Cerebral Hemodynamics in Patients with Chronic Obstructive Carotid Disease by rCBF, rCBV, and rCBV/rCBF Ratio Using SPECT

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To evaluate cerebral hemodynamics, 21 patients with chronic occlusion or severe stenosis of the internal carotid or middle cerebral artery with normal or only lacunar infarction on x-ray CT were studied using single photon emission computed tomography (SPECT). We measured rCBV with ^{99m}Tc erythrocytes after rCBF with ^{133}Xe, and calculated rCBV/rCBF. rCBF and rCBV of the 25 affected hemispheres were classified as (a) patients with normal rCBF {type I (n = 7) and type II (n = 3)}; (b) patients with decreased rCBF {type III (n = 6) and type IV (n = 9)}. These two groups then could be subdivided according to findings of rCBV, normal, and increased blood volumes. rCBV/rCBF increased as the cerebral perfusion pressure dropped from type I to type III. In type IV, other situations but cerebral autoregulation could be assumed. rCBV/rCBF signifies vascular mean transit time. Type III (high rCBV/rCBF) assumed as the increased OEF, misery perfusion as reported in PET. We propose rCBF, rCBV and rCBV/rCBF using SPECT can be an index for cerebral circulatory reserve.

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Positron emission tomography (PET) studies have reported rather good correlation between the regional cerebral blood flow/regional cerebral blood volume (rCBF/rCBV) ratio (*1*) or the rCBV/rCBF ratio (*2*) and the oxygen extraction fraction (OEF). The studies showed that these ratios could provide an index of cerebral circulatory reserve, hemodynamic status of the cerebral circulation in normo-density area on x-ray CT, and this method could be applied using single photon emission computed tomography (SPECT) since rCBF and rCBV could be measured by isotope techniques without PET. To date, semiquantitative analyses of the rCBF/rCBV ratio using SPECT have been reported (*3,4*), but quantitative analysis using SPECT has not yet been reported.

We measured rCBF by xenon-133 (^{133}Xe) inhalation (*5*) and rCBV by in vivo labeled technetium-99m (^{99m}Tc) red blood cells (*6*) quantitatively, and calculated the rCBV/rCBF ratio on the same axial plane of the coordinate using a ring-type SPECT (*7*).

To evaluate cerebral circulatory reserve by rCBF, rCBV, and rCBV/rCBF ratio using that technique, we studied patients with chronic occlusion or severe stenosis of the internal carotid or the middle cerebral artery of normal or with only lacunar infarction on x-ray CT.

MATERIALS AND METHODS

We studied 21 patients (mean age 57.9 ± 8.3 yr) with chronic occlusion or severe stenosis in angiography of the internal carotid or the middle cerebral artery (17 patients with unilateral cases, four patients with bilateral cases) of normal or with only lacunar infarction on x-ray CT (Table 1), and nine normal volunteers, aged 43–70 yr (mean age 59.8 ± 8.3 yr).

We used a ring-type SPECT HEADTOME SET-031 (Shimadzu Corp., Japan) (*8*). It consisted of three detector rings 420 mm in diameter, with 64 NaI crystals arranged per ring. Two types of collimator were used: a high sensitivity (HS) and a high resolution (HR) collimator. The full width at the half maximum (FWHM) of the spatial resolution was 12.4 mm for HR and 19.8 mm for HS. System sensitivity was 5.4 kcps/μ Ci/ml for HR and 27.8 kcps/μ Ci/ml for HS. Slice thickness (FWHM) was 17.5 mm for HR and 29.0 mm for HS at the center of the field of view (*9*).

Studies were performed as follows.

First, to examine accurately on the same plane, the patient's head was fixed with the orbitomeatal (OM) line perpendicular to the axis of rotation throughout the examination.

Second, for subsequent in vivo labeling of red blood cells, half a vial of a pyrophosphate kit with 2 mg of $SnCl_2$ (Daiichi Radioisotope Corp., Japan) was injected intravenously.

Then rCBF was measured by inhalation of 50 mCi of ^{133}Xe and rapid scanning by HS collimator, and calculated by the sequence of picture method (*5*). Approximately 30 min was required to measure and calculate rCBF.

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TABLE 1
Summary of Patient Population*

Case no.	Age (yr)	Sex	Diagnosis		rCBF		rCBV		rCBV/rCBF		Type	
					LH	RH	LH	RH	LH	RH	LH	RH
1	70	M	Left	MCO	48	47	4.2	4.2	5.4	5.4	I	
2	55	F	Left	MCO	48	49	3.5	3.6	4.2	4.2	I	
3	45	M	Right	MCO	41	44	3.5	4.3	5.4	6.0		I
4	66	M	Right	ICS	48	48	3.7	3.7	4.8	4.8	I	I
			Left	ICS								
5	40	M	Left	ICO	42	44	3.1	3.2	4.2	4.2	I	
6	57	M	Right	ICO	54	49	3.6	3.7	4.0	4.5		I
7	65	F	Right	ICS	41	41	5.7	5.3	8.4	7.8	II	II
			Left	ICO								
8	53	M	Right	MCO	38	42	5.2	4.4	8.4	6.0	III	II
			Left	ICO								
9	56	M	Right	ICO	38	26	4.0	5.4	6.6	12.6		III
10	40	M	Right	MCS	39	38	4.7	4.6	7.2	7.2	III	III
			Left	ICO								
11	60	M	Right	ICO	33	26	3.9	5.5	7.2	12.6		III
12	59	M	Right	ICO	35	28	3.8	4.6	6.5	9.9		III
13	52	M	Right	ICO	45	40	4.0	4.0	5.3	6.0		IV
14	70	M	Left	MCS	33	32	4.0	4.0	7.2	7.8	IV	
15	51	M	Left	MCO	37	47	3.4	3.1	5.4	4.2	IV	
16	63	M	Left	MCS	33	33	3.9	3.7	7.2	6.6	IV	
17	57	M	Left	ICO	39	45	4.0	3.7	6.0	4.8	IV	
18	71	F	Left	ICS	35	43	3.9	4.1	6.6	6.0	IV	
19	61	F	Right	ICO	49	34	3.9	3.6	4.8	6.6		IV
20	68	M	Left	MCS	40	41	3.4	3.3	5.1	4.8	IV	
21	57	M	Right	ICO	44	40	3.6	3.6	4.1	5.1		IV

* rCBF = regional cerebral blood flow; rCBV = regional cerebral blood volume; LH = left hemisphere; RH = right hemisphere; ICO = internal carotid artery occlusion; ICS = internal carotid artery severe stenosis; MCO = middle cerebral artery occlusion; MCS = middle cerebral artery severe stenosis. Underlined number: value of the affected hemisphere.

Next, 15 mCi of $^{99m}TcO_4^-$ was injected intravenously. After 20 min, rCBV was scanned by HR collimator for 20 min. A blood sample was taken from the antecubital vein of the uninjected arm during the rCBV scanning. rCBV was calculated by the method proposed by Kuhl (*10*).

We studied rCBF and rCBV on three slices (20, 55, 90 mm) taken above the OM line. The CBV/CBF image was composed as we previously reported (*7*). ROI was placed over both hemispheres of the rCBF image 90 mm above the OM line. Next, ROI was placed over the internal margin (no brain surface vein) of the rCBV image on the same plane. The CBV/CBF ratio was calculated using these two values.

RESULTS

In nine normal volunteers, the mean rCBF was 45.8 ± 5.12 ml/100g brain/min, the mean rCBV 3.98 ± 0.39 ml/100g brain and the mean rCBV/rCBF ratio 5.2 ± 0.57 sec (Table 2).

Table 1 shows the rCBF, rCBV and rCBV/rCBF values for 21 patients. Figure 1 shows the relationship between rCBF and rCBV in the affected hemisphere in the angiography of each patient. In case of both hemispheres, two dots were marked for one patient.

The rCBF and rCBV values of the affected hemispheres of 21 patients (25 lesions) were classified into four types, comparing with the mean rCBF − standard deviation (s.d.) and the mean rCBV + s.d. of the normal volunteers, as follows (Table 1, Fig. 1):

type I (n = 7): rCBF did not decrease, and rCBV did not increase.

type II (n = 3): rCBF did not decrease, while rCBV increased.

type III (n = 6): rCBF decreased, and rCBV increased.

type IV (n = 9): rCBF decreased, but rCBV did not increase.

TABLE 2
Mean rCBF, rCBV, and rCBV/rCBF in Each Type and in Normal Volunteers

Type	rCBF (ml/100 g brain/min)	rCBV (ml/100 g brain)	rCBV/rCBF (sec)
I (n = 7)	46.7 ± 2.4	3.7 ± 0.4	4.8 ± 0.6
II (n = 3)	41.3 ± 0.5	5.1 ± 0.5	7.4 ± 1.0
III (n = 6)	32.5 ± 5.9	5.0 ± 0.4	9.7 ± 2.3
IV (n = 9)	36.8 ± 2.9	3.8 ± 0.2	6.1 ± 0.8
Normals (n = 9)	45.8 ± 5.12	4.0 ± 0.39	5.2 ± 0.57

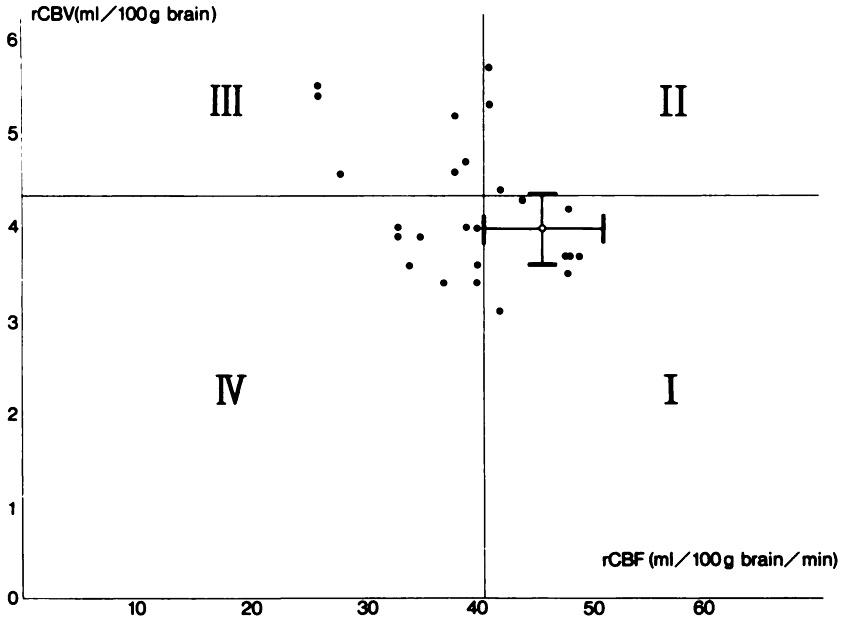

FIGURE 1
Relationship between rCBF and rCBV in each affected hemisphere. Open circle represents the mean value of nine normal volunteers. Closed circle represents thè value in the affected hemisphere of each patient.

Table 2 shows the mean rCBF, rCBV and rCBV/rCBF values of each type.

The mean rCBV/rCBF ratio in type II, type III, and type IV were higher than that in type I. Particularly, the mean rCBV/rCBF ratio in type III was significantly higher than that in type I.

The mean rCBV/rCBF ratio increased from type I to type III. SPECT images are shown in Figures 2–5 in four patients of each type.

DISCUSSION

PET studies have shown negative correlation between the rCBF/rCBV ratio (*1*) and OEF, positive correlation between the rCBV/rCBF ratio (*2*) and OEF on normodensity area of x-ray CT. OEF is an index of the cerebral circulatory reserve. Therefore, the rCBV/rCBF ratio or the rCBF/rCBV ratio using SPECT may provide an index of circulatory reserve without measuring OEF.

However in contrast to the approaches using PET, combined rCBF and rCBV analysis using SPECT is generally impeded by the necessity of using two different radiotracers with relatively long half-lives. Consequently, we measured rCBV with ^{99m}Tc red blood cells 30 min after the measurement of rCBF by ^{133}Xe inhalation on the same day, using a ring-type SPECT. Xenon-133, an inert freely diffusable radioactive gas, is the standard tracer for the clinical evaluation of rCBF using SPECT.

After data are acquired, the tracer can be washed out from the brain in a few minutes, and the gamma-ray energy is relatively lower (81 keV) than ^{99m}Tc (140

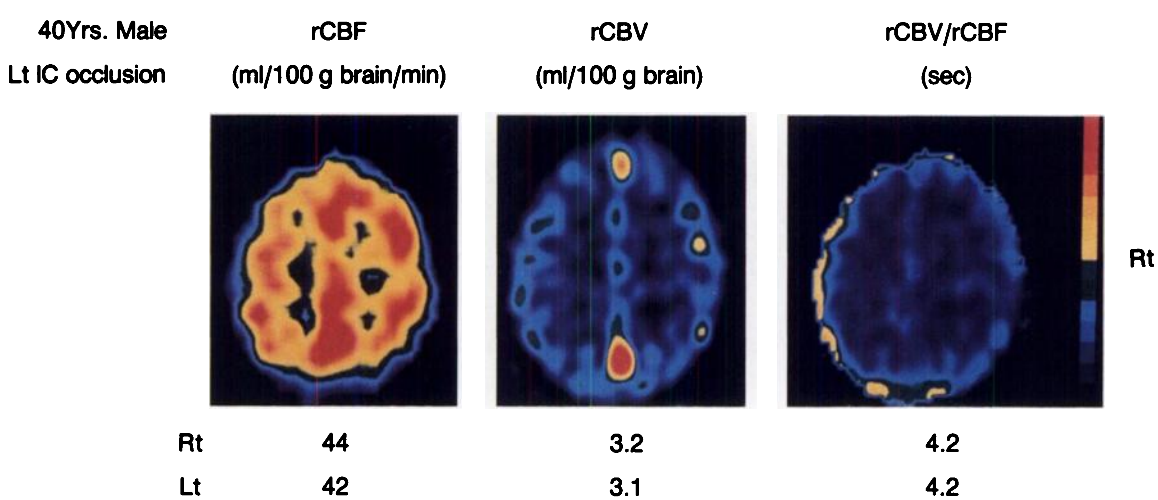

FIGURE 2
Case 5: Male, age 40 yr, with left internal carotid artery occlusion. rCBF did not decrease, rCBV and rCBV/rCBF ratio did not increase in the left hemisphere (Type I).

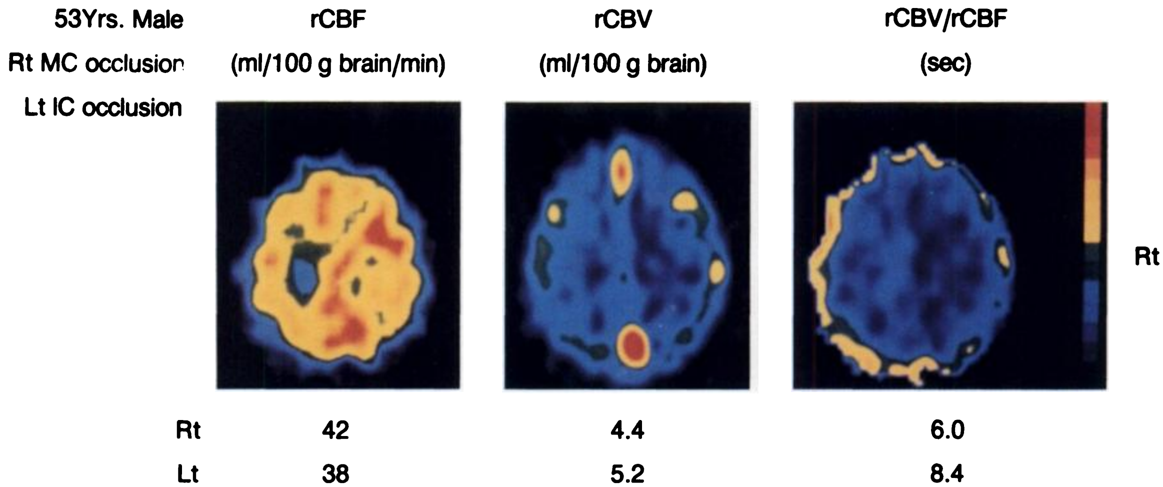

FIGURE 3
Case 8: Male, age 53 yr, with left internal carotid and right middle cerebral artery occlusion. rCBF decreased, rCBV increased and rCBV/rCBF ratio remarkably increased in the left hemisphere (Type III). rCBF did not decrease, while rCBV and rCBV/rCBF ratio increased in the right hemisphere (Type II).

keV), therefore we could sequentially measure rCBV with ^{99m}Tc red blood cells quantitatively without energy subtraction.

In this study, the rCBF and rCBV values of the affected hemispheres of chronic obstructive carotid disease were classified into four types. Figure 6 shows the changes in rCBF, rCBV, and rCBV/rCBF ratio with a decrease in cerebral perfusion pressure. We can analyze

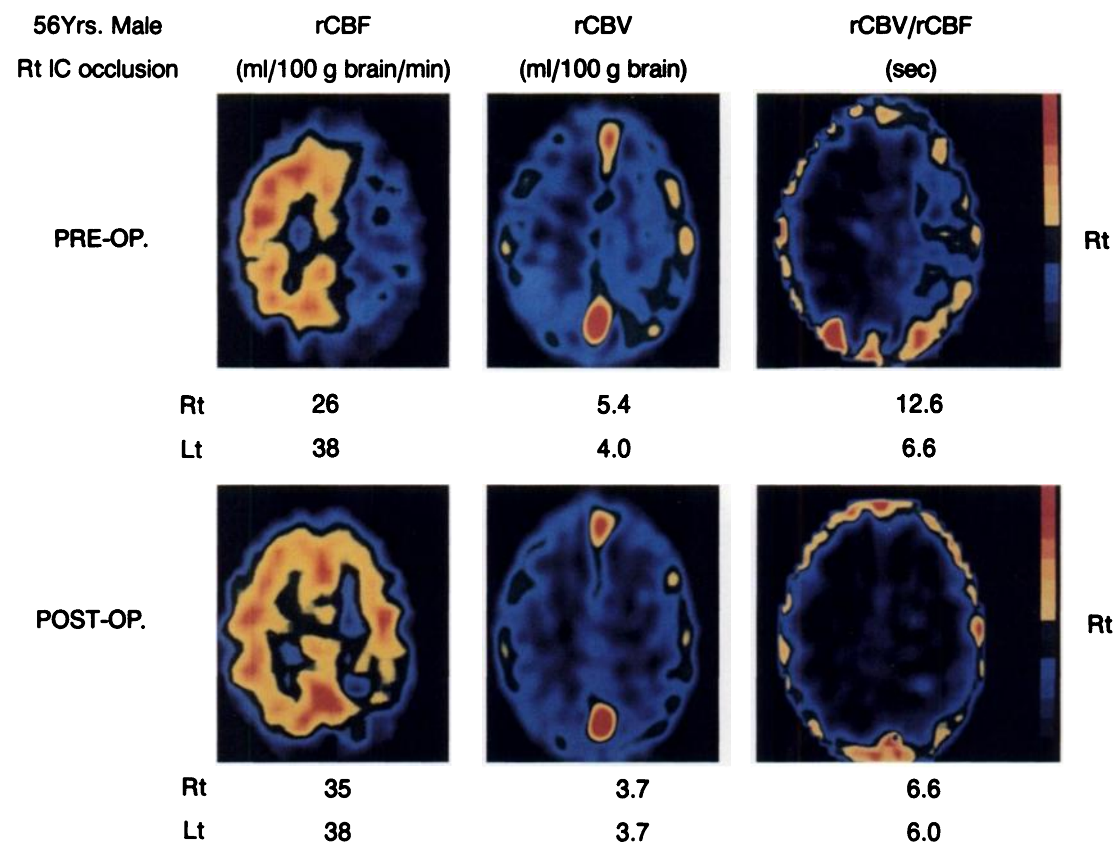

FIGURE 4
Case 9: Male, age 56 yr, with right internal carotid artery occlusion. rCBF decreased, rCBV increased and rCBV/rCBF ratio remarkably increased in the right hemisphere on preoperative SPECT (Type III). Extracranial-intracranial bypass surgery was performed. Postoperative SPECT showed remarkable improvement. That is, increased rCBF and reduced rCBV and rCBV/rCBF ratio in the affected hemisphere were observed.

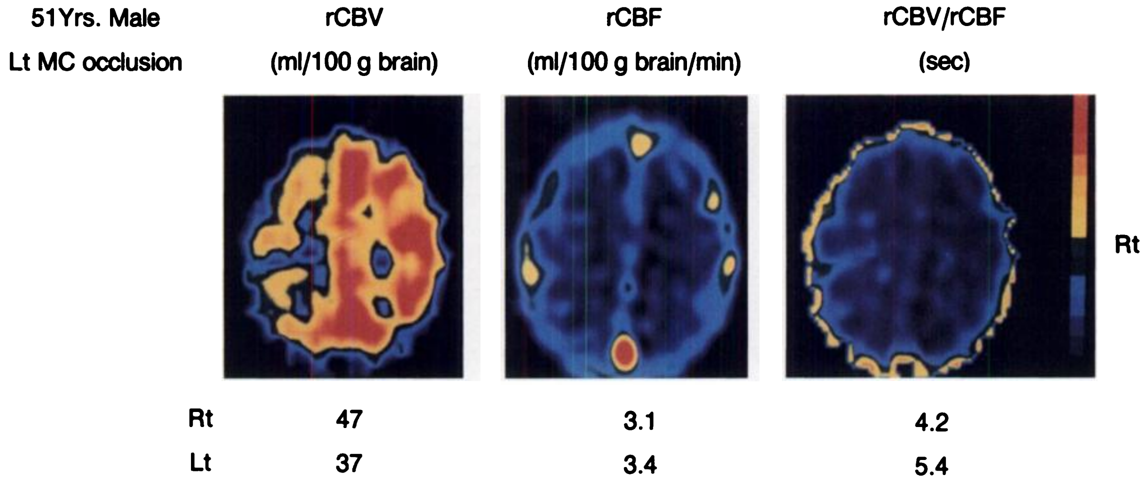

FIGURE 5
Case 15: Male, age 51 yr, with left middle cerebral artery occlusion. rCBF decreased, but rCBV did not increase in the left hemisphere. Thus, rCBV/rCBF ratio increased (Type IV).

Figure 6 by applying cerebral autoregulation as follows: type I is assumed as the state of cerebral perfusion pressure within the normal range. When the cerebral perfusion pressure drops, rCBV increases due to vasodilatation, although rCBF may remain unchanged owing to the perfusion pressure within the autoregulatory range (type II), and rCBF decreases when the cerebral perfusion pressure is below the autoregulation lower limit (type III). In type IV (two dotted lines in Fig. 6), two situations can be assumed.

1. rCBV decreases because of lowered vascular response or metabolism because of chronically decreased rCBF which is apparently normal or with only lacunar infarction on x-ray CT with decreased cerebral perfusion pressure.

2. rCBF decreases with aging or transneural depression in spite of no decrease in cerebral perfusion pressure and increase in rCBV. In type IV, especially aged people showed states of decreased rCBF with no difference between either hemisphere. Thus, we can assume that this is the second situation state of type IV.

The rCBV/rCBF ratio increases as cerebral perfusion pressure drops from type I to type III. The rCBV/rCBF ratio signifies the vascular mean transit time. It is a reasonable supposition that type III is the state of decreased cerebral circulatory reserve because of autoregulation. Therefore, type III can be assumed as the state of remarkably increased OEF, the misery perfusion as reported in PET studies.

But, the increased rCBV/rCBF ratio in type IV does

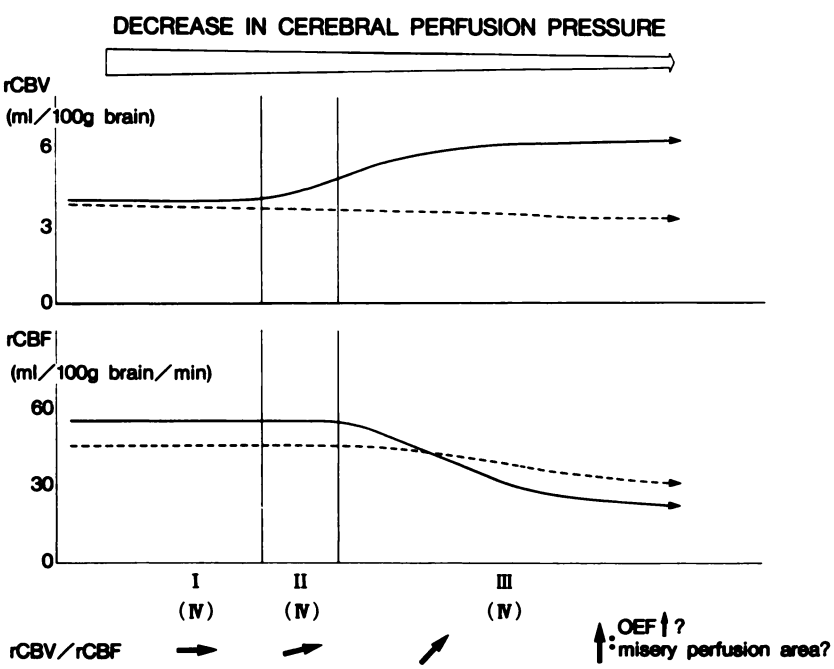

FIGURE 6
Changes in rCBF, rCBV, and the rCBV/rCBF ratio with decrease in cerebral perfusion pressure. Solid line shows the change of Type I to Type III. Dotted line shows the change of Type IV. Type III (high rCBV/rCBF ratio) shows decreased cerebral circulatory reserve when the cerebral perfusion pressure is below the lower limit of autoregulation. Therefore, Type III can be assumed as the state of remarkably increased OEF, misery perfusion.

not mean an increased OEF because of autoregulation. Higano et al. (*2*) reported that rCBF and the oxygen consumption rate ($CMRO_2$) correlatively decreased in most cases of chronic obstructive carotid disease, and that there were few cases of increased OEF in spite of the decreased rCBF in PET studies. We can assume that the former is the state of type IV, and that the latter is the state of type III.

That is, to evaluate the cerebral circulatory reserve using SPECT, we should analyze not only the rCBV/rCBF ratio but also rCBF and rCBV. To detect misery perfusion without PET, measuring rCBV using SPECT is very significant. We propose that the rCBF, rCBV and rCBV/rCBF ratio determined using SPECT can be a good index for evaluating cerebral circulatory reserve.

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