Recovery of Cerebrovascular Reserves after Stenting for Symptomatic Carotid Artery Stenosis

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Summary

Although a decrease in cerebrovascular reserves (CVR) is known to enhance the risk of stroke, changes in this parameter after carotid artery stenting (CAS) have rarely been investigated. The present study is the first to compare CVR recoveries after applying CAS to patients with symptomatic carotid artery disease.

CAS was performed for 31 consecutive patients with symptomatic carotid artery disease. They underwent acetazolamide-challenged single photon emission computed tomography (SPECT) before and after CAS to obtain data on resting stage cerebral blood flow (CBF_{rest} values) in various regions of interest (ROIs) defined by a three-dimensional stereotactic ROI template. CVR values on ipsilateral and contralateral hemispheric sides were then calculated based on the CBF_{rest} data.

The 31 patients were dichotomized into unilateral (n=22) and bilateral (n=9) lesion groups, and no significant between-group differences were observed in CBF_{rest} before and after CAS. In the unilateral group, there were no differences in CVR values before and after CAS. In the bilateral group, however, the CVR values significantly increased in nearly all the investigated ROIs on the contralateral side. Also, the hemispheric CVR values on both sides significantly increased after CAS in the bilateral group, while no such increase was observed in the unilateral group.

CAS in patients with symptomatic bilateral carotid artery disease has the potential utility for their haemodynamic improvement even on the contralateral hemispheric side.

Introduction

Carotid endarterectomy (CEA) has been used as a standard method for preventing stroke episodes in patients with symptomatic unilateral carotid artery stenosis [1,2]. However, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) reported that CEA, when performed in patients with bilateral carotid artery stenosis, increased a perioperative risk up to the relative risk score of 2.3 [3]. Although carotid artery stenting (CAS) is a possible alternative to CEA, the widespread use of CAS remains controversial because of the lack in high-level evidence regarding its effectiveness [1,2]. Meanwhile, a Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) study has shown that CAS as well as CEA is suitable for patients with contralateral carotid artery occlusion with a similar level of effectiveness to prevent their adverse events [4]. Because severe carotid artery diseases, particularly bilateral carotid artery lesions, have an increased risk of not only distal artery-to-artery embolisms but also haemodynamic ischemia, the use of CAS in these severe cases would potentially improve cerebral haemodynamics.

Reportedly, a decrease in cerebrovascular reserves (CVR) enhances the risk of stroke [5-10]. The CVR decrease, as assessed by transcranial sonography (TCD) [11], magnetic resonance imaging (MRI) [12] or single photon emission computed tomography (SPECT) [14], has been recognized as a useful predictor for CEA outcomes. The effectiveness of CAS can also be assessed by the quantitative measurement of CVR [5-10].

The present study first attempted a quantitative analysis of cerebral haemodynamics using acetazolamide (ACZ)-challenged SPECT in CAS-treated patients with carotid artery diseases including contralateral carotid artery lesions (occlusion or severe stenosis).

The CVR values before and after CAS were then compared in different regions of interest (ROIs) defined by a highly reproducible three-dimensional stereotactic ROI template (3DSRT) consisting of 12 regions in each hemisphere. Here we report the results of this pilot study of evaluating the CVR recovery after CAS for treatment of symptomatic carotid artery stenosis, in order to provide new information on the potential risk reduction in ischemic stroke through the recovery of cerebral haemodynamics.

Materials and Methods

Subjects

Patients with symptomatic carotid artery disease (stenosis or occlusion), admitted consecutively to Yokohama Brain and Stroke Center between January 2003 and September 2005, were evaluated by routine diagnostic investigations, and 37 of them were found qualified to undergo CAS based on the NASCET criteria [3]. The CAS procedure was approved by the institutional ethics committee. Of these 37 patients, 31 were enrolled on the basis of the SAPPHIRE criteria, with their agreements as written informed consents. The 31 patients underwent SPECT examinations before and after CAS as described later, and then dichotomized to unilateral (n=22) and bilateral (n=9) groups according to their pre-CAS conditions of the contralateral carotid artery. The unilateral lesion was defined as the case of less than 70% stenosis and the bilateral lesions as that of 70% or higher. The risk factor profiles, including age, sex, hypertension, diabetes mellitus, dyslipidemia, smoking, and history of myocardial infarction and angina pectoris are summarized in Table 1.

Table 1 **Main characteristics of 31 patients with symptomatic unilateral and bilateral carotid artery lesions**

Item	**Unilateral (n=22)**	**Bilateral (n=9)**	***P* Value**
Age (y; mean, SD)	72 (±5.4)	67.8 (±3.6)	0.04*
Sex (% men)	95%	88%	0.76
Cerebrovascular events before CAS			
Minor stroke	21 (95%)	8 (88%)	0.50
Transient ischemic attack	1 (5%)	1 (12%)	0.50
Degree of ipsilateral carotid stenosis (mean±SD)	82% (±8.5)	82% (±5.5)	0.89
Degree of contralateral carotid stenosis (mean±SD)	37% (±12)	91% (±14.8)	0.0001*
Degree of ipsilateral carotid stenosis after CAS(mean)	3%	5%	0.58
Hypertension	17 (69%)	9 (100%)	0.25
Diabetes	5 (21%)	1 (11%)	0.53
Dyslipidemia	12 (48%)	6 (67%)	0.41
Coronary heart disease	1 (4%)	1 (11%)	0.77
Current smoking	15 (65%)	2 (22%)	0.09

Symbols: SD, standard deviation; CAS, carotid artery stenting.
** Statistically significant difference at P < 0.05; Mann-Whitney U-test*

Brain SPECT study

CAS was performed for all the patients (n = 31) using a biplane neuroangiography unit (Neurostar Plus/T.O.P., Siemens, Deutschland) under local (n = 30) or general (n = 1) anaesthesia by a team consisting of vascular surgeons, interventional radiologists and an anaesthesiologist. Appropriate carotid protection devices in the distal internal carotid artery were also used under roadmap guidance; the devices used in the present study were Medtronic PercuSurge Guard Wire Plus (n = 28), Challenge Japan Investment Mint Catch Filter (n = 2) or ArteriA Medical Science Parodi Anti-Emboli System (n = 1). After deployment of the carotid protection device, a self-expandable stent (Boston Scientific Carotid Wallstent) or a nitinol stent (Cordis, Precise; SMART USA) was selected and placed across the stenosis, with local balloon dilatation applied before and after placing the stent. Procedural success in CAS was judged according to complete stent deployment with residual stenosis of lesser than 30% on the completion angiogram. Heparin (5000 IU) was injected intra-arterially once or twice during the intervention, and systemic heparinisation was used at 10^4 units for 24 h after the surgery. During the CAS procedure, the neurological status of each patient was assessed by asking him or her to shake the hands of nurses and talk to them.

Basal and ACZ-challenged ECD SPECT studies were performed using a rotating dual-headed gamma camera (E.CAM, Siemens) equipped with a parallel-hole collimator (128 ´ 128 matrix, 9 mm FWHM) as described [14]. Image slices parallel to the orbitomeatal line were taken with 5-mm centre-to-centre spacing, using a Butterworth filter (cut-off = 0.45 cycles/cm; order = 3) and a Ramp filter for image reconstruction. Pre-operative examinations were carried out two weeks before CAS at an interval of more than one month after the symptomatic transient ischemic attack or minor stroke, and the postoperative studies were conducted approximately one month after CAS. About ten minutes after the initial injection of 400 MBq of [^{99m}Tc] ECD, ACZ (1 g) was intravenously administered for two minutes and then the second injection of 400 MBq of ECD was done 24 minutes after the initial ECD administration. Data collection for basal and ACZ-challenged SPECT images was initiated at nine minutes after each post-injection of 400 MBq of [^{99m}Tc] ECD for 15 min. The quantitative CBF (ml/100g/min) images were obtained using a Patlak plot analysis [15], and each regional CBF (rCBF) was determined using automated ROI analysis software (3D SRT) which permitted the automatic computation of 318 ROIs in each hemisphere within several minutes to avoid possible biases depending on the individual differences [16]. Then, the ROIs were classified into callosomarginal, precentral, central, parietal, angular, temporal, occipital, and pericallosal regions, hippocampus, and lenticular nucleus according to the previously published templates [14,17]. Thalamus and cerebellum regions were excluded from the present analysis to avoid the influence of diaschisis [18]. The ROIs with small but evident infarction on CT and/or MRI were not excluded from the analysis. The CVR was evaluated in both hemispheres by calculating its percent value as follows:

$$CVR(\%)=[(\text{ACZ-challenged CBF}-CBF_{rest})/CBF_{rest}]\times 100$$

where the suffix "rest" stands for resting stage. Incidentally, a normal CBF value was 40-45 ml/100 g/min in our study.

Statistical analysis

Differences in CBF_{rest} and CVR values between unilateral (n=22) and bilateral (n=9) lesion groups were compared using the Mann-Whitney *U* test. Differences in these values between before-CAS and after-CAS evaluations were compared using Wilcoxon's signed-rank test. Statistical significances were detected at P<0.05.

Results

In the bilateral group, when examined by MRI six out of the nine patients showed occlusion and the remaining three exhibited severe stenosis in the contralateral carotid artery. Comparing the hemispheric before-CAS ipsilateral CVR values for the six patients and those of the three patients, we found 28.9% and 30.5%, respectively. Among nine patients with bilateral lesions, six had occlusion on the contralateral side. Of the six patients, four showed collateral flow to the contralateral MCA via anterior communicating artery and two showed the similar event via the posterior communicating artery, and the hemispheric before-CAS contralateral CVR values were 24.5% and

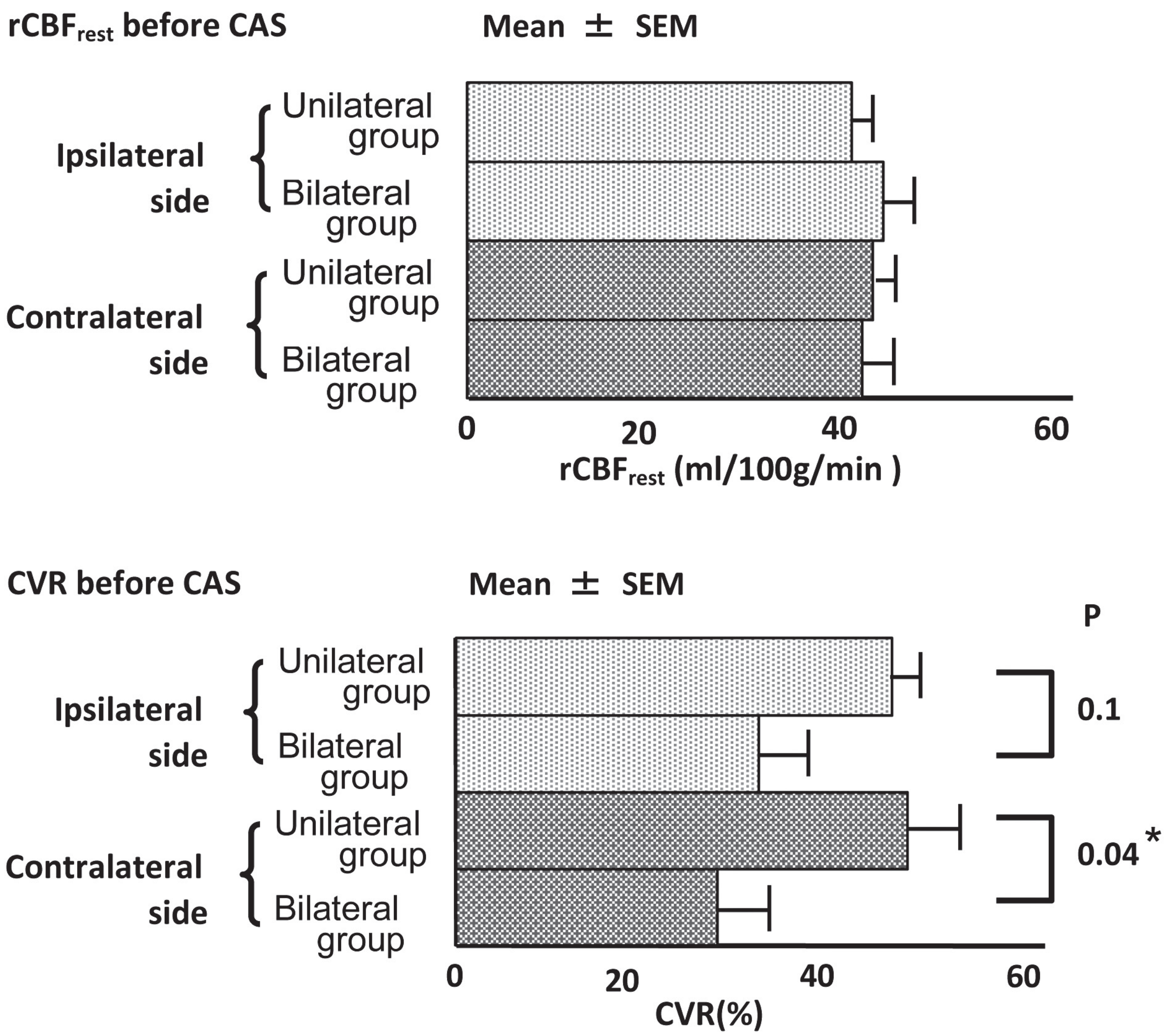
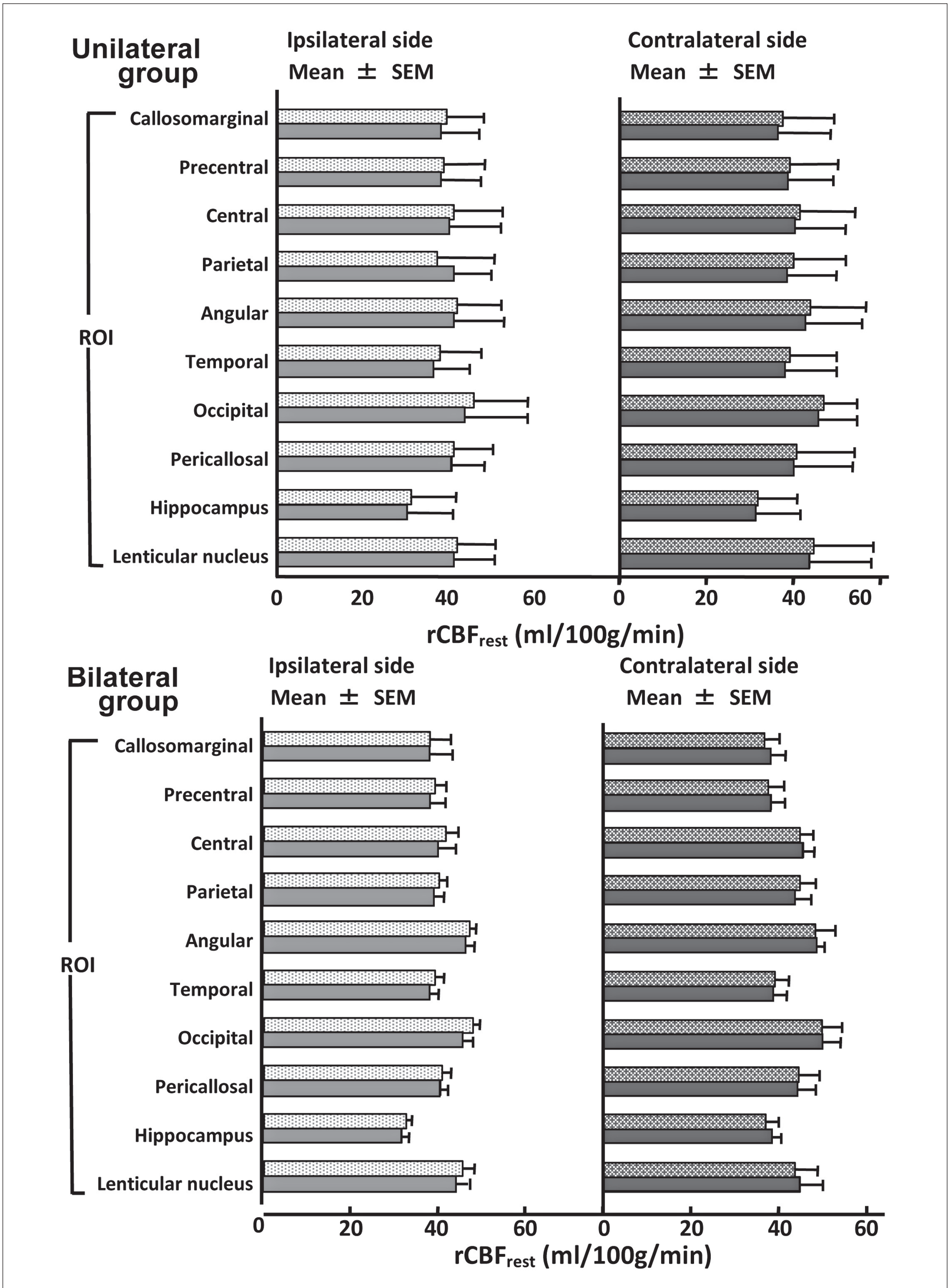


Figure 1 Comparisons of before-CAS $rCBF_{rest}$ values on ipsilateral and contralateral sides of hemispheres between unilateral and bilateral lesion groups. Symbols: rCBF, regional recebral blood flow; CBF_{rest}, resting stage cerebral blood flow; CVR, cerebrovascular reserves; CAS, carotid artery stenting. *Significantly different at $P<0.05$ in Mann-Whitney *U* test.

27.0%, respectively. No the patients displayed any additional neurological deficits after CAS, but four among them had asymptomatic tiny infarctions within the ipsilateral hemisphere. No hyperperfusion syndrome (HPS) was diagnosed among them prior to undergoing after-CAS SPECT. The absence of HPS was confirmed by ECD-SPECT, TCD, monitoring of regional cerebral oxygenation by near-infrared spectroscopy (NIRO-200; Hamamatsu Photonics K.K. Japan).

Figure 1 shows before-CAS data. No statistically significant differences were observed in ipsilateral $rCBF_{rest}$ values between unilateral and bilateral groups. In addition, there were no significant differences in ten ROI $rCBF_{rest}$ values (data not shown). On the other hand, a significant difference in CVR values on the contralateral hemispheric side was observed between unilateral and bilateral groups. In this case, there were significant differences in ten ROI CVR values as well (data not shown). As in Figure 2, $rCBF_{rest}$ values on ipsilateral and contralateral sides remained unchanged after CAS. In terms of CVR values on ipsilateral and contralateral sides, there were no significant differences between before-CAS and after-CAS in the unilateral group. For the bilateral group, however, the observed CVR values were significantly different in the hemisphere and its ten ROIs, except for lenticular nucleus, on the ipsilateral side (Figure 3). A greater difference


Unilateral group
Ipsilateral side
Mean ± SEM
Contralateral side
Mean ± SEM
ROI
Callosomarginal
Precentral
Central
Parietal
Angular
Temporal
Occipital
Pericallosal
Hippocampus
Lenticular nucleus
0 20 40 60 0 20 40 60
rCBFrest (ml/100g/min)
Bilateral group
Ipsilateral side
Mean ± SEM
Contralateral side
Mean ± SEM
ROI
Callosomarginal
Precentral
Central
Parietal
Angular
Temporal
Occipital
Pericallosal
Hippocampus
Lenticular nucleus
0 20 40 60 0 20 40 60
rCBFrest (ml/100g/min)

was observed in these CVR values on the contralateral side. Incidentally, all the CVR values were in the range of 30-50% which were regarded almost normal in the light of the published data [14]. In the case of unilateral disease with an isolated circulation, there was no evidence of CVR changes for patients with very severe (>90%) stenosis.

Discussion

Ischemic stroke in patients with internal carotid artery is mostly due to artery to artery embolism [19,20]. Particularly in the case of symptomatic internal carotid a artery, occlusion ischemic stroke is due to hemodynamic compromise [21,22]. It was reported that when 419 patients with internal carotid artery occlusion were examined by positron emission tomography (PET), an increase in oxygen extraction was observed suggesting that the patients tended to suffer from ischemic stroke [23]. Using XeCT applied to 21 patients with internal carotid lesion, another group showed that they were going to have ischemic stroke due to decreased CO_2 reactivity [24]. It was shown that 22 among 96 ACZ-SPECT treated patients with internal carotid occlusion or middle cerebral artery occlusion became lower in MCA-regional CVR values, with occurrence of ischemic stroke [25]. To reduce the risk of ischemic stroke, CEA and CAS are generally applied to patients with carotid artery diseases. Since these procedures can influence haemodynamics in the brain, perfusion changes have been investigated in such patients. No significant degree of CVR improvement after CEA has generally been presented, although three studies reported that some patients show haemodynamic improvement after CEA [26,27]. Several observations described the cases with haemodynamic improvements after CEA in patients with bilateral carotid artery disease are due to CVR increases in the ipsilateral hemisphere [26,28-30]. Furthermore, there is a paper on the CVR improvement after CEA in four patients with bilateral carotid artery stenosis even in the contralateral hemisphere [12]. These indicate the potential therapeutic benefits of surgical approaches in patients with bilateral carotid artery disease to improve their brain haemodynamics. However, quantitative evaluation of CVR changes associated that CAS using Acz-challenged SPECT has not been presented so far, despite that CAS can be applied to both unilateral and bilateral carotid artery stenosis to reduce the risk of ischemic stroke.

The present study revealed that $rCBF_{rest}$ values remained unchanged after CAS in both unilateral and bilateral lesions (Figure 2). In addition, we showed that patients with bilateral carotid artery disease, but not those with unilateral disease, showed significant CVR increases in the contralateral rather than ipsilateral ROIs (Figure 3). The significant CVR increase in the contralateral hemisphere may suggest a cross-flow via the anterior communicating artery [31,32] and/or the posterior communicating artery leading to haemodynamic improvement. Significant differences in the before-CAS hemispheric CVR values on the contralateral side were found between the unilateral and bilateral groups. However, no such differences were observed in the after-CAS CVR values. Since no information has been provided regarding CAS-mediated CVR improvement in bilateral carotid artery lesions, our findings add a new dimension to current knowledge on the therapeutic value of CAS as an effective method for improving brain haemodynamics. However, our study also has certain limitations. The current data were obtained from a relatively small number of patients. In addition, the disease characteristics of the patients with bilateral carotid artery disease were not uniform: the nine patients comprised three with high degree stenosis and six with occlusion in the contralateral carotid artery. Therefore, the haemodynamic status may not necessarily be similar in all cases. Despite these problems, the present study may be significant in that our attempt is the first to evaluate CVR

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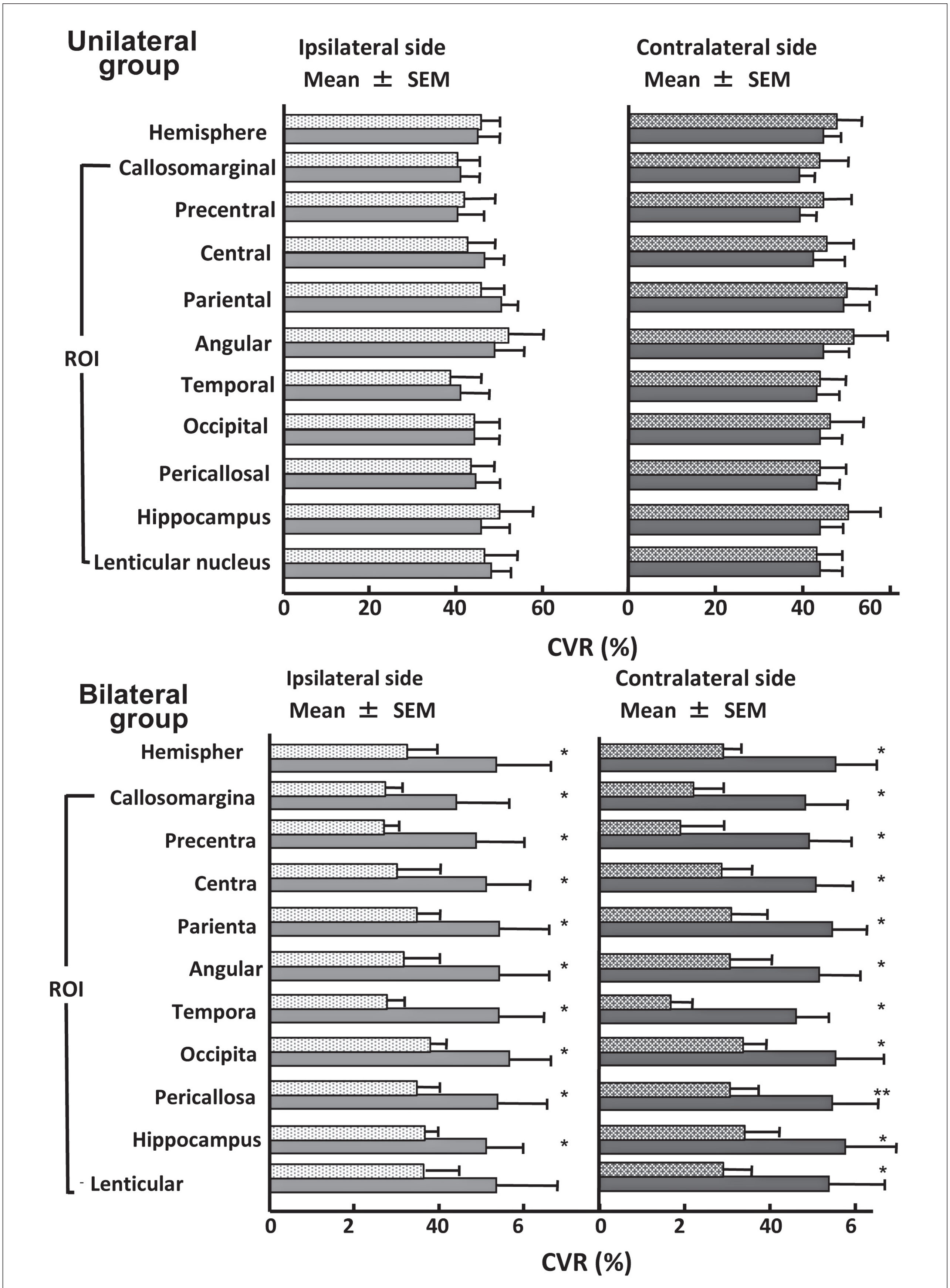
Figure 2 Comparisons of before- and after-CAS $rCBF_{rest}$ values in 10 hemispheric regions of interest on ipsilateral and contralateral sides between unilateral and bilateral carotid artery lesion groups. Symbols: ROI, region of interest; $rCBF_{rest}$, regional cerebral blood flow at resting stage. Dotted and filled columns, before- and after-CAS $rCBF_{rest}$ values, respectively. No significant difference observed at $P<0.05$ in Wilcoxon's signed-rank test. Hemispheric before- and after-CAS $rCBF_{rest}$ values on the ipsilateral side in the unilateral group were 39.0±4.3 and 38.0±4.3, respectively (P=0.20), and those on the contralateral side in the same group were 40.8±3.7 and 39.8±3.8, respectively (P=0.20). Hemispheric before- and after-rCBF values on the ipsilateral side in the bilateral group were 41.9±9.8 and 42.3±7.8, respectively (P=0.68), and those on the contralateral side in the same group were 40.1±12.4 and 40.4±10.3, respectively (P=0.86). All these $rCBF_{rest}$ values showed no significant difference from each other at $P<0.05$.



Unilateral group
Ipsilateral side
Mean ± SEM
Contralateral side
Mean ± SEM
Hemisphere
Callosomarginal
Precentral
Central
Pariental
Angular
Temporal
Occipital
Pericallosal
Hippocampus
Lenticular nucleus
ROI
0 20 40 60
0 20 40 60
CVR (%)
Bilateral group
Ipsilateral side
Mean ± SEM
Contralateral side
Mean ± SEM
Hemispher
Callosomargina
Precentra
Centra
Parienta
Angular
Tempora
Occipita
Pericallosa
Hippocampus
Lenticular
ROI
*
**
0 2 40 6
0 2 40 6
CVR (%)

←
Figure 3 Comparisons of before- and after- CAS CVR values on ipsilateral and contralateral sides in 10 hemispheric regions of interest between unilateral (A) and bilateral (B) lesion groups. For symbols see Figures 1 and 2. Significantly different at $P<0.05$* and $P<0.01$** in Wilcoxon's signed-rank test.

changes after CAS in patients with bilateral carotid artery disease.

Conclusion

The use of CAS for patients with severe symptomatic bilateral carotid artery stenosis can significantly increase their CVR values even on the contralateral hemispheric side. This suggests the potential utility of CAS for risk reduction of ischemic stroke.

References

1 Mas JL, Chatellier G, Beyssen B, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med. 2006; 355: 1660-1671.
2 Ringleb PA, Allenberg J, Bruckmann H, et al. 30 day results from the space trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: A randomised non-inferiority trial. Lancet. 2006; 368: 1239-1247.
3 North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med. 1991; 325: 445-453.
4 Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med. 2004; 351: 1493-1501.
5 Kleiser B, Widder B. Course of carotid artery occlusions with impaired cerebrovascular reactivity. Stroke. 1992; 23: 171-174.
6 Yonas H, Smith HA, Durham SR, et al. Increased stroke risk predicted by compromised cerebral blood flow reactivity. J Neurosurg. 1993; 79: 483-489.
7 Gur AY, Bova I, Bornstein NM. Is impaired cerebral vasomotor reactivity a predictive factor of stroke in asymptomatic patients? Stroke. 1996; 27: 2188-2190.
8 Yamauchi H, Fukuyama H, Nagahama Y, et al. Evidence of misery perfusion and risk for recurrent stroke in major cerebral arterial occlusive diseases from pet. J Neurol Neurosurg Psychiatry. 1996; 61: 18-25.
9 Markus H, Cullinane M. Severely impaired cerebrovascular reactivity predicts stroke and tia risk in patients with carotid artery stenosis and occlusion. Brain. 2001; 124: 457-467.
10 Vernieri F, Pasqualetti P, Matteis M, et al. Effect of collateral blood flow and cerebral vasomotor reactivity on the outcome of carotid artery occlusion. Stroke. 2001; 32: 1552-1558.
11 Vernieri F, Pasqualetti P, Diomedi M, et al. Cerebral hemodynamics in patients with carotid artery occlusion and contralateral moderate or severe internal carotid artery stenosis. J Neurosurg. 2001; 94: 559-564.
12 Kluytmans M, van der Grond J, Eikelboom BC, et al. Long-term hemodynamic effects of carotid endarterectomy. Stroke. 1998; 29: 1567-1572.
13 Cikrit DF, Burt RW, Dalsing MC, et al. Acetazolamide enhanced single photon emission computed tomography (spect) evaluation of cerebral perfusion before and after carotid endarterectomy. J Vasc Surg. 1992; 15: 747-753; discussion 753-744.
14 Takeuchi R, Matsuda H, Yonekura Y, et al. Noninvasive quantitative measurements of regional cerebral blood flow using technetium-99m-l,l-ecd spect activated with acetazolamide: Quantification analysis by equal-volume-split 99mtc-ecd consecutive spect method. J Cereb Blood Flow Metab. 1997; 17: 1020-1032.
15 Matsuda H, Yagishita A, Tsuji S, et al. A quantitative approach to technetium-99m ethyl cysteinate dimer: A comparison with technetium-99m hexamethylpropylene amine oxime. Eur J Nucl Med. 1995; 22: 633-637.
16 Takeuchi R, Yonekura Y, Matsuda H, et al. Usefulness of a three-dimensional stereotaxic roi template on anatomically standardised 99mtc-ecd spet. Eur J Nucl Med Mol Imaging. 2002; 29: 331-341.
17 Tatu L, Moulin T, Bogousslavsky J, et al. Arterial territories of the human brain: Cerebral hemispheres. Neurology. 1998; 50: 1699-1708.
18 De Reuck J, Stevens H, Jansen H, et al. Cobalt-55 positron emission tomography of ipsilateral thalamic and crossed cerebellar hypometabolism after supratentorial ischaemic stroke. Cerebrovasc Dis. 1999; 9: 40-44.
19 Markus H. Transcranial doppler detection of circulating cerebral emboli. A review. Stroke. 1993; 24: 1246-1250.
20 Babikian VL, Hyde C, Pochay V, et al. Clinical correlates of high-intensity transient signals detected on transcranial doppler sonography in patients with cerebrovascular disease. Stroke. 1994; 25: 1570-1573.
21 Itoh M, Hatazawa J, Pozzilli C, et al. Positron ct imaging of an impending stroke. Neuroradiology. 1988; 30: 276-279.
22 Yamauchi H, Fukuyama H, Fujimoto N, et al. Significance of low perfusion with increased oxygen extraction fraction in a case of internal carotid artery stenosis. Stroke. 1992; 23: 431-432.
23 Grubb RL Jr., Derdeyn CP, Fritsch SM, et al. Importance of hemodynamic factors in the prognosis of symptomatic carotid occlusion. J Am Med Assoc. 1998; 280: 1055-1060.
24 Dettmers C, Solymosi L, Hartmann A, et al. Confirmation of ct criteria to distinguish pathophysiologic subtypes of cerebral infarction. Am J Neuroradiol. 1997; 18: 335-342.
25 Moriwaki H, Matsumoto M, Hashikawa K, et al. Hemodynamic aspect of cerebral watershed infarction: Assessment of perfusion reserve using iodine-123-iodoamphetamine spect. J Nucl Med. 1997; 38: 1556-1562.
26 Wiart M, Berthezene Y, Adeleine P, et al. Vasodilatory response of border zones to acetazolamide before and after endarterectomy: An echo planar imaging-dynamic susceptibility contrast-enhanced mri study in patients with high-grade unilateral internal carotid artery stenosis. Stroke. 2000; 31: 1561-1565.
27 Sacca A, Pedrini L, Vitacchiano G, et al. Cerebral spect with 99mtc-hmpao in extracranial carotid pathology: Evaluation of changes in the ischemic area after carotid endarterectomy. Int Angiol. 1992; 11: 117-121.

28 Levine RL, Rozental JM, Nickles RJ. Blood flow asymmetry in carotid occlusive disease. Angiology. 1992; 43: 100-109.
29 Tatemichi TK, Young WL, Prohovnik I, et al. Perfusion insufficiency in limb-shaking transient ischemic attacks. Stroke. 1990; 21: 341-347.
30 Baron JC, Bousser MG, Rey A, et al. Reversal of focal "misery-perfusion syndrome" by extra-intracranial arterial bypass in hemodynamic cerebral ischemia. A case study with 15O positron emission tomography. Stroke. 1981; 12: 454-459.
31 Kluytmans M, van der Grond J, van Everdingen KJ, et al. Cerebral hemodynamics in relation to patterns of collateral flow. Stroke. 1999; 30: 1432-1439.
32 Muller M, Schimrigk K. Vasomotor reactivity and pattern of collateral blood flow in severe occlusive carotid artery disease. Stroke. 1996; 27: 296-299.

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