Clinical Observation of Retinal Vessel Density In Type 2 Diabetic Patients With High Mopyopia

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Research Article

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Abstract

Purpose: To quantitatively analyze the difference of superficial and deep retinal vessel density between diabetic patients with high myopia , diabetic patients without high myopia and normal subjects.

Methods: This cross-sectional study recruited type 2 diabetic patients with no history of ocular treatment in Shijiazhuang, China. Thirty type 2 diabetic patients with high myopia (30 eyes) were included in group A, 30 type 2 diabetic patients (30 eyes) without myopia were included in group B. Another 30 sex-,age-matched healthy volunteers (30 eyes) were included in group C. The superficial and deep retinal vessel density were measured and compared among the three groups to determine the effects of high myopia on diabetes.

Results: No statistically significant differences in central superficial retinal vessel density(CSVD) was found in three groups($P \geq 0.05$). There were significant differences in the temporal superficial retinal vessel density(TSVD),superior superficial retinal vessel density(SSVD), nasal superficial retinal vessel density(NSVD),inferior superficial retinal vessel density(ISVD) between the three groups, respectively ($P \leq 0.05$). TSVD,SSVD,NSVD,ISVD in group A were all lower than those in group B and group C($P \leq 0.05$). ISVD in group B was lower than that in group C and no statistically significant differences in TSVD,SSVD,NSVD were found between groups B and C($P \geq 0.05$). There were significant differences in central deep retinal vessel density(CDVD),temporal deep retinal vessel density(TDVD),superior deep retinal vessel density(SDVD), nasal deep retinal vessel density(NDVD),inferior deep retinal vessel density(IDVD) between the three groups, respectively ($P \leq 0.05$). CDVD in group A was higher than that in group B , but there was no significant difference between group A and group C. TDVD,SDVD,NDVD,IDVD in group A were all lower than those in group B and C($P \leq 0.05$),and those in group B were lower than those in group C($P \leq 0.05$).

Conclusion: Myopia and diabetes are important factors affecting vessel density. The parafoveal superficial and deep vessel density of type 2 diabetic patients with high myopia were lower than those of diabetics and normal persons. However,there was no difference in macular fovea superficial and deep retinal vessel density between diabetic patients with high myopia and normal persons. Myopia did not show a protective effect on retinal vessel density reduction in diabetic patients.

Introduction

The International Diabetes Federation (IDF) has released new figures showing that 537 million adults are now living with diabetes worldwide -a rise of 16% (74 million) since the previous IDF estimates in 2019. IDF projections show that by 2045, 783 million adults will be living with diabetes- or one in eight adults. Globally, over 90% of people with diabetes have type 2 diabetes. China has the largest number of people with diabetes in the world[1]. Diabetic retinopathy (DR) is a progressive microvascular disease of the retina. It is one of the most common and serious complications of diabetes, and a common cause of blindness in the middle age and elderly population[2]. In past clinical experience, we found that diabetic

patients with high myopia had a lower incidence of DR than diabetic patients without myopia. A small number of clinical studies and epidemiological studies have suggested that high myopia could be a protective factor against DR. Bazzazi et al. [3] studied 116 diabetic patients with high myopia anisometropia, it was found that only 27.6% of high myopic eyes had DR, none of them had PDR, while 100% of contralateral eyes had DR, 31% of them had PDR. High myopia was a protective factor against DR. He et al. [4] found that the axial length was negatively correlated with the severity of DR. Man et al. [5] found that longer axial length might be protective factor of DR, independent of refractive status, corneal curvature and anterior chamber depth. Wang et al. [6] also confirmed this view. However, the pathogenesis of a protective role for longer axial length against DR still remains unclear. DR is one of the major microvascular complication of diabetes. Optical coherence tomography angiography (OCTA) is a safe, rapid, and noninvasive technique for visualization of the retina with a resolution exceeding that of fundus fluorescein angiography [7–9]. The retina contains two main capillary plexuses: superficial capillary plexus lies in the nerve fiber layer or ganglion cell layer, while deep capillary plexus is located within the inner nuclear layer. OCTA can show and quantify the superficial and deep vascular plexuses, impaired capillary perfusion with high resolution, it gives us a better understanding of retinal capillary plexuses. In previous studies, there was no study of macular retinal capillary plexus density in diabetic patients with high myopia. In this study, OCTA was employed to evaluate the macular retinal superficial and deep capillary plexus density in diabetic patients with high myopia eyes, diabetic patients eyes, and normal eyes of Chinese population, and the changes in retinal capillary plexus density were analyzed.

Methods

A total of 60 patients treated at the Ophthalmology Department of Hebei General Hospital between November 2019 to September 2021 were recruited for this study. The 30 type 2 diabetic patients with high myopia (30 eyes) were included in group A, and 30 type 2 diabetic patients (30 eyes) without myopia were included in group B. Another 30 sex-, age-matched healthy volunteers (30 eyes) were included in group C. There were no significant differences in age, sex, or intraocular pressure between the three groups (Table 1).

Inclusion criteria were as follows: Group A: a diagnosis of type 2 diabetes made at least 1 year prior to study enrolment and the absence of DR; control serum glucose well (hemoglobin A1C [HbA1c] < 5.7%); spherical equivalent (SE) refractive error ≥ -6.0 diopters (D) and axial length ≥ 26

mm [10]. Group B: a diagnosis of type 2 diabetes made at least 1 year prior to study enrolment and the absence of DR; control serum glucose well (hemoglobin A1C [HbA1c] < 5.7%); SE < -1.0 D or emmetropia (no hyperopia was allowed). Group C: healthy volunteers; SE < -1.0 D or emmetropia (no hyperopia was allowed). Exclusion criteria included poor central fixation; any ocular surgery, laser treatment and ocular trauma in the study eye; media opacity in the study eye; patients with glaucoma, fundus retinopathy, and macular diseases; Patients with systemic diseases that may be related to ocular blood vessels (such as hypertension, cardiovascular and cerebrovascular diseases, nephropathy, etc.). This study followed the

Helsinki Declaration and was approved by the ethics committee of Hebei General Hospital. All subjects and their guardians signed informed consent forms.

Table1 Base line characteristics of the study groups

	eyes n	Age(years)	Sex M/F	IOP mmHg	AL(mm)	Duration of diabets years
Group A	30	50.20±9.10	20/10	14.57±3.06	28.19±1.41	3.87±1.72
Group B	30	54.93±8.49	16/14	16.07±2.23	22.85±0.72	3.47±1.59
Group C	30	53.03±11.28	18/12	15.69±2.60	23.02±0.92	-
$\chi^2/F/t$		1.81	4.34	2.60	247.38	0.94
<i>P</i>		0.17	0.11	0.08	<0.01	0.35

M,male;F,female;IOP,intraocular pressure;AL,axial length

Routine examinations

All subjects underwent comprehensive eye examinations,including slit-lamp microscopy,fundus,IOP measurement,axiallength measurement.

Optical Coherence Tomography Angiography examinations

Angio-retina examinations were performed by a single experienced eye specialist.OCTA images were obtained by the DRI Triton OCT(Topcon, Tokyo, Japan).The scan area was centered on the fovea with a field of view of 3×3mm . This system uses split-spectrum amplitude decorrelation angiography algorithm(IMAGEnet Version 1.28.17642)and operates at an A-scan rate of 100kHz with an axial resolution of 7μm and a lateral resolution of 20μm.OCTA images of the superficial and deep capillary networks were generated separately usingthe automated software algorithm.Based on these default settings,the boundaries of superficial retinal capillary plexus (SCP) extended from 2.6 μ below the internal limiting membrane to 15.6μ below the inner plexiform layer. The deep retinal capillary plexus(DCP) extended from 15.6μ to 70.2μ below the inner plexiform layer.The built-in software automatically divides the retinal capillary plexus into five zones and the calculation of vessel density in each plexus.The location of the segmentation lines that determine each plexus are detailed in Figure 1.We used proprietary software to obtain automated perifoveal VD (%).A good set of scans,with a a quality index >60 (range 0–100) and no motion artefact for each eye[11],was selected for further analysis.

Statistical analysis

This was a retrospective case- control study, and all included cases met the inclusion criteria. SPSS 21.0 statistical software (IBM Corporation, Armonk,NY,USA)was used for statistical analysis. Normally distributed quantitative data are expressed as the mean(standard deviation,SD). The sex composition ratio in the three groups of subjects was compared using a χ^2 test.One-way ANOVA was performed for comparisons of age, axial length,IOP, VD among the three groups. The independent sample t test was used for pair wise comparisons. A value of $P<0.05$ was considered statistically significant.

Results

No statistically significant differences in central superficial retinal vessel density(CSVD) was found in three groups($F=2.318,P=0.105$).There were significant differences in the temporal superficial retinal vessel density(TSVD),superior superficial retinal vessel density(SSVD), nasal superficial retinal vessel density(NSVD),inferior superficial retinal vessel density(ISVD) between the three groups, respectively ($F=9.249,P<0.001$; $F=6.450,P=0.002$; $F=10.420,P<0.001$; $F=9.786,P<0.001$). TSVD,SSVD,NSVD,ISVD in group A were all lower than those in group B and group C($P<0.05$).ISVD in group B was lower than that in group C and no statistically significant differences in TSVD,SSVD,NSVD were found between groups B and C($P>0.05$).

There were significant differences in central deep retinal vessel density(CDVD),temporal deep retinal vessel density(TDVD),superior deep retinal vessel density(SDVD), nasal deep retinal vessel density(NDVD),inferior deep retinal vessel density(IDVD) between the three groups, respectively ($F=8.299,P=0.001$; $F=8.468,P<0.001$; $F=8.244,P=0.001$; $F=12.578,P<0.001$; $F=11.264,P<0.001$).CDVD in group A was higher than that in group B , but there was no significant difference between group A and group C.TDVD,SDVD,NDVD,IDVD in group A were all lower than those in group B and C($P<0.05$),and those in group B were lower than those in group C($P<0.05$)(Table 2).

Table 2 Comparisons of superficial and deep retinal vessel density in three groups

Regions		Group A	Group B	Group C	<i>p</i> -Value A-B	<i>p</i> -Value A-C	<i>p</i> -Value B-C
Superficial	CSVD	18.43±2.09	17.53±2.17	18.82±2.82	0.105	0.550	0.052
	TSVD	46.78±2.51	48.71±2.94	49.61±2.36	0.008*	0.001*	0.199
	SSVD	47.38±3.23	48.87±2.23	49.91±2.70	0.042*	0.002*	0.109
	NSVD	46.08±2.69	47.60±2.41	49.10±2.58	0.011*	0.001*	0.096
	ISVD	46.91±3.29	48.74±3.07	50.25±2.35	0.030*	0.001*	0.037*
Deep	CDVD	18.44±2.67	16.25±2.23	18.50±2.36	0.001*	0.926	0.001*
	TDVD	48.18±4.59	50.34±2.99	51.81±2.30	0.036*	0.036*	0.037*
	SDVD	49.78±4.04	51.57±2.11	53.08±3.02	0.035*	0.001*	0.028*
	NDVD	48.25±2.66	50.14±2.73	51.76±2.75	0.009*	0.001*	0.026*
	IDVD	49.04±3.30	51.15±2.89	52.87±3.20	0.011*	0.001*	0.032*

CSVD,central superficial retinal vessel density;**TSVD**,temporal superficial retinal vessel density;**SSVD**,superior superficial retinal vessel density;**NSVD**,nasal superficial retinal vessel density;**ISVD**,inferior superficial retinal vessel density;**CDVD**,central deep retinal vessel density;**TDVD**,temporal deep retinal vessel density; **SDVD**, superior deep retinal vessel density;**NDVD**,nasal deep retinal vessel density;**IDVD**,inferior deep retinal vessel density

Data are expressed as the mean ± standard deviation

*Significant:independent *t* test

Discussion

DR is a microvascular complication of diabetic retinopathy.In early DR, retinal capillary pericytes and endothelial cell degeneration were seen. Capillary as a structural factor of tissue metabolism, retinal capillary damage to largely extent reflects the pathological changes of diabetic retina, such as vascular occlusion, hypoxia and necrosis[12].Compared with the healthy control population, the retina of diabetes mellitus with no or mild diabetic retinopathy has been relatively hypoxic[13].The macular is the most sensitive part of vision.Microcirculation changes already existed in the macular of diabetes mellitus with no or mild diabetic retinopathy, irreversible damage to the macular and its surrounding vascular tissue caused by abnormal glucose metabolism[14–15].We found that diabetic patients with high myopia had a lower incidence of DR than normal people.Although the topic of a possible connection between myopia and DR is not new in the literature, the reason are still conflicting.The technology of OCTA is a major advance in ophthalmology and offers the opportunity to noninvasively visualize different retinal capillary layers and quantify the retinal capillary without the need for injection of fluorescein sodium dye[16].We

therefore designed this cross-sectional study to determine vessel density in type 2 diabetic patients with/without high myopia to identify the effects of myopia and diabetes on retinal vessel density.

The results of this study showed that there was no significant difference in the CSVD among the three groups, but the TSVD, SSVD, NSVD and ISVD in group A were lower than those in group B and group C; Only ISVD in group B was lower than that in group C, and there was no significant difference in other zones between group B and group C. In the comparison of deep retinal vessel density, CDVD in group A was higher than that in group B, but there was no significant difference compared with group C. TDVD, SDVD, NDVD, IDVD in group B were higher than those in group A and lower than those in group C. Previous studies found that in NDR, NPDR and PDR groups, both parafoveal superficial and deep retinal vessel density gradually decreased, retinal vessel density in OCTA was correlated significantly with disease severity in eyes with DR, and deep retinal vessel density decreased significantly [17–18]. Cao et al. [18] found that retinal circulation may be affected before clinical manifestation in diabetic eyes, retinal vessel density decreased, a few microaneurysms and capillary nonperfusion can be found in NDR by OCTA. This study found that although the superficial and deep retinal vessel density of NDR decreased, the deep retinal vessel density decreased more significantly, which is the same as the research conclusions of Tsai et al. [19] and Sun et al. [20]. In previous studies, there was no report of macular retinal vessel density in diabetic patients with high myopia. We found that the macular central superficial and deep vessel density in diabetic patients with high myopia were not different from those in the healthy control group, but the parafoveal superficial and deep vessel density were lower than those in the diabetic patients without high myopia and normal subjects. Chiu et al. [21] proposed that with the increasing severity of myopia, in order to protect the visual function of macular fovea, human eyes sacrifice the thickness of peripheral retina to ensure the retinal thickness of macular fovea. Li et al. [22] found that when there was no significant fundus degenerative change, patients with high myopia had a decrease in retinal capillary density. Since the diabetic patients with high myopia have lower retinal vessel density in the superficial and deep macular retina than in the diabetic patients without high myopia, what is the reason why the incidence of DR in diabetic patients with high myopia is lower than that in diabetic patients? Although the exact mechanism(s) underlying a protective effect of long axial length against DR is yet to be defined [23–25], several hypotheses have been suggested: Fundus changes in high myopia are often accompanied by thinning and atrophy of the choroidal and retinal tissue, which greatly reduces retinal metabolism. Retinal atrophy and choroid thickness reduction may decrease oxygen requirements [26]. Man et al. [27] found that the difference of retinal arteriovenous oxygen saturation was small in patients with long axial length. These findings suggested that longer axial length have decreased retinal function and oxygen consumption, and thus were relatively less hypoxic in the presence of diabetes, which may partly explain the reduced risk of DR in these eyes. In high myopia, the volume of intraocular contents becomes larger due to eye expansion, which reduces the concentration of VEGF in eyes. It has been reported that the axial length was negatively correlated with the content of intraocular VEGF [28, 29]. Retinal thinning in patients with high myopia increases the diffusion of oxygen from choroid; Vitreum detachment and liquefaction are more prone to occur in patients with long axial

length, the retina is more likely to get oxygen from liquefied vitreum which can reduce the hypoxia, and hypoxia relieved of diabetic retina can reduce VEGF release.

This study still has some limitations. First, the sample size of type 2 diabetic patients with high myopia was limited, and subjects could be drawn from only one center. In the future, a multicenter study including a larger sample of subjects may provide more accurate outcome predictions. Second, When using OCTA to evaluate retinal vessel density in myopic patients (AL > 26 mm), 3×3 mm scan pattern has better repeatability and more accurate than that of 6×6 mm scan pattern [30]. However, the 3×3 scan area is limited. Third, due to the automatic measurement software, automatic partition of the retinal vessel density might have introduced some measurement errors. The more complex the pathological changes of fundus, the lower the accuracy of segmentation.

In conclusion, the parafoveal superficial and deep vessel density of type 2 diabetic patients with high myopia were lower than those of diabetics and normal persons. However, there was no difference in macular fovea superficial and deep retinal vessel density between diabetic patients with high myopia and normal persons. In addition, myopia did not show a protective effect on retinal vessel density reduction in diabetic patients. We speculated that the protective effect of the long axial length against DR is due to decreased metabolism and not to changes in vascular density. Our results increased our understanding of the pathophysiology of retinal vessel density changes in diabetic patients. Other possible mechanisms for high myopia to against diabetic retinopathy need further verification.

Declarations

Conflict of interest All authors declare no conflicts of interest.

Ethical approval All procedures in the study involving human participants were performed in accordance with the ethical standards of the Institutional Research Committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all enrolled study participants.

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Figures

Figure 1

Illustration of the measurement of superficial and deep retinal vessel density at five locations
CSVD,central superficial retinal vessel density;TSVD,temporal superficial retinal vessel density;
SSVD,superior superficial retinal vessel density;NSVD,nasal superficial retinal vessel density;
ISVD,inferior superficial retinal vessel density;CDVD,central deep retinal vessel density;
TDVD,temporal deep retinal vessel density;SDVD,superior deep retinal vessel density;
NDVD,nasal deep retinal vessel density;IDVD,inferior deep retinal vessel density