Available online at www.ijicr.com

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

INDIAN JOURNAL OF INNOVATIVE CLINICAL RESEARCH

Received 16 April 2024
Revised 12 August 2024
Accepted 3 September 2024

RESEARCH ARTICLE

ANALYSIS OF OPHTHALMIC ARTERY MORPHOLOGICAL FEATURES AND RETINAL VESSEL DIAMETER FOR THE IDENTIFICATION OF OCULAR ISCHAEMIC SYNDROME

Sharmistha Behera, Department of Ophthalmology, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Sambalpur, Odisha, India

Abstract

Introduction: Ocular ischemic syndrome (OIS) results from prolonged inadequate blood flow to the eye, often due to carotid artery narrowing, leading to potential vision loss. Early detection is critical, yet diagnosis can be challenging due to subtle initial symptoms and a lack of standardized treatment protocols. This study aims to examine the morphological features of the ophthalmic artery and retinal vessels in individuals with OIS.

Methods: 160 individuals were included in the study, divided into those with OIS and a control group with confirmed carotid artery stenosis but no ocular symptoms. High-resolution fundus photography was used to assess retinal vessel diameters, while computed tomography angiography provided insights into the ophthalmic artery's structure. Morphological measurements and collateral circulation assessments were performed to establish associations with OIS.

Results: The study found significant differences in intraocular pressure (IOP) and best-corrected visual acuity (BCVA) between ocular ischemic syndrome (OIS) eyes and control eyes, with OIS eyes exhibiting poorer visual acuity (BCVA of 1.03 logMAR). Morphological analysis revealed a smaller ophthalmic artery diameter in OIS eyes (1.45 mm) in contrast to fellow (1.58 mm) and control eyes (1.83 mm). Retinal vessel analysis indicated that the central retinal artery equivalent (CRAE) and artery-to-vein ratio (AVR) were notably lower in OIS eyes in contrast to control as well as fellow eyes. The prevalence of internal carotid artery stenosis was markedly higher in OIS patients (median 83%) versus controls (median 61%).

Conclusion: These findings underscore the vascular contributions to ocular ischemic syndrome, particularly regarding impaired ocular hemodynamics and visual outcomes. Further research is warranted to explore

potential therapeutic interventions targeting these vascular abnormalities.

Keywords: Ocular Ischemic Syndrome, Intraocular Pressure, Best-Corrected Visual Acuity, Ophthalmic Artery

BACKGROUND/INTRODUCTION

Ocular ischemic syndrome (OIS) is a serious ailment marked by prolonged insufficient blood flow to the eye, primarily due to significant narrowing or blockage of the carotid artery. This impairment in blood supply can result in irreversible vision loss as the syndrome advances. Unfortunately, the absence of a standardized treatment for OIS, coupled with its subtle early signs, leads to frequent misdiagnoses as other retinal diseases. Therefore, timely and accurate detection of OIS is crucial for improving patient outcomes [1,2].

The exact mechanisms underlying OIS remain inadequately understood. Carotid arteriography typically reveals severe stenosis (around 90%) of the ipsilateral carotid artery in affected individuals [3]. However, it is important to note that some patients with OIS present with less than 50% stenosis, suggesting that carotid artery narrowing alone may not be a reliable predictor of the syndrome. This observation prompts further investigation into additional factors—such as the role of intracranial collateral circulation and the dynamics of the ophthalmic artery—that may significantly influence the risk of developing OIS [4].

Numerous investigations have assessed the alterations in retinal vessels among patients with carotid artery stenosis, focusing on indices such as the central retinal vein equivalent (CRVE), arteriole-to-venule ratio (AVR), as well as central retinal artery equivalent (CRAE) [5,6]. For instance, one investigation noted a prominent reduction in CRAE and AVR in those with severe stenosis in comparison to healthy individuals. Nevertheless, the relationship between these retinal vessel changes and OIS is not well defined. Moreover, OIS can manifest without apparent retinal vascular abnormalities in its early stages, complicating efforts to diagnose the condition based solely on retinal vessel characteristics [6,7].

The primary blood supply to the eye is derived from the ophthalmic artery (OA), a major branch of the internal carotid artery (ICA). Research indicates that individuals with OIS often experience reversed blood flow and decreased velocity in the OA [8]. This presents an opportunity to explore the structural characteristics of the OA, which could provide critical insights into the pathophysiology of OIS and facilitate early diagnosis. However, existing literature lacks comprehensive studies examining these morphological characteristics in OIS patients.

Computed tomography angiography (CTA) has emerged as a non-invasive technique that allows for detailed visualization of the OA and accurately captures its complex anatomical structure [9]. In this study, we aim to utilize advanced computer software

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

to reconstruct three-dimensional (3D) models of the ICA and OA, enabling a thorough morphological analysis of these vessels that reflects their actual state *in vivo* [10-13]. This study aims to explore the structural attributes of the OA and retinal blood vessels in patients with OIS using three-dimensional (3D) reconstruction techniques. This study anticipates a significant reduction in both the OA diameter and the CRAE in eyes affected by OIS. Furthermore, the analysis of OA morphology is expected to provide a more reliable method for diagnosing OIS compared to conventional retinal vessel measurements.

MATERIALS AND METHODS

Study Design

This cross-sectional study sought to examine the association between ICA stenosis and OIS. The study was conducted at a medical facility in Odisha, India.

Study Population

The study involved 160 patients, all receiving treatment between April 2018 and June 2022. These individuals were categorized into two groups: one comprising patients diagnosed with OIS and the other serving as a control group, consisting of individuals without ocular ischemic symptoms but with confirmed ICA stenosis or occlusion through CTA. Both groups were matched according to age, gender, the extent of ICA stenosis, and brain collateral blood flow.

Participant Selection Criteria

The inclusion criteria for this study required patients to be diagnosed with ocular ischemic syndrome (OIS) based on the criteria outlined by Kofoed et al. [14]. Additionally, controls were selected from individuals with ICA stenosis or occlusion, confirmed through CTA, but without any ocular ischemic symptoms. Both the cohorts were aligned for variables like age, gender, the extent of artery narrowing, and alternative brain blood flow pathways to ensure they were comparable for analysis.

The study did not include participants with any eye or vascular conditions affecting the retina or the layer beneath it, such as blocked central retinal veins, detached retinas, or abnormal blood vessels in the choroid. Additionally, individuals with retinal vessel issues caused by systemic disorders like Vogt–Koyanagi–Harada syndrome, Behçet's syndrome, or rheumatoid arthritis were excluded. Those with optic nerve problems, like optic nerve damage from reduced blood flow, or a history of eye injuries or surgeries that could alter retinal or blood vessel structures, were also not part of the study.

Study Duration

This research was carried out over a span of four years, from April 2018 to June 2022, reviewing the records and monitoring information of the participants.

Retinal Vessel Diameter Assessment

A Kowa camera (Kowa, Tokyo, Japan) was used to take high-definition pictures of the retina. Using Ivan

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

software, the widths of the retina's arteries and veins were measured to within 0.5 to 1 times the optic disc's diameter (University of Wisconsin, Madison, WI, USA). The modified Parr-Hubbard approach was used to calculate key parameters, such as the ratio between artery and vein diameters (AVR), central retinal vein width (CRVE), and central retinal artery width (CRAE) [15]. An expert in ocular pathology assessed the image clarity and included only high-quality ones. Strong reliability was ensured by an intraclass correlation coefficient above 0.85, which verified the consistency of the measurements [16].

CTA Acquisition and Imaging Protocols

From the base of the skull to the aortic arch, 64-slice CT scans (called CT angiography, or CTA scans) were carried out using a LightSpeed VCT scanner manufactured by GE Healthcare in Chicago, Illinois, USA. The following were the scanning parameters: 0.8 mm slice spacing, 512 × 512 image resolution, and 0.625 mm pixel spacing. The degree of arterial constriction (ICA stenosis) was assessed using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria, and the anterior and posterior connecting arteries' openness was noted [17].

Data Collection

Information regarding the degree of artery narrowing (ICA stenosis), retinal vessel widths, and other clinical data were gathered from patient records. CTA images were reviewed to evaluate the severity of artery narrowing and the condition of alternative circulation pathways. Retinal vessel measurements were conducted using semi-automated software, and other eye-related data were obtained from comprehensive eye exams, including best-corrected visual sharpness, eye pressure, and slit-lamp biomicroscopy.

Ophthalmic Artery 3D Modelling

Using Mimics 21.0 software (Materialise, Ann Arbour, MI, USA), 3D models of the internal carotid artery (ICA) and ocular artery (OA) were created from CTA images. The classification described by Bouthillier et al. led to the division of the ICA into seven sections (C1–C7). The intracranial, intracanalicular, and intraorbital components of the OA were separated. The width and curvature of the OA and ICA sections were measured, and the angle separating them was computed. The following formula was used to calculate curvature: 1 – (straight distance / path length).

Ethics Approval

The Institutional Review Board (IRB) granted ethics approval for the study (reference number: XXX). Following complete disclosure of the objectives and possible dangers of the study, all participants gave written consent.

Statistical Analysis

All statistical analyses were performed using IBM Corp.'s SPSS Statistics 26.0 (Chicago, IL, USA). For statistical significance, a p-value of less than 0.05 was used. The Shapiro-Wilk test was used to analyse the distribution of the data, and the medians (25th and 75th percentiles) were provided for data that were not

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

normally distributed. Using the Student's t-test or the Mann-Whitney U test, the continuous data between the OIS and control groups was compared based on normality. The chi-square test was used to compare categorical data. Binary logistic regression study identified traits linked to OIS, while a receiver operating characteristic (ROC) curve assessed the ability of OA diameter and CRAE to distinguish between OIS and control eyes.

RESULTS

Patient demographics

The study examined the initial characteristics of participants with ocular ischemic syndrome (OIS) in comparison to control subjects. Key results showed notable differences in eye pressure and best-corrected visual sharpness between eyes with OIS and control eyes, with OIS eyes exhibiting lower visual sharpness (BCVA of 1.03 logMAR) and similar eye pressure (15.60 mmHg). Furthermore, systemic factors revealed a greater occurrence of internal carotid artery narrowing in patients with OIS (median 83%) compared to the controls (median 61%), underscoring the possible vascular influences on the development of OIS, as detailed in Table 1.

Table no.1: Comparison of Baseline Features

Characteristics	OIS Eyes (n = 95)	Fellow Eyes (n = 95)	P Value	Control Eyes (n = 65)	p-value
Systemic Parameters					
Age (y)	68.20 ± 7.30	68.60 ± 6.90	0.810	67.80 ± 6.10	0.850
Male	78 (82.1%)	-	0.720	48 (73.8%)	0.745
BMI (kg/m²)	25.30 ± 3.20	25.10 ± 2.80	0.890	24.80 ± 2.45	0.920
ICA stenosis (%)	83 (65, 98)	43 (23, 59)	<0.001†	61 (36, 92)	0.150
Hypertension	73 (76.8%)	-	0.860	52 (80.0%)	0.880
Diabetes mellitus	61 (64.2%)	-	0.940	36 (55.4%)	0.915
Ischemic heart disease	28 (29.5%)	-	0.630	24 (36.9%)	0.680
Stroke	37 (38.9%)	-	0.930	27 (41.5%)	0.945

Smoking	34 (35.8%)	-	0.180	38 (58.5%)	0.205
Collateral Patency					
ACoA	67 (70.5%)	-	0.245	36 (55.4%)	0.270
Ipsilateral PCoA	21 (22.1%)	-	0.290	22 (33.8%)	0.230
Laboratory Parameters					
SBP (mmHg)	130.50 (122.00, 144.50)	125.50 (114.50, 136.50)	0.242	124.80 (114.00, 135.50)	0.255
DBP (mmHg)	77.30 ± 7.60	75.50 ± 11.50	0.480	75.90 ± 8.90	0.490
TC (mmol/L)	3.75 ± 0.82	4.22 ± 1.05	0.255	4.12 ± 0.95	0.270
Triacylglycerol (mmol/L)	1.20 (1.05, 1.52)	1.14 (0.92, 1.71)	0.535	1.10 (0.94, 1.64)	0.550
HDL (mmol/L)	1.07 (0.90, 1.16)	1.12 (0.96, 1.18)	0.545	1.09 (0.94, 1.17)	0.565
LDL (mmol/L)	2.12 ± 0.54	2.30 ± 0.74	0.230	2.25 ± 0.58	0.245
Glucose (mmol/L)	6.85 (5.42, 9.50)	5.78 (5.12, 8.03)	0.465	5.80 (5.25, 8.10)	0.480
HBA1c (%)	7.08 ± 0.92	6.88 ± 1.15	0.815	6.82 ± 1.07	0.822
Homocysteine (μmol/L)	17.55 (14.60, 20.40)	13.05 (9.00, 17.85)	0.108	12.60 (9.00, 17.75)	0.120
Ocular Parameters					
BCVA (logMAR)	1.03 (0.26, 2.15)	0.25 (0.01, 0.31)	0.013†	0.11 (0.01, 0.15)	<0.001
IOP (mmHg)	15.60 (14.05, 19.45)	14.90 (12.40, 17.45)	0.348‡	16.80 (13.00, 18.45)	0.908

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

Structural Comparison of the OA and the ICA

Ocular ischaemic syndrome (OIS) patients' eyes had an average ophthalmic artery (OA) diameter of 1.45 ± 0.20 mm, which was significantly smaller than the 1.58 ± 0.18 mm of identical colleague eyes (P < 0.001) and the 1.83 ± 0.22 mm of normal control eyes (P. 0.001). There were no significant changes between OIS eyes and control eyes, however OIS eyes had a substantially smaller average C4 segment diameter than colleague eyes (3.30 ± 0.94 mm vs. 4.35 ± 0.61 mm; P = 0.002). Furthermore, no discernible variations were found between the OIS and control eyes in terms of the C5 segment's diameter, the C4–C5 segment's curvature, or the angle and OA's curvature.

Evaluation of Retinal Vessel Diameters

The evaluation covered the retinal vascular diameters of sixteen OIS-affected eyes and the corresponding non-affected eyes. Five eyes of OIS patients had insufficient sight because to opacities in the refractive media; therefore, those eyes were excluded from the analysis. The OIS eyes that were included and those that were excluded did not significantly differ in terms of age, gender, OA diameter, or ICA stenosis ratio. The average CRAE in OIS eyes was considerably lower than that of fellow eyes (133.75 ± 22.10 µm vs. 148.30 ± 18.30 µm; P = 0.004) and control eyes (133.75 ± 22.10 µm vs. 150.24 ± 16.40 µm; P = 0.012). Parallel to this, OIS eyes had an average AVR that was considerably lower than control and buddy eyes (0.45 ± 0.07 vs. 0.50 ± 0.06; P = 0.003). Between OIS eyes and their control or colleague counterparts, there were no appreciable differences in the CRVE (Table 2).

Table no.2: Dimensions of Retinal Blood Vessels in Participants

	OIS Eyes, Mean ± SD	**Fellow Eyes, Mean ± SD**	**p-value**	**Control Eyes, Mean ± SD**	**p-value**
CRAE (µm)	133.75 ± 22.10	148.30 ± 18.30	0.004	150.24 ± 16.40	0.012
CRVE (µm)	298.10 ± 26.30	296.74 ± 22.15	0.812	293.20 ± 24.10	0.689
AVR	0.45 ± 0.07	0.50 ± 0.06	0.003	0.53 ± 0.06	0.002

DISCUSSION

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

This study effectively matched participants in the control and OIS groups based on factors such as age, gender, the extent of ICA narrowing, and alternative circulation pathways. Prior studies have shown that some individuals with ICA blockage do not develop OIS, while others do so even with narrowing below 50%. This variation may be influenced by differences in alternative blood flow [3,4]. Additionally, the condition of collateral vessels impacts blood circulation behind the eye, highlighting the necessity of aligning participants based on the openness of essential collateral arteries, specifically the anterior and posterior communicating arteries [19]. In findings from this study, the occurrence of male individuals with OIS was 82%, consistent with previous research [3]. Notably, this investigation revealed that 64.2% of OIS patients had diabetes, an increase compared to earlier studies where the prevalence was approximately 56% [2-4]. However, there was no substantial difference in diabetes rates between OIS patients and the control group.

The C4 and C5 segments are included in the ICA syphon, which is identified by its S-shaped bend. According to studies, this siphon's twisting affects blood flow dynamics, which may have an impact on target organ circulation, such as the eyes [20]. The C4 segment width in OIS eyes was found to be substantially narrower than in equivalent eyes based on measurements. This observation might be related to processes that automatically regulate blood flow; in order to maintain ICA blood flow, a drop in peripheral vascular resistance usually follows a decrease in blood flow [21]. But in OIS situations, the markedly reduced perfusion pressure upsets this homeostasis, leading to a reduction in ICA flow [22]. Reduced blood flow may eventually cause arterial remodelling, which is characterised by an increase in smooth muscle and endothelial cell loss and a decrease in cell development, ultimately narrowing the ICA [23, 24]. It's interesting to note that although corresponding eyes had a wider C4 width than OIS eyes and control eyes, there was no statistically significant difference between corresponding and control eyes. This observation might indicate that the opposing ICA is providing compensating collateral circulation.

Reduced pressure in the distal ICA in OIS probably causes collateral flow from the opposite side through the anterior communicating artery, which could cause the ICA blood flow to shift laterally [25, 26]. Despite the fact that OIS and matching eyes differed significantly in C4 width, there was no discernible variation in C5 width, which may have been caused by the C4 segment's larger curvature. High curvature regions have been found to have low and variable wall shear stress, which is associated with an atherogenic profile in endothelial cells. This, in turn, promotes inflammation and smooth muscle cell migration, both of which are known to exacerbate atherosclerosis and narrowing [27, 28].

Furthermore, the width of the OA in OIS eyes was significantly smaller than in matched and control eyes. This finding could suggest that inadequate ICA circulation is the cause of reduced blood flow in the

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

OA. In the past, it has been demonstrated that decreased blood flow can lead to growth inhibition, endothelial and smooth muscle cell death, and arterial remodelling and diameter decreases [23]. Poiseuille's principle, which stipulates that shear stress is inversely connected to the cube of the diameter, suggests that low wall shear stress may function as a mediator in arterial remodelling processes [29]. Low shear stress can have deleterious consequences on the shape and function of endothelial cells, leading to a pro-atherosclerotic phenotype. Furthermore, low wall shear stress can reduce nitric oxide synthesis by blocking the expression of endothelial nitric oxide synthase and reducing vascular relaxation. Furthermore, it accelerates the development of atherosclerotic plaque by encouraging the uptake of low-density lipoprotein in arterial walls [30–34].

When there is insufficient blood flow, endothelin-1 can exacerbate vasoconstriction in the OA, mostly via certain receptor pathways, which results in a smaller OA diameter [35, 36]. The study observed a noteworthy difference in OA diameter between corresponding and control eyes. However, the difference did not reach statistical significance, potentially because of the dynamics of collateral blood flow from the opposite ICA. The angle between the ipsilateral ICA and OA was also investigated in this study, but no significant group differences were discovered.

Male gender and higher blood pressure have been associated with narrower retinal arteriolar widths. The average central retinal arteriolar equivalent (CRAE) in OIS eyes was found to be considerably lower in this study compared to controls, who had similar blood pressure and gender [37]. Reduced retinal circulation due to insufficient blood flow from OA may be the cause of this drop in CRAE [38]. Retinal arteries first enlarge by autoregulation in response to a drop in ocular perfusion pressure, although this response has limits [39]. Arterial constriction occurs when retinal blood flow decreases due to a drop in perfusion pressure that surpasses the autoregulatory capacity [40]. The lack of significant variations in the Central Retinal Venous Equivalent (CRVE) between OIS and control eyes was noted in this study. This could be because of the limited sample size and other confounding factors that affect venous width, such as high blood sugar, smoking, and lipid imbalances.

Reduced CRAE and a modest rise in CRVE are the causes of the observed decrease in the Artery-to-Vein Ratio (AVR) in OIS eyes. The AVR is a dimensionless measure that lessens the effect of changes in picture enlargement while conducting evaluations. In patients with OIS, this study found a correlation between CRAE and decreased OA diameter. The OA diameter's potential as a diagnostic marker for OIS was highlighted by the Receiver Operating Characteristic (ROC) curve analysis, which showed that it was a more effective discriminator between OIS and control eyes than CRAE. Although retinal blood vessels are usually easily seen in clinical settings, confounding variables such as age, diabetes,

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

and hypertension might affect the sizes of these veins [37]. However, the OA might more accurately represent variations in the blood flow to the eyes. Previous studies revealed that after ischaemic episodes, changes in the retinal vascular system happened later than changes in OA flow. This implies that tracking OA diameter could help identify OIS early on, which could help with prompt intervention and preventive measures [41].

This study showed that in eyes afflicted by OIS, there is a substantial correlation between a smaller OA diameter and a smaller CRAE. The OA diameter has the potential to be a more accurate diagnostic marker for OIS because the ROC curve analysis showed that it could distinguish between eyes with OIS and healthy controls more successfully than CRAE measures. Retinal arteries can be easily seen in clinical settings, although factors such as age, diabetes mellitus, and hypertension can affect how big they are [42]. On the other hand, the OA might provide a clearer picture of variations in the blood supply to the eyes.

Moreover, research has shown that the OA undergoes vasoconstriction far earlier than retinal damage following ischaemic events, indicating that the OA is more adaptive to blood flow alterations. Reports have also demonstrated that in individuals with ICA obstruction, reversed blood flow in the OA can occur without changes in the central retinal artery and posterior ciliary artery, underscoring the OA's role as an early warning system for changes in the ocular blood supply [25,43]. These findings highlight the critical need of monitoring OA diameter and blood flow in patients with ICA constriction or obstruction, as this may facilitate early identification and treatment of OIS. Further investigation is necessary to determine whether OA may be used as a diagnostic marker for this condition.

The careful matching of control and OIS eyes based on ICA constriction and collateral circulation characteristics is one of the study's many notable strengths. This work used three-dimensional modelling to assess the inner diameter of the OA and offer a more accurate depiction of in vivo vascular conditions. However, given that OIS is often underdiagnosed in clinical settings, this study's limited sample size poses a problem. In addition, patients with diabetes were included in the study, and the perfusion of the OA in OIS patients was not evaluated.

CONCLUSION

This study emphasizes the notable link between the diameter of the OA and the occurrence of OIS, suggesting that OA diameter could function as a dependable diagnostic indicator for OIS. Findings reveal that the decrease in OA diameter, coupled with a reduction in CRAE, is intimately connected to impaired eye blood flow resulting from underlying carotid artery afflictions. These results highlight the necessity of evaluating OA diameter as a possible early signal of modifications in ocular circulation, especially in individuals with carotid artery narrowing or blockage. Although this study provides

significant insights, additional research with larger participant groups and further evaluations of OA circulation are essential to reinforce these conclusions and improve early identification and treatment approaches for OIS.

LIMITATION

Small cohort was the limitation of the study and to confirm the findings of the study more such studies on large cohorts are required.

ACKNOWLEDGEMENT

We express our gratitude towards the hospital staff and participants of the study for their kind cooperation throughout the study.

CONFLICT OF INTEREST

There are no conflicts of interest

REFERENCES

1. Lee D, Tomita Y, Yang L, Negishi Y, Kurihara Y. Ocular ischemic syndrome and its related experimental models. Int J Mol Sci. 2022;23:5249.
2. Luo J, Yan Z, Jia Y, Luo R. Clinical analysis of 42 cases of ocular ischemic syndrome. J Ophthalmol. 2018;2018:2606147.
3. Sivalingam A, Brown GC, Magargal LE, Menduke H. The ocular ischemic syndrome. II. Mortality and systemic morbidity. Int Ophthalmol. 1989;13:187–91.
4. Mizener JB, Podhajsky P, Hayreh SS. Ocular ischemic syndrome. Ophthalmology. 1997;104:859–64.
5. Wang H, Wang Y, Li H. Multimodality imaging assessment of ocular ischemic syndrome. J Ophthalmol. 2017;2017:4169135.
6. Wu DH, Wu LT, Wang YL, Wang JL. Changes of retinal structure and function in patients with internal carotid artery stenosis. BMC Ophthalmol. 2022;22:123.
7. Klijn CJ, Kappelle LJ, van Schooneveld MJ, et al. Venous stasis retinopathy in symptomatic carotid artery occlusion: prevalence, cause, and outcome. Stroke. 2002;33:695–701.
8. Kawaguchi S, Iida J, Uchiyama Y. Ocular circulation and chronic ocular ischemic syndrome before and after carotid artery revascularization surgery. J Ophthalmol. 2012;2012:350475.
9. Zhang T, Fan S, He W, Zhang T, Wang Y. Ophthalmic artery visualization and morphometry by computed tomography angiography. Graefes Arch Clin Exp Ophthalmol. 2015;253:627–31.
10. Mallouhi A, Schocke M, Judmaier W, et al. 3D MR angiography of renal arteries: comparison of volume rendering and maximum intensity projection algorithms. Radiology. 2002;223:509–16.
11. Zhang J, Can A, Mukundan S, et al. Morphological variables associated with

ruptured middle cerebral artery aneurysms. Neurosurgery. 2019;85:75–83.

12. Lu L, Zhang LJ, Poon CS, et al. Digital subtraction CT angiography for detection of intracranial aneurysms: comparison with three-dimensional digital subtraction angiography. Radiology. 2012;262:605–12.
13. Wu LT, Wang JL, Wang YL. Ophthalmic artery morphological and hemodynamic features in acute coronary syndrome. Invest Ophthalmol Vis Sci. 2021;62:7.
14. Kofoed PK, Munch IC, Sander B, et al. Prolonged multifocal electroretinographic implicit times in the ocular ischemic syndrome. Invest Ophthalmol Vis Sci. 2010;51:1806–10.
15. Knudtson MD, Lee KE, Hubbard LD, Wong TY, Klein R, Klein BEK. Revised formulas for summarizing retinal vessel diameters. Curr Eye Res. 2003;27:143–9.
16. Zhao L, Jiang B, Li H, et al. Risk stratification tool for ischemic stroke: a risk assessment model based on traditional risk factors combined with white matter lesions and retinal vascular caliber. Front Neurol. 2021;12:696986.
17. North American Symptomatic Carotid Endarterectomy Trial. Methods, patient characteristics, and progress. Stroke. 1991;22:711–20.
18. Bouthillier A, van Loveren HR, Keller JT. Segments of the internal carotid artery: a new classification. Neurosurgery. 1996;38:425–32; discussion 432–3.
19. Yamamoto T, Mori K, Yasuhara T, et al. Ophthalmic artery blood flow in patients with internal carotid artery occlusion. Br J Ophthalmol. 2004;88:505–8.
20. Liu S, Jin Y, Wang X, et al. Increased carotid siphon tortuosity is a risk factor for paraclinoid aneurysms. Front Neurol. 2022;13:869459.
21. Xiong L, Liu X, Shang T, et al. Impaired cerebral autoregulation: measurement and application to stroke. J Neurol Neurosurg Psychiatry. 2017;88:520–31.
22. Müller M, Schimrigk K. Vasomotor reactivity and pattern of collateral blood flow in severe occlusive carotid artery disease. Stroke. 1996;27:296–9.
23. Cho A, Mitchell L, Koopmans D, Langille BL. Effects of changes in blood flow rate on cell death and cell proliferation in carotid arteries of immature rabbits. Circ Res. 1997;81:328–37.
24. Ward MR, Tsao PS, Agrotis A, Dilley RJ, Jennings GL, Bobik A. Low blood flow after angioplasty augments mechanisms of restenosis: inward vessel remodeling, cell migration, and activity of genes regulating migration. Arterioscler Thromb Vasc Biol. 2001;21:208–13.
25. Wu TC, Chen TY, Ko CC, Chen JH, Lin CP. Correlation of internal carotid artery diameter and carotid flow with asymmetry of the circle of Willis. BMC Neurol. 2020;20:251.
26. Zarrinkoob L, Wåhlin A, Ambarki K, Birgander R, Eklund A, Malm J. Blood flow lateralization and collateral compensatory mechanisms in patients with carotid artery stenosis. Stroke. 2019;50:1081–8.
27. Zhang C, Xie S, Li S, et al. Flow patterns and wall shear stress distribution in human internal

carotid arteries: the geometric effect on the risk for stenoses. J Biomech. 2012;45:83–9.

28. Zhou J, Li YS, Chien S. Shear stress-initiated signaling and its regulation of endothelial function. Arterioscler Thromb Vasc Biol. 2014;34:2191–8.
29. Misra S, Fu AA, Misra KD, Glockner JF, Mukhopadyay D. Evolution of shear stress, protein expression, and vessel area in an animal model of arterial dilatation in hemodialysis grafts. J Vasc Interv Radiol. 2010;21:108–15.
30. Davies PF, Civelek M, Fang Y, Fleming I. The atherosusceptible endothelium: endothelial phenotypes in complex haemodynamic shear stress regions in vivo. Cardiovasc Res. 2013;99:315–27.
31. Won D, Zhu SN, Chen M, et al. Relative reduction of endothelial nitric-oxide synthase expression and transcription in atherosclerosis-prone regions of the mouse aorta and in an in vitro model of disturbed flow. Am J Pathol. 2007;171:1691–704.
32. Moniripiri M, Abandani MHS, Firoozabadi B. Simulation of LDL permeation into multilayer wall of a coronary bifurcation using WSS-dependent model: effects of hemorheology. Biomech Model Mechanobiol. 2023;22:711–27.
33. Berk BC, Abe JI, Min W, Surapisitchat J, Yan C. Endothelial atheroprotective and anti-inflammatory mechanisms. Ann N Y Acad Sci. 2001;947:93–109; discussion 109–11.
34. Deng H, Min E, Baeyens N, et al. Activation of Smad2/3 signaling by low fluid shear stress mediates artery inward remodeling. Proc Natl Acad Sci USA. 2021;118.
35. Blixt FW, Haanes KA, Ohlsson L, Christiansen AT, Warfvinge K, Edvinsson L. Increased endothelin-1-mediated vasoconstriction after organ culture in rat and pig ocular arteries can be suppressed with MEK/ERK1/2 inhibitors. Acta Ophthalmol. 2018;96–25.
36. Blixt FW, Haanes KA, Ohlsson L, et al. MEK/ERK/1/2 sensitive vascular changes coincide with retinal functional deficit, following transient ophthalmic artery occlusion. Exp Eye Res. 2019;179:142–9.
37. Sun C, Liew G, Wang JJ, et al. Retinal vascular caliber, blood pressure, and cardiovascular risk factors in an Asian population: the Singapore Malay Eye Study. Invest Ophthalmol Vis Sci. 2008;49:1784–90.
38. Klefter ON, Kofoed PK, Munch IC, Larsen M. Macular perfusion velocities in the ocular ischemic syndrome. Acta Ophthalmol. 2019;97:113–7.
39. Nagel E, Vilser W. Autoregulative behavior of retinal arteries and veins during changes of perfusion pressure: a clinical study. Graefes Arch Clin Exp Ophthalmol. 2004;242:13–7.
40. Tani T, Nagaoka T, Nakabayashi S, Yoshioka T, Yoshida A. Autoregulation of retinal blood flow in response to decreased ocular perfusion pressure in cats: comparison of the effects of increased intraocular pressure and systemic hypotension. Invest Ophthalmol Vis Sci. 2014;55:360–7.

e-ISSN:
Vol. 1 No. 1 (2024)
September 2024 Issue

41. Toulouie S, Chang S, Pan J, Snyder K, Yiu G. Relationship of retinal vessel caliber with age-related macular degeneration. J Ophthalmol. 2022;2022:8210599.
42. Sun C, Wang JJ, Mackey DA, Wong TY. Retinal vascular caliber: systemic, environmental, and genetic associations. Surv Ophthalmol. 2009;54:74–95.
43. De Caro J, Ciacciarelli A, Tessitore A, et al. Variants of the circle of Willis in ischemic stroke patients. J Neurol. 2021;268:3799–807.