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Original Article

Correlation of glucose and lipid metabolism, renal function and retinopathy in diabetic retinopathy patients using OCTA detection

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Abstract: Objective: To investigate the correlation between glucose and lipid metabolism, renal function, and retinopathy in patients with diabetic retinopathy (DR) based on optical coherence tomography angiography (OCTA). Methods: A total of 584 diabetic patients who underwent treatment at The Second Affiliated Hospital of Dalian Medical University from March 2022 to June 2023 were retrospectively selected as research participants. They were categorized into a NDR group (n=366) and a DR group (n=218) based on the presence or absence of DR. Relevant indexes of glucose and lipid metabolism, renal function, and OCTA findings were collected. Logistic regression analysis was applied to identify the influencing factors of diabetes mellitus complicated with DR. ROC curves were drawn to examine the diagnostic value of the screened influencing factors for diabetes mellitus complicated with DR. Finally, Spearman correlation coefficients were calculated to examine the relevance between influencing factors and the severity of DR Lesions. Results: Logistic regression showed that high levels of angiography 3 × 3 inner vascular density (IVD_33) and angiography 3 × 3 inner perfusion density (IPD_33) were protective factors for diabetes mellitus complicated with DR, and diabetic peridiabetic vascular disease (DPVD), elevated blood urea nitrogen (BUN), and urea levels were risk factors for diabetes mellitus complicated with DR (all $P<0.05$). ROC curve displayed that the areas under the curve (AUC) of IVD_33, DPVD, BUN, IPD_33, and Urea in predicting diabetes mellitus with DR were 0.779, 0.705, 0.621, 0.723, and 0.632, respectively. The AUC of combined prediction with OCTA index was higher than that of combined prediction without OCTA index (0.781 VS 0.84, $P<0.05$). Spearman correlation coefficient displayed that IVD_33 and IPD_33 were negatively correlated with the severity of DR, whereas DPVD and Urea showed a positive correlation ($P<0.05$). Conclusion: Our findings provide valuable insights for the initial clinical assessment of diabetic patients with DR and aid in the early determination of DR severity. Corresponding intervention measures should be formulated as early as possible to remedy patients' outcomes.

Keywords: Diabetic retinopathy, OCTA, glucose and lipid metabolism, renal function, risk factors, correlation

Introduction

Diabetes is a global health concern, projected to impact 642 million people by 2024. Diabetic retinopathy (DR) is a prevalent complication, affecting 1/3 of diabetic patients and standing as the main cause of adult blindness [1]. Early DR manifests with microaneurysm, retinal haemorrhage and hard exudates, which are referred to as non-proliferative diabetic retinopathy (NPDR). Advanced stages, known as proliferative diabetic retinopathy (PDR), involve neovascularization leading to severe visual impairment and irreversible retinal damage [2]. Therefore, early diagnosis and timely intervention are crucial for improving outcomes in DR patients.

Optical coherence tomography angiography (OCTA) is an emerging DR diagnostic technique. Using the principle of three-dimensional imaging, it can not only observe the changes in microvessels but also quantitatively analyze the retinal vascular density and vascular perfusion density. Compared with fluorescence angiography, OCTA offers advantages such as non-invasiveness, high repeatability and superior resolution [3]. At present, there is no specific treatment for DR in clinical practice, posing

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challenges in clinical management. Metabolomics, an emerging research technique for identifying and quantifying metabolites in a system, holds promise in elucidating disease mechanisms and discovering new biomarkers. Several studies [4-6] have shown that glucose and lipid metabolism disorders play an important role in the progression of DR, which has a profound meaning for the discovery of potential target metabolites for DR prevention and personalized treatment. Diabetic kidney disease and DR are both complications caused by diabetic microangiopathy. They have common predisposing factors and pathogenesis. Studies [7-9] have shown that the progression of DR is closely related to the changes in multiple related indicators of renal function. Given this, based on previous studies, this study used OCTA to further analyze the correlation between glucose and lipid metabolism, renal function, and retinopathy in DR patients, aiming to afford a scientific basis for the diagnosis and therapy of DR.

Subjects and methods

Research subjects

A retrospective analysis of 584 diabetic patients who underwent treatment at the Second Affiliated Hospital of Dalian Medical University from March 2022 to June 2023 was conducted. Inclusion criteria: (1) Confirmed diagnosis of diabetes [10]; (2) Age ≥18 years; (3) Availability of complete data required for the study. Exclusion criteria: (1) Presence of primary eye diseases, including glaucoma, cataract, and optic nerve atrophy; (2) Severe opacity of refractive media such as cornea and lens that seriously affecting the fundus examination; (3) Those who had undergone retinal laser photocoagulation or intraocular surgery; (4) Presence of retinal vascular occlusion, ocular ischemic syndrome or other ocular diseases that may change retinal hemodynamics; (5) Patients with serious hepatic and renal insufficiency; (6) Presence of systemic infection. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Dalian Medical University.

DR diagnostic standard

DR severity can be categorized into light, moderate, and severe NPDR and PDR. The diagnosis was based on fundus examination under a mydriasis slit lamp, fundus colour photography and fundus fluorescein angiography. According to the international classification standard [11], mild NPDR: only microaneurysms; moderate NPDR: microaneurysms, but less severe than severe NPDR; severe NPDR: no PDR manifestations, with more than 20 retinal haemorrhages in any quadrant, or more than 2 quadrants of venous beaded changes, or significant retinal microvascular abnormalities in more than 1 quadrant; PDR: obvious neovascularization, retinal haemorrhage or vitreous haemorrhage.

Data collection

General data were gathered from the hospital's electronic information system, including age, sex, body mass index (BMI), underlying diseases, smoking and drinking history, and diabetic complications [diabetic kidney disease (DKD), diabetic peripheral neuropathy (DPN), and diabetic peridiabetic vascular disease (DPVD)]. Lipid and renal function indicators: Within 24 hours of admission, a fasting venous blood sample of 4 mL was collected from the patient and centrifuged at 3000 $r \cdot min^{-1}$. The serum was separated and analyzed using an automated biochemical analyzer (Roche Company, Roche Cobas 8000). Fasting blood glucose (FBG), cholesterol (TC), triglycerides (TG), very low-density lipoprotein (VLDL-C), low-density lipoprotein (LDL-C), creatinine (Scr), and blood urea nitrogen (BUN) were measured using enzymatic methods. Glycated hemoglobin (HbA1c) levels were determined by high-pressure liquid chromatography. A morning clean midstream urine sample of 20 mL was collected for the measurement of creatinine (Ucr) and Urea using enzymatic methods. Glomerular filtration rate (GFR) was calculated using the simplified MDRD formula: GFR=175 × Scr - 1.154 × age - 0.203 (+ female correction factor × 0.742), where Scr was measured in mg/dL and age is in years. Random urine protein quantitative test results were reported as follows: (-): <0.15 g/L; (+): 0.3 g/L; (++): 1 g/L; (+++): 3 g/L; (++++) or more: ≥5 g/L.

OCTA examination

Macular OCTA angiography was obtained using an optical coherence tomography scanner

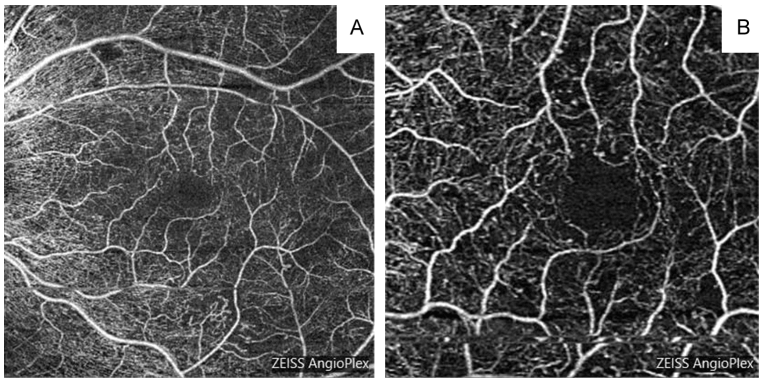

Figure 1. Vascular imaging generated by optical coherence tomography angiography. A: The superficial retinal capillary layer of the macula in non-diabetic retinopathy patients; B: The superficial retinal capillary layer of the macula in diabetic retinopathy patients.

(Zeiss, Criius HD-OCT 5000) using an angio retina mode Angiography 3 × 3 and Angiography 6 × 6, respectively. Angiography 3 × 3 is a circle with a radius of 1.5 mm around the foveal avascular zone (FAZ), the center is a circle with a radius of 0.5 mm around the FAZ, and the inner layer is the complete area excluding the center area. Angiography 6 × 6 is a circle with a radius of 3 mm around the FAZ, the center is a circle with a radius of 0.5 mm around the FAZ, the inner layer is a circle with a radius of 1.5 mm excluding the central area, and the outer layer is a complete area excluding the center and inner area. The linear density and perfusion density of blood vessels in the superficial retinal regions within this range were auto-measurement by the built-in analysis software, including angiography 3 × 3 central vascular density (CVD_33), angiography 3 × 3 inner vascular density (IVD_33), angiography 3 × 3 whole vascular density (WVD_33), angiography 3 × 3 central perfusion density (CPD_33), angiography 3 × 3 inner perfusion density (IPD_33), angiography 3 × 3 whole perfusion density (WPD_33), angiography 6 × 6 central vascular density (CVD_66), angiography 6 × 6 inner vascular density (IVD_66), angiography 6 × 6 whole vascular density (WVD_66), angiography 6 × 6 central perfusion density (CPD_66), angiography 6 × 6 inner perfusion density (IPD_66), and angiography 6 × 6 whole perfusion density (WPD_66). All the above measurements ensured a signal intensity ≥8. Due to the variability in the deep vascular layer, this study only selected the superficial retinal capillary layer of the macular of the retina, as shown in **Figure 1**.

Statistical methods

Data analysis was conducted using SPSS 26.0. Quantitative data fitted the Gaussian distribution were described as mean ± standard deviation ($\bar{x}$ ± s), and an independent sample t-test was adopted. Quantitative data that did not match the Gaussian distribution were expressed as a median and interquartile range [M (Q_{25}, Q_{75})], and a Wilcoxon rank sum test was adopted. Binomial data were described as numbers and percentages [n (%)], and the chi-square test was adopted for comparison. Correlation analysis was performed using Spearman correlation analysis. The influencing factors were examined by the logistic regression. The diagnostic value of influencing factors for DR was examined by the receiver operating characteristic (ROC) curve. Statistical significance was set at $P<0.05$.

Results

General information

A total of 366 patients without DR (NDR group) and 218 patients with DR (DR group) were included in the study. There was no significant difference in age, BMI, history of alcohol consumption, type of diabetes, and presence of hypertension between the two groups (all $P>0.05$). However, statistically significant differences were observed in gender, smoking history, duration of diabetes, diabetic kidney disease, diabetic peripheral neuropathy, and DPVD between the two groups (all $P<0.05$, **Table 1**).

Glycolipid metabolism

There were no statistical differences in FBG, TG and LDL-C levels between the two groups. The levels of HbAlc, TC, and VLDL-C in the DR group were significantly higher than those in the NDR group (all $P<0.05$, **Figure 2**).

Renal function

The GFR level in the DR group was significantly lower than that in the NDR group, while the Ucr,

Table 1. General information of the two groups [n (%)]

	NDR group (n=366)	DR group (n=218)	x^2	*P*
Age			2.507	0.113
<53 years	191 (52.19)	99 (45.41)		
≥53 years	175 (48.81)	119 (54.59)		
Sex			8.776	0.003
Male	232 (63.39)	164 (75.23)		
Female	134 (36.61)	54 (24.77)		
BMI			0.007	0.933
<24.6 kg/m^2	180 (49.18)	108 (49.54)		
≥24.6 kg/m^2	186 (50.82)	110 (50.46)		
Smoking	115 (31.42)	92 (42.20)	6.940	0.008
Drinking	70 (19.13)	48 (22.02)	0.709	0.400
Diabetes type			0.016	0.992
II	347 (94.81)	207 (94.95)		
I	10 (2.73)	6 (2.75)		
Else	9 (2.46)	5 (2.29)		
Diabetes course			19.637	<0.001
<10 years	250 (68.31)	112 (51.38)		
10-20 years	98 (26.78)	80 (36.70)		
>20 years	18 (4.92)	26 (11.93)		
Complicated HTN	174 (47.54)	115 (52.75)	1.484	0.223
Combined with DKD	58 (15.85)	114 (52.29)	87.345	<0.001
Combined with DPN	73 (19.95)	111 (50.92)	60.731	<0.001
Combined with DPVD	144 (39.34)	175 (80.28)	92.346	<0.001

BMI: body mass index; HTN: hypertension; DKD: diabetic kidney disease; DPN: diabetic peripheral neuropathy; DPVD: diabetic peridiabetic vascular disease.

Scr, Urea, and BUN levels in the DR group were all notably higher than those in the NDR group (all *P*<0.05, **Figure 3**). The results of urine protein quantitative test also showed a statistically higher positive rate in the DR group compared to the NDR group (*P*<0.05), as shown in **Table 2**.

OCTA examination

The CVD_33, IVD_33, WVD_33, IPD_33, WPD_33, IVD_66, WVD_66, IPD_66, and WPD_66 in the DR group were all lower than those in the NDR group, and the differences were statistically significant (all *P*<0.05, **Table 3**).

Risk factors of diabetes mellitus complicated with DR

Using the random forest algorithm for indicator selection, the Gini coefficient is represented on the horizontal axis, and the logistic regression equation utilizes the top 10 indicators (**Figure 4**) as independent variables. The assignment of variables is presented in **Table 4**, where a binary variable indicates whether DR is merged (0= no, 1= yes). The logistic analysis results showed that high levels of IVD_33 [OR: 0.085 (0.042-0.172)] and IPD_33 [OR: 0.321 (0.191-0.540)] were protective factors for diabetes mellitus complicated with DR. DPVD [OR: 5.741 (3.375-9.767)], high levels of BUN [OR: 1.279 (1.124-1.455)] and Urea [OR: 1.077 (1.012-1.146)] were risk factors for diabetes mellitus complicated with DR (*P*<0.05, **Table 5**).

ROC curve analysis

The areas under curve (AUC) of IVD_33, DPVD, BUN, IPD_33, and Urea in predicting diabetes with DR were 0.779, 0.705, 0.621, 0.723, and 0.632, respectively, with sensitivities of 60.00%, 78.5%, 36.20%, 68.10%, and 42.20%, and specificities of 82.40%, 60.70%, 84.70%, 65.70%, and 82.00%, respectively. The AUC of combined prediction of DPVD, BUN and Urea (Unite 1) was 0.781, with a sensitivity of 79.4% and a specificity of 67.8%. Adding OCTA indicators (Unite 2) resulted in an AUC of 0.847, with a sensitivity of 84.3% and a specificity of 71.4%. The AUC of Unite 2 was higher than that of Unite 1 (*Z*=4.391, *P*<0.001). See **Figures 5**, **6** and **Table 6**.

Correlation analysis of DR lesion degree

IVD_33 (*r*=-0.306) and IPD_33 (*r*=-0.211) demonstrated a negative correlation with the severity of DR, while DPVD (*r*=0.147) and Urea (*r*=0.162) demonstrated a positive correlation with the severity of DR (*P*<0.05, **Table 7**).

Discussion

At present, the treatment options for diabetic retinopathy (DR) have become more extensive and refined. However, their primary therapeutic

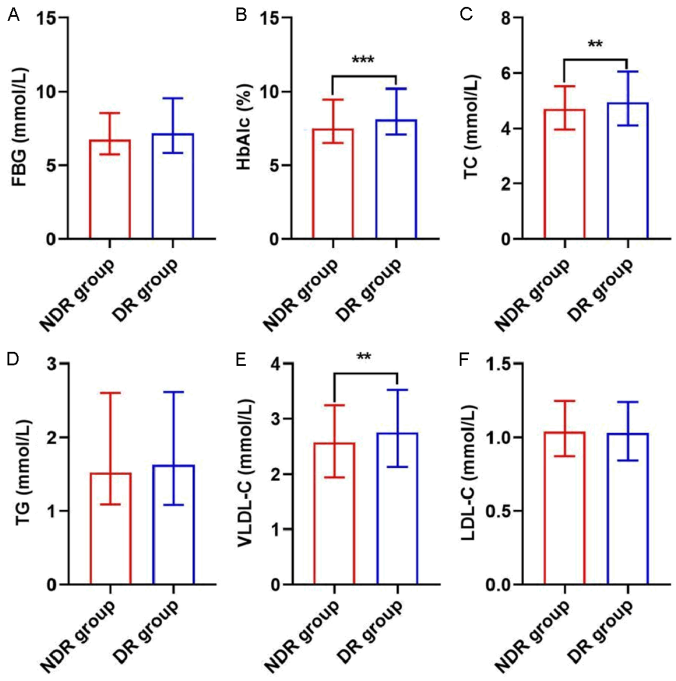

Figure 2. Comparison of glucose and lipid metabolism indexes between the two groups. A: Comparison of FBG levels between the two groups; B: Comparison of HbA1c levels between two groups; C: Comparison of TC levels between the two groups; D: Comparison of TG levels between the two groups; E: Comparison of VLDL-C levels between the two groups; F: Comparison of LDL-C levels between the two groups. FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; TC: cholesterol; TG: triglyceride; VLDL-C: very low-density lipoprotein; LDL-C: low-density lipoprotein; ***: $P<0.001$; **: $P<0.01$.

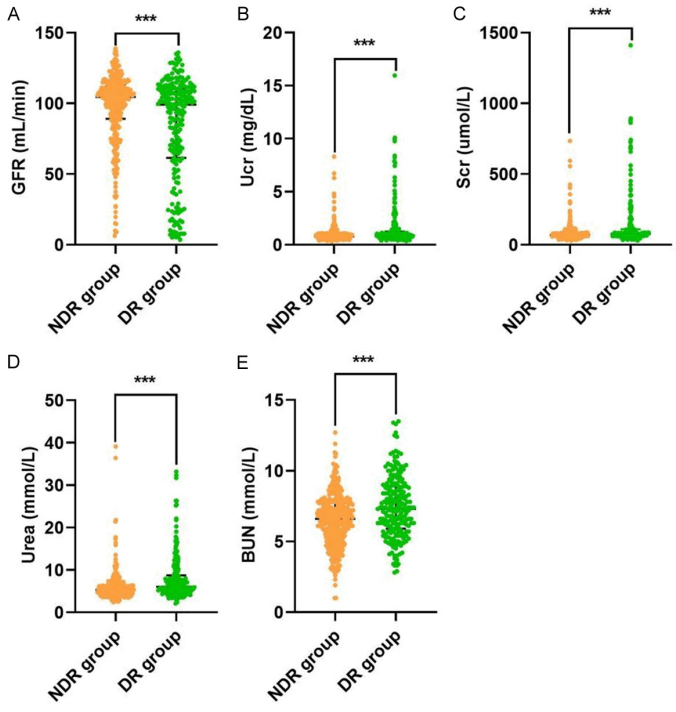

Figure 3. Comparison of renal function indexes between the two groups. A: Comparison of GFR levels between the two groups; B: Comparison of Ucr levels between the two groups; C: Comparison of Scr levels between the two groups; D: Comparison of Urea levels between the two groups; E: Comparison of BUN levels between the two groups. GFR: glomerular filtration rate; Ucr: urine creatinine; Scr: serum creatinine; BUN: blood urea nitrogen; ***: $P<0.001$.

purpose is still limited to delaying or preventing disease progression and retaining its residual function. Therefore, it is imperative to explore biomarkers associated with the progression of DR for early diagnosis and intervention.

Traditional fundus fluorescein angiography (FFA) is considered the gold standard for diagnosing diabetic retinopathy (DR), but it is an invasive procedure that involves contrast agent injection, resulting in longer imaging time and limited to two-dimensional images. The process takes 10-30 minutes and has several limitations in clinical application [12]. FFA primarily examines the superficial blood vessels of the retina, making it challenging to accurately diagnose deep retinal capillaries due to light scattering issues [13]. Furthermore, complications such as contrast agent allergies, nausea, vomiting, and even anaphylactic shock restrict its use among patients with allergies or those requiring repeated examinations. In contrast, optical coherence tomography angiography (OCTA) calculates changes and flow of red blood cells within the microvascular network of the retina over time. Compared to traditional FFA, OCTA offers numerous advantages. It is non-invasive and does not require contrast agent injections, making it more convenient for dynamic monitoring of diabetic patients. Advances in traditional optical coherence tomography (OCT) have enabled OCTA to produce faster, three-dimensional images of different layers of capillary networks, systematically im-

Table 2. Comparison of random urine qualitative results for proteinuria between the two groups [n (%)]

	(-)	(+)	(++)	(+++)	(++++)	Total positive cases
NDR group (n=366)	310 (84.70)	41 (11.20)	11 (3.01)	4 (1.09)	0	56 (15.30)
DR group (n=218)	113 (51.83)	52 (23.85)	22 (10.09)	25 (11.47)	6 (2.75)	105 (48.17)
x^2						87.764
P						<0.05

Table 3. Comparison of OCTA examination indicators between the two groups

	NDR group (n=366)	DR group (n=218)	*t/Z*	*P*
CVD_33	8.30±2.63	7.46±2.71	3.367	<0.001
IVD_33	20.06±2.01	17.74±2.39	11.824	<0.001
WVD_33	18.73±1.97	16.53±2.39	11.320	<0.001
CPD_33	0.14±0.05	0.13±0.05	1.918	0.056
IPD_33	0.36±0.03	0.33±0.04	9.115	<0.001
WPD_33	0.34±0.03	0.31±0.04	8.667	<0.001
CVD_66	7.03±2.78	6.56±2.86	1.931	0.054
IVD_66	16.73±2.07	15.14±2.67	7.379	<0.001
WVD_66	16.94±1.73	15.49±2.34	7.752	<0.001
CPD_66	0.16 (0.11, 0.20)	0.14 (0.10, 0.19)	1.934	0.053
IPD_66	0.41 (0.37, 0.43)	0.38 (0.33, 0.42)	6.531	<0.001
WPD_66	0.43 (0.40, 0.45)	0.40 (0.36, 0.43)	7.104	<0.001

_33: Angiography 3 × 3; _66: Angiography 6 × 6; CVD: central vascular density; IVD: inner vascular density; WVD: whole vascular density; CPD: central perfusion density; IPD: inner perfusion density; WPD: whole perfusion density.

aging retinal blood vessels at precise axial positions. Additionally, OCTA allows quantitative measurements of size and length of new blood vessels [14]. These advantages have significantly increased the utilization of OCTA in DR diagnosis.

In 2015, Jia et al. [15] pioneered the quantitative analysis of OCTA images in patients with DR. Since then, numerous quantitative indicators pertaining to diabetes and DR have been developed. The linear density of blood flow is to skeletonize the blood vessels and depict each blood vessel line to account for the rate of the linear length to the area in the region. The vascular perfusion density calculates the ratio of the area occupied by the vascular network to the total scanned area. Cao et al. [16] reported a reduction in central foveal vascular density in clinically undiagnosed DR patients compared to healthy individuals, indicating early changes in retinal microvasculature. Sun et al. [17] demonstrated that multiple OCTA parameters, particularly lower deep vascular plexus density and fractal dimension, could predict the incidence of DR in diabetic patients, highlighting the potential of OCTA parameter indicators for early diagnosis of DR. Further studies have shown that as DR progresses, both retinal vascular linear density and vascular perfusion density gradually decline [18-20]. This study found that IVD_33 and IPD_33 were independent influencing factors of DR in diabetic patients, and negatively correlated with the severity of DR lesions. In OCTA imaging, the superficial retinal capillary plexus is situated between the retinal nerve fibers and the ganglion cell layer, while the intermediate and deep capillary plexus are positioned at the inner and outer margins of the inner nuclear layer, respectively [21]. The intermediate capillary plexus, nerve plexus, and deep capillary plexus are structurally similar to nearby small blood vessels and are usually classified as deep capillary complexes [22]. As the severity of the disease progresses, retinal microvascular damage gradually increases, which induces the expression of pro-angiogenic factors, such as VEGF, which further promotes angiogenesis and expands the FZA area, thereby reducing vascular linear density and vascular perfusion density [23]. Therefore, IVD_33 and IPD_33 can reflect the severity of retinal microvascular injury, and then serve as indicators for diagnosing DR and evaluating the severity of the disease.

Peripheral vascular disease (PVD), particularly affecting the tibial artery and the common peroneal artery, is characterized by the formation of atherosclerotic plaques in the lower

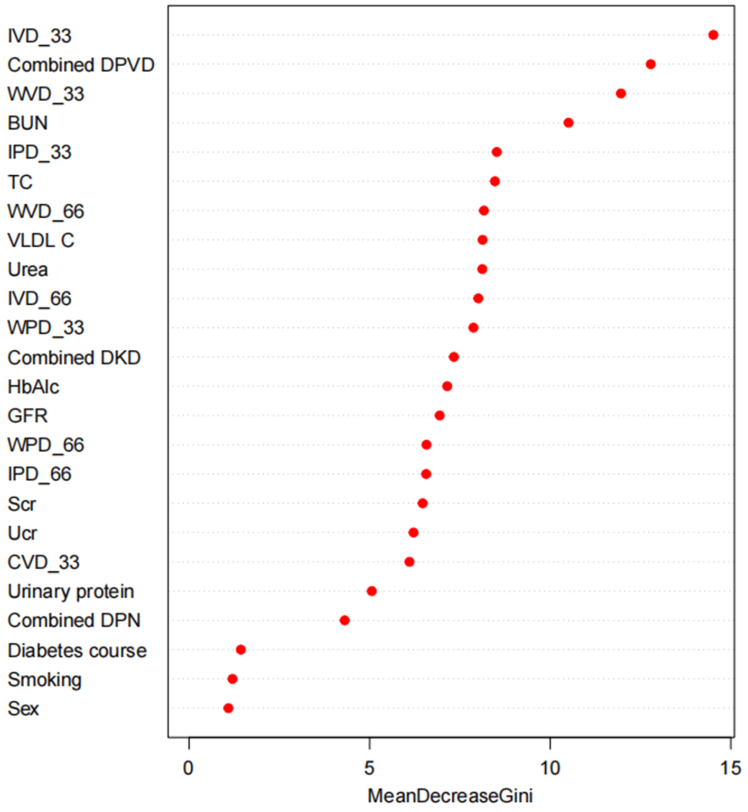

Figure 4. Variable screening. _33: Angiography 3 × 3; _66: Angiography 6 × 6; CVD: central vascular density; IVD: inner vascular density; WVD: whole vascular density; IPD: inner perfusion density; WPD: whole perfusion density; DPVD: diabetic peridiabetic vascular disease; BUN: blood urea nitrogen; TC: cholesterol; VLDL-C: very low-density lipoprotein; DKD: diabetic kidney disease; HbA1c: glycosylated hemoglobin; GFR: glomerular filtration rate; Ucr: urine creatinine; Scr: serum creatinine; DPN: diabetic peripheral neuropathy.

Table 4. The assignment table

Variable	Assignment
IVD_33	Original value input
DPVD	1= yes, 2= no
WVD_33	Original value input
BUN	Original value input
IPD_33	Original value input
TC	Original value input
WVD_66	Original value input
VLDL-C	Original value input
Urea	Original value input
IVD_66	Original value input

_33: Angiography 3 × 3; _66: Angiography 6 × 6; IVD: inner vascular density; WVD: whole vascular density; IPD: inner perfusion density; DPVD: diabetic peridiabetic vascular disease; BUN: blood urea nitrogen; TC: cholesterol; VLDL-C: very low-density lipoprotein.

extremity arterial lumen. This process involves the deposition of lipids and the accumulation of carbohydrates in the affected arterial intima, eventually leading to the proliferation of fibrous tissue and the deposition of calcium. These changes result in arterial stenosis and occlusion, causing chronic ischemia in the lower extremities over time [24]. This study found that DPVD is an influencing factor of diabetic patients with DR, and DPVD is positively correlated with the severity of DR lesions. The reason is that DR and DPVD are common complications of diabetes, which are closely related in epidemiology and have some common pathogenesis. When diabetic patients also have peripheral vascular disease, the overall vascular damage tends to be more severe. This systemic vascular dysfunction can further exacerbate retinal microvascular damage, thereby promoting the development of DR. Moreover, peripheral vascular disease may induce circulatory disorders and local ischemia, rendering the retinal microvasculature more susceptible to damage and destruction [25]. However, the precise mechanism underlying this interrelation remains incompletely understood, necessitating further in-depth research to clarify their interrelationship.

Blood urea nitrogen (BUN) and Urea are principal end products of protein metabolism in the body, excreted via glomerular filtration. They serve as crucial indicators to measure renal function in clinical practice, with elevated levels indicating organic renal dysfunction [26, 27]. This study identified BUA and Urea as the influencing factors for diabetic patients with DR, and Urea was positively correlated with the severity of DR lesions. The correlation between renal function and DR has been extensively

Table 5. The Logistic regression of influencing factors for diabetes mellitus complicated with DR

Independent variable	*β*	*SE*	*Wald* χ^2	*P*	*OR (95% CI)*
IVD_33	-2.466	0.360	46.906	<0.001	0.085 (0.042-0.172)
DPVD	1.748	0.271	41.553	<0.001	5.741 (3.375-9.767)
WVD_33	0.159	0.193	0.686	0.408	1.173 (0.804-1.711)
BUN	0.246	0.066	13.979	<0.001	1.279 (1.124-1.455)
IPD_33	-125.505	17.888	49.228	<0.001	0.321 (0.191-0.540)
TC	-0.038	0.137	0.076	0.783	0.963 (0.736-1.259)
WVD_66	-0.103	0.170	0.364	0.546	0.902 (0.647-1.259)
VLDL-C	0.378	0.203	3.453	0.063	1.459 (0.980-2.174)
Urea	0.074	0.032	5.480	0.019	1.077 (1.012-1.146)
IVD_66	0.025	0.146	0.029	0.864	1.025 (0.770, 1.365)

_33: Angiography 3 × 3; _66: Angiography 6 × 6; IVD: inner vascular density; WVD: whole vascular density; IPD: inner perfusion density; DPVD: diabetic peridiabetic vascular disease; BUN: blood urea nitrogen; TC: cholesterol; VLDL-C: very low-density lipoprotein.

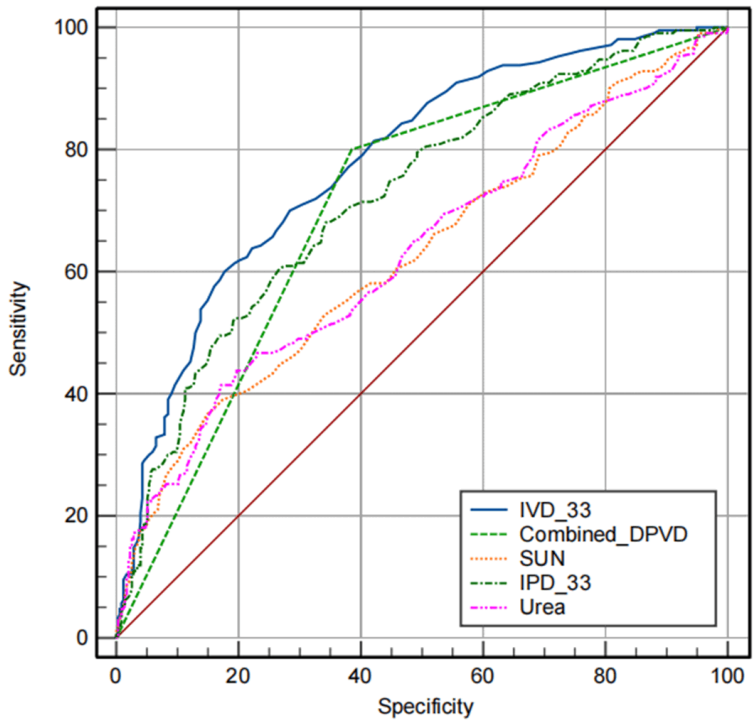

Figure 5. ROC curve analysis of different indicators in predicting diabetes combined with DR. _33: Angiography 3 × 3; IVD: inner vascular density; DPVD: diabetic peridiabetic vascular disease; BUN: blood urea nitrogen; IPD: inner perfusion density.

studied, revealing that as DR severity increases, renal function tends to decline [28]. Furthermore, research has shown that as diabetic nephropathy progresses to the end stage, DR similarly advances from the background stage to proliferative diabetic retinopathy (PDR) [29]. In T2DM, the degree of renal function damage is proportional to the degree of eye damage, with a clear temporal sequence where renal damage typically precedes retinal damage [30]. This can be attributed to the shared embryonic origin, developmental processes, and structural similarities between the kidneys and retina. Both organs feature extensive capillary networks, and early thickening of the basement membrane in these capillaries is a hall mark of diabetic nephropathy and DR. Additionally, similarities exist in the pathways governing glomerular filtration barrier and blood-retina barrier, contributing to common pathogenic mechanisms between diabetic nephropathy and DR [31, 32].

In this study, several predictors including IVD_33, DPVD, BUN, IPD_33, and Urea were analyzed. The combined use of the two OCTA detection indexes, IVD_33 and IPD_33, showed superior predictive capability compared to individual use, indicating that the combined OCTA detection index has a good diagnostic efficiency for diabetes mellitus with DR. This study presents an innovative integration of OCTA detection indicators with renal function indicators as predictive fac-

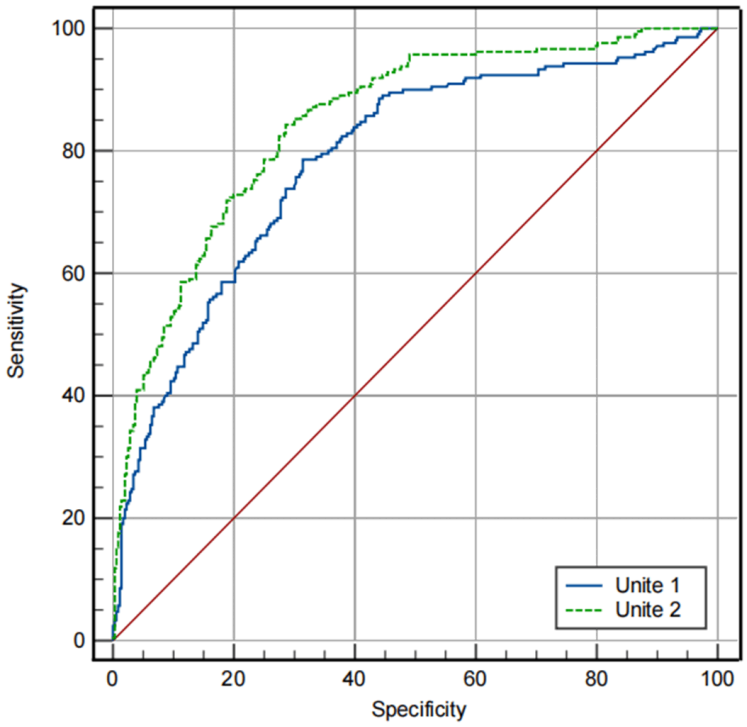

Figure 6. ROC curve analysis for combined prediction of diabetes with DR.

Table 6. The predictive value of different indicators for diabetes mellitus with DR

	AUC	Sensitivity	Specificity	Yoden index	*P*	*95% CI*
IVD_33	0.779	60.00	82.40	18.40	<0.001	0.743-0.813
DPVD	0.705	78.5	60.7	-	<0.001	0.666-0.741
BUN	0.621	36.20	84.70	8.1	<0.001	0.580-0.661
IPD_33	0.723	68.1	65.7	0.354	<0.001	0.685-0.760
Urea	0.632	42.20	82.00	6.83	<0.001	0.592-0.672
Unite 1	0.784	79.4	67.8	-	<0.001	0.748-0.816
Unite 2	0.847	84.30	71.40	-	<0.001	0.814-0.875

_33: Angiography 3 × 3; IVD: inner vascular density; IPD: inner perfusion density; DPVD: diabetic peridiabetic vascular disease; BUN: blood urea nitrogen.

Table 7. Correlation analysis of predictors with DR lesion severity

	DR lesion severity	
	r	*P*
IVD_33	-0.306	<0.001
DPVD	0.147	0.030
BUN	0.007	0.923
IPD_33	-0.211	0.002
Urea	0.162	0.017

_33: Angiography 3 × 3; IVD: inner vascular density; IPD: inner perfusion density; DPVD: diabetic peridiabetic vascular disease; BUN: blood urea nitrogen.

tors for DR. This interdisciplinary and technologically diverse combination, facilitated by the adoption of OCTA technology, broadens research perspectives, enabling comprehensive data analysis and exploring new clinical avenues. These findings offer novel ideas and methodologies for DR research and treatment. However, it is important to note that this retrospective study that relied on a single data source with a limited sample size. Subgroup analysis based on diabetes type was not conducted, which may introduce bias into the results. Future studies should aim to validate these findings using larger sample sizes and prospective follow-up studies.

In summary, our findings provide valuable insights for the initial clinical evaluation of diabetic patients with DR and are conducive to the preliminary judgment of the degree of DR lesions. Corresponding intervention measures should be formulated as early as possible to remedy patients' outcomes.

Disclosure of conflict of interest

None.

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