics Ipsilateral to Carotid Stenosis Before and After CEA

The altered pattern of the BFVs of the ipsilateral ACA, MCA, and PCA before and after CEA at different time-points are summarized in Table I. The BFV of the ipsilateral ACA significantly increased from 98.3 ± 43.7 cm/s preoperatively to 118.8 ± 43.0 cm/s during the following several days after CEA ($p = 0.029$). 2-16 months later, the BFV of the ipsilateral ACA decreased from 118.8 ± 43.0 cm/s at several days postoperatively to 109.4 ± 35.5 cm/s ($p = 0.338$) and was no longer statistically different from the preoperative value (109.4 ± 35.5 vs. 98.3 ± 43.7 cm/s, $p = 0.264$).

The BFV of the ipsilateral MCA was markedly elevated from 146.6 ± 80.0 cm/s preoperatively to 160.3 ± 76.6 cm/s during the following several days after CEA ($p = 0.012$). 2-16 months later, the BFV of the ipsilateral MCA was reduced from 160.3 ± 76.6 cm/s at several days postoperatively to 149.9 ± 75.2 cm/s ($p = 0.109$) and did no longer statistically differ from the preoperative value (149.9 ± 75.2 vs. 146.6 ± 80.0 cm/s, $p = 0.572$).

There were no significant differences on the BFVs of the ipsilateral PCA preoperatively, during the following several days after CEA and 2-16 months later.

Changes in Cerebral Hemodynamics Contralateral to Carotid Stenosis Before and After CEA

The BFVs of the contralateral ACA, MCA, and PCA before and after CEA at different time-points are shown in Table II. Statistically significant dif-

Table I. The cerebral BFVs of the ipsilateral ACA, MCA, and PCA preoperatively, at several days postoperatively, and on 2-16 months after CEA.

	Preoperatively	Several days after CEA	2-16 months later
BFVs of ipsilateral ACA, cm/s	98.3 ± 43.7	$118.8 \pm 43.0^*$	$109.4 \pm 35.5^\#$
BFVs of ipsilateral MCA, cm/s	146.6 ± 80.0	$160.3 \pm 76.6^*$	$149.9 \pm 75.2^\#$
BFVs of ipsilateral PCA, cm/s	62.3 ± 14.6	$65.3 \pm 16.4^\#$	$62.9 \pm 18.1^\#$

* $p < 0.05$ vs. preoperatively; $^\#p \geq 0.05$ vs. preoperatively. BFV, blood flow velocity; ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; CEA, carotid endarterectomy.

Table II. The cerebral BFVs of the contralateral ACA, MCA, and PCA preoperatively, at several days postoperatively, and 2-16 months after CEA.

	Preoperatively	Several days after CEA	2-16 months later
BFVs of contralateral ACA, cm/s	122.2 ± 60.2	111.8 ± 41.3 [#]	106.4 ± 40.9 [#]
BFVs of contralateral MCA, cm/s	148.5 ± 58.7	150.2 ± 57.9 [#]	139.3 ± 59.3 [#]
BFVs of contralateral PCA, cm/s	63.7 ± 18.7	67.2 ± 19.4 [#]	60.3 ± 13.0 [#]

[#] $p \geq 0.05$ vs. preoperatively.

BFV, blood flow velocity; ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; CEA, carotid endarterectomy.

ference on the BFV of the contralateral ACA was not observed preoperatively and during the following several days after CEA (122.2 ± 60.2 vs. 111.8 ± 41.3 cm/s, $p = 0.458$). Likewise, the BFV of the contralateral ACA on 2-16 months after CEA was not statistically different from the preoperative value (106.4 ± 40.9 vs. 122.2 ± 60.2 cm/s, $p = 0.298$).

There was no statistically significant difference on the BFV of the contralateral MCA between preoperatively and during the following several days after CEA (148.5 ± 58.7 vs. 150.2 ± 57.9 cm/s, $p = 0.769$). Likewise, the BFV of the contralateral MCA on 2-16 months after CEA did not statistically differ from the preoperative value (139.3 ± 59.3 vs. 148.5 ± 59.3 cm/s, $p = 0.313$).

Similarly, there were no significant differences on the BFVs of the contralateral PCA preoperatively, during the following several days after CEA and 2-16 months later.

Changes in Ocular Hemodynamics Ipsilateral to Carotid Stenosis Before and After CEA

The altered pattern of the BFVs of the ipsilateral CRA and SPRA before and after CEA at the different time-points are summarized in Table III. Although the BFV of the ipsilateral CRA increased from 8.6 ± 3.0 cm/s preoperatively to 11.2 ± 4.7 cm/s during the following several days after CEA, the difference did not reach statistical significance ($p = 0.055$). Similarly, the BFV of the ipsilateral CRA on 2-16 months after CEA was not statistically different from the preoperative value (12.2 ± 6.0 vs. 8.6 ± 3.0 cm/s) ($p = 0.599$).

The BFV of the ipsilateral SPCA significantly increased from 10.0 ± 2.4 cm/s preoperatively to 13.7 ± 4.8 cm/s during the following several days after CEA ($p = 0.008$). 2-16 months later, the BFV of the ipsilateral SPCA decreased from 13.7 ± 4.8 cm/s at several days postoperatively to 12.2 ± 4.9 cm/s ($p = 0.232$) and was no longer statistically significant from the preoperative value (12.2 ± 4.9 vs. 10.0 ± 2.4 cm/s, $p = 0.110$).

Changes in Ocular Hemodynamics Contralateral to Carotid Stenosis Before and After CEA

The BFVs of the contralateral CRA and SPCA before and after CEA at the different time-points are shown in Table IV. There was no statistically significant difference on the BFV of the contralateral CRA preoperatively, during the following several days after CEA and 2-16 months later.

There was no statistically significant difference on BFV of the contralateral SPCA preoperatively and during the following several days after CEA (9.9 ± 2.3 vs. 12.0 ± 4.0 cm/s, $p = 0.084$). Likewise, the BFV of the contralateral SPCA on 2-16 months after CEA did not differ from the preoperative value (9.6 ± 3.2 vs. 9.9 ± 2.3 cm/s, $p = 0.838$).

Illustrative Cases

A 62-year-old man complained of headache with a medical history of minor disabling stroke two months ago. A left CEA successfully removed the 85% stenosis of the left carotid bifur-

Table III. The ophthalmic BFVs in the ipsilateral CRA and SPCA preoperatively, at several days postoperatively, and 2-16 after CEA.

	Preoperatively	Several days after CEA	2-16 months later
BFVs of ipsilateral CRA, cm/s	8.61 ± 3.02	11.16 ± 4.70 [#]	12.23 ± 5.98 [#]
BFVs of ipsilateral SPCA, cm/s	9.96 ± 2.35	13.72 ± 4.75 [*]	12.23 ± 4.90 [#]

^{*} $p < 0.05$ vs. preoperatively; [#] $p \geq 0.05$ vs. preoperatively. BFV, blood flow velocity; CRA, central retinal artery; SPCA, short posterior ciliary artery; CEA, carotid endarterectomy.

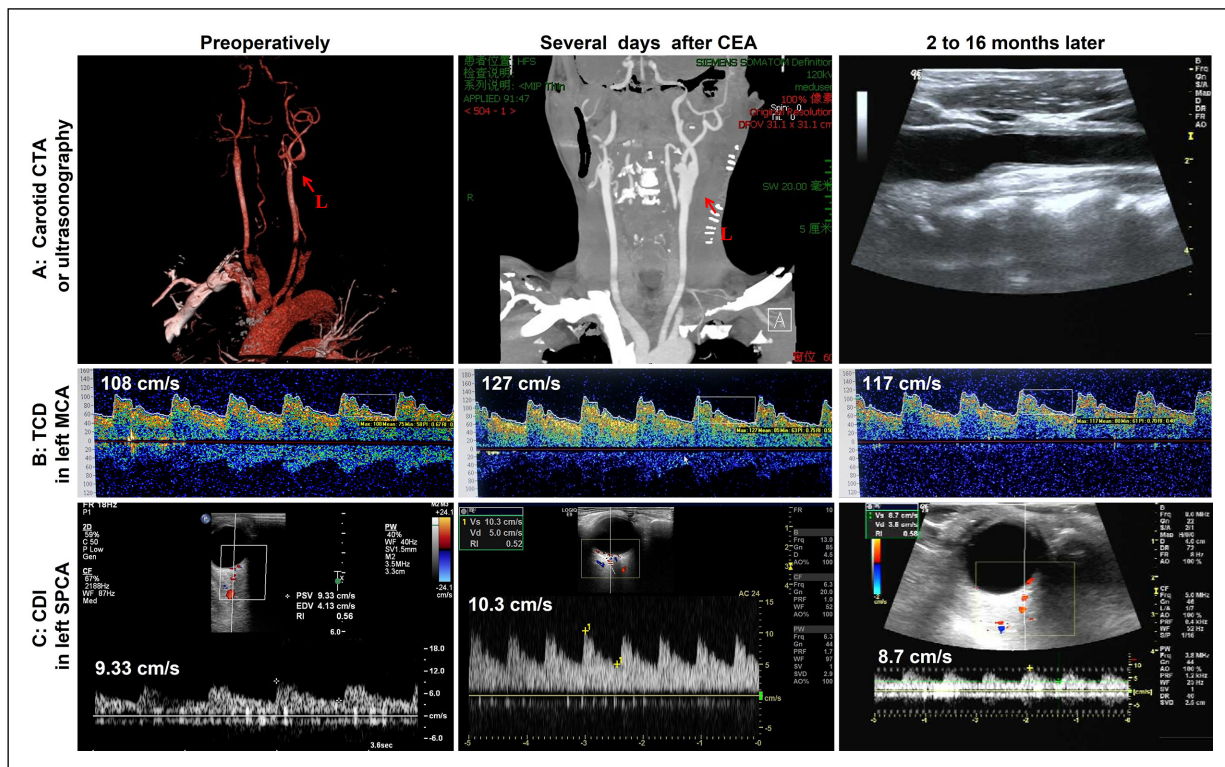


Figure 1. Image data acquired from a 62-year-old man with left 85% carotid stenosis. **A**, Left-sided CEA was successfully performed to resolve carotid stenosis, and good patency of carotid artery was confirmed by postoperative CTA and three-month follow-up color Duplex ultrasound scanning. **B**, The BFVs of left MCA increased from 108.0 cm/s to 127.0 cm/s at three days postoperatively, and eventually decreased to 117.0 cm/s at the follow-up of three months following CEA. **C**, The BFVs of left SPCA increased from 9.3 cm/s at three days postoperatively, and eventually decreased to 8.7 cm/s at the follow-up of three months following CEA. CEA, Carotid endarterectomy; CTA, computed tomography angiography; BFV, blood flow velocity; MCA, middle cerebral artery; SPCA, short posterior ciliary artery.

ation (Red arrowheads, Figure 1A). The patency of CEA was confirmed by carotid CTA at three days postoperatively and color Duplex ultrasound scanning on three months after surgery (Figure 1A). The BFV of left MCA increased from 108.0 cm/s preoperatively to 127.0 cm/s at three days postoperatively (Figure 1B). Three months later, the BFV of the left MCA decreased from 127.0 cm/s early after surgery to 117.0 cm/s (Figure 1B). Likewise, CEA resulted in an elevation on the BFV of the left SPCA from 9.3 cm/s preoper-

atively to 10.3 cm/s at three days postoperatively (Figure 1C). The BFV of the left SPCA was reduced to 8.7 cm/s at the end of three-month follow-up period (Figure 1C).

A 68-year-old woman complained of declining visual acuity in the right eye with a medical history of minor disabling stroke twice four months and one year ago. A right CEA successfully removed the 95% stenosis of the left carotid bifurcation (Red arrowheads, Figure 2A). The patency of CEA was confirmed by carotid CTA at four

Table IV. The ophthalmic BFVs of the contralateral CRA and SPCA preoperatively, at several days postoperatively, and 2-16 months after CEA.

	Preoperatively	Several days after CEA	2-16 months later
BFVs in contralateral CRA, cm/s	9.4 ± 3.0	11.3 ± 2.4 [#]	10.1 ± 2.7 [#]
BFVs in contralateral SPCA, cm/s	9.9 ± 2.3	12.0 ± 4.0 [#]	9.6 ± 3.2 [#]

[#]*p* ≥ 0.05 vs. preoperatively. BFV, blood flow velocity; CRA, central retinal artery; SPCA, short posterior ciliary artery; CEA, carotid endarterectomy.

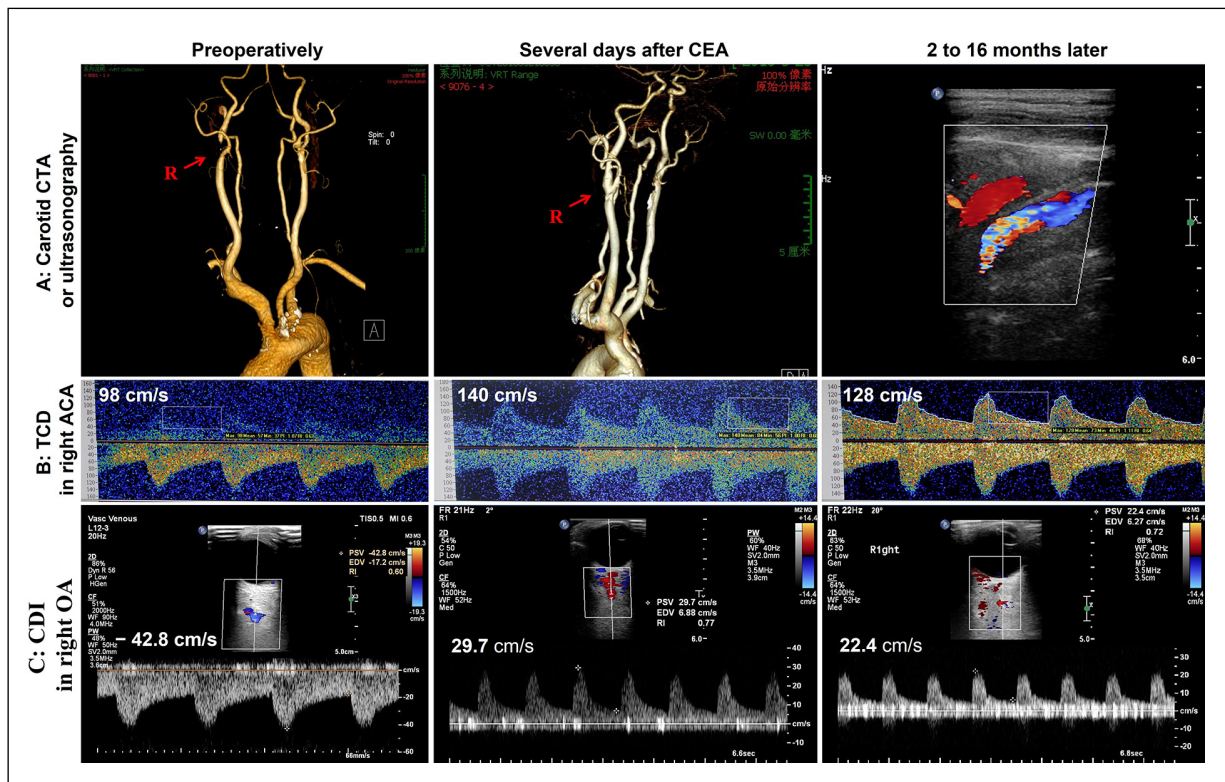


Figure 2. Image data acquired from a 68-year-old woman with right 95% carotid stenosis. **A**, Right-sided CEA was successfully performed to resolve carotid stenosis, and good patency of carotid artery was confirmed by postoperative CTA and two-month follow-up color Duplex ultrasound scanning. **B**, The BFVs in right ACA increased from 98.0 cm/s to 140.0 cm/s at three days postoperatively, and eventually decreased to 128.0 cm/s at the follow-up of two months following CEA. **C**, Preoperative reversed OA flow resolved after undergoing CEA. The postoperative BFVs of the ipsilateral OA were 29.7 cm/s and 22.4 cm/s at three days postoperatively and two months later, respectively. CEA, Carotid endarterectomy; CTA, computed tomography angiography; BFV, blood flow velocity; ACA, anterior cerebral artery; OA, ophthalmic artery.

days postoperatively and color Duplex ultrasound scanning on two months after surgery (Figure 2A). The BFV of the left ACA increased from 98.0 cm/s preoperatively to 140.0 cm/s at three days postoperatively (Figure 2B). Two months later, the BFV of the left MCA displayed the decrement from 140.0 cm/s early after surgery to 128.0 cm/s (Figure 2B). The right CDI showed reversed flow in the OA and the BFV was -42.8 cm/s (Figure 2C). The flow direction of the OA returned to antegrade direction following CEA, and the BFVs were 29.7 cm/s and 22.4 cm/s at three days after CEA and two months later, respectively (Figure 2C).

Discussion

This recent study had two most important findings. First, in symptomatic patients with unilateral carotid stenosis, CEA resulted in a significant BFV

increase in ipsilateral ACA, MCA and SPCA during the following several days after CEA before discharge. Second, 2-16 months after surgery, the BFVs of the ipsilateral ACA, MCA and SPCA tended to decrease and returned to their preoperative values.

Successful CEA is associated with a significant improvement in cerebral and ocular hemodynamics ipsilateral to carotid stenosis early after surgery. These changes can be interpreted as an increase of the perfusion pressure because of the recovery of normal diameter and flow in the ICA early after CEA. Similar results have been reported in our previous study¹³ and elsewhere¹⁴. It is interesting to note that the increased flow velocities have the tendency to decrease and approached the preoperative measurements at the follow-up of 2-16 months after surgery. The restored cerebrovascular autoregulation function (CAF) might be responsible for the observation that BFVs returned to their preoperative levels¹⁹. Improvement of cerebral autoregulation was in-

dependent of changes in cerebral BFV¹⁹. CAF is impaired in patients with carotid stenosis as the cerebral vessels are already vasodilated to compensate for the reduction in cerebral perfusion pressure¹⁹. If intracranial microcirculation is maximally dilated, then CAF is exhausted. In patients with the severe carotid stenosis, the dilated cerebral vessels can be maintained, which may lead to cerebral hyperperfusion early after removal of the carotid plaque^{20,21}. This constant dilation of arterioles can interfere with the ability of the cerebral vessels to constrict in response to the increased ICA perfusion pressure early after CEA^{20,21}. With the duration of postoperative recovery, CAF is improved in intracranial vessels due to the progressive restoration of cerebrovascular tone and arterial vasoconstriction response^{20,21}. Bishop et al²² indicated that CEA restored the ability of cerebral microcirculation to autoregulate properly at 6 months after surgery. Müller et al²³ also reported that pulsatility index was significantly increased compared to preoperative value at 6 months after CEA. Consequently, the long-term benefit of CEA may be related to a decrement on resting cerebral BFVs and an improvement in the CAF.

Our findings agree with some previous studies^{22,23}, but are in conflict with several reports^{24,25}. Bishop et al²² reported that CBF was significantly increased at 3 hours after CEA and had returned to its preoperative value at 6 months postoperatively, but CAF was significantly improved in the long-term follow-up. Müller et al²³ indicated that BFV of MCA ipsilateral to CEA was increased at 7 days after surgery and had returned to the preoperative level after 3 months. Zachrisson et al²⁴ demonstrated that significant increase in BFV was observed in the ipsilateral MCA the first few days after CEA, but the BFV of the ipsilateral MCA had returned to normal at the follow-up 3-12 months after CEA. In contrast, Blohmé et al²⁵ reported that the BFV of the ipsilateral MCA was significantly increased six days postoperatively compared to the preoperative value and was still elevated at the late follow-up after 3-12 months. Several factors may be responsible for the conflicting findings. First, in the study, all patients were symptomatic, mean stenosis was 78.2%, and in 12 of the 20 cases stenosis was > 70%. It is known that symptomatic subjects with high-grade carotid stenosis may present the decrease in cerebral perfusion, the insufficient collateral circulation, and the impaired cerebrovascular reserve. Therefore, it is conceivable that a relative vasodilation persists in intracranial vessels early after removal of a hemodynamically significant

carotid stenosis. As a result, the BFVs of the ipsilateral hemisphere are at the higher levels when full perfusion pressure was restored. An intracranial vasoconstriction results from the restored cerebrovascular reserve and is also compatible with a reduction in the BFVs of the ipsilateral anterior circulation in the long-term follow-up. Second, the modality of measurements should be considered: various techniques were utilized in previous studies^{15,16}, including MRI, single photon emission computed tomography¹⁷, intravenous xenon-133 technique²², and TCD^{18,23-25}. However, because these techniques focus mainly on the flow velocity, flow volume or metabolic information of the brain, comparisons with different studies are difficult.

Limitations

A limitation of this study is the relatively small sample size. However, the sample size was large enough to demonstrate short-term improvement and long-term normalization of cerebral and ocular hemodynamics after CEA. In the present study, no flow volume measurements were performed in the intracranial and ocular branching arteries. Flow volume quantification by MRI has been demonstrated to be valuable for monitoring the effect of CEA on cerebral and ocular hemodynamics^{15,16}.

Conclusions

In summary, CEA resulted in a significant increase of BFVs in the ipsilateral anterior circulation and SRCA during the several days after surgery before discharge. This effect was not maintained with the duration of postoperative recovery. The BFVs of the ipsilateral anterior circulation and SPCA tended to decrease and approached the preoperative levels at the follow-up of 2-16 months after surgery. Therefore, the advantage of the CEA might be related to the early improvement of cerebral and ocular hemodynamics and the long-term restoration of cerebrovascular reserve.

Conflict of Interest

The authors declare that there is no conflict of interest.

Ethics Approval

This study was conducted with the approval of the institutional review board of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

Informed Consent

Because this was a retrospective study, no informed consent was required.

Availability of Data and Material

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

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Authors' Contributions

Z.Y.: collection and/or assembly of data, provision of study material or patients, data analysis and interpretation; Q.W.: collection and/or assembly of data, data analysis and interpretation, provision of study material or patients; J.W.: financial support, conception and design, manuscript writing, final approval of manuscript.

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