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ORIGINAL ARTICLE

Retrospective Study

Quantitative analysis of early diabetic retinopathy based on optical coherence tomography angiography biological image

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Author contributions: Shi Y and Lin PY design the study; Ruan YM and Lin CF drafted the work and collected the data; Hua SS and Li B analysed and interpreted data and wrote the article.

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Abstract

BACKGROUND

With the development of the economy and improvements in living standards, the incidences of diabetes mellitus (DM) and diabetic retinopathy (DR), which is a complication of DM, are on the rise.

AIM

To analyze early DR in patients with macular zone changes in biological images using optical coherence tomography angiography

METHODS

A prospective case study was performed on 59 participants: 35 healthy eyes (control group), 35 eyes with diabetes but no DR group (no DR group), and 35 eyes with mild DR (NPDR group). All quantitative comparisons of parameters, including the fovea vascularity area, circularity index, and vascular complexity parameters, were performed using a biological image analysis software.

RESULTS

The foveal avascular zone (FAZ) area, FAZ circularity index, number of branches in the area, and the total of the single branches' length in the area was 0.366 ± 0.031, 0.834 ± 0.037, 3241.8 ± 268.3, and 3.860 × 10^7 ± 0.194 × 10^7, and 0.421 ± 0.030, 0.739 ± 0.023, 2956.6 ± 476.4, and 3.177 × 10^7 ± 0.161 × 10^7 in the no DR group and the NPDR group, respectively, which were significantly different from the corresponding parameters of the control group ($P < 0.05$). Moreover, there were significant differences between these two groups ($P < 0.05$).

CONCLUSION

This study shows that early microcirculation changes in the macular area of the retina is associated with disease progression. Early changes in DR can be analyzed using optical coherence tomography angiography.

additional data are available.

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Core Tip: Optical coherence tomography angiography has the advantage of being rapid, noninvasive, high-resolution, repeatable, and consistent. It can also be used as an early fundus screening method for patients with diabetes mellitus.

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INTRODUCTION

Diabetic retinopathy (DR) occurs in 24.8% to 37.5% of patients with diabetes mellitus (DM) in China according to the latest epidemiological survey data from the International Diabetes Federation. With the development of the economy and improvements in living standards, the incidence of DM and DR, which is a complication of DM, are on the rise[1]. DR is characterized by lesions caused by microvascular retinal damage. Macular ischemia is a significant feature of DR and is thought to be caused by occlusion, loss, or degeneration of the capillary network in the macular area[2,3]. This condition is characterized by a reduction in the capillary network in the fovea. DR is the main cause of blindness in most developing countries[4]. Its early prevention and treatment are challenging and represent urgent public health problems.

Fluorescein angiography is used to visualize the vascular structures in DR for staging purposes. However, this is an invasive technique that only produces images of whole blood vessels and obscures the details of the individual layers of blood vessels. In recent years, noninvasive blood flow imaging technology, known as optical coherence tomography angiography (OCTA), has been developed. It has the advantage of being rapid, noninvasive, high-resolution, repeatable, and consistent[5]. To date, some scholars have applied the OCTA built-in program for DR analysis, but OCTA and biographic software are yet to be used to evaluate changes in microvessels in the macular area in patients with early DM. In this study, OCTA was used to evaluate the macular area and demonstrate that it can be used as an early fundus screening method for DR in patients with DM.

MATERIALS AND METHODS

Study design and participant selection

This was a prospective case study. There were 59 participants in this study. Thirty-eight patients with DM (70 eyes) underwent fundus fluorescein angiography (FFA) at Ningbo First Hospital from May 2019 to December 2019. The group included 18 male patients (35 eyes) and 20 female patients (35 eyes), aged 38-70 years (mean ± SD: 53.11 ± 6.21 years). There were 35 eyes that had no diabetic retinopathy (no DR) and 35 eyes that had non proliferative diabetic retinopathy (NPDR). Another 21 healthy subjects (35 eyes) with matched age participated as the control group and included 13 males (20 eyes) and 8 females (15 eyes), aged 36-63 years (mean ± SD: 53.11 ± 5.81 years).

Exclusion criteria were as follows: (1) Proliferative diabetic retinopathy observed on fundus examination after pupil dilatation; (2) Failure to cooperate with the required examination; (3) History of glaucoma and uveitis; (4) History of retinal photocoagulation, vitrectomy, and other intraocular surgery in any form; and (5) The refractive media was cloudy. In this study, all participants and their families were informed of the details of the study and signed an informed consent form. This study was approved by the Medical Ethics Committee of Ningbo First Hospital.

Methods

All selected participants underwent examination for best-corrected visual acuity and intraocular pressure (IOP), optometry, slit lamp examination, fundus examination, FFA, and OCTA (Heidelberg Engineering, Germany). Both FFA and OCTA were performed on the same day by the same ophthalmologist. DR staging was confirmed by FFA and confirmed by another ophthalmologist. Before OCTA, the participants' pupils were dilated with compound tropicamide eye drops for about 30 min, with the pupils dilated to at least 5 mm. Participants were asked to sit in front of the OCTA instrument, and a series of OCTA images were collected.

Image analysis and observation

The software used was ImageJ analysis (version 1.52 p, http://imagej.nih.gov/ij/; Provided in the public Domain by the National Institutes of Health, Bethesda, MD, United States)[6]. The superficial plexus (SCP) indexes were used in this study because the foveal avascular zone (FAZ) is more superficial and more abstract. SCP imaging and selection tool were used to draw the outline of the FAZ manually, and the circumference and area of FAZ were calculated automatically by this software. Then the circularity index (CI) of FAZ was measured using the following formula: FAZ CI = (4π x area)/(circumference)^2. CI is the expression of shape regularity, and the closer its value is to 1, the more similar its shape is[7]. The images were converted to 8-bit, subjected to binarization, and skeletonized for image skeletal analysis, focusing on two parameters: number of branches in the area (NoB) and total of the single branches' length in the area (tBL)[8].

Statistical methods

All data were analyzed using SPSS 25.0, and variable data are presented as mean ± SD. A one-way ANOVA was used for each variable, and a Scheffe test was used for comparison among groups. Statistical significance was set at $P < 0.05$.

RESULTS

General information

There were no statistically significant differences in age, sex, IOP, or visual acuity between the groups ($P > 0.05$).

Macular area parameter data

All parameters of the no DR group and the NPDR group were significantly different from those of the control group ($F = 136.94$, 105.41, 74.96, 130.22, $P = 0.000$, 0.000; $P = 0.035$, 0.000; $P = 0.000$, 0.000; $P = 0.033$, 0.000), and there were significant differences in parameters between the no DR and NPDR groups ($P = 0.000$, 0.000, and 0.002; Table 1).

The box diagrams in Figures 1-4 indicate that the FAZ area gradually increased with the development of DR, while FAZ CI, NoB, and tBL gradually decreased with the development of DR.

DISCUSSION

OCTA is a newly introduced clinical method that can provide a detailed image of the retinal microvascular system by segmenting the retinal vascular layers. It is a non-ninvasive imaging technique that measures the related and phase characteristics of the signal strength in seconds to generate high-resolution angiographic images of retinal blood flow. Images of the retina and choroid microvasculature can be compared by calculating the position of the retina during repeated scanning movements. OCTA is advantageous for the examination of non-perfused areas in DR microcirculation assessment.

Recently, Gildea[9] published a review of the diagnostic value of OCTA in evaluating multiple microvascular parameters in patients with DM, highlighting the role of OCTA in the identification and location of small aneurysms, preoperative neovascularization and capillary non-perfusion visualization, detection of FAZ amplification, and the reconstruction and quantification of vascular perfusion and branching complexity. Several studies have used OCTA to focus on FAZ measurements as markers of microvascular injury, demonstrating that the FAZ region is larger in patients with DM than in healthy controls[10-14]. The following data are shown in our study of OCTA

Table 1 Parameters and data of macular area

Parameters	Control group	No DR group	NPDR group
FAZ	0.312 ± 0.019	0.366 ± 0.031[b]	0.421 ± 0.030[b,c]
FAZ CI SCP	0.857 ± 0.044	0.834 ± 0.037[a]	0.739 ± 0.023[b,c]
NoB SCP	3896.4 ± 162.2	3241.8 ± 268.3[b]	2956.6 ± 476.4[b,c]
tBL SCP	$4.006 \times 10^7 \pm 0.307 \times 10^7$	$3.860 \times 10^7 \pm 0.194 \times 10^7$[a]	$3.177 \times 10^7 \pm 0.161 \times 10^7$[b,c]

[a]$P < 0.05$ (comparison with control group).
[b]$P < 0.01$ (comparison with control group).
[c]$P < 0.01$ (comparison between the two groups).
FAZ: The foveal avascular zone; CI: Circularity index; SCP: Superficial plexus; NoB: Number of branches in the area; tBL: Total of the single branches' length in the area.

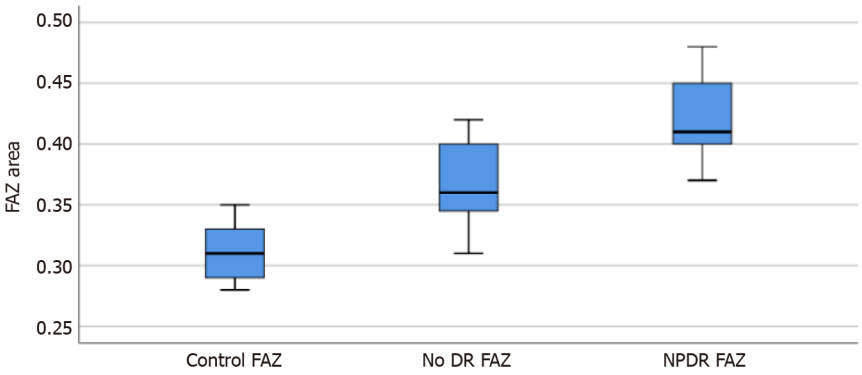

Figure 1 Foveal avascular zone area changes with diabetic retinopathy progress. FAZ: Foveal avascular zone; DR: Diabetic retinopathy; NPDR: Non proliferative diabetic retinopathy.

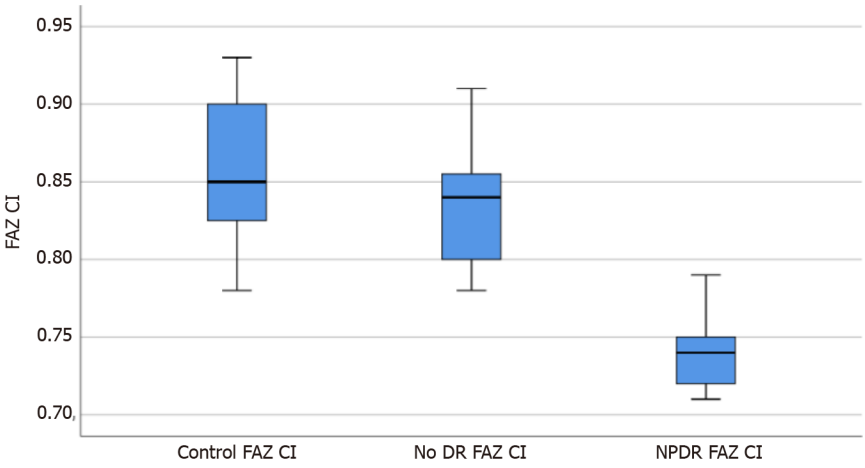

Figure 2 Foveal avascular zone circularity index changes with diabetic retinopathy progress. FAZ: Foveal avascular zone; DR: Diabetic retinopathy; NPDR: Non proliferative diabetic retinopathy; CI: Circularity index.

measurement: The FAZ area was significantly larger in the no DR and NPDR groups than in the control group. For patients with no DR, although the fundus examination showed no obvious pathological changes, the FAZ area expansion indicated that macular occlusion and a nonperfusion status had started. Additionally, we found that the FAZ area in the early period of DM was significantly different between patients without DR and patients with NPDR. As retinopathy progressed, the FAZ area increased, suggesting that macular retinal capillary occlusion and nonperfusion increased in severity.

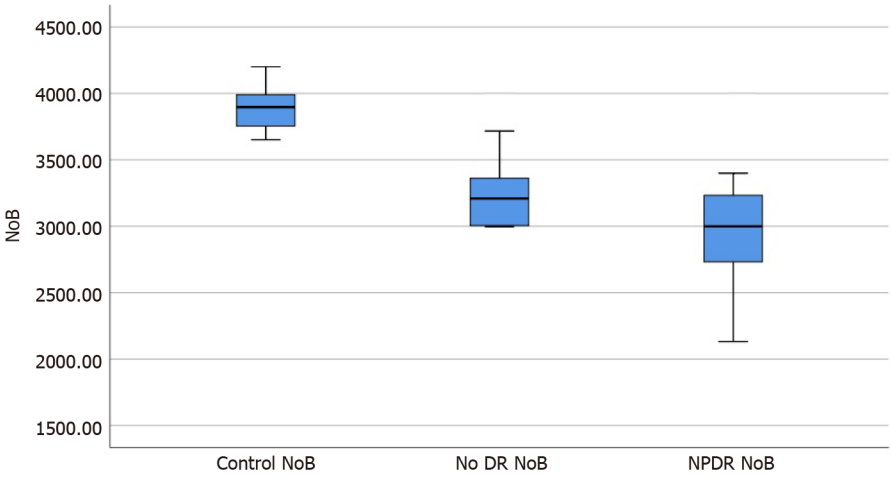

Figure 3 Number of branches in the area changes with diabetic retinopathy progress. DR: Diabetic retinopathy; NPDR: Non proliferative diabetic retinopathy; NoB: Number of branches in the area.

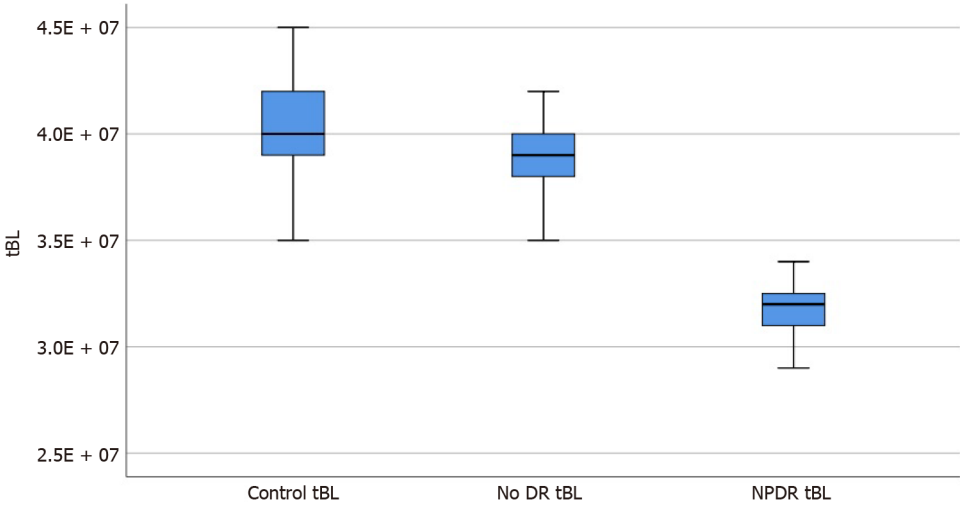

Figure 4 Total of the single branches' length in the area changes with diabetic retinopathy progress. DR: Diabetic retinopathy; NPDR: Non proliferative diabetic retinopathy; tBL: Total of the single branches' length in the area.

Recently, different quantitative methods for the evaluation of roundness of the FAZ in patients with DM have been proposed[15,16]. In this study, CI was an early parameter for FAZ variation in the SCP. From the control group to the no DR and DR groups, there was a significant downward trend in CI, indicating that with the progression of retinal microvascular injury caused by diabetes, the regularity of the FAZ gradually changed significantly in patients with DM compared with that in the control participants.

In this study, we found that compared with the values in the control group, NoB and tBL in the macular area in the NPDR group were significantly decreased. The findings were consistent with the conclusion of Stela V[17], where the same method was used to study the area around the optic disc in patients with DM. They found that patients with DM without clinical DR symptoms had a significant reduction in the area around the optic discs compared with that in healthy participants. Therefore, we believe that the decrease in NoB and tBL may be due to the loss of small branch vessels, which leads to a reduction in retinal branch complexity[18]. Additionally, these findings support the hypothesis that the complexity of the microvascular network decreases gradually as DR severity increases[18].

This study had some limitations. OCTA cannot be applied to all patients with DR, as patients need to have a clear refractive media and good vision. Thus, it is challenging to perform in patients with poor vision, such as those with PDR. A larger sample size is also needed to understand better the exact extent of microvascular damage in the early stages of DR.

CONCLUSION

In summary, this study shows that in patients with DM, fundus lesions with vascular parameters were visible through quantitative OCTA analysis before microcirculation changes in the macular area. OCTA is a new screening tool for patients with DM, and timely monitoring of clinical fundus changes before disease progression might allow for early diagnosis and treatment of DR.

ARTICLE HIGHLIGHTS

Research background

According to the latest epidemiological survey data from the International Diabetes Federation, diabetic retinopathy (DR) occurs in 24.8% to 37.5% of patients with diabetes mellitus (DM) in China.

Research motivation

The early prevention and treatment of DR are challenging and are urgent problems to be solved.

Research objectives

Optical coherence tomography angiography (OCTA) was used to evaluate the macular area and demonstrate that it can be used as an early fundus screening method for patients with DM.

Research methods

All selected participants underwent examination for best-corrected visual acuity and intraocular pressure, optometry, slit lamp examination, fundus examination, fundus fluorescein angiography, and OCTA (Heidelberg Engineering, Germany).

Research results

The values of the foveal avascular zone (FAZ), FAZ circularity index, number of branches in the area, and the total of the single branches' length in the area of the no DR group and the NPDR groups were statistically different from the control group. The said parameters are also statistically different between the two groups.

Research conclusions

OCTA is a new screening tool for patients with DM, and timely monitoring of clinical fundus changes before disease progression might allow for early diagnosis and treatment of DR.

Research perspectives

A novel approach provides novel insights for the diagnosis and treatment of diseases.

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