ISSN 1949-8470 (online)

World Journal of *Radiology*

World J Radiol 2024 September 28; 16(9): 375-496

Published by Baishideng Publishing Group Inc

World Journal of Radiology

Contents

Monthly Volume 16 Number 9 September 28, 2024

EDITORIAL

ORIGINAL ARTICLE

Retrospective Study

Observational Study

CASE REPORT

World Journal of Radiology

Monthly Volume 16 Number 9 September 28, 2024

Contents

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Radiology*, Roberto Grassi, MD, Professor, Chief, Department of Radiology, University of Campania Luigi Vanvitelli, Napoli, 80138, Italy. roberto.grassi@unicampania.it

AIMS AND SCOPE

The primary aim of *World Journal of Radiology* (*WJR*, *World J Radiol*) is to provide scholars and readers from various fields of radiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJR mainly publishes articles reporting research results and findings obtained in the field of radiology and covering a wide range of topics including state of the art information on cardiopulmonary imaging, gastrointestinal imaging, genitourinary imaging, musculoskeletal imaging, neuroradiology/head and neck imaging, nuclear medicine and molecular imaging, pediatric imaging, vascular and interventional radiology, and women's imaging.

INDEXING/ABSTRACTING

The *WJR* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJR* as 1.4; JIF without journal self cites: 1.4; 5-year JIF: 1.8; JIF Rank: 132/204 in radiology, nuclear medicine and medical imaging; JIF Quartile: Q3; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Wen-Bo Wang*; **Production Department Director:** *Xu Guo*; **Cover Editor:** *Jia-Ping Yan*.

NAME OF JOURNAL
World Journal of Radiology

ISSN
ISSN 1949-8470 (online)

LAUNCH DATE
January 31, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Thomas J Vogl

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1949-8470/editorialboard.htm

PUBLICATION DATE
September 28, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Radiology

Submit a Manuscript: https://www.f6publishing.com

World J Radiol 2024 September 28; 16(9): 407-417

DOI: 10.4329/wjr.v16.i9.407

ISSN 1949-8470 (online)

ORIGINAL ARTICLE

Observational Study

Retinal microcirculation changes in prediabetic patients with short-term increased blood glucose using optical coherence tomography angiography

Bing-Jing Lv, Hang-Jia Zuo, Qi-Fu Li, Fan-Fan Huang, Tong Zhang, Rong-Xi Huang, Shi-Jie Zheng, Wen-Juan Wan, Ke Hu

Specialty type: Radiology, nuclear medicine and medical imaging

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade C, Grade D

Novelty: Grade B, Grade C

Creativity or Innovation: Grade B, Grade C

Scientific Significance: Grade B, Grade C

P-Reviewer: Saloň A

Received: January 30, 2024

Revised: August 3, 2024

Accepted: September 9, 2024

Published online: September 28, 2024

Processing time: 240 Days and 16.3 Hours

Bing-Jing Lv, Chongqing Medical University, Chongqing 400000, China

Bing-Jing Lv, Department of Ophthalmology, Dianjiang People's Hospital of Chongqing, Chongqing 4008300, Chongqing, China

Hang-Jia Zuo, Tong Zhang, Wen-Juan Wan, Ke Hu, The First Affiliated Hospital of Chongqing Medical University, Chongqing Medical University, Chongqing 400016, China

Qi-Fu Li, Department of Endocrinology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China

Fan-Fan Huang, Shi-Jie Zheng, Department of Ophthalmology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China

Rong-Xi Huang, Chongqing People's Hospital, Chongqing 400000, China

Co-first authors: Bing-Jing Lv and Hang-Jia Zuo.

Co-corresponding authors: Wen-Juan Wan and Ke Hu.

Corresponding author: Ke Hu, MD, PhD, Doctor, Professor, Researcher, The First Affiliated Hospital of Chongqing Medical University, Chongqing Medical University, No. 1 Yuanjiagang Youyi Road, Yuzhong District, Chongqing 400016, China. cqhuke@hospital.cqmu.edu.cn

Abstract

BACKGROUND

Retinal microcirculation alterations are early indicators of diabetic microvascular complications. Optical coherence tomography angiography (OCTA) is a noninvasive method to assess these changes. This study analyzes changes in retinal microcirculation in prediabetic patients during short-term increases in blood glucose using OCTA.

AIM

To investigate the changes in retinal microcirculation in prediabetic patients experiencing short-term increases in blood glucose levels using OCTA.

METHODS
Fifty volunteers were divided into three groups: Group 1 [impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)], Group 2 (both IFG and IGT), and a control group. Retinal microcirculation parameters, including vessel density (VD), perfusion density (PD), and foveal avascular zone (FAZ) metrics, were measured using OCTA. Correlations between these parameters and blood glucose levels were analyzed in both the fasting and postprandial states.

RESULTS
One hour after glucose intake, the central VD ($P = 0.023$), central PD ($P = 0.026$), and parafoveal PD ($P < 0.001$) were significantly greater in the control group than in the fasting group. In Group 1, parafoveal PD ($P < 0.001$) and FAZ circularity ($P = 0.023$) also increased one hour after glucose intake. However, no significant changes were observed in the retinal microcirculation parameters of Group 2 before or after glucose intake ($P > 0.05$). Compared with the control group, Group 1 had a larger FAZ area ($P = 0.032$) and perimeter ($P = 0.018$), whereas Group 2 had no significant differences in retinal microcirculation parameters compared with the control group ($P > 0.05$). Compared with Group 1, Group 2 had greater central VD ($P = 0.013$) and PD ($P = 0.008$) and a smaller FAZ area ($P = 0.012$) and perimeter ($P = 0.010$). One hour after glucose intake, Group 1 had a larger FAZ area ($P = 0.044$) and perimeter ($P = 0.038$) than did the control group, whereas Group 2 showed no significant differences in retinal microcirculation parameters compared with the control group ($P > 0.05$). Group 2 had greater central VD ($P = 0.042$) and PD ($P = 0.022$) and a smaller FAZ area ($P = 0.015$) and perimeter ($P = 0.016$) than Group 1. At fasting, central PD was significantly positively correlated with blood glucose levels ($P = 0.044$), whereas no significant correlations were found between blood glucose levels and OCTA parameters one hour after glucose intake.

CONCLUSION
A short-term increase in blood glucose has a more pronounced effect on retinal microcirculation in prediabetic patients with either IFG or IGT.

Key Words: Prediabetes; Blood glucose; Optical coherence tomography angiography; Retinal microcirculation; Central vessel density; Impaired fasting glucose; Impaired glucose tolerance

Core Tip: Explore prediabetes-related retinal microcirculation changes with Optical coherence tomography angiography. Categorizing volunteers into Impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and controls, our study reveals postprandial shifts in vessel density, perfusion density (PD), and foveal avascular zone (FAZ) metrics. Noteworthy findings include increased FAZ circularity in IFG/IGT, larger FAZ area/perimeter in IFG, and positive correlation of fasting PD with blood glucose. This novel analysis provides insights into the nuanced impact of short-term blood glucose elevation on retinal microcirculation in prediabetes. Clinicians and researchers, stay tuned for potential clinical implications!

Citation: Lv BJ, Zuo HJ, Li QF, Huang FF, Zhang T, Huang RX, Zheng SJ, Wan WJ, Hu K. Retinal microcirculation changes in prediabetic patients with short-term increased blood glucose using optical coherence tomography angiography. *World J Radiol* 2024; 16(9): 407-417
URL: https://www.wjgnet.com/1949-8470/full/v16/i9/407.htm
DOI: https://dx.doi.org/10.4329/wjr.v16.i9.407

INTRODUCTION

Diabetes is a common chronic metabolic disease, and its incidence continues to rise with improvements in living standards and changes in eating habits[1,2]. The disease mainly manifests clinically as typical symptoms such as polydipsia, polyuria, polydipsia, and weight loss, which have a serious impact on health[3,4]. The main complications of diabetes include diabetic retinopathy (DR), nephropathy, and neuropathy[5]. Among these, DR involves pathological changes in the retinal microcirculation and is the leading cause of blindness in most developing countries[6]. During the transition from the high-risk stage to the diagnosis of diabetes, patients experience the prediabetes stage, which is characterized by impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), as determined through oral glucose tolerance tests (OGTTs). IFG is defined as a fasting blood glucose level greater than 5.6 mmol/L, with a blood glucose level of less than 7.8 mmol/L two hours after the administration of an oral glucose solution; the other is IGT, which is defined as a level of blood glucose greater than 7.8 mmol/L but less than 11.1 mmol/L two hours after the administration of an oral glucose solution[7,8]. A short-term increase in blood sugar may cause insulin resistance[9]. In patients with prediabetes, it is necessary to observe changes in the retinal microcirculation for early diagnosis, intervention and prevention of DR and other complications of diabetes.

Optical coherence tomography angiography (OCTA) has emerged as a novel, noninvasive imaging technology that visualizes the microvascular structures of the retina and choroid[10-12]. This method provides detailed images of the retinal and choroidal vasculature without the need for dye injections, making it a safer and more convenient alternative to traditional angiographic techniques[13]. In recent years, as an auxiliary examination, OCTA has been widely used in systemic diseases that cause pathological manifestations in the eyes[14,15]. It can be employed to quantify relevant indicators of the fundus, including vessel density (VD), perfusion density (PD), and the area, perimeter and circularity of the foveal avascular zone (FAZ). Studies have suggested that OCTA can diagnose a significant proportion of diabetic patients with fundus microvascular abnormalities overlooked by other ocular tests, indicating its importance in the early diagnosis of diabetes[16]. However, most research has focused on patients with type 2 diabetes, whose retinal microcirculation are affected by factors such as age, hypertension, and coronary heart disease[17,18]. Additionally, older diabetic patients may face issues such as unclear refractive media, poor examination coordination, and susceptibility to OCTA motion artifacts, which can affect measurement accuracy[19,20].

Prediabetic patients, primarily those who are young or middle-aged, generally exhibit greater examination tolerance and fewer ocular and systemic diseases, leading to more reliable OCTA results. However, the literature on retinal microcirculation changes in prediabetic patients remains limited[21-23]. This study aimed to explore the effects of short-term blood glucose increases on retinal microcirculation in the macular area of prediabetic patients, emphasizing the importance of early detection and intervention.

MATERIALS AND METHODS

Basic information

In this prospective study, 50 patients underwent OGTTs at the Laboratory of the Endocrinology Department of the First Affiliated Hospital of Chongqing Medical University. All participants were informed, and their consent was obtained. The experimental data were collected from September 1 to November 30, 2020, and patients were divided into a control group (22 patients, 22 eyes), a group with either IFG or IGT (14 patients, 14 eyes, Group 1), and a group with both IFG and IGT (13 patients, 13 eyes, Group 2). After the subjects signed the informed consent form, their basic information, including sex, age, history of systemic diseases, and best corrected visual acuity, was collected. Then, OGTTs were performed after fasting blood glucose levels were recorded. To conduct the OGTTs, we dissolved 75 g of glucose powder in 200 mL of warm water, mixed it well, and instructed the patients to take it within 5 minutes, after which their blood sugar levels were recorded 1 and 2 hours after oral intake of the glucose solution. This study was approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University, with approval No. 2021-648 and an approval date of December 30, 2024.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) Aged 20-60 years; (2) Best-corrected visual acuity of 0.8 or above; (3) The refractive media of both eyes is transparent under slit lamp examination; (4) Normal intraocular pressure; and (5) No history of ocular trauma or surgery.

The exclusion criteria were as follows: (1) The subject was diagnosed with other ophthalmological diseases, such as glaucoma, high myopia (≥ -6.0 DS), uveitis, hypertensive retinopathy, *etc.*; (2) The signal strength of OCTA image scanning was less than 6 (total signal strength was 10); (3) The patient poorly cooperated, and the OCTA image had obvious artifacts; or (4) The patient had been diagnosed with diabetes, had recently used glucose-controlling drugs, or had been diagnosed with malignant tumors, autoimmune system diseases, or blood system diseases.

Image acquisition

All images were collected independently by two experienced ophthalmologists from the entire study group, and the average of their results was used as statistical data. All images were collected using the Zeiss OCTA (Cirrus HD-OCT, 5000, Germany) in angiography 3 mm × 3 mm mode. Each region was scanned three times to ensure data validity, and images with a signal strength greater than 6 were selected. The built-in Forum software automatically identified and displayed indicators of the superficial retina in the macular area. The OCTA images revealed four layers: The choroidal, choriocapillaris and retinal nerve epithelium layers and the vitreoretinal interface. We analyzed data from the avascular layer, deep retinal layer, superficial retinal layer, and color depth encoding map. This study focused on the superficial retinal layer, with the scanning area divided on the basis of ETDRS standards into concentric circles centered on the fovea (1 mm and 3 mm in diameter). The retina was segmented into a 1 mm circular area, a 1 mm to 3 mm annular area, and a 3 mm circular area. The VD and PD were calculated for each area. The quantitative parameters included the VD, PD, and the area, perimeter, and circularity index of the FAZ. VD was the ratio of vessel length to area[24], PD was the ratio of vascular coverage to area, and the FAZ circularity index ranged from 0 (no circularity) to 1 (perfect circle), indicating the impact of disease on FAZ morphology. We collected data from the same eye (left eye) for each subject, as a literature review indicated that most OCTA measurements analyze data from the same eye for consistency[25,26]. Each subject underwent measurements at two time points: Fasting and one hour after oral glucose solution intake. Each time, three measurements were taken, and the average of these measurements was used for statistical analysis.

Statistical analysis

SPSS 23.0 software was used for statistical analysis and processing. Fisher's exact test was used for the statistical analysis of categorical data. Normality and homogeneity of variance tests were used on continuous data. According to the results, a one-way analysis of variance or the Kruskal-Wallis *H* test was performed for group comparisons, and Bonferroni correction was used for pairwise comparisons. The data are expressed as the means and standard deviations. The comparison between patients before and after the OGTT was performed *via* paired *t* tests; otherwise, the paired Wilcoxon signed-rank test was used. According to the normality of the data, Pearson's or Spearman's correlation analysis between blood glucose and OCTA indicators was used. A P value < 0.05 indicated that the difference was statistically significant.

RESULTS

General information

The average ages of the normal control group (CN), Group 1 and Group 2 were 29.57 ± 3.92, 30.79 ± 6.92 and 34.15 ± 8.53 years, respectively. The male-to-female ratios of these three groups were 2:21, 1:13 and 2:11, respectively (Table 1). There were no statistically significant differences in age (P = 0.248) or sex (P = 0.707) between the control group, Group 1 and Group 2.

Comparison of OCTA indices in the superficial retina between fasting conditions and after one hour of OGTT

In the control group, the central VD and PD increased one hour after the subjects consumed the glucose solution (P = 0.023, P = 0.026). One hour after the oral intake of the glucose solution in Group 1, the FAZ circularity was greater than that in the fasting condition (P = 0.023). In Group 2, there were no significant changes in the retinal microcirculation one hour before or after the OGTT (P > 0.05; Table 2). Detailed data on the vascular density, perfusion density, and FAZ under fasting conditions and after one hour of glucose intake can be found in Supplementary Table 1.

Comparison of OCTA indices in the superficial retinal layer among the three groups during fasting

The FAZ area and perimeter were greater in Group 1 than in the control group (P = 0.032, P = 0.018). There was no significant difference in the retinal microcirculation indices between the control group and Group 2 (P > 0.05). The central VD and PD of Group 2 were greater (P = 0.013, P = 0.008) than those of Group 1, while the FAZ area and perimeter were smaller (P = 0.012, P = 0.010; Table 3).

Comparison of OCTA indices in the superficial retinal layer among the three groups after one hour of OGTT

One hour after oral intake of the glucose solution, the FAZ area and perimeter of Group 1 were greater than those of the control group (P = 0.044, P = 0.038), whereas there was no significant difference between the retinal microcirculation indices of the control group and those of Group 2 (P > 0.05). The center VD and PD of Group 2 were greater (P = 0.042, P = 0.022) than those of Group 1, while the FAZ area and perimeter were lower (P = 0.015, P = 0.016; Table 4). Typical examples of VD and PD changes in a 30-year-old female from the control group, a 23-year-old female from Group 1 and a 33-year-old female from Group 2 under fasting conditions and one hour after the OGTT are shown in Figure 1.

Correlations between blood glucose levels and OCTA indices in the superficial retina

Under fasting conditions, the central PD and blood glucose of the three groups were significantly positively correlated (r = 0.286, P = 0.044), while the other OCTA indices were not significantly correlated with blood glucose (all P > 0.05). There was no significant correlation between the blood glucose level one hour after the OGTT and the OCTA metrics (all P > 0.05; Table 5).

DISCUSSION

This study aimed to investigate the changes in retinal microcirculation in prediabetic patients during short-term blood glucose elevation. Our study subjects were divided into three groups: The CN, the group with IFG or IGT (Group 1), and the group with both IFG and IGT (Group 2).

In the control group, the blood glucose level peaked one hour after the OGTT. Therefore, we examined blood glucose levels and performed OCTA examinations at this time point for all participants. One hour after the administration of the glucose solution, the central VD and PD in the macular area of the retina in the control group were significantly greater than those in the fasting group. This increase may be attributed to the relatively stable and normal function of the vascular endothelial cells in the control group. These cells can respond to short-term changes in blood glucose levels by increasing microvascular blood flow and oxygen-carrying capacity, demonstrating a stress response to glycemic variation [26,27]. When blood glucose levels rise, as observed one hour after glucose intake, these endothelial cells can respond promptly and efficiently. The increased central VD and PD in the CN are likely due to the ability of these endothelial cells to produce nitric oxide (NO) and other vasodilatory substances in response to elevated glucose levels, thereby increasing blood flow and perfusion in the retinal microcirculation. This response helps ensure adequate oxygen and nutrient delivery to retinal tissues during short-term glucose fluctuations. In Group 1, which was characterized by prediabetes with either IFG or IGT, FAZ circularity was greater one hour after the OGTT than during fasting. This could be due to the

Table 1 The average ages and male-to-female ratios of the control group, group 1, and group 2 were not significantly different ($P > 0.05$)

Group	Control (CN)	Group 1 (IFG or IGT)	Group 2 (IFG and IGT)	*P* value
Average age (years)	29.57 ± 3.92	30.79 ± 6.92	34.15 ± 8.53	0.248
Male to female ratio	2:21	1:13	2:11	0.707

CN: Control group; IFG: Impaired fasting glucose; IGT: Impaired glucose tolerance.

Table 2 Correlations between blood glucose levels and optical coherence tomography angiography indicators in the superficial retinal layer of the three groups

Index	Fasting		After OGTT	
	Coefficient	*P* value	Coefficient	*P* value
Central VD	0.264	0.064	-0.145	0.314
Lateral VD	0.093	0.520	0.020	0.891
Full VD	0.148	0.306	-0.038	0.793
Central PD	0.286	0.044	-0.137	0.344
Lateral PD	0.127	0.379	0.038	0.792
Full PD	0.231	0.106	-0.016	0.915
FAZ area	-0.190	0.187	0.147	0.308
FAZ perimeter	-0.216	0.131	0.162	0.261
FAZ circularity	0.049	0.734	-0.079	0.586[1]

[1]Correlations between blood glucose level and optical coherence tomography angiography metrics *via* Spearman's correlation analysis; the others were evaluated *via* Pearson's correlation analysis.
OGTT: Oral glucose tolerance test; VD: Vessel density; PD: Perfusion density; FAZ: Foveal avascular zone.

Table 3 Comparison of optical coherence tomography angiography indices in the superficial retina between fasting conditions and one hour after the oral glucose tolerance test

Index	CN ($n = 23$)		*P* value	Group 1 ($n = 14$)		*P* value	Group 2 ($n = 13$)		*P* value
	Fasting	Postprandial		Fasting	Postprandial		Fasting	Postprandial	
Central VD	9.21 ± 2.35	9.74 ± 2.61	0.023	7.58 ± 2.82	7.81 ± 2.96	0.464	10.49 ± 2.50	10.37 ± 2.15	0.733
Lateral VD	21.44 ± 1.07	21.71 ± 1.29	0.268	21.35 ± 1.16	21.75 ± 1.03	0.321	21.44 ± 1.70	21.90 ± 1.21	0.722[1]
Full VD	20.06 ± 1.02	20.38 ± 1.28	0.186	19.79 ± 1.17	20.15 ± 1.12	0.347	20.21 ± 1.65	20.59 ± 1.14	0.807[1]
Central PD	0.15 ± 0.04	0.16 ± 0.04	0.026	0.13 ± 0.05	0.13 ± 0.05	0.662	0.18 ± 0.04	0.18 ± 0.04	0.616
Lateral PD	0.38 ± 0.02	0.38 ± 0.02	0.270	0.38 ± 0.02	0.39 ± 0.02	0.306	0.38 ± 0.03	0.39 ± 0.02	0.649[1]
Full PD	0.35 ± 0.02	0.36 ± 0.02	0.231	0.35 ± 0.02	0.36 ± 0.02	0.741	0.36 ± 0.03	0.36 ± 0.02	0.834[1]
FAZ area	0.31 ± 0.11	0.32 ± 0.11	0.207	0.41 ± 0.13	0.41 ± 0.13	0.716	0.28 ± 0.09	0.29 ± 0.09	0.357
FAZ perimeter	2.35 ± 0.38	2.34 ± 0.38	0.581[1]	2.73 ± 0.44	2.69 ± 0.45	0.232	2.26 ± 0.38	2.25 ± 0.36	0.509
FAZ circularity	0.70 ± 0.08	0.71 ± 0.07	0.602	0.69 ± 0.06	0.72 ± 0.05	0.023	0.69 ± 0.06	0.71 ± 0.08	0.162

[1]Comparison between fasting conditions and one hour after the oral glucose tolerance test *via* the paired Wilcoxon signed-rank test; the other tests were paired *t* tests.
Group 1 comprised patients with either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT); Group 2 comprised patients with both IFG and IGT. CN: Control group; VD: Vessel density; PD: Perfusion density; FAZ: Foveal avascular zone.

Table 4 Comparison of optical coherence tomography angiography indicators in the superficial retinal layer among the three groups during fasting

Index	CN (*n* = 23)	Group 1 (*n* = 14)	Group 2 (*n* = 13)	Statistics value	*P* value	*P*1	*P*2	*P*3
Central VD	9.21 ± 2.35	7.58 ± 2.82	10.49 ± 2.50	4.525	0.016[1]	0.188	0.455	0.013
Lateral VD	21.44 ± 1.07	21.35 ± 1.16	21.44 ± 1.70	0.026	0.974[1]			
Full VD	20.06 ± 1.02	19.79 ± 1.17	20.21 ± 1.65	2.652	0.266[2]			
Central PD	0.15 ± 0.04	0.13 ± 0.05	0.18 ± 0.04	4.999	0.011[1]	0.280	0.218	0.008
Lateral PD	0.38 ± 0.02	0.38 ± 0.02	0.38 ± 0.03	0.775	0.679[2]			
Full PD	0.35 ± 0.02	0.35 ± 0.02	0.36 ± 0.03	2.078	0.354[2]			
FAZ area	0.31 ± 0.11	0.41 ± 0.13	0.28 ± 0.09	5.312	0.008[1]	0.032	1.000	0.012
FAZ perimeter	2.35 ± 0.38	2.73 ± 0.44	2.26 ± 0.38	5.804	0.006[1]	0.018	1.000	0.010
FAZ circularity	0.70 ± 0.08	0.69 ± 0.06	0.69 ± 0.06	0.257	0.775[1]			

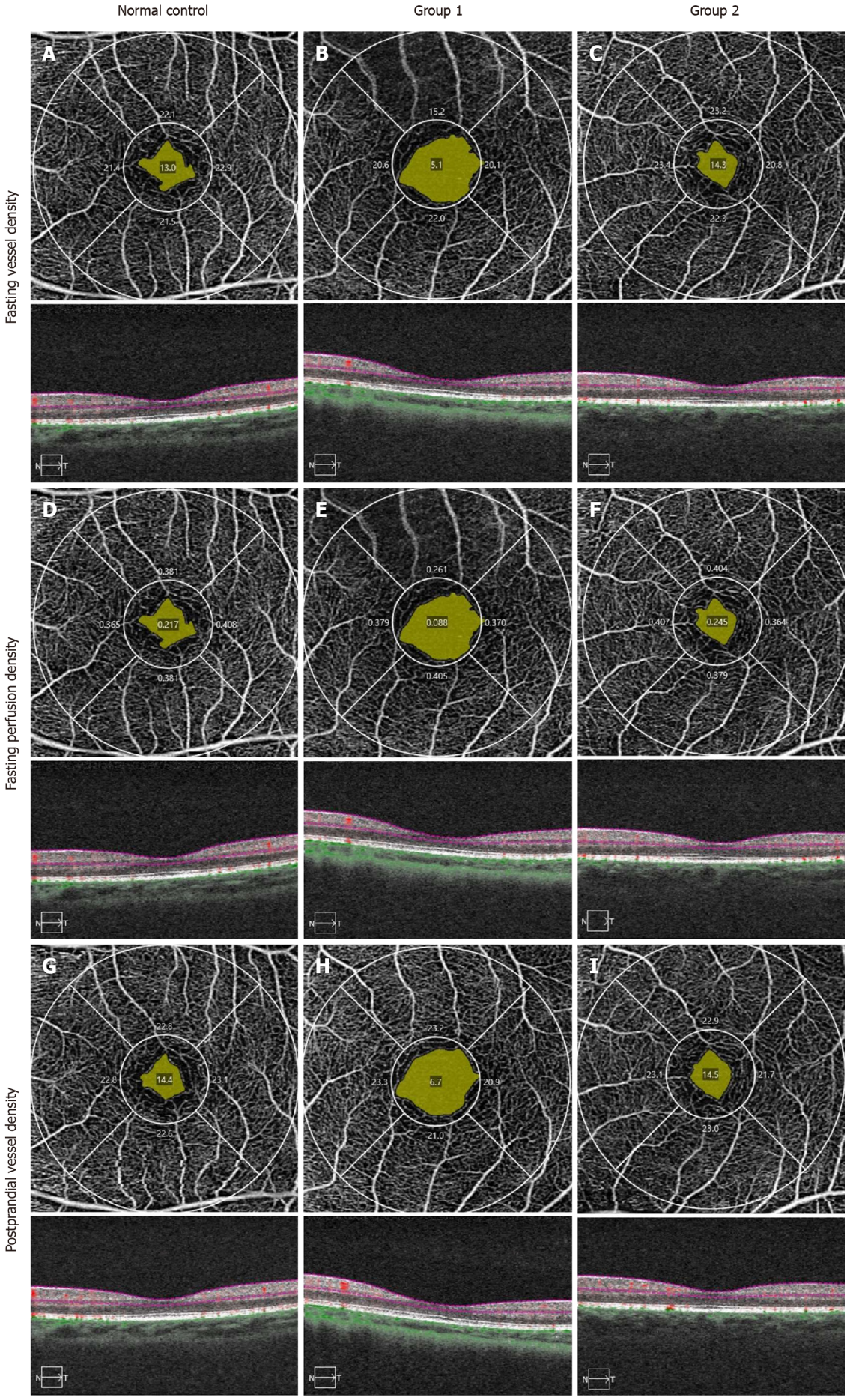
[1]Comparisons among groups were performed *via* one-way analysis of variance.
[2]Comparisons among groups were performed *via* the Kruskal-Wallis *H* test.
*P*1: Comparisons between the control group (CN) and group 1; *P*2: Comparisons between the CN and group 2; *P*3: Comparisons between group 1 and group 2. All *P* values were adjusted with the Bonferroni correction. Group 1 comprised patients with either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT); Group 2 comprised patients with both IFG and IGT. CN: Control group; VD: Vessel density; PD: Perfusion density; FAZ: Foveal avascular zone.

Table 5 Comparison of oral glucose tolerance test indicators in the superficial retinal layer among the three groups after one hour of oral glucose tolerance test

Index	CN (*n* = 23)	Group 1 (*n* = 14)	Group 2 (*n* = 13)	Statistics value	*P* value	*P*1	*P*2	*P*3
Central VD	9.74 ± 2.61	7.81 ± 2.96	10.37 ± 2.15	3.706	0.032	0.101	1.000	0.042
Lateral VD	21.71 ± 1.29	21.75 ± 1.03	21.90 ± 1.21	0.106	0.899			
Full VD	20.38 ± 1.28	20.15 ± 1.12	20.59 ± 1.14	0.449	0.641			
Central PD	0.16 ± 0.04	0.13 ± 0.05	0.18 ± 0.04	4.271	0.020	0.092	1.000	0.022
Lateral PD	0.38 ± 0.02	0.39 ± 0.02	0.39 ± 0.02	0.093	0.911			
Full PD	0.36 ± 0.02	0.36 ± 0.02	0.36 ± 0.02	0.241	0.787			
FAZ area	0.32 ± 0.11	0.41 ± 0.13	0.29 ± 0.09	4.963	0.011	0.044	1.000	0.015
FAZ perimeter	2.34 ± 0.38	2.69 ± 0.45	2.25 ± 0.36	4.967	0.011	0.038	1.000	0.016
FAZ circularity	0.71 ± 0.07	0.72 ± 0.05	0.71 ± 0.08	0.115	0.891			

*P*1: Comparisons between the control group (CN) and Group 1; *P*2: Comparisons between the CN and Group 2; *P*3: Comparison between Group 1 and Group 2. All *P* values were adjusted with the Bonferroni correction. Group 1 comprised patients with either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT); Group 2 comprised patients with both IFG and IGT. *P*: Comparisons among groups were performed *via* one-way analysis of variance. CN: Control group; VD: Vessel density; PD: Perfusion density; FAZ: Foveal avascular zone.

partial insulin resistance present in these individuals. Although insulin efficiency in promoting glucose uptake and utilization is reduced, the body compensates by secreting more insulin[28,29]. This compensatory mechanism may still allow some level of glucose regulation, enabling a stress response to short-term glucose changes, thereby maintaining a more regular FAZ shape. Conversely, in Group 2, which included individuals with both IFG and IGT, no significant changes were observed in retinal microcirculation indicators one hour after glucose intake. This lack of response may be attributed to severe and persistent insulin resistance in these patients. Specifically, insulin resistance impairs the ability of endothelial cells to produce NO and other vasodilatory substances in response to elevated glucose levels[30]. Additionally, chronic hyperglycemia can cause endothelial dysfunction through increased oxidative stress and inflammation, further compromising the ability of retinal blood vessels to adapt to short-term changes in blood glucose[31]. Consequently, the microvasculature in the retina becomes less responsive to acute fluctuations in blood glucose. This diminished capacity for vascular adaptation may lead to a consistent state of poor blood flow regulation and reduced


Normal control
Group 1
Group 2
Fasting vessel density
Fasting perfusion density
Postprandial vessel density
A
B
C
D
E
F
G
H
I
22.1
21.4
13.0
22.9
21.5
15.2
20.6
5.1
20.1
22.0
23.2
23.4
14.3
20.8
22.3
0.381
0.365
0.217
0.408
0.381
0.261
0.379
0.088
0.370
0.405
0.404
0.407
0.245
0.364
0.379
22.8
22.8
14.4
23.1
22.6
23.2
23.3
6.7
20.9
21.0
22.9
23.1
14.5
21.7
23.0

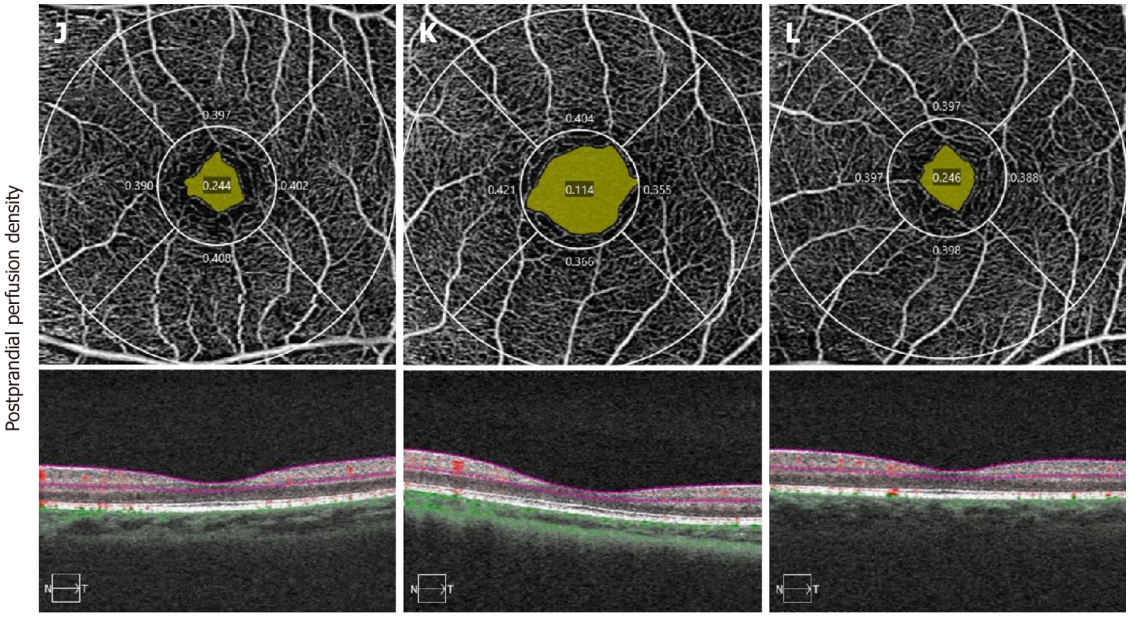


Figure 1 Comparison of central vessel density in fasting state and one hour after oral glucose solution intake across different glycemic groups. A: The central vessel density (VD) in the fasting state of the normal control group; B: The central VD in the fasting state of the impaired fasting glucose or impaired glucose tolerance group; C: The central VD in the fasting state of the group with both impaired fasting glucose and impaired glucose tolerance; D: The central perfusion density (PD) in the fasting state of the normal control group; E: The central PD in the fasting state of the impaired fasting glucose or impaired glucose tolerance group; F: The central PD in the fasting state of the group with both impaired fasting glucose and impaired glucose tolerance; G: The central VD one hour after oral glucose solution intake in the normal control group; H: The central VD one hour after oral glucose solution intake in the impaired fasting glucose or impaired glucose tolerance group; I: The central VD one hour after oral glucose solution intake in the group with both impaired fasting glucose and impaired glucose tolerance; J: The central PD one hour after oral glucose administration in the normal control group; K: The central PD one hour after oral glucose administration in the impaired fasting glucose or impaired glucose tolerance group; L: The central PD one hour after oral glucose administration in the group with both impaired fasting glucose and impaired glucose tolerance.

nutrient and oxygen delivery to retinal tissues.

Both under fasting conditions and one hour after the oral intake of the glucose solution, the FAZ area and perimeter of Group 1 were larger than those of the control group. Al-Sheikh *et al*[32] reported that during the nonproliferative DR period, the VD of the superficial blood vessels of the affected eye was lower than that of the control eye, and the FAZ area of the superficial capillary plexus in the early stage of DR was larger than that of the deep capillary plexus[32]. Moreover, macular ischemia is a typical feature of DR. In patients who have not been diagnosed with diabetes but tend to develop the disease, the FAZ area can be used as a sensitive indicator of microcirculation changes. Relevant studies have confirmed that the area of the FAZ expands as the condition of diabetic patients worsens[33,34], which is consistent with our experimental results. However, compared with those of Group 1, the central VD and PD of Group 2 were greater, and the FAZ area and perimeter were smaller. This may be due to severe insulin resistance in patients with both IFG and abnormal glucose tolerance, which entails an insignificant response to blood sugar fluctuations. Given the effect of diabetes on fundus microcirculation, increased expression of adhesion molecules such as intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 in the retina occurs when blood sugar levels are elevated. These molecules play crucial roles in mediating leukocyte adhesion and infiltration, contributing to local inflammation. This inflammatory response can lead to blood-retinal barrier damage and microvascular endothelial cell injury, causing stenosis, occlusion, and atrophy or degeneration of the capillary lumen. The chronic increase in glucose levels can activate several signaling pathways, including the NF-kB pathway, further amplifying the expression of these adhesion molecules and exacerbating retinal vascular pathology[32]. The inflammatory response under elevated blood sugar conditions causes monocytes and granulocytes to block retinal capillaries[35], which also affects the formation of capillaries. In addition, increases in blood sugar may also destroy the neurovascular self-regulatory mechanism, resulting in a decrease in retinal VD[36]. In fasting patients, the blood glucose level was significantly positively correlated with central PD, indicating that PD may be more sensitive to changes in blood glucose than the VD- and FAZ-associated metrics.

In OCTA imaging, the scan size of the image is inversely proportional to its resolution, implying that the image resolution in the scope of 3 mm × 3 mm is the highest; thus, it was chosen as the scanning scope of this study[37]. Kim *et al*[23] reported that the superficial capillary plexus of the retina was less prone to delamination errors than the deep capillary plexus, the blood VD of the superficial capillary plexus was a sensitive vascular indicator for early DR, and the superficial retinal blood vessels were thicker than the deep ones were[24]. Considering that microvascular changes in early diabetic patients may first appear in the superficial retina[24,38], this study measured the data through OCTA of the superficial capillary plexus of the retina.

This study has the following limitations: (1) The sample size is small, which may affect the representativeness and reliability of the results. Future studies should consider increasing the sample size for more robust data and conclusions; (2) The study was only conducted in the 3 mm × 3 mm area of the superficial retina in the macular region. While this area

is significant for visual function, this limitation may restrict the applicability of the results to larger areas and deeper retinal microcirculation; and (3) Blood glucose levels and microcirculation indices (through OCTA) were measured before and one hour after the OGTT. However, there was no long-term follow-up of the fundus condition of the patients, which may reveal chronic or cumulative changes in microcirculation rather than just immediate responses.

This study demonstrated that a short-term increase in blood glucose had a more significant effect on central retinal microcirculation in patients with either IFG or IGT. Specifically, we found that in the control group, central VD and PD increased significantly one hour after glucose intake. In Group 1, the circularity of the FAZ increased, whereas no significant changes were observed in Group 2. Additionally, under fasting conditions, the FAZ area and perimeter of Group 1 were greater than those of the control group, and Group 2 presented greater central VD and PD and a smaller FAZ area and perimeter than Group 1. These findings suggest that OCTA can be a valuable tool for monitoring retinal microcirculation changes in the macular area of prediabetic patients. This study provides insights into the early alterations in the retinal microvasculature associated with prediabetes, which could help in the early detection, intervention, and prevention of diabetes and DR. Future research should focus on larger sample sizes and long-term follow-up to validate these findings and further explore the utility of OCTA in predicting and managing the progression of diabetes and its complications.

CONCLUSION

This study demonstrated that a short-term increase in blood glucose had a more significant effect on central retinal microcirculation in patients with either IFG or IGT. Specifically, we found that in the control group, central VD and PD increased significantly one hour after glucose intake. In Group 1, the circularity of the FAZ increased, whereas no significant changes were observed in Group 2. Additionally, under fasting conditions, the FAZ area and perimeter of Group 1 were greater than those of the control group, and Group 2 presented greater central VD and PD and a smaller FAZ area and perimeter than Group 1. These findings suggest that OCTA can be a valuable tool for monitoring retinal microcirculation changes in the macular area of prediabetic patients. This study provides insights into the early alterations in the retinal microvasculature associated with prediabetes, which could help in the early detection, intervention, and prevention of diabetes and DR. Future research should focus on larger sample sizes and long-term follow-up to validate these findings and further explore the utility of OCTA in predicting and managing the progression of diabetes and its complications.

ACKNOWLEDGEMENTS

We are indebted to the help and cooperation of the First Affiliated Hospital of Chongqing Medical University, Chongqing Key Laboratory of Ophthalmology, Chongqing Eye Institute, and Endocrinology Laboratory, Chongqing Medical University, Chongqing, China.

FOOTNOTES

Author contributions: Lv BJ and Zuo HJ participated in the data curation, investigation, methodology, writing, and original draft of this article; Li QF, Huang FF, and Zhang T participated in the formal analysis and data curation; Wan WJ was involved in the formal analysis and validation; Ke H participated in the conceptualization, funding acquisition, writing, review and editing, and supervision; Lv BJ and Zuo HJ contributed equally to this work, and Hu K and Wan WJ contributed equally to this work.

Supported by The Project Foundation of Chongqing Science and Technology Commission of China, No. cstc2018jcyjAX0798.

Institutional review board statement: This study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University, with approval No. 2021-648 and an approval date of December 30, 2021.

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Conflict-of-interest statement: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data sharing statement: No additional data are available.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

Country of origin: China

ORCID number: Hang-Jia Zuo 0009-0005-0881-6252; Ke Hu 0000-0002-8055-389X.

S-Editor: Li L
L-Editor: A
P-Editor: Yuan YY

REFERENCES

1 **American Diabetes Association**. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. *Diabetes Care* 2020; **43**: S14-S31 [PMID: 31862745 DOI: 10.2337/dc20-S002]
2 **Saeedi P**, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE, Bright D, Williams R; IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. *Diabetes Res Clin Pract* 2019; **157**: 107843 [PMID: 31518657 DOI: 10.1016/j.diabres.2019.107843]
3 **Xie Z**, Xiao X. Novel biomarkers and therapeutic approaches for diabetic retinopathy and nephropathy: Recent progress and future perspectives. *Front Endocrinol (Lausanne)* 2022; **13**: 1065856 [PMID: 36506068 DOI: 10.3389/fendo.2022.1065856]
4 **Wu Y**, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. *Int J Med Sci* 2014; **11**: 1185-1200 [PMID: 25249787 DOI: 10.7150/ijms.10001]
5 **Wolter JR**. Diabetic retinopathy. *Am J Ophthalmol* 1961; **51**: 1123-1141 [PMID: 13786453 DOI: 10.1016/0002-9394(61)91802-5]
6 **Resnikoff S**, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP, Mariotti SP. Global data on visual impairment in the year 2002. *Bull World Health Organ* 2004; **82**: 844-851 [PMID: 15640920]
7 **Nassif A**, Katoue MG, Wake DJ, George J. Management of Low Density Lipoprotein Cholesterol at a primary care diabetes clinic in Kuwait. *Prim Care Diabetes* 2019; **13**: 259-265 [PMID: 30578166 DOI: 10.1016/j.pcd.2018.11.003]
8 **Alberti KG**, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998; **15**: 539-553 [PMID: 9686693 DOI: 10.1002/(SICI)1096-9136(199807)15:7<539::AID-DIA668>3.0.CO;2-S]
9 **Plummer MP**, Deane AM. Dysglycemia and Glucose Control During Sepsis. *Clin Chest Med* 2016; **37**: 309-319 [PMID: 27229647 DOI: 10.1016/j.ccm.2016.01.010]
10 **Spaide RF**, Klancnik JM Jr, Cooney MJ. Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography. *JAMA Ophthalmol* 2015; **133**: 45-50 [PMID: 25317632 DOI: 10.1001/jamaophthalmol.2014.3616]
11 **de Carlo TE**, Romano A, Waheed NK, Duker JS. A review of optical coherence tomography angiography (OCTA). *Int J Retina Vitreous* 2015; **1**: 5 [PMID: 27847598 DOI: 10.1186/s40942-015-0005-8]
12 **Coscas G**, Lupidi M, Coscas F, Chhablani J, Cagini C. Optical Coherence Tomography Angiography in Healthy Subjects and Diabetic Patients. *Ophthalmologica* 2018; **239**: 61-73 [PMID: 29268269 DOI: 10.1159/000485323]
13 **Tan ACS**, Tan GS, Denniston AK, Keane PA, Ang M, Milea D, Chakravarthy U, Cheung CMG. An overview of the clinical applications of optical coherence tomography angiography. *Eye (Lond)* 2018; **32**: 262-286 [PMID: 28885606 DOI: 10.1038/eye.2017.181]
14 **Karaca I**, Yılmaz SG, Afrashi F, Nalçacı S. Assessment of macular capillary perfusion in patients with inactive Vogt-Koyanagi-Harada disease: an optical coherence tomography angiography study. *Graefes Arch Clin Exp Ophthalmol* 2020; **258**: 1181-1190 [PMID: 32363500 DOI: 10.1007/s00417-020-04676-x]
15 **Yang JY**, Wang Q, Yan YN, Zhou WJ, Wang YX, Wu SL, Yuan MX, Wei WB, Jonas JB. Microvascular retinal changes in pre-clinical diabetic retinopathy as detected by optical coherence tomographic angiography. *Graefes Arch Clin Exp Ophthalmol* 2020; **258**: 513-520 [PMID: 31897704 DOI: 10.1007/s00417-019-04590-x]
16 **Ayhan Z**, Kaya M, Ozturk T, Karti O, Hakan Oner F. Evaluation of Macular Perfusion in Healthy Smokers by Using Optical Coherence Tomography Angiography. *Ophthalmic Surg Lasers Imaging Retina* 2017; **48**: 617-622 [PMID: 28810036 DOI: 10.3928/23258160-20170802-03]
17 **Lee WH**, Park JH, Won Y, Lee MW, Shin YI, Jo YJ, Kim JY. Retinal Microvascular Change in Hypertension as measured by Optical Coherence Tomography Angiography. *Sci Rep* 2019; **9**: 156 [PMID: 30655557 DOI: 10.1038/s41598-018-36474-1]
18 **von Jagow B**, Ohrloff C, Kohnen T. Macular thickness after uneventful cataract surgery determined by optical coherence tomography. *Graefes Arch Clin Exp Ophthalmol* 2007; **245**: 1765-1771 [PMID: 17619896 DOI: 10.1007/s00417-007-0605-6]
19 **Anvari P**, Ashrafkhorasani M, Habibi A, Falavarjani KG. Artifacts in Optical Coherence Tomography Angiography. *J Ophthalmic Vis Res* 2021; **16**: 271-286 [PMID: 34055264 DOI: 10.18502/jovr.v16i2.9091]
20 **Li Rudvan AL**, Can ME, Efe FK, Keskin M, Beyan E. Evaluation of retinal microvascular changes in patients with prediabetes. *Niger J Clin Pract* 2021; **24**: 911-918 [PMID: 34121741 DOI: 10.4103/njcp.njcp_193_20]
21 **Arias JD**, Arango FJ, Parra MM, Sánchez-Ávila RM, Parra-Serrano GA, Hoyos AT, Granados SJ, Viteri EJ, Gaibor-Santos I, Perez Y. Early microvascular changes in patients with prediabetes evaluated by optical coherence tomography angiography. *Ther Adv Ophthalmol* 2021; **13**: 25158414211047020 [PMID: 34708184 DOI: 10.1177/25158414211047020]
22 **Ratra D**, Dalan D, Prakash N, Kaviarasan K, Thanikachalam S, Das UN, Angayarkanni N. Quantitative analysis of retinal microvascular changes in prediabetic and diabetic patients. *Indian J Ophthalmol* 2021; **69**: 3226-3234 [PMID: 34708778 DOI: 10.4103/ijo.IJO_1254_21]
23 **Kim AY**, Chu Z, Shahidzadeh A, Wang RK, Puliafito CA, Kashani AH. Quantifying Microvascular Density and Morphology in Diabetic Retinopathy Using Spectral-Domain Optical Coherence Tomography Angiography. *Invest Ophthalmol Vis Sci* 2016; **57**: OCT362-OCT370 [PMID: 27409494 DOI: 10.1167/iovs.15-18904]
24 **Javed A**, Khanna A, Palmer E, Wilde C, Zaman A, Orr G, Kumudhan D, Lakshmanan A, Panos GD. Optical coherence tomography angiography: a review of the current literature. *J Int Med Res* 2023; **51**: 3000605231187933 [PMID: 37498178 DOI: 10.1177/03000605231187933]

25 **Félétou M**, Vanhoutte PM. Endothelial dysfunction: a multifaceted disorder (The Wiggers Award Lecture). *Am J Physiol Heart Circ Physiol* 2006; **291**: H985-1002 [PMID: 16632549 DOI: 10.1152/ajpheart.00292.2006]

26 **Joussen AM**, Poulaki V, Le ML, Koizumi K, Esser C, Janicki H, Schraermeyer U, Kociok N, Fauser S, Kirchhof B, Kern TS, Adamis AP. A central role for inflammation in the pathogenesis of diabetic retinopathy. *FASEB J* 2004; **18**: 1450-1452 [PMID: 15231732 DOI: 10.1096/fj.03-1476fje]

27 **Catrina SB**, Zheng X. Disturbed hypoxic responses as a pathogenic mechanism of diabetic foot ulcers. *Diabetes Metab Res Rev* 2016; **32** Suppl 1: 179-185 [PMID: 26453314 DOI: 10.1002/dmrr.2742]

28 **Fujii H**, Kawada N; Japan Study Group Of Nafld Jsg-Nafld. The Role of Insulin Resistance and Diabetes in Nonalcoholic Fatty Liver Disease. *Int J Mol Sci* 2020; **21** [PMID: 32485838 DOI: 10.3390/ijms21113863]

29 **Kahn SE**, Prigeon RL, McCulloch DK, Boyko EJ, Bergman RN, Schwartz MW, Neifing JL, Ward WK, Beard JC, Palmer JP. Quantification of the relationship between insulin sensitivity and beta-cell function in human subjects. Evidence for a hyperbolic function. *Diabetes* 1993; **42**: 1663-1672 [PMID: 8405710 DOI: 10.2337/diab.42.11.1663]

30 **Sena CM**, Pereira AM, Seiça R. Endothelial dysfunction - a major mediator of diabetic vascular disease. *Biochim Biophys Acta* 2013; **1832**: 2216-2231 [PMID: 23994612 DOI: 10.1016/j.bbadis.2013.08.006]

31 **Ting DS**, Cheung GC, Wong TY. Diabetic retinopathy: global prevalence, major risk factors, screening practices and public health challenges: a review. *Clin Exp Ophthalmol* 2016; **44**: 260-277 [PMID: 26716602 DOI: 10.1111/ceo.12696]

32 **Al-Sheikh M**, Akil H, Pfau M, Sadda SR. Swept-Source OCT Angiography Imaging of the Foveal Avascular Zone and Macular Capillary Network Density in Diabetic Retinopathy. *Invest Ophthalmol Vis Sci* 2016; **57**: 3907-3913 [PMID: 27472076 DOI: 10.1167/iovs.16-19570]

33 **Simonett JM**, Scarinci F, Picconi F, Giorno P, De Geronimo D, Di Renzo A, Varano M, Frontoni S, Parravano M. Early microvascular retinal changes in optical coherence tomography angiography in patients with type 1 diabetes mellitus. *Acta Ophthalmol* 2017; **95**: e751-e755 [PMID: 28211261 DOI: 10.1111/aos.13404]

34 **de Carlo TE**, Chin AT, Bonini Filho MA, Adhi M, Branchini L, Salz DA, Baumal CR, Crawford C, Reichel E, Witkin AJ, Duker JS, Waheed NK. Detection of microvascular changes in eyes of patients with diabetes but not clinical diabetic retinopathy using optical coherence tomography angiography. *Retina* 2015; **35**: 2364-2370 [PMID: 26469537 DOI: 10.1097/IAE.0000000000000882]

35 **Schröder S**, Palinski W, Schmid-Schönbein GW. Activated monocytes and granulocytes, capillary nonperfusion, and neovascularization in diabetic retinopathy. *Am J Pathol* 1991; **139**: 81-100 [PMID: 1713023]

36 **Abcouwer SF**, Gardner TW. Diabetic retinopathy: loss of neuroretinal adaptation to the diabetic metabolic environment. *Ann N Y Acad Sci* 2014; **1311**: 174-190 [PMID: 24673341 DOI: 10.1111/nyas.12412]

37 **Borrelli E**, Sacconi R, Brambati M, Bandello F, Querques G. In vivo rotational three-dimensional OCTA analysis of microaneurysms in the human diabetic retina. *Sci Rep* 2019; **9**: 16789 [PMID: 31728070 DOI: 10.1038/s41598-019-53357-1]

38 **Toprak I**, Fenkci SM, Fidan Yaylali G, Martin C, Yaylali V. Early retinal neurodegeneration in preclinical diabetic retinopathy: a multifactorial investigation. *Eye (Lond)* 2020; **34**: 1100-1107 [PMID: 31654034 DOI: 10.1038/s41433-019-0646-1]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com