Risk Factors for Diabetic Retinopathy

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Objective To explore the risk factors for retinopathy (DR) in patients with diabetes mellitus (DM). Methods 1866 patients diagnosed with DM in our hospital from September 2016 to February 2020 were selected as the research subjects. They were divided into non-DR group and DR group according to whether DR occurred. The age, gender, and smoking status of the two groups of patients were retrospectively analyzed. History composition ratio, hypertension composition ratio, body mass index (BMI), DM course and low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), blood urea, blood creatinine, triglycerides (TG), total cholesterol (TC), urinary microalbumin/urinary creatinine ratio (UACR) data, and the receiver operating curve (ROC) analysis of statistically significant continuous variables have diagnostic value for DR in DM patients. Logistic multifactor analysis was performed on the risk factors that may affect the occurrence of DR in DM patients.

Result Among 1866 DM patients, 707 patients developed DR, with an incidence rate of 37.89% (707/1866), and the remaining 1159 patients did not develop DR, accounting for 62.11%. The duration of DM, hypertension composition ratio, HbA1c, anterior chamber depth, axial length, UACR, and serum creatinine levels in the DR group were significantly higher than those in the non-DR group (P <0.05). There were no significant differences in age, gender, BMI, smoking composition ratio, LDL-C, HDL-C, TG, TC and blood urea levels between the DR group and the control group (P > 0.05). The duration of DM, HbA1c, anterior chamber depth, axial length, UACR, and serum creatinine area under the curve (AUC) were 0.877, 0.822, 0.968, 0.824, 0.888, and 0.799 respectively, and the optimal cutoff values were 8 years, 6.84%, and 2.78mm respectively. , 23.32mm, 213.91mg/g, 73.94 μ mol/L. Statistically significant variables such as DM duration, hypertension composition ratio, HbA1c, anterior chamber depth, axial length, UACR, and serum creatinine levels were included in the multifactor

logistic model, and relevant variables were assigned values. The results showed that DM duration, hypertension Blood pressure, HbA1c, ocular axis and UACR level can all be used as independent risk factors for the occurrence of DR in DM patients.

Conclusion The occurrence of DR in DM patients is affected by many factors such as the duration of DM, hypertension, HbA1c, and ocular axis. In the management of this type of patients, especially those with long duration of DM, history of hypertension, short ocular axis, and high HbA1c and UACR levels The risk of DR can be reduced by early identification of high-risk groups and timely and effective control intervention.

Keywords. diabetes; retinopathy; risk factors; prevalence

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease mainly characterized by hyperglycemia, and retinopathy (DR) is one of the most common microvascular complications of the disease [1]. In recent years, with the rapid social and economic development, people's living standards have been significantly improved, and the incidence of DR has shown a significant increasing trend [2]. Vision damage caused by DR will limit patients' activities, cause anxiety and depression, and also reduce their quality of life. The clinical prognosis is not ideal, and it has become the primary cause of blindness in DM patients, which brings great harm to patients and society. brings a heavy burden [2-4]. The clinical symptoms of DR are not significant, and its risks have not received much attention. Therefore, early and accurate and effective fundus examination may delay the progression of DR in DM patients to a certain extent [6]. However, due to factors such as economic level and medical technology, some DM patients fail to undergo timely and effective fundus examination, which greatly increases the risk of DR [7-8]. Therefore, early identification of risk factors for DR in DM patients and timely and effective intervention are of great significance to reduce the risk of DR and improve prognosis. Based on the above background, this study selected 1866 patients diagnosed with DM in our hospital from September 2016 to February 2020 as the research subjects, and further analyzed the risk factors for the

occurrence of DR, in order to provide a reference for scientific prevention of the disease.

1 MATERIALS AND METHODS

1.1 Normal information

1866 patients diagnosed with DM in our hospital from September 2016 to February 2020 were selected as the research subjects, and their clinical data were retrospectively analyzed. There were 1,284 male patients and 582 female patients. The average age was (57.20±12.27) years, the average body mass index (BMI) was (22.74±4.25) kg/m^2 , and the average duration of DM was (7.64±3.11) years. , Glycated hemoglobin (HbA1c) is (7.23±3.11)%, low-density lipoprotein cholesterol (LDL-C) is (3.70±0.43) mmol/L, and high-density lipoprotein cholesterol (HDL-C) is (1.02±0.09) mmol/L, triglyceride (TG) is (1.97±0.24) mmol/L, total cholesterol (TC) is (5.83±0.39) mmol/L, blood urea is (9.28±0.98) mmol/L, and trace amounts of white urine are The protein/urinary creatinine ratio (UACR) was (213.90±42.96) mg/g, and the serum creatinine was (72.70±11.12) μ mol/L.

Inclusion criteria: (1) all meet the diagnostic criteria for DM in the Chinese Medical Association's "Guidelines for the Prevention and Treatment of Type 2 Diabetes (2020 Edition) (Part 1)" [9]; (2) all have complete clinical data; (3) all Non-mydriatic fundus photography examination was performed in our hospital; (4) All were diagnosed for the first time; (5) All were approved by the hospital ethics committee (approval number: FJTCM IACUC2018178). Exclusion criteria: (1) Failure to perform non-mydriatic fundus photography Those who have undergone fundus photography or have blurred fundus images; (2) Those who have undergone vitreoretinal surgeries in the past; (3) Those who are pregnant or lactating; (4) Those with a large number of missing laboratory indicators; (5) Those with malignant tumors ; (6) Those with severe organ dysfunction.

1.2 Method

1.2.1 Grouping and Judgment Criteria

1866 DM patients were divided into non-DR group and DR group according to whether DR occurred. Specific methods: All patients underwent fundus photography examination using a CR-2AF digital fundus camera (purchased from Canon, Japan). Then, in accordance with the relevant specifications, the DM patient's eyes are photographed with the fundus optic papilla and macula as the center. At the same time, the lesion-centered photography needs to be carried out according to the condition of the disease. The obtained fundus images need to be independently read by two highly qualified physicians, and judged according to the diagnostic criteria for DR in the "Chinese Clinical Diagnosis and Treatment Guidelines for Diabetic Retinopathy (2014)" [10] . If there is a disagreement, a more qualified physician can be asked to intervene, which ensures consistency in diagnosis. If DR is not found in both eyes of patients with DM, they are classified into the non-DR group; if DR is found in one or both eyes, the patient is classified into the DR group.

1.2.2 Clinical data collection

General data such as age, gender, smoking history, duration of DM, and history of hypertension were collected for the 1866 DM patients included in the basic information collection form made by our hospital. Information collection personnel need to go through a unified process Professional training, conducted in a question-and-answer format. The body weight and height of DM patients were measured using the SH-201 ultrasonic height and weight measuring instrument (purchased from Zhengzhou Shanghe Electronic Technology Co., Ltd.). BMI (kg/m ^{2}) = body weight (kg)/height (m) ^{2} . (2) Laboratory examination: 5 mL of fasting cubital venous blood was drawn from DM patients in the early morning, and the blood samples were centrifuged in a GL0650R desktop high-speed and low-temperature centrifuge (Beijing Puma Precision Medical Technology Co., Ltd.) at a speed of 3000 r//min. , take the upper serum. The levels of LDL-C, HDL-C, TG, TC, blood urea and blood creatinine in DM patients were measured by DP-180 fully automatic biochemical analyzer (purchased from Guangzhou Dongtang Electronic Technology Co., Ltd.). HbA1c levels in DM patients were measured by HLC-723G11

glycosylated hemoglobin analyzer (purchased from Shanghai Tosoh Biotechnology Co., Ltd.). (3) Ophthalmic examination: Measure the axial length and anterior chamber depth of patients with DM through non-contact tonometer.

1.3 Observation indicators

(1) Calculate the incidence of DR in patients with DM; (2) Compare the age, gender, smoking history composition ratio, hypertension composition ratio, BMI, DM course, LDL-C, HDL-C, TG, TC, blood urea and blood creatinine levels and other data; (3) analyze the diagnostic value of various risk factors for the occurrence of DR in DM patients; (4) analyze the independent risk factors that affect the occurrence of DR in DM patients.

1.4 Statistical methods

Data analysis was processed by the SPSS 21.0 software package. Count data were expressed by n (%), and pairwise comparisons were made by the x^2 test. Measurement data were expressed by ($\bar{x} \pm s$), and pairwise comparisons were made by the independent sample *t* test. The diagnostic value of various risk factors for DR in DM patients was analyzed through the receiver operating curve (ROC). Logistic multifactor analysis was performed on the risk factors that may affect the occurrence of DR in DM patients. P <0.05 means the difference is statistically significant.

2 RESULTS

2.1 Analysis of the occurrence of DR in DM patients

Among 1866 DM patients, 707 patients developed DR, with an incidence rate of 37.89% (707/1866), and the remaining 1159 patients did not develop DR, accounting for 62.11%. see picture 1.

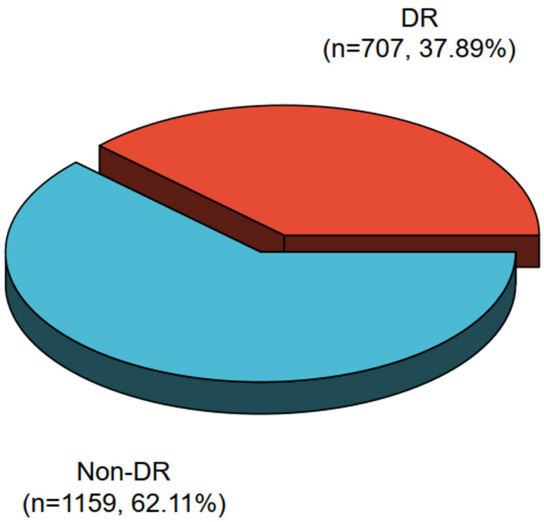

Figure 1 Three-dimensional pie chart of the occurrence of DR in DM patients

2.2 Analysis of clinical data of two groups

The duration of DM, hypertension composition ratio, HbA1c, anterior chamber depth, axial length, UACR, and serum creatinine levels in the DR group were significantly higher than those in the non-DR group (P <0.05). There were no significant differences in age, gender, BMI, smoking composition ratio, LDL-C, HDL-C, TG, TC and blood urea levels between the DR group and the control group (P > 0.05). See Table 1.

Table 1 General data analysis of the two groups [($\bar{x} \pm s$), n(%)]

clinical information	Non-DR group (n= 1159)	DR group (n= 707)	t / x^2	P
Age	57.18±12.31	57.23±12.19	0.049	0.961
gender			3.615	0.057
Male	752 (64.88)	489 (69.17)		
Female	407 (35.12)	218 (30.83)		
BMI (kg/m ^{2})	22.70±4.29	22.81±4.20	0.540	0.589
Duration of DM (years)	6.05±2.01	10.21±3.60	28.839	0.000
Smoking history			0.125	0.723
Have	378 (32.61)	225 (31.82)		
None	781 (67.39)	482 (68.18)		
Hypertension			13.357	0.000
Have	898 (77.48)	597 (84.44)		

None	261 (22.52)	110 (15.56)		
HbA1c (%)	7.75±1.01	6.45±0.90	25.747	0.000
LDL-C (mmol/L)	3.68±0.42	3.65±0.44	1.521	0.128
HDL-C (mmol/L)	1.02±0.09	1.03±0.08	0.913	0.361
TG (mmol/L)	1.97±0.25	1.98±0.22	0.913	0.364
TC (mmol/L)	5.84±0.39	5.82±0.38	1.111	0.267
Anterior chamber depth (mm)	3.10±0.25	2.60±0.12	14.465	0.000
Eye axis (mm)	24.23±1.17	23.44±1.52	11.802	0.000
Blood urea (mmol/L)	9.28±0.98	9.27±0.97	0.211	0.833
UACR（mg/g）	191.10±15.19	251.30±46.55	33.324	0.000
Serum Cr (μ mol/L)	67.82±3.59	80.70±14.22	23.635	0.000

2.3 ROC curve analysis

The duration of DM, HbA1c, anterior chamber depth, axial length, UACR, and serum creatinine area under the curve (AUC) were 0.877, 0.822, 0.968, 0.824, 0.888, and 0.799 respectively, and the optimal cutoff values were 8 years, 6.84%, and 2.78mm respectively. , 23.32mm, 213.91mg/g, 73.94 μ mol/L. See Table 2 Figure 2

Table 2 ROC curve analysis

index	AUC	SE	95%CI	*P*	optimal cutoff value	Sensitivity (%)	Specificity (%)
DM course	0.877	0.009	0.960~0.893	0.000	≤8	89.10	71.10
HbA1c	0.822	0.011	0.802~0.840	0.000	>6.84	79.98	68.65
Anterior chamber depth	0.968	0.005	0.958~0.976	0.000	>2.78	89.94	94.72
eye axis	0.824	0.011	0.804~0.842	0.000	＞23.32	79.98	72.61
UACR	0.888	0.011	0.871~0.903	0.000	≤213.91	94.27	80.20
Serum creatinine	0.799	0.014	0.779~0.819	0.000	≤73.94	95.77	68.65

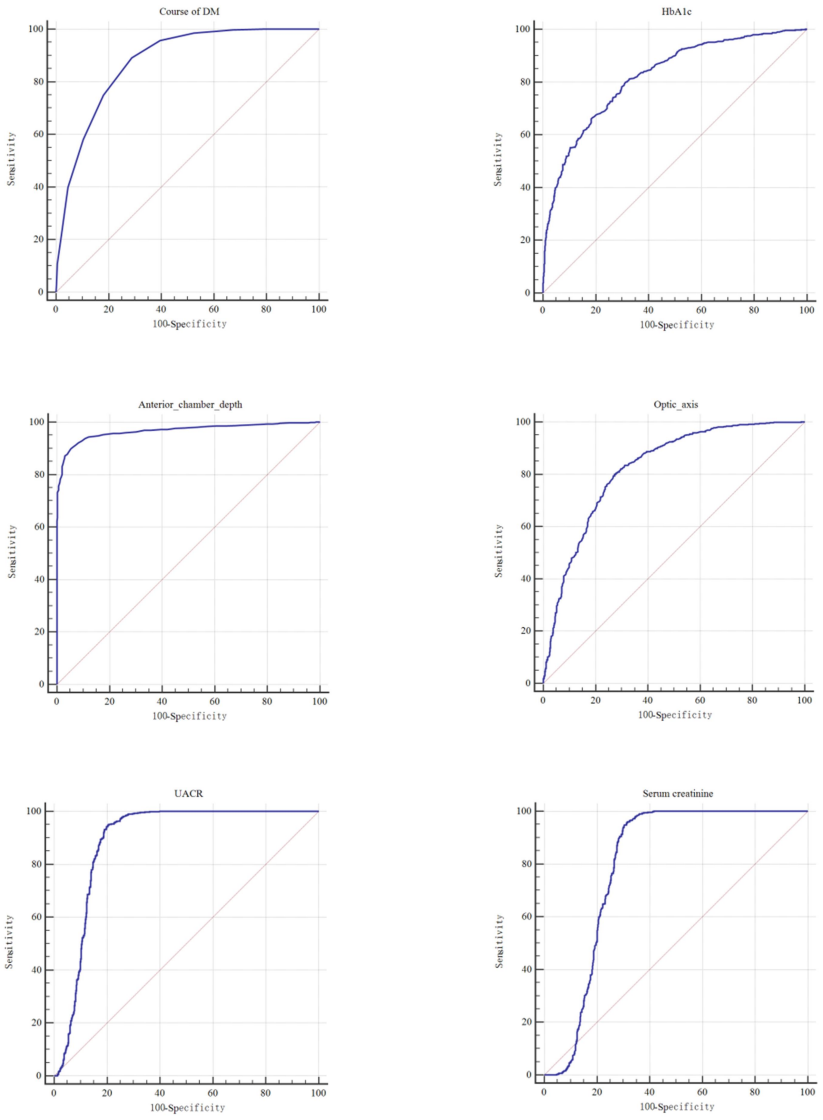

Figure 2 ROC curve analysis

2.4 Variable assignment

Statistically significant variables in Table 1, such as DM duration, hypertension constituent ratio, HbA1c, anterior chamber depth, axial length, UACR, and serum creatinine levels, were included in the multifactor logistic model, and relevant variables were assigned values. See Table 3 for assignment information.

Table 3 Variable assignment

variable	Assignment
DM course	⩽8 years=0, >8 years=1

hypertension	None=0, Yes=1
HbA1c	≤6.84 % =0, >6.84 % =1
Anterior chamber depth	≤2.78mm=0，＞2.78mm=1
eye axis	＞23.32mm=0，≤23.32mm=1，
UACR	≤213.91 mg/g =0, >213.91 mg/g =1
Serum creatinine	≤73.94 μ mol/L =0, >73.94 μ mol/L =1

Logistic multifactor analysis affecting the occurrence of DR in DM patients

Logistic multifactor analysis results showed that the duration of DM, hypertension, HbA1c, axial length, and UACR level can be used as independent risk factors for the occurrence of DR in DM patients. See Table 4.

Table 4 Logistic multifactor analysis affecting the occurrence of DR in DM patients

variable	*β*	*SE* value	*Wald* value	*P* value	*OR* value	95% *CI*
DM course	0.95 4	0.312	9.800	0.000	2.596	1.659~3.120
hypertension	0.503	0.301	6.656	0.037	1.654	1.156~2.102
HbA1c	0.640	0.295	7.354	0.008	1.897	1.563~2.596
Anterior chamber depth	0.210	0.225	4.148	0.096	1.234	0.956~1.369
eye axis	0.742	0.352	5.989	0.043	2.101	1.967~3.154
UACR	0.37 8	0.244	6.349	0.040	1.459	0.697~1.598
Serum creatinine	0.529	0.352	4.237	0.092	1.698	0.959~1.775

3 DSICUSSION

DM is caused by the combined effect of genetic factors and environmental factors. In these patients, the body's insulin is insufficient, which in turn leads to reduced glucose uptake, eventually leading to DM [11]. DR is caused by changes in

retinal blood vessels caused by abnormal insulin metabolism in the body, resulting in exudation and edema in the blood vessel walls, the formation of new blood vessels and proliferative membranes, which ultimately leads to visual dysfunction and impaired eye nutrition. It is a serious complication in patients with DM [12]. DR brings a huge threat to people's lives. It can cause vision loss and blurred vision in patients. In severe cases, it can even lead to retinal detachment and blindness [13-14]. However, due to factors such as economic level and medical technology, some DM patients fail to undergo timely and effective fundus examination, which greatly increases the risk of DR. Therefore, early identification of risk factors for DR in DM patients and timely and effective intervention are of great significance to reduce the risk of DR and improve prognosis. Based on the above background, this study selected patients diagnosed with DM in our hospital as the research subjects, and further analyzed the risk factors for the occurrence of DR, in order to provide a reference for scientific prevention of the disease.

1866 DM patients included in this study , 707 patients developed DR, with an incidence rate of 37.89% (707/1866), and the remaining 1159 patients did not develop DR, accounting for 62.11%. Patients with DM were divided into DR group and non-DR group according to whether DR occurred, and their clinical data were comparatively analyzed. The results showed that in the DR group, the duration of DM, hypertension composition ratio, HbA1c, anterior chamber depth, axial length, UACR , blood The creatinine level was significantly increased compared with the non-DR group (P <0.05). Previous studies have shown that the course of DM can be used as an independent risk factor for the occurrence of DR, and the two are significantly positively correlated. The longer the course of the disease, the higher the degree of damage to the fundus structure and function of the patient, and the greater the risk of DR [15-17]. Both DM and hypertension can lead to microvascular disease. There have been many reports confirming that hypertension is related to the occurrence of DR, especially in patients with elevated systolic blood pressure. If the patient's blood pressure is controlled and intervened, the blood pressure can be reduced by 10mmHg,

DR The risk of occurrence also decreases, about 34% [18-20]. Pathological changes will occur in the blood vessels of patients with hypertension, which can cause retinal ischemia and hypoxia, thereby causing hemangiomas. In addition, retinal blood vessels are in a state of continuous hyperperfusion, which can lead to endothelial cell destruction and ultimately lead to an exacerbation of retinal lesions [21-22]. Excessive HbA1c level can be used as an independent risk factor for DR. As a product of non-enzymatic protein glycation reaction, its formation is slow, continuous and irreversible. The level of HbA1c in the body is closely related to the contact time between blood sugar and hemoglobin and blood sugar concentration, and changes in its level can reflect the recent blood sugar control in DM patients [23-25]. Retinal blood flow in patients with long axial length is reduced, which is beneficial to improving blood vessel wall leakage and retinal ischemia, greatly reducing the risk of occurrence and progression of DR [26]. In patients with long axial length, the thickness of the retina and choroid will be reduced, and the metabolic rate and oxygen consumption of the former will be reduced, which can effectively reduce the massive secretion of inflammatory mediators caused by hypoxia [27]. In addition, patients with longer axial length, especially those with pathological myopia, experience vitreous liquefaction and posterior vitreous detachment earlier, which results in the lack of scaffolds required for neovascular proliferation in the vitreous, which is beneficial to delaying the progression of DR [28]. Excessive UACR levels can reflect endothelial dysfunction. In addition, it plays a vital role in the process of retinal microvascular disease. It has important diagnostic value in determining the occurrence of DR in patients with type 2 DM, and its level is positively correlated with the incidence of the disease. This is because sustained high levels of blood sugar can lead to metabolic abnormalities, aggravation of oxidative stress, secretion of a large amount of cytokines, and ultimately damage to the blood-retinal barrier. Therefore, if the UACR level is found to be too high, timely fundus examination is required. Exclude DR [29-30].

This study used the ROC curve to analyze the diagnostic value of statistically

significant continuous variables for DR in DM patients. The results showed that the duration of DM, HbA1c , anterior chamber depth, axial length, UACR, and serum creatinine AUC were 0.877, 0.822, and 0.968 respectively. ,0.824,0.888,0.799, and the optimal cutoff values are 8 years, 6.84%, 2.78mm, 23.32mm, 213.91mg/g, and 73.94 μ mol/L respectively. Statistically significant variables such as DM duration, hypertension composition ratio, HbA1c, anterior chamber depth, axial length, and UACR level were included into the multifactor logistic model, and relevant variables were assigned values. The results showed that DM duration, hypertension, HbA1c , ocular axis , UACR, and serum creatinine levels can all be used as independent risk factors for the occurrence of DR in DM patients.

In general, the occurrence of DR in DM patients is affected by multiple factors such as the duration of DM, hypertension, HbA1c, and eye axis. In the management of this type of patients, especially long duration of DM, a history of hypertension, short eye axis, and HbA1c And people with high UACR levels can reduce the risk of DR by early identification of high-risk groups and timely and effective control intervention. This study has its limitations. The samples are all from the same hospital and are relatively single. The results and results obtained can provide certain clues to clinical disease occurrence. However, whether it is suitable for disease screening among the general public remains to be conducted in multi-center studies. Further verification will provide new ideas for early prevention and treatment of DR patients, and provide theoretical support for building a suitable work model for preventing blindness.

Data Availability

The experimental data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declared that they have no conflicts of interest regarding this work.

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