Comparison of Ophthalmic Artery Morphological Characteristics and Retinal Vessel Diameter for Identifying Ocular Ischemic Syndrome

Xue-ru Cheng,[1,2] Lu Zhao,[1] Ying-xiang Huang,[1] Yan-ling Wang,[1,2] and Jia-lin Wang[1,2]

[1]Department of Ophthalmology, Beijing Friendship Hospital, Capital Medical University, Beijing, China
[2]Institute of Ophthalmology, Capital Medical University, Beijing, China

Correspondence: Jia-lin Wang, Department of Ophthalmology, Beijing Friendship Hospital, Capital Medical University, 95 Yong'an Road, Xicheng District, Beijing 100050, China;
wangjialin@bjmu.edu.cn.
Yan-ling Wang, Department of Ophthalmology, Beijing Friendship Hospital, Capital Medical University, 95 Yong'an Road, Xicheng District, Beijing 100050, China;
wangyanl@ccmu.edu.cn.

YW and JW contributed equally to this work and should therefore be regarded as equivalent authors.

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Purpose. To investigate the morphological characteristics of the ophthalmic artery (OA) and retinal vessels in ocular ischemic syndrome (OIS) and to compare their ability to identify OIS.

Methods. This cross-sectional observational study included 21 patients with unilateral OIS and 17 controls matched for age, sex, degree of internal carotid artery (ICA) stenosis, and cerebral collateral patency. This study used a three-dimensional reconstruction based on computed tomographic angiography to measure the morphological characteristics of the OA and the ICA. Quantitative measurements of retinal vessel diameter were performed using the Integrative Vessel Analysis software. Receiver operating characteristic (ROC) curve analysis was performed to assess the ability of the OA diameter and the central retinal artery equivalent (CRAE) to identify OIS.

Results. The diameter of the OA (odds ratio = 0.001; $P = 0.001$) and the CRAE (odds ratio = 0.951; $P = 0.028$) were significantly associated with the presence of OIS after adjusting for age, sex, and the degree of the ICA stenosis. The areas under the curve for the OA diameter and the CRAE were, respectively, 0.871 ($P < 0.001$) and 0.744 ($P = 0.017$) according to the ROC curves analysis.

Conclusions. The OA diameter measurement identified OIS better than CRAE measurement. The OA may reflect the changes in ocular blood supply in patients with OIS earlier than retinal vessels. The OA of eyes with OIS may undergo arterial wall remodeling, leading to a decrease in OA diameter and further reduction in blood flow.

Keywords: ocular ischemic syndrome, ophthalmic artery, retinal vessel diameter, arterial remodeling

Ocular ischemic syndrome (OIS) is a clinical syndrome caused by chronic ocular hypoperfusion, which commonly results from carotid artery stenosis or occlusion.[1] Irreversible visual impairment may occur as the disease progresses, and there is currently no standardized treatment for OIS. In clinical practice, the incidence of OIS may be underestimated because the condition is often missed or misdiagnosed as other retinal diseases due to the lack of specific manifestations in the early stage.[2] Early detection and prevention of OIS are important for improving prognosis.

The definite pathogenesis of OIS remains unclear. Carotid arteriography in patients with OIS typically reveals a stenosis of the ipsilateral carotid artery of at least 90%.[3] However, Mizener et al.[4] reported that some patients with an ipsilateral carotid artery stenosis less than 50% developed OIS. Such differences may be related to the blood supply from the intracranial collateral and ophthalmic artery (derived from the external carotid artery). Therefore, the risk of OIS cannot be accurately assessed solely based on the degree of internal carotid artery (ICA) stenosis.

Some studies have reported the morphological and hemodynamic changes of retinal vessels in patients with ICA stenosis.[5,6] Retinal vessel diameter indices include the central retinal artery equivalent (CRAE), central retinal vein equivalent (CRVE), and the arteriole-to-venule ratio (AVR; CRAE/CRVE). Wu et al.[6] found that the CRAE and AVR were significantly decreased in patients with ipsilateral severe ICA stenosis compared with healthy controls. The correlation between retinal vessel diameter and OIS has not been previously reported. In addition, Klijn et al.[7] found that some patients with carotid artery occlusion developed OIS despite no retinal vascular abnormalities in the early stage of occlusion, indicating that retinal vascular characteristics may not accurately assess the risk of OIS in the early stage of the disease. The blood supply to the eye originates from the ophthalmic artery (OA) as the first major branch of the ICA. Kawaguchi et al.[8] reported reversed OA flow and decreased OA blood velocity in patients with chronic OIS. Evaluating

morphological characteristics of OA in OIS contributes to early detection and prevention of OIS, as well as the exploration of the potential pathogenesis of OIS. However, the morphological characteristics of OA in OIS have not been previously examined.

Computed tomography angiography (CTA) is a noninvasive method for visualization of the OA, and it can display the complex course of the OA.[9] In this study, morphological parameters of the ICA and the OA were measured by reconstructing three-dimensional (3D) models using computer software that has been used for the observation and morphological analysis of small arteries,[10–13] and which can reflect the actual state of blood vessels in vivo.

This study aimed to investigate the morphological characteristics of the OA and retinal vessels in patients with OIS and compare their ability to identify OIS. We hypothesized that OA diameter and CRAE decreased in eyes with OIS and that morphological measurement of the OA would identify OIS better than the retinal vessel diameter measurement.

Methods

Study Participants

This cross-sectional observational study was performed in accordance with the tenets of the Declaration of Helsinki. Ethics approval was obtained from the Medical Research Ethics Committee of Beijing Friendship Hospital, which is affiliated with Capital Medical University (reference number: 2020-P2-008). All participants provided informed consent to participate in this study after receiving an explanation of the nature and possible consequences of the study.

The medical records of all patients admitted to Beijing Friendship Hospital between January 2016 and December 2022 with a diagnosis of OIS and those of controls with no ocular ischemic symptoms who underwent CTA and were diagnosed with ICA stenosis or occlusion were reviewed. The control group and the OIS group were matched for age, sex, the degree of ICA stenosis, and cerebral collateral circulation. All patients underwent CTA and ocular examination, including measurement of best-corrected visual acuity, intraocular pressure measured by non-contact tonometry, slit-lamp biomicroscopy, fundus color photography, and fundus fluorescein angiography (Fig. 1). The diagnostic criteria for OIS were those described by Kofoed et al.[14] The exclusion criteria were as follows: (1) retinal or choroidal diseases, such as ischemic central retinal vein occlusion, retinal detachment, or polypoidal choroidal vasculopathy; (2) retinal vascular lesions caused by Vogt–Koyanagi–Harada disease, Behçet's disease, or rheumatoid disease; (3) optic neuropathy, such as anterior ischemic optic neuropathy; and (4) history of ocular trauma.

Retinal Vessel Diameter Measurement and Analysis

A high-resolution fundus camera (Kowa, Tokyo, Japan) was used for digital fundus photography of all patients, and the diameters of the retinal vessels coursing through a specified area (0.5–1 disk diameter from the optic disk margin) were measured using a semi-automated vessel measurement system (Ivan software, University of Wisconsin at Madison, Madison, WI, USA) (Fig. 2A). The software was used according to the software developer's instructions. The CRAE, CRVE, and AVR were calculated according to the modified Parr–Hubbard formula revised by Knudtson et al. in 2003.[15] The quality of color fundus images was assessed by an experienced ophthalmologist. If the vascular architecture was not clearly visible because of media opacities, the eye was not included in the analysis of the retinal blood vessel diameter. Measurements of the retinal vessel diameter in all eyes were completed by a trained grader. These measurements have been shown to be highly reproducible in previous studies,[16] and the consistency of the measurements has

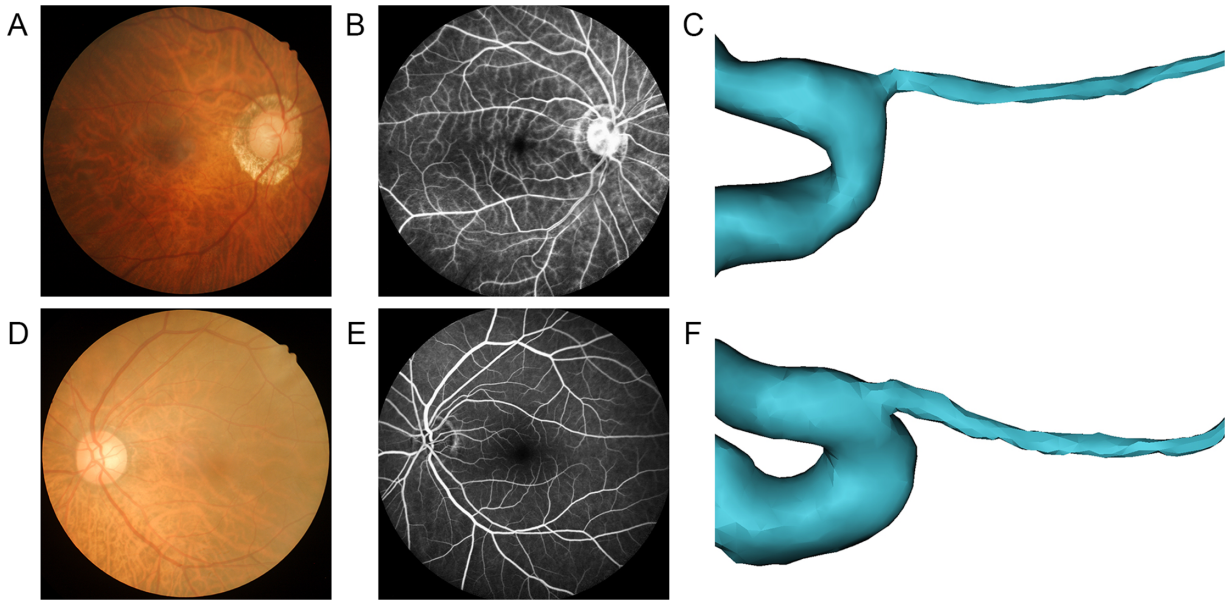

Figure 1. Characteristic fundus photographs, fundus fluorescein angiography (FFA) images, and the 3D models of the OA reconstructed by using CTA images in patients with OIS and controls. (**A–C**) Fundus photograph, FFA image, and 3D model of the OA in a 70-year-old male with OIS. (**D–F**) Fundus photograph, FFA image, and 3D model of the OA in a 69-year-old female control.

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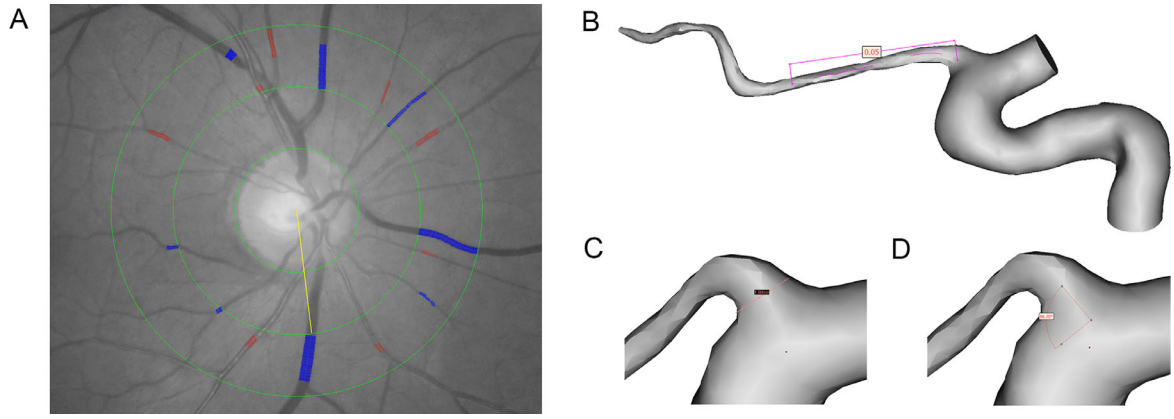

FIGURE 2. Measurement of retinal blood vessel diameter (**A**) and morphological measurements of the OA (**B–D**). (**B**) A three-dimensional model of the OA and C4–C6 segments of the ICA, and measurement of OA tortuosity. (**C**) Measurement of the diameter of the initial part of the OA. (**D**) Measurement of the angle between the OA and the ICA.

been confirmed. The intraclass correlation coefficient for all measured parameters was >0.85.[16]

CTA Data Acquisition

CTA was performed from the aortic arch to the skull base by using a 64-row multidetector computed tomography scanner (LightSpeed VCT; GE Healthcare, Chicago, IL, USA). The detailed scanning parameters were as follows: pixel spacing, 0.625 mm; image resolution, 512 × 512; layer spacing, 0.8 mm. The degree of ICA stenosis in all patients was assessed based on CTA, according to the criteria of the North American Symptomatic Carotid Endarterectomy Trial Collaborators (NASCET).[17] The maximum degree of stenosis among multiple stenoses of the ICA was recorded, as well as the patency of the anterior communicating artery and posterior communicating artery.

Three-Dimensional OA Reconstruction

Using CTA images, a 3D model of the ICA and OA was reconstructed in Mimics 21.0 (Materialise, Ann Arbor, MI, USA) (Fig. 1). Image segmentation technology was used to extract clear contour data of the OA and the ICA from CT images. The entire ICA was divided into seven segments designated C1 through C7, according to the classification system proposed by Bouthillier et al.[18,19] The OA was divided into intracranial, intracanalicular, and intraorbital segments,[20] and the intraorbital course of the OA was divided into three sections.[20] Mimics software was used to measure the centerline best-fit diameter of the initial part of the OA (corresponding to the intracranial segment) (Fig. 2C), the tortuosity of OA (from the beginning of the intracranial segment to the terminal section of the first part of the intraorbital segment, because these segments were clearer, compared with distal segments) (Fig. 2B), the angle between the OA and the ipsilateral ICA (Fig. 2D), and the diameter and the tortuosity of C4 and C5 segments of the ICA. The measured diameter parameter was the lumen diameter. The tortuosity of certain segments is calculated by the formula of 1 – (linear distance/length along the centerline).

Statistical Analyses

SPSS Statistics 26.0 (IBM Corp., Chicago, IL, USA) was used for all statistical analyses. $P \leq 0.05$ indicated statistical significance. The Shapiro–Wilk test was performed for data normality. Data of normal continuous variables are presented as means ± standard deviations (SDs), and those of skewed variables are presented as medians (25th percentile, 75th percentile). Categorical variables are summarized as numbers (percentages). According to data normality, the continuous variables were compared using the Student's *t*-test or the Mann–Whitney *U* test between OIS eyes and control eyes. The two-sided paired *t*-test or the Wilcoxon signed-rank test was used to compare OIS eyes and fellow eyes according to the normality of *D* values. The χ^2 test was performed for the comparison of categorical data. Binary logistic regression analysis was performed for both OIS eyes and control eyes to analyze parameters associated with OIS. The receiver operating characteristic (ROC) curve analysis was performed to assess the ability of the OA diameter and the CRAE to discriminate between OIS eyes and control eyes.

RESULTS

Patient Baseline Clinical Characteristics

In total, 21 OIS eyes and 21 fellow eyes of patients with unilateral OIS (mean age, 67.62 ± 7.16 years; male sex, 85.7%) and 17 eyes of 17 controls (mean age, 67.18 ± 6.45 years; male sex, 76.5%) were enrolled in this study. Table 1 presents the baseline data of all participants. There was no significant difference in the median stenosis ratio of the ipsilateral ICA between OIS eyes and control eyes (80% vs. 60%; $P = 0.168$), although a significant difference in this parameter was detected between OIS eyes and fellow eyes (80% vs. 40%; $P < 0.001$). The best-corrected visual acuity of OIS eyes was significantly worse than that of fellow eyes (median logMAR, 1.00 vs. 0.22; $P = 0.016$) and control eyes (median logMAR, 1.00 vs. 0.10; $P < 0.001$). There were no significant differences in age, sex, other clinical characteristics, or intraocular pressure between patients with OIS and controls.

Table 1. Baseline Characteristics of Participants

Characteristics	OIS (n = 21)				
	OIS Eyes	Fellow Eyes	P	Control Eyes (n = 17)	P^*
Systemic Parameters					
Age (y)	67.62 ± 7.16			67.18 ± 6.45	0.844
Male	18 (85.7)			13 (76.5)	0.750
BMI (kg/m^2)	25.00 ± 3.49			25.11 ± 2.40	0.910
ICA stenosis (%)	80 (63, 99)	40 (20, 60)	<0.001†	60 (35, 95)	0.168
Hypertension	16 (76.2)			14 (82.4)	0.875
Diabetes mellitus	13 (61.9)			10 (58.8)	0.976
Ischemic heart disease	6 (28.6)			7 (41.2)	0.644
Stroke	8 (38.1)			7 (41.2)	0.976
Smoking	7 (33.3)			10 (58.8)	0.196
Collateral Patency					
ACoA	12 (70.6)			11 (52.4)	0.254
Ipsilateral PCoA	4 (19.0)	4 (19.0)		6 (35.3)	0.258
Laboratory Parameters					
SBP (mmHg)	129.50 (120.00, 143.50)			124.00 (113.50, 136.00)	0.234
DBP (mmHg)	76.95 ± 7.85			74.71 ± 11.88	0.496
TC (mmol/L)	3.73 ± 0.80			4.14 ± 1.18	0.251
Triacylglycerol (mmol/L)	1.20 (1.07, 1.44)			1.10 (0.89, 1.72)	0.546
HDL (mmol/L)	1.00 (0.88, 1.15)			1.07 (0.93, 1.18)	0.558
LDL (mmol/L)	2.08 ± 0.52			2.35 ± 0.79	0.244
Glucose (mmol/L)	6.73 (5.39, 9.67)			5.65 (5.03, 8.08)	0.476
HBA1c (%)	7.00 ± 0.95			6.89 ± 1.24	0.829
Homocysteine (μmol/L)	17.30 (14.48, 20.48)			12.90 (8.80, 17.90)	0.107
Ocular Parameters					
BCVA (logMAR)	1.00 (0.22, 2.00)	0.22 (0.00, 0.30)	0.016†	0.10 (0.00, 0.10)	<0.001
IOP (mmHg)	15.00 (13.98, 19.00)	14.65 (12.15, 17.00)	0.362‡	16.60 (12.83, 18.00)	0.901

Data are presented as mean ± SD, number (%), or median (25th percentile, 75th percentile). OIS, ocular ischemic syndrome; BMI, body mass index; ICA, internal carotid artery; ACoA, anterior communicating artery; PCoA, posterior communicating artery; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high-density protein; LDL, low-density protein; HBA1c, hemoglobin A1c; BCVA, best-corrected visual acuity; IOP, intraocular pressure.

* Comparison between OIS eyes and control eyes.

† Paired t-test between OIS eyes and fellow eyes.

‡ Wilcoxon signed-rank test between OIS eyes and fellow eyes.

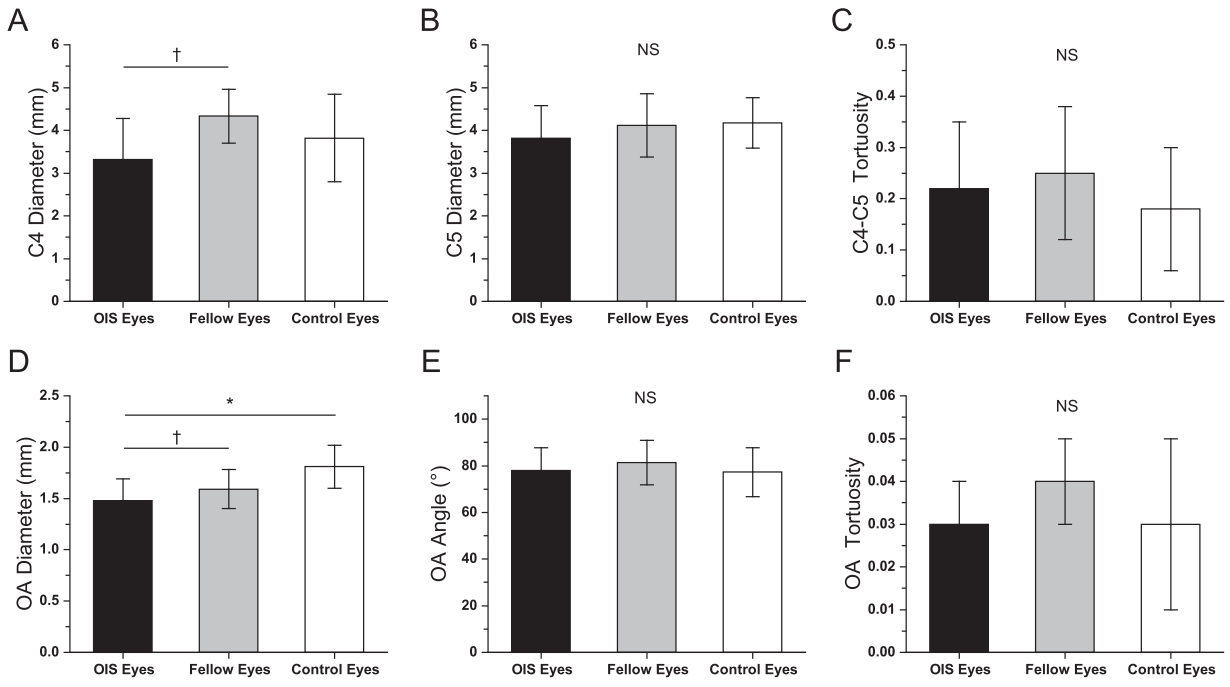

Figure 3. Comparison of morphological features of the OA and the ICA in OIS eyes, fellow eyes, and control eyes. *P < 0.05 compared with OIS eyes calculated by Student's t-test; †P < 0.05 compared with OIS eyes calculated by paired t-test; NS, not significant.

Morphological Comparison of the OA and the ICA

The mean diameter of the OA in OIS eyes (1.48 ± 0.21 mm) was significantly smaller than that in fellow eyes (1.59 ± 0.19 mm; $P < 0.001$) and control eyes (1.81 ± 0.21 mm; $P < 0.001$). The mean C4 segment diameter in OIS eyes was significantly smaller than that in fellow eyes (3.32 ± 0.96 vs. 4.33 ± 0.63 mm; $P = 0.001$), whereas there was no significant difference between OIS eyes and control eyes. No significant differences were found between OIS eyes and control eyes in the angle and tortuosity of the OA, the diameter of the C5 segment, and the tortuosity of the C4–C5 segment (Fig. 3).

Comparison of Retinal Blood Vessel Diameters

Retinal blood vessel diameters of 16 eyes with OIS and 16 fellow eyes were calculated and included in the analysis. Retinal blood vessels in the remaining five patients with OIS were excluded from the analysis, as these were not clearly visible due to refractive medium opacities. There were no significant differences in age, sex, ICA stenosis ratio, and OA diameter between included and excluded OIS eyes. The mean CRAE in OIS eyes was significantly smaller than that in fellow eyes (135.41 ± 21.94 µm vs. 150.80 ± 17.62 µm; $P = 0.003$) and control eyes (135.41 ± 21.94 µm vs. 152.63 ± 15.98 µm; $P = 0.015$). The mean AVR in OIS eyes was significantly smaller than that in fellow eyes (0.46 ± 0.06 vs. 0.51 ± 0.05; $P = 0.002$) and control eyes (0.46 ± 0.06 vs. 0.52 ± 0.05; $P = 0.001$). No significant differences were found in the CRVE between OIS eyes and fellow eyes or control eyes (Table 2).

Logistic Regression Analysis of Parameters Associated With OIS

In the logistic regression analysis, the diameter of the OA (odds ratio [OD] = 0.001; 95% confidence interval [CI], 0.000–0.060; $P = 0.001$) and the CRAE (OR = 0.951; 95% CI, 0.910–0.995; $P = 0.028$) were significantly associated with OIS after adjusting for age, sex, and stenosis ratio of the ICA.

ROC Curve Analysis of Parameters Associated With OIS

The ROC curve was used to assess the ability of the OA diameter and CRAE to discriminate between OIS eyes and control eyes. The areas under the curve for the OA diameter and the CRAE were 0.871 (95% CI, 0.746–0.997; $P < 0.001$) and 0.744 (95% CI, 0.574–0.915; $P = 0.017$), respectively (Fig. 4).

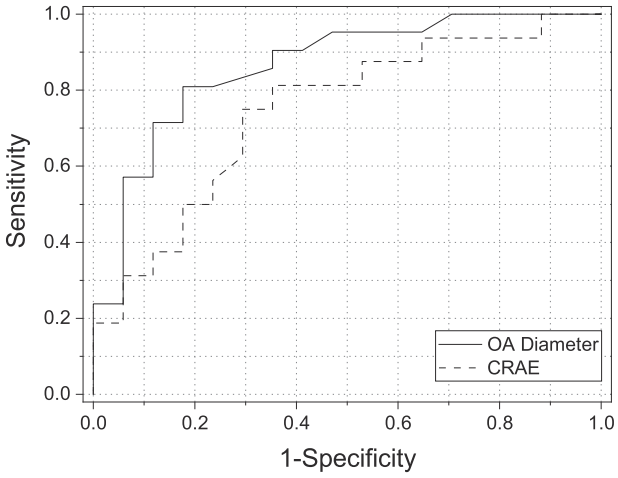

Figure 4. ROC curves for identification of eyes with OIS using the OA diameter measurement and CRAE measurement.

Discussion

In this study, the control and OIS group were matched for age, sex, degree of ICA stenosis, and cerebral collateral circulation. A previous study reported that some patients with ipsilateral ICA occlusion did not develop OIS, whereas others developed OIS despite an ipsilateral ICA stenosis of less than 50%; these results may be attributed to differences in the collateral circulation.[4] Furthermore, the capacity of collaterals also affects the retrobulbar circulation.[21] Therefore, patients with OIS and controls in this study were matched for the collateral patency of the anterior communicating artery and posterior communicating artery to mitigate the impact of the collateral circulation and explore the correlation of ocular parameters with OIS. The proportion of male patients with OIS in our study was 86%, which was consistent with the findings of previous studies.[3] In addition, in previous studies, about 56% of patients with OIS had diabetes.[2–4] In our study, 62% of patients with OIS had diabetes. There was no significant difference in diabetes between patients with OIS and controls.

The ICA siphon is an S-shaped bend upstream of the origin of the OA, including the C4 and C5 segments.[18] Previous studies have reported that the tortuosity of the ICA siphon affects the blood outflow patterns,[22] which might affect the perfusion of the target organ, such as eyes. Therefore, we measured the diameters of the C4 and C5 segments of the ICA, as well as the tortuosity of the C4–C5 segment. The diameter of the C4 segment of the ICA in OIS eyes was significantly smaller than that in fellow eyes. We postulated that this may be associated with the automatic regulation of

Table 2. Retinal Vessel Diameters of Participants

	OIS, Mean ± SD				
	OIS Eyes ($n = 16$)	Fellow Eyes ($n = 16$)	P^*	Control Eyes, Mean ± SD ($n = 17$)	$P^\dagger$
CRAE (µm)	135.41 ± 21.94	150.80 ± 17.62	0.003	152.63 ± 15.98	0.015
CRVE (µm)	296.08 ± 25.46	295.49 ± 21.74	0.816	292.33 ± 23.71	0.664
AVR	0.46 ± 0.06	0.51 ± 0.05	0.002	0.52 ± 0.05	0.001

OIS, ocular ischemic syndrome; CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; AVR, arteriole to venule ratio.

[*] Two-sided paired *t*-test between OIS eyes and fellow eyes.

[†] Two-sided Student's *t*-test between OIS eyes and control eyes.

blood flow. When blood flow decreases, peripheral vascular resistance decreases to maintain the ICA blood flow.[23] However, automatic regulation on the OIS side is impaired because of severely decreased perfusion pressure, resulting in decreased ICA blood flow.[24] Conversely, decreased ICA blood flow may lead to arterial remodeling, characterized by downregulation of proliferation and upregulation of apoptosis of the endothelial cell and smooth muscle cells,[25] as well as increased migration of smooth muscle cells,[26] which leads to further reduction in the ICA diameter. In addition, our results showed that the C4 diameter in fellow eyes was larger than that in OIS eyes and control eyes, although the difference between fellow eyes and control eyes was not significant. This may be associated with collateral compensation for contralateral ICA. In brief, in OIS there is a decrease in the pressure of the distal ICA, and the pressure difference causes collateral flow from the contralateral side toward the ipsilateral side via the anterior communicating artery, leading to ICA blood flow lateralization.[27,28] There was a significant difference in C4 diameter between OIS eyes and fellow eyes, although no significant difference in C5 diameter was observed. The likely explanation for this finding is the higher curvature of the C4 segment compared to that of the C5 segment. Research indicates that regions with high curvature had low and highly oscillatory wall shear stress in the inner or the outer wall of arterial vessel bends.[29] Low and oscillating shear stress promotes the atheroprone phenotype of the endothelial cells, with increased inflammation, leukocyte adhesion, lipoprotein uptake, and migration of smooth muscle cells, thus contributing to atherosclerosis and stenosis.[30]

The diameter of the OA in OIS eyes was significantly smaller than that in fellow eyes and control eyes, which might be associated with the decrease in OA blood flow as a result of decreased ICA blood flow. Cho et al.[25] found that reduced blood flow can trigger apoptosis and inhibit the proliferation of smooth muscle and endothelial cells in carotid arteries of immature rabbits, contributing to arterial remodeling and decreases in diameter. According to Poiseuille's law, shear stress is proportional to the flow and to the inverse cube of the diameter.[31] Therefore, we postulate that arterial remodeling is mediated by low wall shear stress (WSS). Low WSS induces changes in the structure and function of endothelial cells, leading to transition to the atherosusceptible endothelial phenotype.[32] Furthermore, low WSS induces downregulation of endothelial nitric oxide synthase expression,[33] leading to a decrease in the production of nitric oxide and impaired OA relaxation response. Moreover, low WSS increases the uptake and synthesis of endothelial low-density lipoprotein, leading to the accumulation of low-density lipoprotein in the intima of the arterial wall, promoting atherosclerotic plaque progression.[34] Low WSS also enhances expression of the pro-inflammatory gene by stimulating mitogen-activated protein kinases[35] and activates Smad2/3 signaling, which promotes endothelial–mesenchymal transition, severe inflammation, and arterial wall remodeling.[36] In addition, when ischemia occurs, the endothelin-1–mediated vasoconstriction in the OA increases, primarily through the endothelin receptor type B (ETB) receptor and the mitogen-activated protein kinase kinase (MEK)/extracellular signal-regulated kinase (ERK)1/2 pathway, which may also result in a decrease in OA diameter.[37,38] We found that the OA diameter in fellow eyes was smaller than that in control eyes, although the difference was not significant. We hypothesized that this might be associated with collateral flow from the contralateral ICA to the OIS side. Although blood flow in the dominant ICA increased, it may not maintain sufficient OA blood supply in fellow eyes, leading to a decrease in OA blood flow. In addition, the angle between arteries or arterial segments might affect the hemodynamics.[39,40] Therefore, we evaluated the angle between the OA and the ipsilateral ICA. However, no significant difference was found between two groups.

A smaller retinal arteriolar diameter was reported to be associated with higher blood pressure and male sex.[41] The results of this study indicate that the mean CRAE in OIS eyes was significantly smaller than that in control eyes matched for blood pressure and sex. We postulate that this may be associated with decreased retinal blood perfusion caused by insufficient OA blood supply.[42] When ocular perfusion pressure decreases, the retinal arterial diameter initially increases by autoregulation.[43] However, the autoregulative capability of retinal vessels is limited. When the decrease in ocular perfusion pressure exceeds the compensatory limit of the retinal vessels, retinal blood flow decreases and the retinal arteries contract.[44] No significant differences were found in CRVE between OIS eyes and control eyes, probably because the retinal venous diameter is influenced by more confounding factors, such as current smoking, dyslipidemia, and hyperglycemia.[41] In addition, this result may also be related to the small sample size. The significantly decreased AVR in OIS eyes was considered to be related to the decreased CRAE and slightly increased CRVE. AVR is a dimensionless ratio that mitigates, to some extent, the impact of variations in image magnification during measurement.[45]

In this study, decreased OA diameter and decreased CRAE were found to be associated with the presence of OIS. ROC curve analysis showed that the ability of the OA diameter to discriminate between OIS eyes and control eyes was better than that of CRAE, suggesting that measurement of the OA diameter identifies OIS better than CRAE measurement. The OA diameter may be a potential diagnostic marker for OIS. Although the retinal blood vessels are easily visualized clinically, the retinal vessel diameter is often affected by confounding factors, such as age, hypertension and diabetes mellitus.[46] The OA is considered to directly reflect the changes in ocular blood supply. Blixt et al.[38] found that the endothelin-1 mediated vasoconstriction in the OA significantly increased 48 hours after global ischemia, whereas retinal damage occurred 72 hours after ischemia, indicating that the OA can reflect changes in ocular blood supply earlier than the retinal vascular system. Moreover, it was reported that, when the OA blood flow was reversed in patients with ICA occlusion, the blood flow velocity of the central retinal artery and the posterior ciliary artery had not changed,[21,47] which also indicates that OA may reflect changes in ocular blood supply in patients with ICA stenosis or occlusion earlier than the central retinal artery and the posterior ciliary artery. These findings have prompted ophthalmologists to focus on the reduction of OA diameter and reversed blood flow of the OA in patients with ICA stenosis or occlusion, which may reflect changes in ocular blood supply in the early stage of OIS, contributing to early detection and prevention. In the future, studies are needed on the significance of the OA as a potential diagnostic marker for OIS.

The strengths of this study are that the control eyes were matched with eyes with OIS for ICA stenosis, collateral patency, and other systemic characteristics. We measured the inner diameter of the OA by 3D modeling, which can reflect

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the actual state of blood vessels in vivo. This study had several limitations. First, the sample size was small because OIS is underdiagnosed in clinical practice. Second, the perfusion of the OA in patients with OIS was not evaluated. Third, this study included diabetic patients.

Our findings suggest that the OA diameter identifies OIS better than CRAE. The OA may reflect changes in the ocular blood supply of patients with OIS earlier than retinal vessels. The arterial wall remodeling may occur in the OA of eyes with OIS, leading to a decrease in OA diameter and further reduction in blood flow.

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