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Use of Orbital Color Doppler Imaging for Detecting Internal Carotid Artery Stenosis in Patients with Amaurosis Fugax

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Purpose: To determine whether orbital color Doppler imaging (CDI) can be used to detect internal carotid artery stenosis (ICAS) in patients with amaurosis fugax (AF).

Methods: Twenty patients with AF (20 symptomatic eyes) and 14 normal controls (14 randomly selected eyes) were studied. The AF patients were divided by magnetic resonance angiography or carotid arteriography into those without ICAS (Group 1, n = 14), and those with ICAS (Group 2, n = 6). The peak systolic velocities (PSV) and end diastolic velocities (EDV) of the ophthalmic artery (OA) and the central retinal artery (CRA) were determined by orbital CDI, and the values were compared between the three groups.

Results: There were no significant differences in the PSV and EDV of the CRA between the three groups. However, the PSV and EDV of the OA were significantly lower in Group 2 than in the other two groups. From the distribution of PSV-OA and EDV-OA in AF patients, Group 2 could be separated from Group 1 by the PSV-OA value of 10 cm/s.

Conclusions: The PSV-OA of 10 cm/s can be used to identify AF patients with ICAS. It is concluded that orbital CDI is a valuable method for detecting ICAS in AF patients. **Jpn J Ophthalmol 2003;47:276–280** © 2003 Japanese Ophthalmological Society

Key Words: Amaurosis fugax, internal carotid artery stenosis, orbital color Doppler imaging.

Introduction

Ophthalmologists are often the first to examine patients who present with symptoms of amaurosis fugax (AF), but the ocular examinations frequently show no abnormal findings. Although the majority of AF patients do not have internal carotid artery stenosis (ICAS), some AF patients do have ICAS accompanying other treatment-resistant diseases, such as cerebral infarction, rubeotic glaucoma, and central retinal artery occlusion.[1,2]

Carotid color Doppler imaging (CDI), magnetic resonance angiography (MRA), or carotid arteriography (CA) is usually performed on patients with AF to determine whether ICAS is present. However, there are two problems associated with carotid CDI; one is that the area of the carotid that can be examined by carotid CDI is limited, so that ICAS situated in the upper regions of the carotid are sometimes missed. The second problem is that it is very difficult for an ophthalmologist to perform carotid CDI, because the carotid artery is too long to trace in one slice of CDI. MRA and CA cannot be performed successfully in some cases. Thus, an easier way to examine AF patients for ICAS should be found.

To determine whether there is a better way to examine patients with AF for ICAS, orbital CDI was tested. Orbital CDI is a recently developed objective method that enables the ophthalmologist to make reproducible, noninvasive measurements of the hemodynamics of orbital vessels.[3,4] We shall show that orbital CDI can differentiate patients with ICAS from patients without ICAS with high sensitivity and specificity.

Materials and Methods

The charts of 20 consecutive patients with AF and 14 normal controls examined between January 1998 and December 2000 were reviewed. The AF patients were divided into two groups based on the results of MRA or

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CA. AF patients without ICAS were placed in Group 1, and AF patients with ICAS were placed in Group 2. There were 14 cases (10 men, 4 women) in Group 1 with a mean age of 64.8 ± 5.8 years (range, 56–75 years). Five (36%) of these had diabetes, 5 (36%) had hypertension, 4 (29%) had atrial fibrillation, 2 (14%) smoked, and 2 (14%) had been treated with percutaneous transluminal coronary angioplasty (PTCA). Thirteen cases showed no remarkable ocular findings, and 1 case had preproliferative diabetic retinopathy in both eyes. Thirteen of the 14 cases in Group 1 were examined by MRA, and no ICAS was observed; 2 cases had stenosis of the middle cerebral artery. One case was scheduled for CA at neurosurgery, so MRA was not performed. The CA showed 2 cases with middle cerebral artery stenosis and no ICAS (Table 1).

Group 2 was made up of 6 cases (6 men, no women) with a mean age of 69.2 ± 8.3 years (range, 61–80 years). Six (100%) smoked, 4 (67%) had diabetes, 3 (50%) had hypertension, and 2 (33%) had been treated with PTCA. Five cases showed no remarkable ocular findings. One case had multiple cotton wool patches in both eyes. He was treated with interferon for a metastatic lung lesion from a renal cell carcinoma. The cotton wool patches continued after internal carotid endarterectomy but disappeared after the completion of the interferon therapy. All 6 cases in Group 2 were examined by CA and severe ICAS (99% stenosis) was detected. One case was also examined by MRA, and the result was similar to that obtained by CA (Table 1).

The normal control group was composed of 14 cases (10 men, 4 women) with a mean age of 66.1 ± 9.9 years (range, 51–85 years). They had no remarkable medical history or abnormal ocular findings.

All of the subjects in the three groups were examined by orbital CDI (HDI 3000; ATL Ultrasound, Bothell, WA, USA). A 5–10 MHz broadband linear transducer was used to examine the patients according to the method of Lieb et al.[3] In brief, with the patient in a supine position, sterile ophthalmic gel was applied to the closed eyelid as a couplant, and the probe was positioned on the eyelid gently with minimal pressure. The peak systolic velocity (PSV) and end diastolic velocity (EDV) of the ophthalmic artery (OA) and the central retinal artery (CRA) were determined.

The velocities in symptomatic eyes of patients with AF and the randomly selected eyes of normal controls were compared using one-way analysis of variance with the Tukey test between each group. $P < .001$ was considered as statistically significant.

Informed consent was obtained from all patients after an explanation of the purpose of the testing. The procedures conformed to the tenets of the Declaration of Helsinki.

Results

The differences in age, sex, and blood pressure between the normal controls, Group 1, and Group 2 were not statistically significant.

Table 1. Medical History, Ocular History, and Internal Carotid Artery Findings

Group 1 AF without ICAS				Group 2 AF with ICAS			
No.	Age	Sex	History	No.	Age	Sex	History
1 OD	70	M	None	1 OS	67	M	OA-regular flow; smoking, DM, Renal cancer with lung meta interferon retinopathy, 99% ICAS
2 OS	62	M	DM, Af	2 OD	63	M	OA-regular flow; smoking, DM, PTCA, 99% ICAS
3 OS	73	M	Smoking, HT	3 OS	80	M	OA-reverse flow; smoking, HT, PTCA, 99% ICAS
4 OD	67	F	HT	4 OD	61	M	OA-reverse flow; smoking, DM, HT, 99% ICAS
5 OS	61	F	HT	5 OD	65	M	OA-reverse flow; smoking, DM, 99% ICAS
6 OD	75	M	DM, PTCA, Af	6 OS	79	M	OA-reverse flow; smoking, HT, TIA, 99% ICAS
7 OS	69	M	DM, Af, Hypothyroid				
8 OS	68	M	TIA				
9 OD	59	F	None				
10 OS	56	M	PTCA, HL				
11 OS	61	F	None				
12 OS	66	M	DM, HT				
13 OD	62	M	Smoking, DM, HT, Pre-PDR				
14 OS	58	M	Af, TB				

AF: amaurosis fugax, ICAS: internal carotid artery stenosis, OD: right eye, OS: left eye, M: male, F: female, DM: diabetes mellitus, Af: atrial fibrillation, HT: hypertension, PTCA: percutaneous transluminal coronary angioplasty, PDR: proliferative diabetic retinopathy, TIA: transient ischemic attack, HL: hyperlipidemia, TB: tuberculous.

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In the normal group, orbital CDI showed no reverse flow in the OA in any of the cases, and the PSV-OA ranged from 21.2 to 46.8 cm/s with a mean of 29.9 ± 6.3 cm/s (Table 2). The EDV-OA in the normal group ranged from 4.5 to 11.6 cm/s with a mean of 7.0 ± 2.3 cm/s. The PSV-CRA ranged from 6 to 13.7 cm/s with a mean of 8.9 ± 3.0 cm/s, and the EDV-CRA ranged from 1.7 to 4.0 cm/s with a mean of 2.6 ± 0.7 cm/s.

In Group 1, orbital CDI also showed no reverse flow in the OA in any of the cases, and the PSV-OA ranged from 18.5 to 45.6 cm/s with a mean of 27.8 ± 8.0 cm/s (Table 2). The EDV-OA ranged from 2.8 to 15.3 cm/s with a mean of 7.3 ± 3.8 cm/s. The PSV-CRA in Group 1 ranged from 4.4 to 10.4 cm/s with a mean of 7.8 ± 1.7 cm/s, and the EDV-CRA ranged from 1.3 to 3.1 cm/s with a mean of 2.0 ± 0.5 cm/s.

In Group 2, orbital CDI showed that 2 cases had regular flow and 4 cases had reverse flow in the OA. The PSV-OA in Group 2 ranged from −26.8 to 9.8 cm/s with a mean of −11.3 ± 15.3 cm/s, and the EDV-OA ranged from −7.5 to 2.8 cm/s with a mean of −3.4 ± 4.5 cm/s (Table 2). The PSV-CRA in Group 2 ranged from 2.6 to 7 cm/s with a mean of 5.0 ± 1.7 cm/s, and the EDV-CRA ranged from 1.2 to 2.3 cm/s with a mean of 1.7 ± 0.4 cm/s.

The means of the PSV-CRA and EDV-CRA in Group 2 did not differ significantly from those in Group 1 and from normal controls; however, the means of the PSV-OA and EDV-OA in Group 2 were significantly lower than those in the other two groups (Table 2, Figure 1).

The distribution of PSV-OA and EDV-OA in AF patients is shown in Figure 2. In this study, the AF patients were clearly divided into two groups at the PSV-OA value of 10 cm/s; all of the patients with a PSV-OA of more than 10 cm/s were from Group 1, while all of the patients with a PSV-OA of less than 10 cm/s were from Group 2. There was, however, an overlap in the EDV-OA in the two Groups of AF patients (Figure 2).

The minimum, mean and maximum of PSV-OA and EDV-OA of regular flow OA cases in Group 2 (n = 2) and normal controls are shown in Figure 3. The PSV-OA values of the regular flow OA cases in Group 2 were approximately the same as those of the EDV-OA of normal controls.

Discussion

AF is defined as a monocular, transient visual loss lasting minutes and is a symptom common to many diseases.[2] Because of the loss of vision, ophthalmologists are generally the first physicians to examine AF patients. It has been reported that the frequency of recurrent vascular ischemic events is highest during the first month from the first onset and then decreases during the second and third months.[5] Thus, it is important to rule out other ocular diseases which cause a vision loss and to determine whether an internal carotid arterial lesion is present at the first examination.

The manifestations of ocular ischemic syndrome are divided into acute and chronic signs.[6] The acute signs are bright plaques, cotton wool patches, retinal artery occlusion, and anterior ischemic optic neuropathy. The chronic signs are peripheral blot hemorrhages, neovascularization on the disk, and rubeotic glaucoma. Unfortunately, the usual signs of ocular ischemic syndrome are rarely found in AF patients,[7] and those signs also were not found in our patients.

Table 2. Characteristics and Hemodynamic Parameters of Patients with Amaurosis Fugax and Normal Controls

Parameter	Normal Controls (n = 14)	AF Patients Without ICAS Group 1 (n = 14)	AF Patients With ICAS Group 2 (n = 6)
Age (years)	66.1 ± 9.9	64.8 ± 5.8	69.2 ± 8.3
Sex			
Male/Female	10/4	10/4	6/0
SBP (mm Hg)	125.3 ± 16.3	120.3 ± 16.5	127.3 ± 25.4
DBP (mm Hg)	72.3 ± 8.4	68.1 ± 10.0	66.7 ± 6.4
PSV-CRA (cm/s)	8.9 ± 3.0	7.8 ± 1.7	5.0 ± 1.7
EDV-CRA (cm/s)	2.6 ± 0.7	2.0 ± 0.5	1.7 ± 0.4
OA direction	Regular 14	Regular 14	Regular 2 Reverse 4
PSV-OA (cm/s)	29.9 ± 6.3	27.8 ± 8.0	−11.3 ± 15.3*
EDV-OA (cm/s)	7.0 ± 2.3	7.3 ± 3.8	−3.4 ± 4.5*

AF: amaurosis fugax, ICAS: internal carotid artery stenosis, SBP: systolic blood pressure, DBP: diastolic blood pressure, CRA: central retinal artery, PSV: peak systolic velocities, EDV: end diastolic velocities, OA: ophthalmic artery.

*$P < .001$.

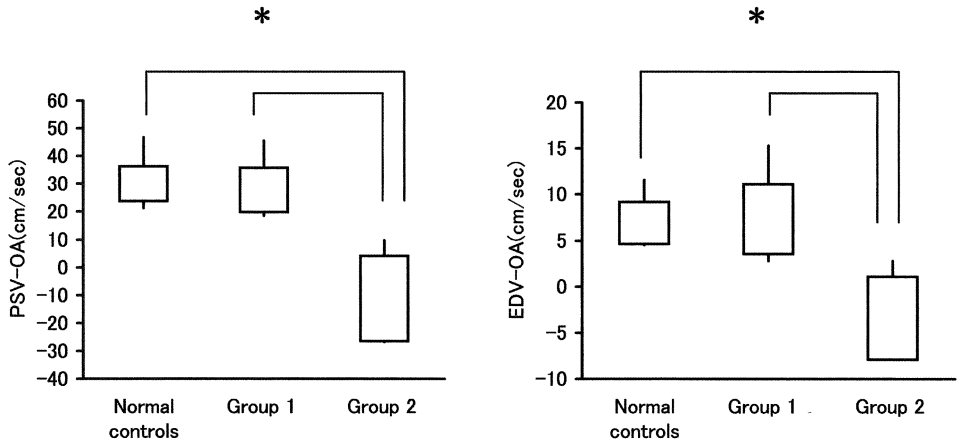

Figure 1. Peak systolic velocities (PSV) for the ophthalmic artery (OA) (left) and end diastolic velocities (EDV) for the OA (right) in normal controls, Group 1, and Group 2. Group 1 had amaurosis fugax (AF) without internal carotid artery stenosis (ICAS). Group 2 had AF with severe ICAS. PSV-OA values were significantly lower in Group 2 patients than in the other two groups. $*P < .001$.

Carotid CDI, MRA, and CA are performed on patients with AF to determine whether ICAS is present, but our results have shown that orbital CDI can also be used to separate AF patients into those with ICAS and those without ICAS by the PSV-OA value. It has been reported that the PSV-OA does not decrease until the internal carotid artery is almost completely blocked,[7] and our results showed that a significantly reduced PSV-OA is highly correlated with severe ICAS. We found that a PSV-OA value of 10 cm/s was a useful index to indicate the presence of ICAS, because it separated the two groups of AF patients. Interestingly, this value of 10 cm/s is approximately the maximum EDV-OA in the normal controls. Thus, if a patient presents with AF, a PSV-OA of less than 10 cm/s would strongly indicate the presence of ICAS and either MRA or CA should be carried out.

The mean of the EDV-OA was also significantly lower in Group 2 than in Group 1. However, the EDV-OA value was not an effective index to separate the two groups because cases with the same EDV-OA existed in both groups.

It was interesting that the PSV and EDV of the CRA were not significantly different between the three groups.

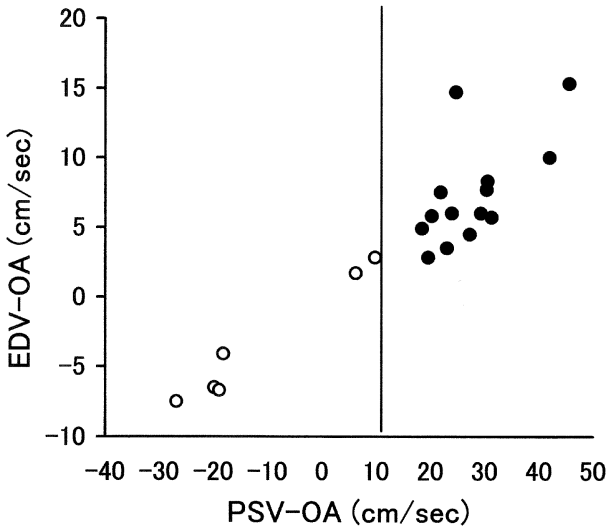

Figure 2. Distribution of peak systolic velocities (PSV) for the ophthalmic artery (OA) and end diastolic velocities (EDV) for the OA in amaurosis fugax (AF) patients. Group 1 (●) had AF without ICAS. Group 2 (○) had AF with severe ICAS.

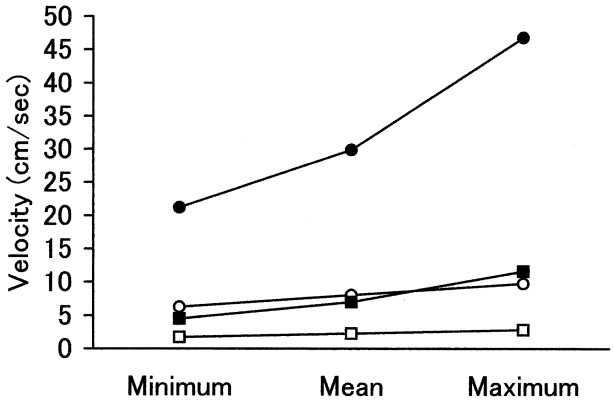

Figure 3. Comparison of peak systolic velocities (PSV) for the ophthalmic artery (OA) and end diastolic velocities (EDV) for the OA of regular flow OA cases in Group 2 and normal controls. —○—: PSV-OA of regular flow OA cases in Group 2, —●—: PSV-OA of normal controls, —□—: EDV-OA of regular flow OA cases in Group 2, —■—: EDV-OA of normal controls.

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These findings would suggest that vascular autoregulation was functioning at the retina level. When the PSV and EDV of the CRA were measured, none of these patients reported loss of vision. So we suggest that the flow in the CRA was sufficient then and the AF occurred when the flow in the CRA was significantly reduced. A PSV-OA of less than 10 cm/s and a reverse OA flow would most likely induce a transient but significant reduction of the flow in the CRA.

The PSV and EDV of the posterior ciliary artery (PCA) was not measured in our study, even though Ho et al reported that poor vision was correlated with the absence of PCA signals on CDI.[8] However, the poor vision in their patients was due to a continuous visual loss and not to AF. The PCA values do not seem like a good index for detecting ICAS because of the numerous PCAs around the optic nerve.

The resistance index also was not considered because it represents the downstream resistance of the end organ's vascular bed, and the internal carotid artery is upstream.

The question arises regarding the occurrence of false positives and false negatives if orbital CDI is used as a detector of ICAS in AF patients. It was determined that the score of 10 cm/s for PSV-OA is the critical value for segregating AF patients into those with ICAS and those without ICAS (Figure 2). Using this value, all of the patients with PSVs in the OA higher than 10 cm/s did not have ICAS, and all of the patients with PSVs in the OA lower than 10 cm/s had ICAS confirmed by MRA or CA. Thus, there were no false positives or false negatives in this study. However, the number of cases in this study is limited, and we are testing more AF cases as they become available. It should be noted that a case giving false-positive results has been reported. Ward et al have reported that abnormal blood flow in the OA existed in the absence of ICAS.[9] This case had stenosis in the left vertebral artery and hypoplasia in the right vertebral artery. This report confirms that it is necessary for cases with abnormal blood flow in the OA to be examined by MRA or CA. False-negative cases can also be found; we have examined two cases of severe ICAS in the absence of abnormal blood flow in the OA. Our findings indicated good OA flow from the vertebral arteries and the contralateral carotid artery. These patients had no symptoms of AF and were thus not included in this study.

The main reasons for the AF in Group 1 (14 cases without ICAS) were considered to be from atrial fibrillation (4 cases), middle cerebral artery stenosis (2 cases), low blood pressure (2 cases), brain hemorrhage (1 case), lacuna (1 case), and unknown causes (4 cases). In these unknown cases, it can be assumed that some disorder might have disturbed their systemic circulation. In the two middle cerebral artery stenosis cases, the patients may have mistaken homonymous hemianopia for an AF incident.

Factors in the past history of the patients in Group 2 were 100% smoking, 67% diabetes, and 50% hypertension. Therefore, when patients presenting with AF have these risk factors, orbital CDI examination is strongly recommended.

Orbital CDI is noninvasive, very easy to perform for an ophthalmologist, can be completed in 10 minutes on one eye, and can be performed on any patients. Therefore, we conclude that orbital CDI has a very important place in the examination of AF patients even if they show no ocular signs of ischemia.

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