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ORIGINAL PAPER

Optical coherence tomography angiography characteristics and correlated factors with visual acuity in retinal arterial occlusion

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Abstract

Purpose To reveal the characteristics of vascular changes in retinal arterial occlusion (RAO) using optical coherence tomography angiography (OCTA) and determine the correlated factors with best-corrected visual acuity (BCVA).

Methods This retrospective study recruited 54 RAO patients and 27 healthy individuals. Ophthalmic examinations including BCVA and OCTA were performed in all the patients and individuals. The OCTA outcomes were analyzed using SPSS software, and the characteristics of vascular changes and BCVA-related factors were summarized.

Results The vessel density in all areas except fovea of both superficial capillary plexus (SCP) and deep capillary plexus (DCP) was significantly reduced in RAO eyes compared with the fellow eyes and normal control eyes ($P < 0.05$). The vessel density of DCP in all areas except fovea was significantly reduced in the fellow eyes compared with that in the normal control eyes as well ($P < 0.05$). The retinal thickness in fovea was significantly increased in RAO eyes compared with that in the fellow eyes and normal control eyes ($P < 0.05$), without any differences in other areas between the RAO eyes and the other two groups ($P > 0.05$). The retinal thickness in whole area and retinal thickness in fovea were correlated with BCVA, respectively (whole area: r = 0.295, P = 0.030; fovea: r = 0.322, P = 0.018).

Conclusions OCTA is a fast, noninvasive, and effective examination means for RAO that can display the vascular density and retinal thickness quantitatively and distinctly. RAO patients had reduced vascular density in both eyes and increased foveal retinal thickness in RAO eyes, showing a correlation with BCVA.

Keywords Retinal arterial occlusion · Optical coherence tomography angiography · Vessel density · Retinal thickness

Introduction

Retinal arterial occlusion (RAO) often presents an acute onset and causes devastating damages to visual acuity (VA) or visual field. Generally, RAO can be divided into central retinal artery obstruction (CRAO), branch retinal artery obstruction (BRAO), cilioretinal artery obstruction (CLRAO), combined retinal artery and vein obstruction, and cotton-wool spots [1]. RAO is essentially acute ocular ischemia, just like stroke of retina [2]. The period from the onset of RAO to the significant functional inner retinal infarction is

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acknowledged as a golden time of treatment, but unfortunately, this therapeutic window is very short [3]. Therefore, doctors are required to identify RAO and formulate a proper therapeutic regime in a quite short time. In addition to slit lamp and ophthalmoscope, optical coherence tomography angiography (OCTA) is also a useful diagnostic tool for RAO, which has been applied in the detection of precise vessel density of superficial retinal layer (superficial capillary plexus, SCP) and deep retinal layer (deep capillary plexus, DCP) in recent years. In this backdrop, our study attempted to observe the retinal vessel density and retinal thickness of RAO patients using OCTA and analyze the correlation between the outcomes and VA.

Methods

Study design and participants

This was a retrospective observational study conducted in the Ocular Trauma and Fundus Disease Department of Eye Hospital of China Academy of Chinese Medical Science. This study enrolled 54 patients who had been diagnosed with RAO monocularly. The inclusion criteria included patients who had first-ever CRAO as principal diagnosis from December 2018 to June 2020. The exclusion criteria included giant cell arteritis, any previous or current eye diseases except for RAO or a signal index lower than 6 in OCTA. Twenty-seven age- and gender-matched individuals with normal fundus were recruited as normal control group. The cases were divided into three groups, including affected eyes, fellow eyes of 54 patients with RAO, and normal control eyes of 27 individuals with normal fundus. Only one eye (the right) of normal control individuals was selected for the statistical analyses. The fundus images are shown in Fig. 1. This study was approved by the Ethics Committee of Eye Hospital China Academy of Chinese Medical Science on September 19th, 2018.

Measurements

The examinations including slit-lamp biomicroscopy (BM 900, HAAG-STREIT International, Switzerland), intraocular pressure (CT-80, Topcon, Japan), fundus examination using the ophthalmoscope, best-corrected visual acuity (BCVA), and OCTA (RTVue XR, Optovue, USA) were performed in all participants and the measurement results were analyzed.

BCVA was conducted using the early treatment diabetic retinopathy study chart (ETDRS, Wenzhou Xingkang Medical Tech. Co., Ltd, China) and the results were converted to logarithm of the minimum angle of resolution (LogMAR). The patients with the counting fingers of BCVA from 6 to 40 cm were assigned logMAR values of 2.1 to 2.9, hand movements, 3.0, light perception, 4.0, no light perception, 5.0.

OCTA scanning was conducted using the central macular under Angio Retina mode (3 × 3 mm). The retinal thickness and vessel density of SCP and DCP within a circle 3 mm in diameter from the center of macular were automatically quantified using the software (RTVue-XR version 2017.1.0.155). The whole quantified area was divided into fovea (the area within a diameter of 1 mm in the center of the macula) and parafovea (the area with a diameter from 1 to 3 mm). Then, the parafovea area was divided into four regions: superior, inferior, temporal, and nasal, and finally, a total of five areas were obtained [4, 5]. SCP starts from 3 μm above the inner limiting membrane to 15 μm below the inner plexiform layer, mainly consisting of the optic nerve fiber layer and ganglion cell layer. DCP stars from 15 to 70 μm below the inner plexiform layer, mainly including the kernel layer [6].

Statistical analysis

Statistical analysis was performed using IBM SPSS 24.0, and all quantified values were presented as mean ± standard deviation (SD). The normal distribution was verified, and then the independent sample t test was used for the comparisons of vessel density and retinal thickness among the three groups, with a 95% confidence interval. The Spearman correlation coefficient was used for correlation evaluation. A value of $P < 0.05$ was regarded statistically significant and was shown in boldface in the Table.

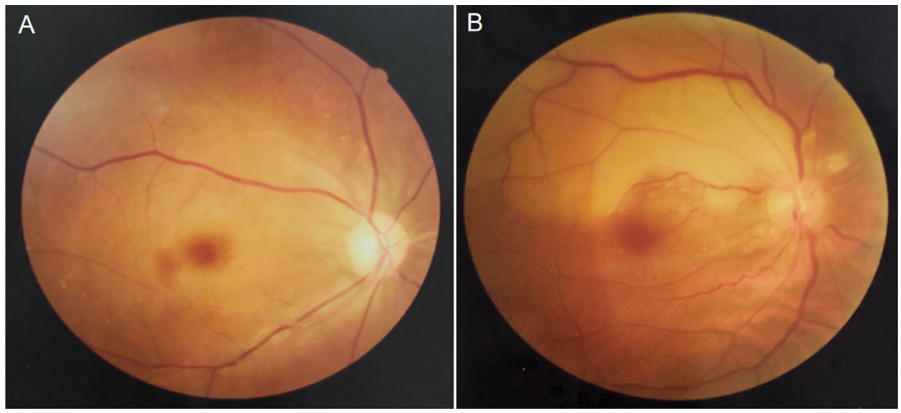

Fig. 1 Fundus images of CRAO (**a**) and BRAO (**b**), a: Fundus image of CRAO b: Fundus image of BRAO

Results

General information

Fifty-four patients (54 eyes) diagnosed with RAO monocular were enrolled in this study. All these patients had an onset time within 3 months, of which 49 patients (90.7%) had an onset time from 3 h to 1 month (1 month included), and the other five patients (9.3%) had an onset time from 1 to 3 months (3 months included), including 40 males (74.1%) and 14 females (25.9%), with an average age of (61.9 ± 12.0), ranging from 42 to 81 years old.

Among them, 29 patients (29 eyes, 53.7%) were diagnosed with CRAO; 24 patients (24 eyes, 44.4%) were diagnosed with BRAO, and one patient (one eye, 1.9%) was diagnosed with CLRAO. Furthermore, among the 24 cases of BRAO, 12 cases were involved in supratemporal branch retinal artery (12 eyes, 50.0%); 10 cases were involved in subtemporal branch retinal artery (10 eyes, 41.6%); one case was involved in temporal branch retinal artery (one eye, 4.2%), and one case was involved in nasal branch retinal artery (one eye, 4.2%).

In addition, 27 age- and gender-matched individuals (27 eyes) without any fundus disorder were enrolled as the normal controls.

BCVA

BCVA of the affected eyes of RAO patients ranged from 0 to 4, with an average of (1.54 ± 1.18), while the fellow eyes ranged from -0.1 to 0.2, with an average of (0.07 ± 0.15). BCVA of normal control eyes ranged from -0.1 to 0, with an average of (0.01 ± 0.05).

OCTA findings (Fig. 2 shows OCTA of CRAO eye; Fig. 3 shows BRAO eye; Fig. 4 shows normal eye).

Vessel density

The normality test confirmed that the data of vessel density of SCP and DCP were all in normal distribution. A significant reduction of vessel density was observed in SCP and DCP except the fovea of the affected eyes, compared with both the fellow eyes and normal control eyes (the vessel density of SCP is shown in Table 1 and vessel density of DCP is shown in Table 2).

In addition, the vessel density of DCP in the fellow eyes was significantly reduced except fovea, compared with that in the normal control eyes (Table 1). However, there was no significant difference in SCP between the two groups (Table 2).

Retinal thickness (Table 3)

The normality test confirmed that the data of retinal thickness were in normal distribution. The retinal thickness of the affected eyes was significantly increased only in fovea, compared with that of both the fellow eyes and normal control eyes, without significant difference between the fellow eyes and normal control eyes. There was no significant difference in other areas among these three groups.

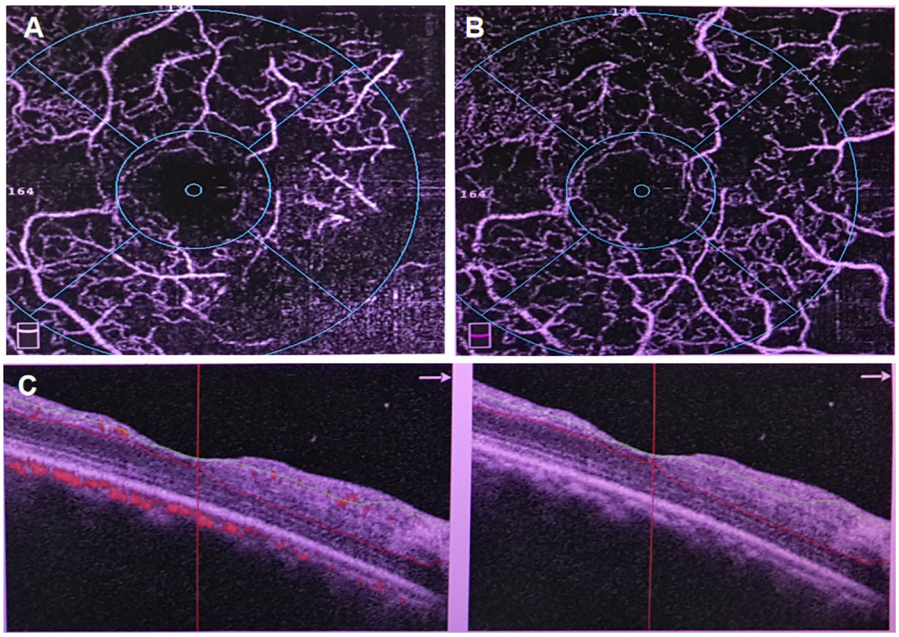

Fig. 2 OCTA of CRAO eye, **a**: vascular image of SCP. Vessel density of SCP decreased in parafovea, including temporal, superior, nasal and inferior regions. **b**: vascular image of DCP. Vessel density of DCP decreased in parafovea, including temporal, superior, nasal and inferior regions. **c**: retinal image

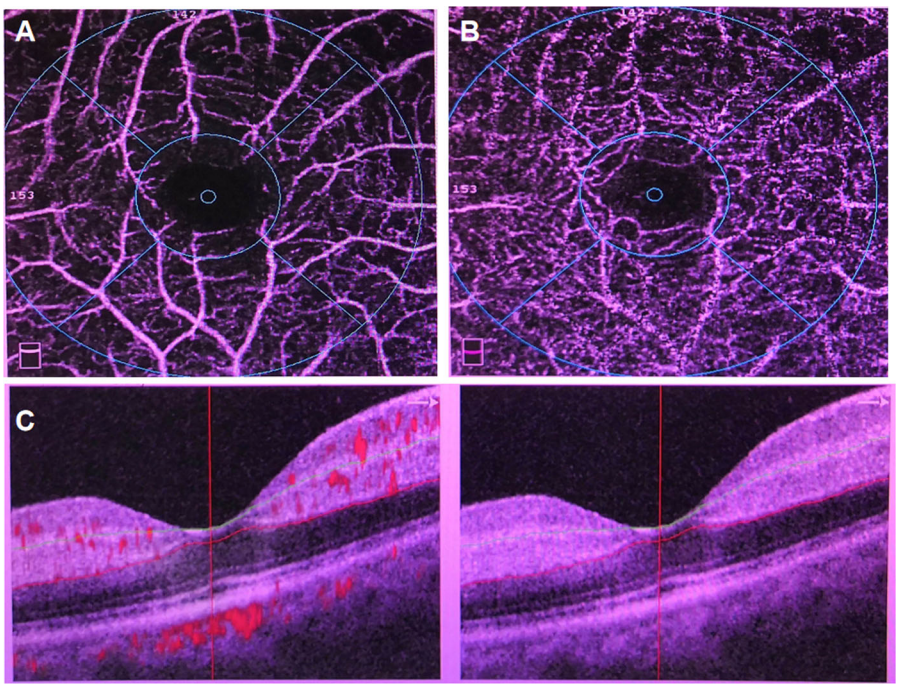

Fig. 3 OCTA of BRAO eye **a**: vascular image of SCP. Vessel density of SCP decreased in parafovea, including temporal, superior, nasal and inferior regions. **b**: vascular image of DCP. Vessel density of DCP decreased in parafovea, including temporal, superior, nasal and inferior regions. **c**: retinal image

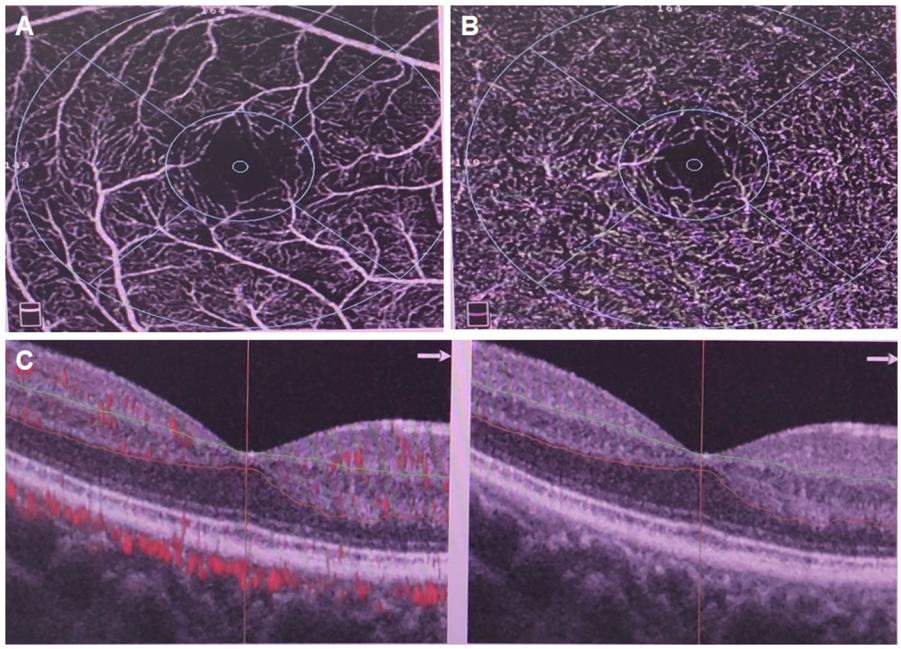

Fig. 4 OCTA of normal eye **a**: vascular image of SCP **b**: vascular image of DCP **c**: retinal image

Table 1 Comparison of vessel density of SCP between affected eyes, fellow eyes, and normal control eyes (%)

	Affected eyes	Fellow eyes	Normal control eyes	P1	P2	P3
N	54	54	27			
Whole	37.90 ± 4.85	46.37 ± 4.39	47.01 ± 3.39	**0.000**	**0.000**	0.510
Fovea	17.20 ± 5.05	17.19 ± 4.86	17.23 ± 5.52	0.989	0.980	0.971
Parafovea	40.43 ± 5.87	48.99 ± 4.78	50.08 ± 3.89	**0.000**	**0.000**	0.308
Temporal	40.50 ± 6.14	48.39 ± 5.32	48.36 ± 3.63	**0.000**	**0.000**	0.979
Superior	40.31 ± 6.95	50.08 ± 4.52	51.67 ± 4.50	**0.000**	**0.000**	0.139
Nasal	40.16 ± 7.56	48.23 ± 4.51	49.10 ± 4.05	**0.000**	**0.000**	0.402
Inferior	40.39 ± 6.62	49.67 ± 6.48	51.18 ± 4.46	**0.000**	**0.000**	0.280

A value of $P < 0.05$ was shown in boldface

P1: comparisons of affected eyes vs fellow eyes

P2: comparisons of affected eyes vs normal control eyes

P3: comparisons of fellow eyes vs normal control eyes

Correlation information (Table 4)

Spearman correlation analysis indicated that BCVA was significantly correlated with both the retinal thickness in fovea and retinal thickness in the whole scanned area, but the correlation between BCVA and retinal thickness in fovea was stronger, with the r-value of 0.322 ($P = 0.018$) versus 0.295 ($P = 0.030$). On the contrary, there was no correlation between BCVA and vessel density in SCP or DCP.

Discussion

RAO represents an ophthalmic emergency resulted from retinal ischemia and hypoxia due to an acute decrease of retinal artery perfusion, with an extremely short effective therapeutic window [7]. The current knowledge describes CRAO as a stroke both in ophthalmologic and medical emergency and deems intravenous fibrinolysis as an effective management with a quite small therapeutic window of 4.5–6 h

Table 2 Comparison of vessel density of DCP between affected eyes, fellow eyes, and normal control eyes (%)

	Affected eyes	Fellow eyes	Normal control eyes	P1	P2	P3
N	54	54	27			
Whole	41.14 ± 5.29	47.88 ± 3.94	52.10 ± 2.18	**0.000**	**0.000**	**0.000**
Fovea	28.37 ± 6.58	29.37 ± 5.11	29.23 ± 6.73	0.378	0.583	0.916
Parafovea	44.25 ± 6.44	51.85 ± 3.51	54.92 ± 2.42	**0.000**	**0.000**	**0.000**
Temporal	45.46 ± 6.99	52.03 ± 3.92	54.92 ± 2.93	**0.000**	**0.001**	**0.001**
Superior	43.17 ± 7.40	52.37 ± 4.00	55.00 ± 2.24	**0.000**	**0.002**	**0.002**
Nasal	45.17 ± 6.78	52.26 ± 4.39	55.30 ± 2.53	**0.000**	**0.001**	**0.001**
Inferior	43.77 ± 6.84	50.69 ± 4.95	54.44 ± 3.17	**0.000**	**0.001**	**0.001**

A value of $P < 0.05$ was shown in boldface

P1: comparisons of affected eyes vs fellow eyes

P2: comparisons of affected eyes vs normal control eyes

P3: comparisons of fellow eyes vs normal control eyes

Table 3 Comparison of retinal thickness between affected eyes, fellow eyes, and normal control eyes (%)

	Affected eyes	Fellow eyes	Normal control eyes	P1	P2	P3
N	54	54	27			
Whole	304.6 ± 51.0	302.4 ± 14.8	303.1 ± 14.1	0.758	0.882	0.830
Fovea	262.1 ± 43.4	244.0 ± 13.2	244.4 ± 17.3	**0.005**	**0.046**	0.898
Parafovea	319.6 ± 51.7	316.3 ± 15.4	316.0 ± 15.1	0.655	0.722	0.927
Temporal	306.6 ± 48.5	308.6 ± 14.8	307.3 ± 15.6	0.777	0.942	0.724
Superior	328.1 ± 61.7	320.2 ± 15.8	320.3 ± 15.4	0.364	0.520	0.976
Nasal	327.7 ± 53.4	318.9 ± 17.6	320.3 ± 16.1	0.253	0.482	0.732
Inferior	316.9 ± 60.1	317.5 ± 17.2	317.0 ± 15.9	0.938	0.994	0.885

A value of $P < 0.05$ was shown in boldface

P1: comparisons of affected eyes vs fellow eyes

P2: comparisons of affected eyes vs normal control eyes

Table 4 Spearman correlation between BCVA and other parameters

	N	VD in SCP	VD in DCP	RT in whole area	RT in fovea
R	54	−0.114	−0.251	0.295	0.322
P	54	0.411	0.067	**0.030**	**0.018**

A value of $P < 0.05$ was shown in boldface

[8–10]. Clinically, the diagnosis of RAO mainly depends on the typical medical history, optical symptoms, and fundus examinations by the ophthalmologist. The application of fundus fluorescein angiography (FFA) is limited although it is a golden standard for the diagnosis of retinal vascular diseases [11, 12]. Instead, OCTA emerges as a novel noninvasive imaging technique that can finish the examination in a short time without any harm to the patient [13], which has been extensively applied in the examination of retinal vascular diseases, such as diabetic retinopathy (DR) and retinal vein occlusion (RVO) [14, 15]. Accordingly, this study adopted OCTA to show the changes in vessel density and retinal thickness in RAO patients, the two most critical characteristics of RAO.

Two independent blood supply systems provide oxygen and nutrition to retina. The inner retina is supplied by the retinal artery system, while the outer retina is supplied by the choroidal circulation system. OCTA is endowed with the ability to analyze the vascular density of two layers separately. The vessel density of SCP reflects the circulation condition of the inner retina (the retinal artery system), while the vessel density of DCP reflects the circulation condition of the outer retina (the choroidal circulation system). The vessel density of SCP is demonstrated to be

significantly reduced in the affected eyes compared with that in the fellow eyes when RAO occurs [16, 17]. Consistent with the previous studies [12, 18], our results exhibited an obvious reduction of vessel density of SCP and DCP. Yang et al. elucidated that the vessel density of SCP in the fellow eyes of RAO patients is decreased compared with that in the normal eyes [19], and also, our results demonstrated a similar trend in DCP. Some experts mentioned the vascular perfusion of SCP and DCP in the fellow eyes of RVO patients is reduced compared with that in the normal control eyes, which has been suggested as a sign of the previous asymptomatic [20]. When people suffer from a certain monocular vascular disease, the abnormal changes not only occur in the affected eye, but also in the other eye [20]. A study on a consecutive series of patients with isolated acute retinal ischemia shows that 20% of patients are complicated with acute silent brain infarcts, among which 30% of cases are ipsilateral to the acute retinal ischemia and 70% of cases are involved different and/or multiple vascular territories [21]. These pieces of evidence indicate that ocular vascular diseases may be accompanied by other chronic microvascular changes in the whole arterial system.

Intriguingly, this study found a different phenomenon in RAO that had not been mentioned in previous studies. The foveal vessel density did not show a decreasing trend either in SCP or DCP, which may be related to the special anatomical structure of fovea. However, the foveal vessel density also shows a big difference in normal individuals [22].

Retina edema in affected areas is a common sign of RAO, resulting in a remarkable increase of retinal thickness [23]. Nevertheless, edema can only be observed in the early stage and tends to resolve with the subsequent atrophic changes within weeks [12, 24]. The fovea is a special area with the thinnest thickness and highest incidence of edema. Central macular thickness (CMT) refers to the retinal thickness of the area within a diameter of 1 mm in the center of the macula, which is often used to describe the degree of fovea edema and is found to be increased significantly in RAO eyes [19]. In this study, no difference in retinal thickness was found in all areas except fovea between the affected eyes and the fellow eyes or normal eyes, which may be due to the fact that all different stages of RAO patients were recruited in this study.

In recent years, numerous experts have focused on the correlation factors of VA and unveiled a statistically significant correlation between VA and the vascular density of both the superficial and deep networks in familial exudative vitreoretinopathy and DR patients [25–27]. It is reported that foveal avascular zone (FAZ) size can be significantly enlarged in RVO and DR eyes, with a strong correlation with VA, despite the variability of FAZ size in normal individuals [28–30]. A retrospective observational study about RAO clarifies that no difference is observed in FAZ between the affected eyes and fellow eyes, and the correlation is observed between CMT and BCVA[19]. The vessel density of SCP and DCP, as well as the retinal thickness in the whole area and fovea were analyzed in this study, respectively, and the results exhibited that the retinal thickness, rather than vessel density, was the key related factor of BCVA.

There are some limitations of this study. Firstly, since this study is a retrospective study with small sample size, some of the results and conclusions may have limitations, and consequently, a further large prospective study is needed. Secondly, this study fails to analyze different types of RAO such as CRAO and BRAO due to the fact that the incidence rate of RAO is low to 1/10000. Thirdly, this study merely analyzes 3×3 mm of the central macular and lacks the analysis of the other areas.

Conclusions

RAO is an ophthalmic emergency, mainly manifested as retina ischemic changes. OCTA can reveal the changes in vascular density and retinal thickness quantitatively and distinctly, representing an effective means for doctors to diagnose and follow up this disease. This study demonstrates that the vascular density is significantly decreased in the affected eye of RAO patients, which can serve as a potential predictor of systemic vascular diseases. Decreased vascular density in the fellow eye indicates that the microvascular change may exist before the onset of RAO. Therefore, the reduced vessel density might act as a potential predictive factor for RAO. When RAO occurs, the retinal thickness is increased in fovea and has a strong correlation with BCVA. Given the

limitations of this study, more researches on RAO are warranted.

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Authors' contribution Like Xie finished study design, Xuan Li, Xiaofeng Hao, Jie Luo, and Yixin Qi finished experimental studies, Xuan Li, Jinhua Luo, Hang Yuan finished data analysis, and Xuan Li finished manuscript editing. All authors read and approved the final manuscript.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical statement This was a retrospective observational study conducted in the Ocular Trauma and Fundus Disease Department of Eye Hospital of China Academy of Chinese Medical Science.

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