• Clinical Research •

Changes of retinal vessel density in low to moderate myopic eyes with orthokeratology evaluated by optical coherence tomography angiography

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Abstract

● **AIM:** To explore the effect of orthokeratology (OK) fitting on retinal vessel density in low to moderate myopia adolescents by using optical coherence tomography angiography.

● **METHODS:** Children aged 10 to 14y with a cycloplegic spherical equivalent refraction of −0.50 diopter (D) to −5.00 D and astigmatism with more than −1.50 D were recruited. The enrolled adolescents were divided into OK group and spectacle group. During regular follow-up, adolescents were measured respectively at pre-wear, 1, 3, and 6mo after treatment. The follow-up included uncorrected distance visual acuity (UDVA), axial length (AL), superficial capillary plexus density (SCPD), deep capillary plexus density (DCPD), central retinal thickness (CRT), foveal avascular zone area (FAZ-A), foveal avascular zone perimeter (FAZ-P) and foveal vessel density in a 300-μm-wide region around foveal avascular zone (FD-300). The collected data were analyzed using statistical methods.

● **RESULTS:** By one month, SCPD significantly increased in the fovea and superior retina, and DCPD significantly increased inferiorly in OK group compared to spectacle group (P<0.05). By three months, there were significant increases in SCPD in the fovea and inferior retina, and DCPD in the parafovea, superior, and inferior retina in OK group (P<0.05), while the increase in SCPD and DCPD in the fovea were observed by six months (P<0.05). The FD-300 significantly increased at every follow-up in OK group compared to spectacle group (P<0.05). No significant differences in the CRT, FAZ-A and FAZ-P and FD-300 were observed between two groups (P>0.05). OK group showed a significant improvement in UDVA after wearing OK, compared to spectacle group (P<0.01), while the AL did not show a significant difference between two groups (P>0.05).

● **CONCLUSION:** Short-term OK worn can increase local retinal vessel density in adolescents with low-to-moderate myopia.

● **KEYWORDS:** optical coherence tomography angiography; orthokeratology; myopia; axial length; retinal capillary plexus density

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INTRODUCTION

Myopia has become a major public health problem worldwide, and it is predicted that by 2050 the number of people with myopia will reach 4.758 billion worldwide (49.8% of the total population), and that the number of people with high myopia will reach 938 million (9.8% of the total population)[1]. The prevalence of myopia among children and adolescents in China was 52.7% in 2019, with patients showing young ages and rapid myopia progression[2]. Individuals with myopia, especially high myopia, are prone to cataracts, glaucoma and other eye diseases that seriously affect vision and even cause blindness. Therefore, further research into the pathogenesis of myopia and methods of prevention and control are urgently needed. Recent studies have confirmed that ischemia and hypoxia of the eye may be factors in myopia[3-4]. Many studies have been carried out on fundus blood flow density in myopia, but studies to control fundus blood flow density during the development of myopia

are extremely rare. Orthokeratology (OK) has been shown to be a safe and effective measure to control the progression of myopia[5-7], however, to date there does not seem to be any published studies on changes in retinal microcirculation following the use of OK. Optical coherence tomography angiography (OCTA) is a new, non-invasive technique for imaging the blood vessels in the fundus, using the principle of decoherence and frequency separation to construct images of the macula and optic disc area in three dimensions. This facilitates tracking the movement of blood cells in the retina and thereby clearly imaging the microcirculatory structures of the retina[8]. OCTA can therefore be used to examine changes in the microcirculation of the retinal layers following OK. The non-invasive and rapid nature of OCTA is also more acceptable to young people with myopia.

Many studies have analyzed showed that superficial and deep macular vessel density were significantly negatively correlated with axial length (AL). And it has been observed that the effect of fundus vessel density varies with the degree of myopia, many studies have confirmed that among patients with non-pathological myopia, retinal vessel density is significantly lower in patients with high myopia[9-11]. Studies on the microcirculation in the fundus of myopic adolescents have also been ongoing, and these studies suggest that myopia similarly reduces retinal vessel density in adolescents[12-13]. However, there is a relative paucity of studies on controlling retinal blood flow density in patients after myopia progression. This experiment was carried out by applying OCTA in this direction to investigate the possible changes in retinal vessel density in adolescents after myopia control.

SUBJECTS AND METHODS

Ethical Approval The study was approved by the Ethics Committee of the South Hospital of the Sixth People's Hospital, School of Medicine (approval number: 20220608). All adolescents and their guardians signed an informed consent form.

Subjects Select This is a retrospective study of data from adolescent patients who attended the ophthalmology department of the Sixth People's Hospital of Shanghai Jiao Tong University South Hospital, from April 2021 to June 2022. Including criteria were: 1) axial myopia; 2) age 10 to 14y; 3) uncorrected visual acuity ≤0.6, best-corrected visual acuity (BCVA) of 1.0 and pre-intervention intraocular pressure of 10–21 mm Hg; 4) spherical equivalent refractive error of −0.50 diopter sphere (DS) to −5.00 DS, and corneal astigmatism (with-the-rule) >−1.50 diopter cylinder (DC); 5) corneal curvature of 40.0 to 46.0 D; 6) healthy eyes, with no inflammation of the cornea or conjunctiva, and no systemic immune system disorders; 7) no significant complaints of ocular dryness, tear break-up time ≥10s. The enrolled participants showed good compliance in wearing their glasses, and good hygiene habits, and were able to follow medical advice to complete regular evaluations. Good compliance included all adolescents wearing the lenses for at least 8h per day and following regular follow-up for regular reviews. No ocular adverse reactions such as epithelial damage to the cornea of degree II or more has occurred during lenses wear (Chinese Medical Association classification: mild, punctate corneal epithelial damage; moderate, extensive corneal epithelial loss and fusion; severe, extensive corneal epithelial loss or corneal stromal ulcer formation[14]).

Examination Methods All participants completed the following eye examinations, performed by the same special examiner between 8–10 *a.m*.

Visual acuity examination Using the international standard visual acuity chart at a viewing distance of 5 m, the right first, and then left, eyes were tested separately. The decimal recording method was used. The results were converted into logarithmic minimum resolution (logMAR) visual acuity for statistical analysis.

Computerized optometry An autorefractor (CV-7000, TOPCO, Japan) was used for refraction. Before refraction, optometry: an autorefractor was used for refraction. Before refraction, cycloplegia with a compound tropicamide eye solution, peak ciliary muscle paralysis 45min after dosing, the computerized refraction was performed, with the instrument automatically taking the average of the valid measurements.

Comprehensive optometry Comprehensive optometry was performed using the VT-10 comprehensive phoropter (VT-10, TOPCON, Japan) and BCVA to 0.0 (logMAR) for all adolescents.

Axial length examination A optical biometer (Len-Star900, Colin Corporation, USA) was used to measure the AL. For this test and the following, as applicable, the patient was asked to keep his or her gaze steadily directed at the fixation lamp in the instrument, to ensure accurate and reliable measurements. The Len-Star automatically averaged the values from three consecutive measurements.

Corneal curvature examination The Len-Star900 biometer was also used to measure corneal curvature. The horizontal and vertical corneal curvature values were measured three times in each eye and averaged to calculate the corneal curvature value.

Corneal topography A corneal topographer (TMS-4N, Tomey, Japan) was used to measure corneal morphology before and after the intervention. Rational selection of different image modes aids in the assessment of corneal status and fitting of OK[15].

Optical coherence tomography angiography examination The OCTA scanner (Optovue OCTA, Colin Corporation, USA) was used to evaluate the fundus of the eye. The scanning

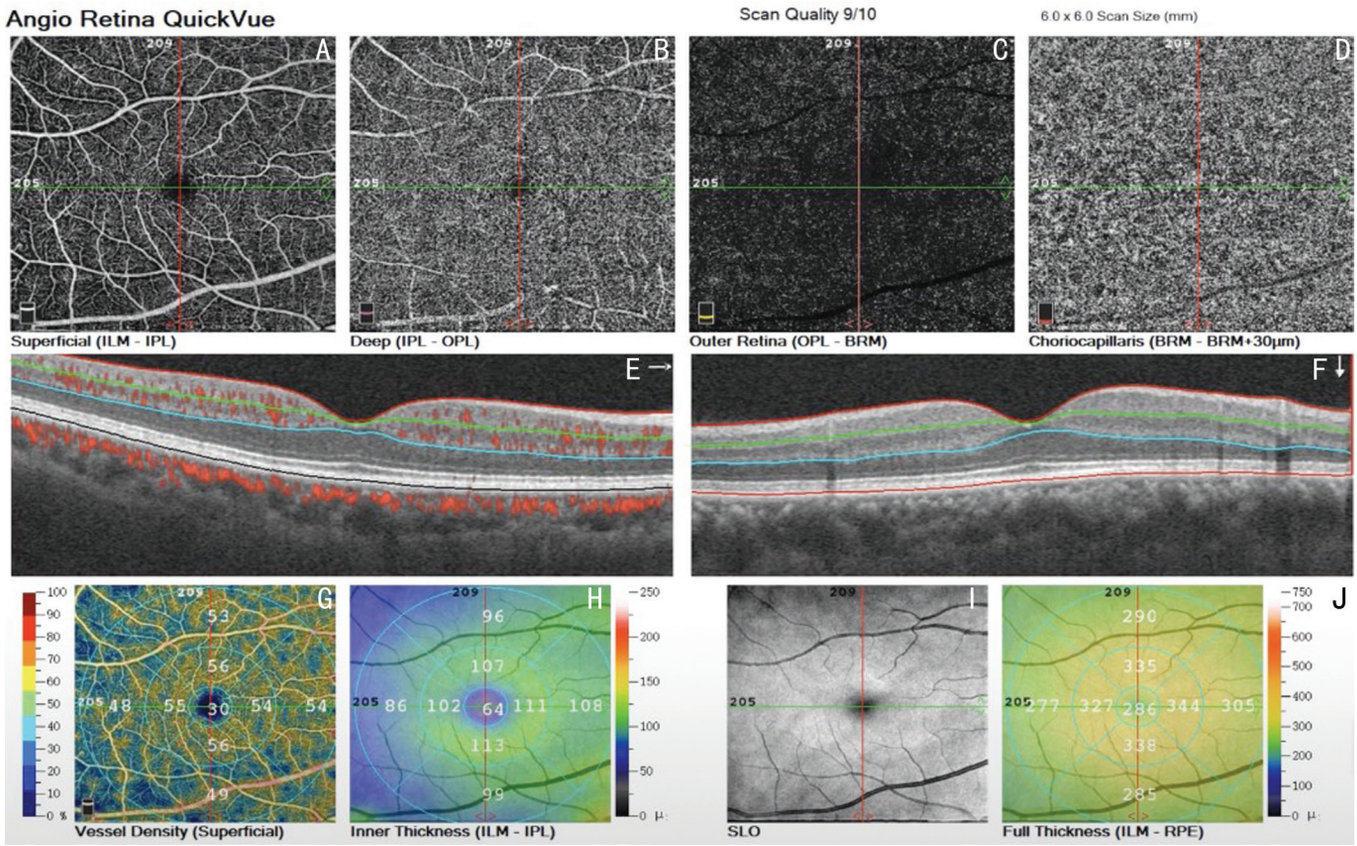

Figure 1 Quantitative measurements using OCTA in a right eye, Angio Retina Quick Vue (6.0×6.0 mm^2 scan size) A: Superficial vessel density; B: Deep vessel density; C: Outer retina; D: Choriocapillaris (BRM-BRM+30 μm); E: OCT horizontal tomography with red vessel signal superimposition (green, blue and white signal lines show preset layering); F: OCT vertical tomography (green blue and red signal lines show preset layering); G: Quantitative data of superficial vessel density; H: Quantitative data of inner thickness; I: Enface SLO image of full structure; J: Quantitative data of full thickness. OCT: Optical coherence tomography; OCTA: Optical coherence tomography angiography; ILM: Inner limiting membrane; IPL: Inner plexiform layer; OPL: Outer plexiform layer; BRM: Brunch membrane; RPE: Retinal pigment epithelium; SLO: Scanning laser ophthalmoscopy.

modes used were HD Angio-Retina 6×6 mm^2, and HD Angio-Disc 4.5×4.5 mm^2. Each scan was centered on the fovea in the retina 6×6 mm^2 scans and on the optic disc in the 4.5×4.5 mm^2 scans. The superficial capillary plexus density (SCPD), deep capillary plexus density (DCPD), central retinal thickness (CRT), FAZ area, FAZ perimeter (PERIM) and foveal vessel density in a 300-μm wide region around FAZ (FD-300) of the patients were analyzed using the OCTA machine's built-in analysis software. Images were selected for inclusion if the data scan quality index was ≥6/10 (Figures 1-3). Post-scan data shown in Tables 1, 2.

Orthokeratology Testing and Fitting The practitioner is informed of the benefits and risks of fitting OK, the need for follow-up, adverse effects, and precautions before the formal fitting. Depending on the patient's condition and the practitioner's experience, the lens is observed for centration and movement under dynamic conditions by slit lamp and corneal fluorescein staining. The lenses are also evaluated under static conditions to check for fluorescence arc staining and refractive changes after removal, and parameters are compared and adjusted to arrive at the final prescription for ordering the lenses. The patient verifies the lens information prior to collection and confirms that he/she will go for the lens

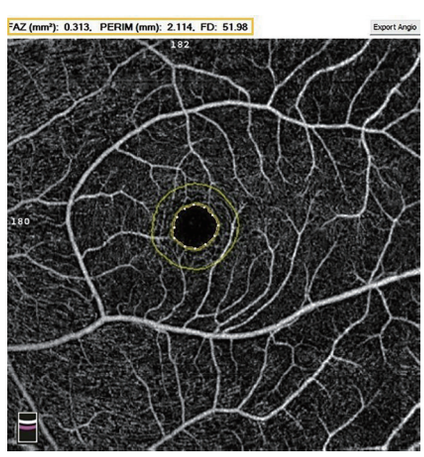

Figure 2 Quantitative measurement of FAZ in a right eye The yellow border shows the FAZ measurement data, including FAZ area, PERIM and FD, all based on whole retinal vessel measurements. FAZ: Foveal avascular zone; FD: Foveal density; ILM: Inner limiting membrane; OPL: Outer plexiform layer; PERIM: FAZ perimeter.

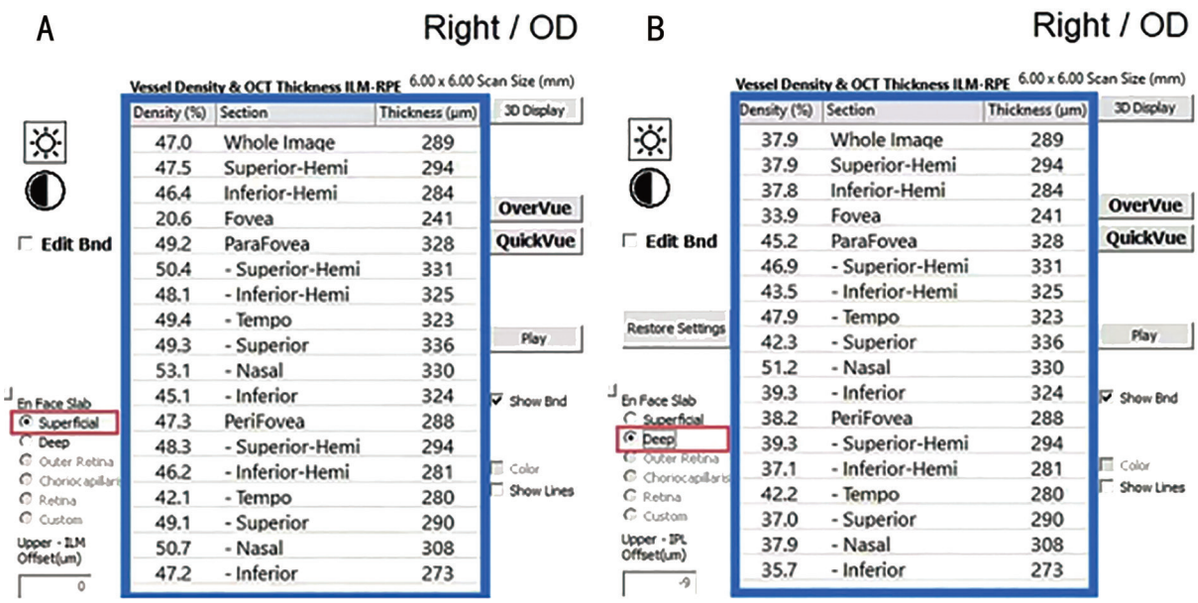

Figure 3 Quantitative measurement of retinal vessel density in a right eye A: The data of superficial in different subdivisions; B: The data of deep in different subdivisions. The red border shows the preset stratification, the blue border shows the data.

Table 1 Comparison of general information on adolescents in both groups

Items	OK group	Spectacle group	*t*	*P*
Age	12.00±1.518	13.00±1.241	-1.31	0.93
Height (m)	1.6156±0.075	1.6536±0.067	-0.45	0.97
Weight (kg)	50.118±9.444	48.426±7.427	0.77	0.63
CECD (/mm²)	2747.529±204.870	2758.398±247.756	-9.2	0.67
UDVA	0.424±0.154	0.435±0.149	-0.17	0.91
SE (D)	-2.206±1.861	-2.1304±1.039	1.24	0.21
K1 value (D)	42.475±1.221	43.109±1.561	-0.78	0.15
E value	0.573±0.085	0.516±0.067	0.32	0.29
IOP (mm Hg)	19.21±1.321	18.63±1.476	0.93	0.82
AL (mm)	24.923±0.840	24.895±0.738	0.91	0.78

OK: Orthokeratology; CECD: Corneal endothelial cell density; UDVA: Uncorrected distant visual acuity; SE: Spherical equivalent; IOP: Intraocular pressure; K1 value: Flat meridian; E value: Corneal eccentricity; AL: Axial length.

Table 2 Comparison of UDVA at different time points in two groups

Group	Pre-intervention	1mo	3mo	6mo
OK	0.397±0.208	0.015±0.040	0.024±0.043	0.000±0.000
Spectacle	0.313±0.351	0.397±0.216	0.421±0.194	0.467±0.186
t	9.701	31.031	30.986	32.603
P	0.720	0.038[b]	0.039[b]	0.033[b]

OK: Orthokeratology; UDVA: Uncorrected distance visual acuity. [b]*P*<0.01.

collection examination when the patient is in good ocular and general health. After verification, the child and his/her parents are trained by the same doctor on cleaning and maintenance of the lenses and eventually need to ensure that the wearer is either able to perform the complete procedure of lens removal, fitting and care on his/her own and with the help of a guardian. Attention is paid to reviewing the procedures for removing, putting on and caring for the lens wearer to reinforce safety awareness[16]. Adverse reactions include: ocular surface abnormalities: 1) conjunctival adverse reactions, mainly including non-infectious conjunctivitis, infectious conjunctivitis and allergic conjunctivitis; 2) corneal adverse reactions, mainly including non-infectious keratopathy and infectious keratitis; 3) tear membrane abnormalities, including dry eye symptoms and signs. Visual abnormalities include the naked eye and corrected symptoms and signs such as poor vision, fluctuating vision, double vision, and glare[17].

Statistical Analysis The SPSS 25.0 statistical software was used to process the data. Mean±standard deviations are shown for the measured data; independent-samples *t*-tests were used for comparisons between groups. Differences were considered statistically significant at $P<0.05$.

RESULTS

Comparison of the General Information of the Two Groups of Participants Before Treatment A total of 70 patients with low to moderate adolescent myopia were included in this study. After a comprehensive eye examination, 40 patients were fitted with OK and 30 patients were fitted with single-vision spectacle lenses according to the examination results and the compliance of patients and parents. In the spectacle group, there were 28 cases and 28 eyes completed the follow-up, and 2 cases and 2 eyes were lost. The right eye was selected as the test eye for binocular treatment, and if a single eye was treated, that eye was selected as the test eye. There was no statistically significant difference between the two groups of participants with different degrees of myopia when comparing the general information before treatment ($P\geq0.05$), as shown in Table 1.

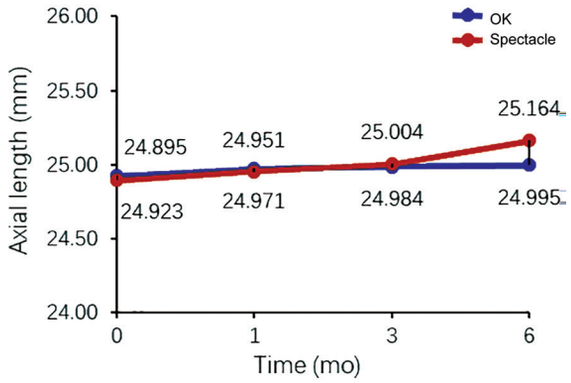

Figure 4 Comparison of eye axes in the OK and spectacle groups.

Table 3 Comparison of AL at different time points in two groups mm

Group	Pre-intervention	1mo	3mo	6mo
OK	24.923±0.840	24.971±0.822	24.984±0.815	24.995±0811
Spectacle	24.895±0.738	24.951±0.731	25.004±0.720	25.164±0.716
t	0.138	0.096	0.067	0.015
P	0.891	0.924	0.988	0.393

OK: Orthokeratology; AL: Axial lengh.

Comparison of Uncorrected Distant Visual Acuity Before and After Treatment Between Two Groups The uncorrected distance visual acuity (UDVA) in the OK and spectacle groups before the intervention were 0.397±0.208 and 0.313±0.351, respectively. The UDVA of the adolescents in the OK group was significantly better at 1, 3, and 6mo after the start of the intervention than before, whereas UDVA of the adolescents in the spectacle group was lower at 1, 3 and 6mo than before the intervention. The differences between the two groups were statistically significant (P<0.001; Table 2).

Comparison of Axial Length Before and After Treatment Between Two Groups Before the intervention, the AL of the OK and the spectacle group were 24.923±0.840 and 24.895±0.738 mm, respectively; the difference was not statistically significant (P>0.05). After wearing OK there was no statistically significant difference in AL between the two groups at 1, 3 and 6mo (P>0.05; Table 3, Figure 4).

Comparison of Superficial Capillary Plexus Density Before and After Treatment Between Two Groups The SCPD increased from baseline at all time points in the experiment group. The difference in SCPD measured in the fovea and superiorly was statistically significant between the two groups at 1, 3 and 6mo (P<0.05; Table 4, Figure 5).

Comparison of Deep Capillary Plexus Density Before and After Treatment Between Two Groups The difference between the two groups in DCPD measured in the inferior retina was statistically significant at 1mo (P<0.05). The difference in DCPD between the two groups measured in the parafovea, and superior and inferior retina was statistically significant at 3mo (P<0.05). Finally, there was a significant difference between the two groups in DCPD measured in the fovea at 6mo (P<0.05; Table 5, Figure 6).

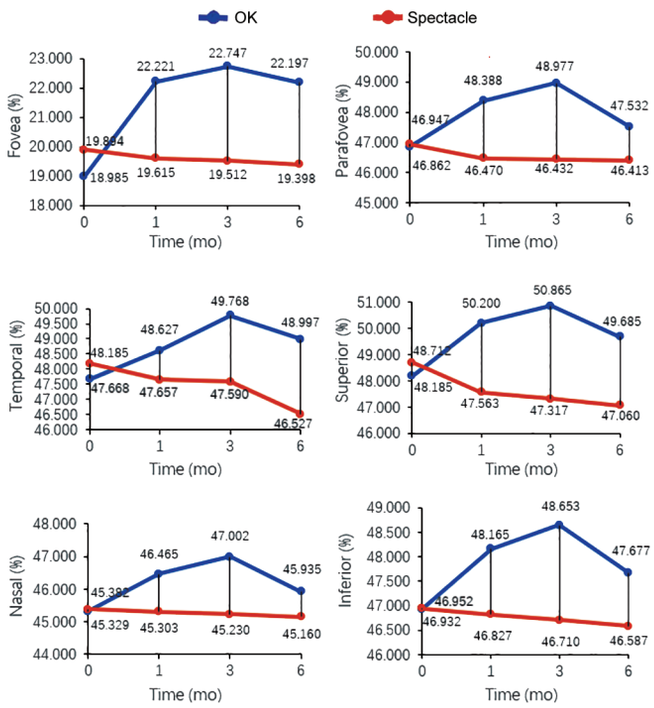

Figure 5 Comparison of superficial capillary plexus density (%) in the OK group and spectacle group OK: Orthokeratology.

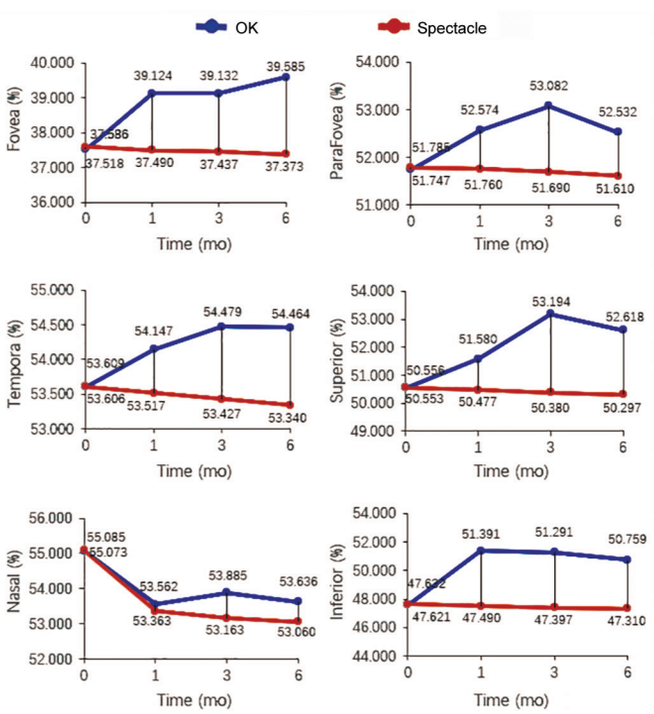

Figure 6 Comparison of DCPD (%) in the OK group and spectacle group DCPD: Deep capillary plexus density; OK: Orthokeratology.

Comparison of Central Retinal Thickness Before and After Treatment Between Two Groups CRT increased in the OK group at all times after the intervention, compared with before the intervention, but the difference was not statistically significant between the spectacle group (P>0.05; Table 6).

Comparison of FAZ Area, PERIM, FD-300 Before and After Treatment Between Two Groups During follow-up, the differences between the OK and spectacle groups FD-300

Table 4 Comparison of SCPD at different time points in two groups %

Group	Fovea	Parafovea	Temporal	Superior	Nasal	Inferior
Pre-intervention						
OK	18.985±5.882	46.862±5.203	47.668±6.495	48.185±5.733	45.329±5.693	46.932±6.054
Spectacle	19.894±5.075	46.947±5.545	48.185±5.733	48.712±6.111	45.382±6.164	46.952±6.570
t	-0.902	0.195	0.082	0.272	0.142	0.475
P	0.843	0.371	0.935	0.971	0.787	0.891
1mo						
OK	22.221±1.810	48.388±4.267	48.627±4.382	50.200±4.257	46.465±5.746	48.165±5.042
Spectacle	19.615±4.823	46.470±4.115	47.657±4.036	47.563±4.021	45.303±5.680	46.827±5.102
t	4.029	0.689	0.378	2.926	0.346	1.543
P	0.006[b]	0.496	0.707	0.006[b]	0.732	0.132
3mo						
OK	22.747±5.856	48.977±4.408	49.768±4.942	50.865±4.672	47.002±5.596	48.653±4.779
Spectacle	19.512±5.785	46.432±4.111	47.590±4.036	47.317±4.528	45.230±5.874	46.710±4.153
t	3.907	0.949	0.753	1.042	0.542	2.363
P	0.004[b]	0.349	0.456	0.304	0.591	0.024[a]
6mo						
OK	22.197±6.666	47.532±5.111	48.997±4.603	49.685±4.949	45.935±5.621	47.677±6.501
Spectacle	19.398±6.776	46.413±5.095	46.527±4.015	47.060±4.360	45.160±5.151	46.587±5.971
t	3.032	0.374	1.862	0.596	0.801	0.287
P	0.024[a]	0.710	0.071	0.555	0.429	0.776

SCPD: Superficial capillary plexus density; OK: Orthokeratology. [a]*P*<0.05; [b]*P*<0.01.

Table 5 Comparison of DCPD at different time points in two groups %

Groups	Fovea	Parafovea	Tempora	Superior	Nasa	Inferior
Pre-intervention						
OK	37.518±6.354	51.747±4.427	53.606±5.079	50.553±6.376	55.073±4.291	47.621±6.629
Spectacle	37.586±6.562	51.785±4.423	53.609±5.073	50.556±6.380	55.085±4.293	47.632±6.625
t	0.084	-0.036	-0.002	-0.002	-0.011	-0.007
P	0.933	0.972	0.998	0.998	0.991	0.994
1mo						
OK	39.124±5.980	52.574±4.591	54.147±4.958	51.580±4.781	53.562±4.817	51.391±4.698
Spectacle	37.490±5.128	51.760±4.217	53.517±4.130	50.477±4.090	53.363±4.179	47.490±4.140
t	1.589	1.020	0.739	1.342	-0.963	4.817
P	0.122	0.315	0.465	0.189	0.342	0.001[c]
3mo						
OK	39.132±6.585	53.082±3.607	54.479±4.331	53.194±3.962	53.885±4.611	51.291±4.353
Spectacle	37.437±6.129	51.690±3.200	53.427±4.146	50.380±3.091	53.163±4.063	47.397±4.165
t	1.498	2.212	1.408	4.129	-0.099	5.174
P	0.143	0.034[a]	0.168	0.015[a]	0.922	0.001[c]
6mo						
OK	39.585±5.953	52.532±4.581	54.464±4.147	52.618±5.048	53.636±4.544	50.759±4.651
Spectacle	37.373±5.133	51.610±4.191	53.340±4.121	50.297±5.050	53.050±4.090	47.310±4.151
t	20161	0.344	1.572	2.680	1.099	4.298
P	0.038[a]	0.733	0.125	0.437	0.975	0.213

DCPD: Deep capillary plexus density; OK: Orthokeratology. [a]*P*<0.05; [c]*P*<0.001.

had significantly increased (*P*<0.05), and in FAZ area and PERIM were not statistically significant (*P*>0.05; Table 7).

DISCUSSION

There is no definite conclusion about the pathogenesis of myopia. In recent years, a large number of studies have confirmed that ischemia and hypoxia of the eye may be among the influential factors causing myopia[3-4], so the alteration of microcirculation in the fundus of myopic patients is one

Table 6 Comparison of CRT at different time points in two groups μm

Group	Fovea	Parafovea	Temporal	Superior	Nasal	Inferior	Whole
Pre-intervention							
OK	247.41±19.89	309.91±12.02	302.00±11.81	313.21±11.73	314.51±13.97	309.32±11.89	273.76±9.86
Spectacle	245.04±27.67	309.85±11.99	302.13±12.06	314.01±12.85	314.01±13.80	309.78±12.48	274.00±9.76
t	-0.518	0.020	0.000	0.000	0.000	0.000	-0.099
P	0.606	0.984	0.940	0.972	0.995	0.994	0.922
1mo							
OK	249.03±22.14	310.32±12.93	302.67±12.53	313.91±13.01	315.00±13.66	309.41±13.31	274.44±10.57
Spectacle	245.80±21.82	308.76±12.26	302.03±12.29	312.59±12.47	313.11±12.84	308.38±12.74	273.82±10.27
t	0.232	0.510	0.215	0.428	0.585	0.326	0.244
P	0.817	0.612	0.722	0.830	0.560	0.746	0.808
3mo							
OK	247.41±22.83	310.00±12.25	302.06±12.11	314.29±12.04	314.32±13.44	309.03±11.64	275.41±11.15
Spectacle	245.79±20.18	308.98±11.95	301.74±12.01	312.35±11.81	312.59±12.61	308.26±11.08	274.44±10.72
t	0.473	0.351	0.111	0.325	0.549	0.277	0.366
P	0.638	0.727	0.810	0.912	0.585	0.782	0.716
6mo							
OK	245.91±20.92	310.71±12.29	303.32±12.58	313.9412.41	315.73±13.93	310.38±12.82	274.26±11.91
Spectacle	243.76±20.12	309.47±11.96	301.73±12.46	312.03±12.17	312.76±13.11	309.32±12.47	273.03±11.15
t	0.431	0.420	0.194	0.306	0.601	0.345	0.442
P	0.668	0.6765	0.830	0.747	0.550	0.731	0.660

OK: Orthokeratology; CRT: Central retinal thickness.

Table 7 Comparison of FAZ-area, PERIM and FD-300 at different time points in two group

Groups	FAZ-area, mm^2	PERIM, mm	FD-300, %
Pre-intervention			
OK	0.251±0.688	1.906±0.277	49.608±6.315
Spectacle	0.223±0.469	1.816±0.212	49.452±6.181
t	1.514	1.165	0.118
P	0.36	0.250	0.906
1mo			
OK	0.253±0.870	1.967±0.401	52.661±6.668
Spectacle	0.236±0.949	1.888±0.424	49.389±6.082
t	0.654	0.658	2.473
P	0.546	0.514	0.015[a]
3mo			
OK	0.242±0.810	1.881±0.324	52.769±5.786
Spectacle	0.216±0.065	1.744±0.306	49.327±6.005
t	1.155	1.442	2.755
P	0.254	0.156	0.007[b]
6mo			
OK	0.244±0.072	1.898±0.268	52.146±5.420
Spectacle	0.219±0.055	1.786±0.216	49.2621±5.951
t	1.121	1.482	2.370
P	0.268	0.145	0.020[a]

FAZ: Foveal avascular zone; PERIM: FAZ perimeter; FD-300: Foveal vessel density in a 300-μm-wide region around FAZ; OK: Orthokeratology. [a]*P*<0.05; [b]*P*<0.01.

of the research directions explored in recent years. In the past, most studies that measured blood flow density in the fundus used laser Doppler velocimetry and scanning laser Doppler flowmetry, but those experiments mainly focused on the large blood vessels, and there were limitations in the detection of the surface of the retinal capillary layer[18-19]. The recent development of OCTA has made it possible to measure capillary morphology and blood flow density in a non-invasive manner in all layers of the retina and choroid, so OCTA has become the main detection means these days. On OCTA images, the inner border membrane up to 10 μm above the inner plexiform layer is identified as the superficial vascular layer, and 10 μm above the inner plexiform layer to 10 μm below the outer plexiform layer is identified as the deep vascular layer. The existing OCTA techniques have primarily been applied in myopia in two areas: first, OCTA can reveal the retinal and choroidal blood density and thickness in a stratified and partitioned manner, monitor the ischemia of the fundus in myopic patients, and further understand the pathogenesis of myopia by analyzing correlation between these characteristics. Second, OCTA allows for the early diagnosis and treatment of complications secondary to high myopia and can be used for long-term follow up[20-21].

The aim of the present experiment was to use OCTA to look at possible changes in retinal vessel density in adolescents with refractive errors, after wearing OK or regular glasses. We found that the UDVA in the OK group improved significantly within 1d after OK wear, that the UDVA was stable from 1 to 6mo, and the rate of increase in AL was reduced compared

with that in the spectacle group. Cho *et al*[22] found that the ocular AL increased by 0.14 mm per year in their OK group, compared with 0.27 mm per year in their frame group over a 2-year period, suggesting that OK significantly slowed down the progression of myopia. It was also confirmed that OK significantly delayed the progression of myopia. Liu *et al*[23] used OCTA to study 208 eyes of 208 patients and found that micro-bleed density was highest in the superficial and deep retinal layers, and throughout the whole retina, in the group of patients with mild myopia, followed by the moderate-myopia group and then by the high-myopia group; the density was lowest in the very-high-myopia group. Other studies on the vessel density of myopic patients have also confirmed that myopia will affect the retinal vessel density and reduce the retinal vessel density to varying degrees. The experiment confirmed that retinal vessel density decreases with the development of myopia; that OK are effective in slowing myopia progression compared to ordinary spectacle glasses; and that local retinal vessel density increases within a short period of time after OK wear in this experiment using OCTA; From these conditions, it is hypothesized that the possible mechanism by which OK controls the progression of myopia is that OK slows the progression of myopia by improving retinal vessel density. Compared to the OK group, the retinal vessel density in the spectacle group has decreased, suggesting that it is believed that during the development of uncontrolled myopia, the density of vessel in the fundus of myopic adolescents also decreases gradually with the development of myopia. Thus, we suggest that the decrease in retinal vessel density may also have contributed to the development of myopia. This theory is also supported by other studies in recent years[24-25]. In addition, this study found that changes in macular vessel density in myopic adolescents occurred earlier than changes in AL. It is assumed that 1) OK directly slows myopia progression by increasing retinal vessel density; 2) OK first improves the blood supply to the fundus, which slows the growth of the AL and thus controls myopia progression. In addition, this pilot study suggests that macular blood flow density could be an indicator of early myopia progression. The FAZ is the most central area of the macula lacking retinal capillaries and is the area with the highest oxygen consumption near the density of cone photoreceptors. Gołębiewska *et al*[12] used OCTA to observe at myopic and non-myopic children to show that the FAZ area was larger in myopic children than in non-myopic children, that FAZ perimeter was positively correlated with area, and that SCPD was lower. The results of our experiment showed an increase in FD-300 after controlling for myopia by OK, but no change in FAZ area and FAZ perimeter outcomes, presumably the structural damage to the FAZ from myopia is irreversible.

Regarding the effect of eye movement on the scan results: The Angio Vue system uses an orthogonal calibration algorithm (montion correction technic) to capture a second set of frames perpendicular to the first set orthogonally, thus minimising motion artefacts. Regarding the effect of AL on vessel density scans: The Angio Vue system sets up an automatic correction formula for the effect of AL, which excludes the effect of AL on vessel density scan results. Regarding the effect of pupil size on scan results: OCTA engineers explained that pupil size can have an effect on the quality of scanned images, but less on blood flow quantification data, keeping the examination room light uniform and selecting images with a scan quality index ≥6/10 to exclude the effect of pupil on the quality of scanned images.

To better understand the changes in the fundus microcirculatory system after wearing OK, future research will include more children with suitable lenses worn for a longer period of time. Patients with high myopia were not included in this study. According to the conditions for fitting OK, the equivalent spherical lens should not exceed -5.0 DS, and the use of OK with too high a degree of myopia increases the probability of corneal punctal detachment, which poses a safety risk. There are many factors that influence myopia[3], such as adjustment lag, retinal imaging quality, retinal peripheral refractive status, and parental myopia genetics. The influence of these factors on the observed results was not considered in this study, but experimental studies should be designed in future studies to exclude these confounding factors in order to reduce error and bias.

OCTA revealed an increase in local macular vessel density including SCPD, DCPD and FD-300 after short-term wear of OK. In conclusion, the effect of OK to improve UDVA is significant, and the safety of standardized wear is high.

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