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Original Article

Short-term glycemic control improves macular microvascular parameters in type 2 diabetic patients without diabetic retinopathy

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Abstract: Objective: To explore the effects of short-term intensive glycemic control on macular microvascular parameters in patients with type 2 diabetes mellitus (T2DM) without diabetic retinopathy (DR), and to develop a risk predictive model for poor glycemic control. Methods: Clinical data of 320 T2DM patients without DR (Mar 2021-Sep 2024) were retrospectively collected. The cohort was randomly allocated in a 7:3 ratio into a training set (n=224) and a validation set (n=96). Within each dataset, patients were further divided into an intensive glycemic control group and a conventional control group. Macular microvascular parameters were assessed at baseline and 14 days after treatment, with a 3-month follow-up for glycemic control status. Multivariate logistic regression was used to identify independent risk factors for poor glycemic control and to establish a predictive model, which was verified by receiver operating characteristic (ROC) curve analysis. Results: After 14 days of treatment, the intensive group exhibited significantly reduced foveal avascular zone (FAZ) and retinal thickness (RT), as well as increased macular capillary density (MCD), compared with the control group (all $P<0.001$). The incidence of poor glycemic control was significantly lower in the intensive group than the control group (9.7% vs. 37.0%; $P<0.001$). FAZ, MCD, RT and HbA1c were identified as independent risk factors for poor glycemic control. The combined predictive model achieved an area under ROC curve (AUC) of 0.905 in the training set and 0.960 in the validation set, outperforming individual parameters. Conclusion: Short-term intensive glycemic control improves macular microvascular perfusion in T2DM patients without DR. The combined predictive model demonstrates stable and high diagnostic performance for identifying patients at risk of poor glycemic control.

Keywords: Short-term blood glucose control, diabetic retinopathy, macular microvascular parameters, foveal avascular zone, capillary density

Introduction

Type 2 difabetes mellitus (T2DM), accounting for over 90% of global diabetes cases, is a chronic metabolic disorder characterized by persistent hyperglycemia secondary to insulin secretory dysfunction, insulin resistance, and aberrant lipid and protein metabolism, posing a substantial threat to patients' long-term survival and quality of life [1, 2]. Diabetic retinopathy (DR), the most prevalent microvascular complication of T2DM, remains a leading cause of irreversible vision impairment and blindness worldwide, primarily driven by progressive retinal microcirculatory dysfunction [3]. As the anatomical and functional center of human central vision, the structural integrity of the macular microvascular network plays a pivotal role in maintaining visual acuity and visual function in diabetic patients [4]. Accumulating clinical evidence has demonstrated that subclinical microvascular impairment may be present in diabetic patients even before the onset of clinically evident DR, and these early microvascular alterations are closely associated with long-term glycemic control status [5]. Therefore, timely and optimized glycemic control at the pre-DR stage is critical for preventing or delaying the progression of subclinical macular microvascular damage and subsequent vision loss in patients with T2DM.

In the clinical management of T2DM, long-term oral hypoglycemic therapy remains the cornerstone of treatment [6]. Although this strategy is effective in maintaining glycemic targets and

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reducing the risk of chronic complications, its clinical utility is limited by adverse events such as hypoglycemia, weight gain, and gastrointestinal intolerance, which may compromise treatment adherence and long-term outcomes [7]. Short-term intensive insulin pump therapy, including continuous subcutaneous insulin infusion (CSII), has been widely adopted in clinical practice as an optimized glycemic control strategy due to its ability to reduce glycemic variability and lower the risk of hypoglycemic events [8]. However, existing studies have predominantly focused on the effects of hypoglycemic control strategies on fundus lesion progression in patients with confirmed DR. Limited evidence is available regarding the dynamic effects of different short-term glycemic control regimens on macular microvascular parameters in T2DM patients without DR, and the association between macular microvascular alterations and subsequent glycemic control outcomes remains insufficiently elucidated.

In this context, this retrospective study aimed to investigate the dynamic effects of short-term intensive glycemic control on macular microvascular parameters in T2DM patients without DR, to clarify the correlation between macular microvascular indicators and the risk of poor glycemic control, and to develop and validate a risk predictive model for poor glycemic control based on these noninvasive microvascular parameters. Our findings are expected to provide an objective and quantitative basis for the early identification of T2DM patients at high risk of poor glycemic control, optimization of individualized hypoglycemic management strategies, and a shift toward earlier prevention of DR in clinical practice.

Materials and methods

Patients' selection

Clinical data of 368 T2DM patients treated in the Departments of Endocrinology and Ophthalmology of Xi'an People's Hospital between March 2021 and September 2024 were retrospectively collected. Inclusion criteria: (1) diagnosis of T2DM according to established clinical criteria; (2) absence of diabetic retinopathy (DR, ETDRS grade 0), confirmed by fundus photography and optical coherence tomography angiography (OCTA); (3) age between 18 and 80 years; (4) completion of at least 14 days of standardized hypoglycemic treatment and 3 months of regular follow-up; (5) availability of high-quality OCTA images of the macular region suitable for accurate measurement of foveal avascular zone (FAZ), macular capillary density (MCD), retinal thickness (RT), and other microvascular parameters; (6) complete clinical data, including baseline characteristics, glycemic indices, imaging data, and follow-up records. Exclusion criteria: (1) presence of any degree of diabetic retinopathy (mild non-proliferative DR or above); (2) coexisting retinal diseases, including age-related macular degeneration, retinal vein occlusion, uveitis, glaucoma, or high myopia retinopathy; (3) history of ocular surgery, ocular trauma, or severe refractive media opacity affecting image quality; (4) severe systemic diseases, including cardiac, hepatic, or renal insufficiency, malignant tumors, hematological diseases, or autoimmune diseases; (5) pregnancy or lactation; (6) poor adherence to insulin treatment, loss to follow-up, or missing key data; and (7) other factors potentially affecting glycemic control or macular microvascular status.

The flowchart of participant selection is illustrated in **Figure 1**. A total of 320 eligible patients were included and randomly allocated into a training set (n=224) and a validation set (n=96) at a ratio of 7:3. Within each dataset, patients were further divided into a control group (conventional subcutaneous insulin therapy) and an observation group (short-term intensive glycemic control) according to their glycemic management strategy. Specifically, the training set comprised 100 patients in the control group and 124 in the observation group, while the validation set included 46 and 50 patients, respectively. This study was approved by the Ethics Committee of Xi'an People's Hospital (Xi'an Fourth Hospital). All procedures were conducted in accordance with the Declaration of Helsinki.

Data extraction

Both groups received standardized diabetes education, including dietary guidance, exercise recommendations, and training in self-monitoring of blood glucose. Patients in both groups received treatment for 14 consecutive days.

Patients in the control group received conventional subcutaneous insulin therapy. Insulin

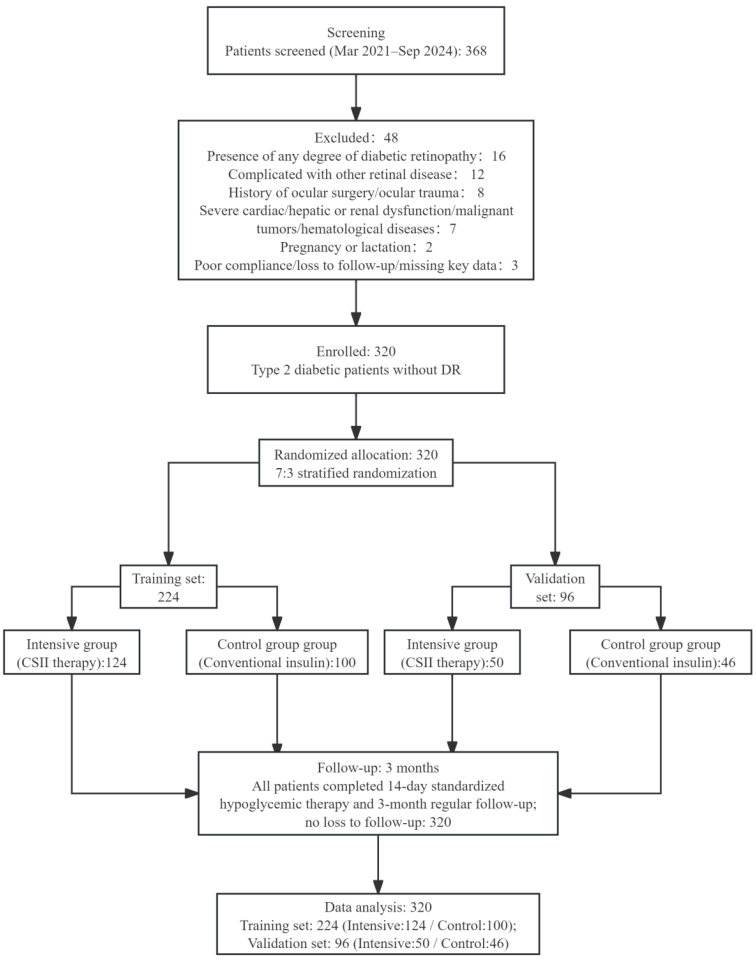


Figure 1. Flowchart for patient selection.

aspart injection (approval number: S20153001, 3 mL: 300 U) was administered subcutaneously before each of the three daily meals at an initial dose of 0.1 U/(kg·d). In addition, insulin glargine injection (approval number: S20201000, 3 mL: 300 U) was injected subcutaneously once daily before bedtime at an initial dose of 0.2 U/(kg·d). Blood glucose levels were closely monitored throughout treatment, and insulin dosages were adjusted individually according to glycemic response.

Patients in the observation group received short-term intensive glycemic control using continuous subcutaneous insulin infusion (CSII) with insulin aspart injection (approval number: S20200008, 3 mL: 300 U). A subcutaneous indwelling catheter was inserted into the abdominal wall as the infusion site. The initial total daily insulin dose was 0.3 U/kg, equally divided into two portions. One portion was delivered as a continuous basal infusion via the insulin pump; the other portion was equally subdivided and injected as bolus doses before breakfast, lunch, and dinner, respectively.

Data collection

Primary indicators

Incidence of poor glycemic control events: The occurrence of poor glycemic control events was recorded during the 3-month follow-up period, and the incidence was calculated. Poor glycemic control was defined as the presence of any of the following conditions: persistent fasting blood glucose (FBG) >7.0 mmol/L or 2-hour postprandial blood glucose (2hPBG) >10.0 mmol/L; glycated hemoglobin (HbA1c) >7.5%; occurrence of hypoglycemia (blood glucose <3.9 mmol/L) on two or more occasions; requirement for adjustment of the treatment regimen due to marked glycemic fluctuations.

Adverse reactions: The occurrence of adverse reactions in both groups was counted, including constipation, gastrointestinal reactions, urinary tract infections, and hypoglycemia.

Secondary indicators

Baseline data: The collected data included sex, age, disease duration, body mass index (BMI), history of hypertension, FBG, 2hBG, and HbA1c.

Macular microvascular parameters: Parameters, including FAZ area, MCD, and RT, were collected from both groups at baseline and 14 days after treatment.

Statistical analysis

Statistical analyses were performed using SPSS 26.0 and R 4.2.0 software. Continuous variables were expressed as mean ± standard deviation (SD). Between-group comparisons were performed using the independent-samples t-test, while within-group comparisons

Table 1. Baseline data of the training and validation sets [n (%), $\bar{x}$±sd]

	Training set (n=224)	Validation set (n=96)	t/χ^2	*P*
Age (yr)	55.57±2.53	55.61±2.53	0.130	0.897
Gender			0.010	0.922
Male	118 (52.7)	50 (52.1)		
Female	106 (47.3)	46 (47.9)		
Disease duration (yr)	5.18±0.65	5.20±0.66	0.251	0.802
BMI (kg/m^2)	22.81±1.61	22.76±1.54	0.258	0.797
Hypertension			1.200	0.273
Yes	130 (58.0)	62 (64.6)		
No	94 (42.0)	34 (35.4)		
Smoking history			0.053	0.818
Yes	144 (64.3)	63 (65.6)		
No	80 (35.7)	33 (34.4)		
Drinking history			0.101	0.751
Yes	121 (54.0)	50 (52.1)		
No	103 (46.0)	46 (47.9)		
FBG (mmol/L)	10.60±1.62	10.62±1.63	0.101	0.920
2hBG (mmol/L)	17.58±1.50	17.55±1.45	0.166	0.867
HbA1c (%)	7.99±0.58	7.96±0.56	0.204	0.839

Notes: BMI: body mass index; FBG: fasting blood glucose; 2hBG: 2-hour postprandial blood glucose; HbA1c: glycated hemoglobin.

Table 2. Baseline data of the observation and control group in the training set [n (%), $\bar{x}$±sd]

	Observation group (n=124)	Control group (n=100)	t/χ^2	*P*
Age (yr)	55.60±2.76	55.54±2.22	0.176	0.860
Gender			0.799	0.371
Male	62 (50.0)	56 (56.0)		
Female	62 (50.0)	44 (44.0)		
Disease duration (yr)	5.17±0.72	5.20±0.56	0.342	0.733
BMI (kg/m^2)	22.58±2.49	22.55±2.52	0.113	0.910
Hypertension			0.412	0.521
Yes	70 (55.8)	60 (60.0)		
No	54 (44.2)	40 (40.0)		
Smoking history			0.040	0.841
Yes	79 (63.7)	65 (65.0)		
No	45 (36.3)	35 (35.0)		
Drinking history			0.647	0.421
Yes	64 (51.6)	57 (57.0)		
No	60 (49.4)	43 (43.0)		
FBG (mmol/L)	10.59±1.79	10.62±1.40	0.137	0.891
2hBG (mmol/L)	17.57±1.65	17.58±1.29	0.055	0.956
HbA1c (%)	7.95±0.54	8.04±0.62	1.418	0.158

Notes: BMI: body mass index; FBG: fasting blood glucose; 2hBG: 2-hour postprandial blood glucose; HbA1c: glycated hemoglobin.

before and after treatment were analyzed using paired-samples t-test. Categorical variables were expressed as rates (%) and compared using the chi-square (χ^2) test.

Variables with P<0.1 in univariate analysis were entered into multivariate logistic regression to identify independent risk factors for poor glycemic control. Optimal cutoff values for continuous variables were determined using the maximum Youden index from receiver operating characteristic (ROC) curve analysis, and variables were subsequently dichotomized for model construction. The predictive performance of the model was evaluated using ROC curve analysis, and the area under the curve (AUC), sensitivity, and specificity were calculated. A two-sided *P* value of <0.05 was considered statistically significant.

Results

Baseline characteristics of the training and validation sets

There were no significant differences in baseline characteristics, including sex, age, disease duration, BMI, hypertension history, FBG, 2hBG, and HbA1c, between the training set and the validation set (all P>0.05, **Table 1**).

Baseline characteristics of the control and observation groups in the training cohort

No significant differences were observed in baseline characteristics, including sex, age, disease duration, BMI, hypertension history, FBG, 2hBG, or HbA1c between the observation and control groups (all P>0.05, **Table 2**).

Table 3. Comparison of macular microvascular parameters between the observation and control groups before and after treatment ($\bar{x}$±sd)

Groups	n	FAZ (mm^2)		t	P	MCD (mm/mm^2)		t	P	RT (μm)		t	P
		Before treatment	14 d after treatment			Before treatment	14 d after treatment			Before treatment	14 d after treatment		
Observation group	124	0.37±0.05	0.28±0.02*	18.610	<0.001	22.43±1.55	26.13±1.19*	21.084	<0.001	265.78±16.03	228.79±14.10*	19.294	<0.001
Control group	100	0.38±0.03	0.30±0.03*	18.856	<0.001	22.41±1.52	24.93±1.24*	13.054	<0.001	264.63±15.21	239.19±14.24*	12.210	<0.001
t		1.760	5.962			0.097	7.363			0.546	5.464		
P		0.080	<0.001			0.923	<0.001			0.585	<0.001		

Notes: FAZ: foveal avascular zone; MCD: macular capillary density; RT: and retinal thickness. *within-group comparison before and after treatment, P<0.001.

Table 4. Comparison of the incidence of adverse reactions and poor glycemic control events between the two groups after treatment [n (%)]

Groups	n	Adverse reactions					Occurrence of poorly controlled blood glucose events	
		Constipation	Gastrointestinal reactions	Urinary tract infections	Hypoglycemia	Incidence of adverse reactions	Yes	No
Observation group	124	3 (2.4)	2 (1.6)	0 (0.00)	4 (3.2)	9 (7.3)	12 (9.7)	112 (90.3)
Control group	100	5 (5.0)	2 (2.0)	2 (2.0)	1 (1.0)	10 (10.0)	37 (37.0)	63 (63.00)
χ^2						1.497		24.181
P						0.221		<0.001

Table 5. Comparison of the baseline data and macular microvascular parameters between patients with different glycemic control outcomes [n (%), $\bar{x}\pm sd$]

	Poorly controlled blood glucose group (n=49)	Well-controlled blood glucose group (n=175)	t/χ^2	*P*
Age (yr)	55.37±2.64	55.63±2.50	0.636	0.526
Gender			0.501	0.479
Male	28 (57.1)	90 (51.4)		
Female	21 (42.9)	85 (48.6)		
Disease duration (yr)	5.23±0.67	5.17±0.65	0.567	0.571
BMI (kg/m^2)	22.86±1.68	22.74±1.54	0.551	0.582
Hypertension			0.262	0.609
Yes	30 (61.2)	100 (57.1)		
No	19 (38.8)	75 (42.9)		
Smoking history			0.123	0.940
Yes	32 (65.3)	112 (64.0)		
No	17 (34.7)	63 (36.0)		
Drinking history			0.227	0.634
Yes	25 (51.0)	96 (54.9)		
No	24 (49.0)	79 (46.1)		
FBG (mmol/L)	10.64±1.66	10.59±1.62	0.190	0.850
2hBG (mmol/L)	17.56±1.54	17.58±1.49	0.082	0.934
HbA1c (%)	8.52±0.59	7.84±0.48	8.318	<0.001
FAZ (mm^2)	0.31±0.03	0.28±0.02	8.234	<0.001
MCD (mm/mm^2)	24.41±1.13	25.93±1.21	7.882	<0.001
RT (μm)	247.17±13.81	229.59±13.03	8.239	<0.001

Notes: BMI: body mass index; FBG: fasting blood glucose; 2hBG: 2-hour postprandial blood glucose; HbA1c: glycated hemoglobin; FAZ: foveal avascular zone; MCD: macular capillary density; RT: and retinal thickness.

Comparison of macular microvascular parameters between the observation and control groups before and after treatment (training set)

As shown in **Table 3**, no significant differences in FAZ, MCD, or RT were observed between the two groups at baseline (P>0.05). After treatment, FAZ and RT were significantly decreased, while MCD was significantly increased in both groups. Compared with the control group, the observation group exhibited a more significant reduction in FAZ and RT, as well as a greater increase in MCD (all P<0.001).

Comparison of adverse events and incidence of poor glycemic control between the observation and control groups (training set)

As shown in **Table 4**, the incidence of adverse reactions was 7.3% (9/124) in the observation group and 10.0% (10/100) in the control group, with no significant difference between the groups (P>0.05). The incidence of poor glycemic control was significantly lower in the observation group than that in the control group (9.7% [12/124] vs. 37.0% [37/100]; P<0.001).

Comparison of baseline characteristics and macular microvascular parameters between patients with different glycemic control outcomes

As shown in **Table 5**, there were no significant differences in age, sex, disease duration, BMI, hypertension, smoking history, drinking history, FBG, or 2hBG between the poor glycemic control group and the well-controlled group. However, FAZ, RT, and HbA1c were significantly higher in the poor control group (all P<0.05).

Univariate and multivariate analyses of factors affecting the glycemic control

Variables showing significant differences in **Table 5** were dichotomized according to the optimal cut-off values derived from the maxi-

Table 6. Assignment of influencing factors

Influencing factors	Assignment
FAZ	0: <0.305 mm^2
	1: ≥0.305 mm^2
MCD	0: ≥25.185 mm/mm^2
	1: <25.185 mm/mm^2
RT	0: <241.825 μm
	1: ≥241.825 μm
HbA1c	0: <8.26%
	1: ≥8.26%

Notes: FAZ: foveal avascular zone; MCD: macular capillary density; RT: and retinal thickness; HbA1c: glycated hemoglobin.

mum Youden index in ROC curve analysis, with the assignment details presented in **Table 6**. Univariate and multivariate logistic regression analyses (**Tables 7** and **8**) identified FAZ ≥0.305 mm^2, MCD <25.185 mm/mm^2, RT ≥241.825 μm, and HbA1c ≥8.26% as independent risk factors for poor glycemic control.

Nomogram construction and validation

In the training set, the nomogram demonstrated that MCD contributed the greatest weight to the prediction of glycemic control outcomes, followed by FAZ, whereas RT and HbA1c showed relatively smaller contributions (**Figure 2A**). In the validation set, MCD remained the strongest predictor, followed by FAZ and HbA1c, while RT exerted a relatively weak effect (**Figure 2B**).

Calibration curves confirmed favorable predictive performance of the combined model incorporating FAZ, MCD, RT, and HbA1c in both the training set (χ^2=1.344, P=0.719, **Figure 2C**) and the validation set (χ^2=3.631, P=0.304, **Figure 2D**).

ROC curve analysis of predictive performance

As shown in **Table 9** and **Figure 3**, ROC curve analysis in the training set demonstrated that FAZ, MCD, RT, and HbA1c had acceptable individual predictive values for poor glycemic control. The combined model achieved significantly superior predictive performance compared with any single indicator (**Figure 3A**). Consistent findings were observed in the validation set, where the combined model similarly outperformed individual parameters (**Figure 3B**).

Discussion

DR is the most prevalent microvascular complication in patients with T2DM. The underlying pathogenesis is primarily attributed to retinal microvascular damage and neurodegenerative alterations induced by persistent hyperglycemia [9, 10]. Therefore, early and optimal glycemic intervention prior to the onset of clinically evident DR may help delay or prevent the progression of subclinical retinal microvascular impairment [11, 12]. In clinical practice, continuous subcutaneous insulin infusion (CSII)-based short-term intensive therapy has been widely adopted as an effective strategy to achieve stable and near-target glycemic control [13]. In the present study, we demonstrated that short-term intensive glycemic management significantly improved macular microvascular perfusion in T2DM patients without DR, and the constructed combined predictive model exhibited favorable and stable predictive performance.

The macula is the anatomical center of central vision, and its microvascular integrity plays a critical role in maintaining visual function [14, 15]. In the present study, 14 days of CSII therapy significantly reduced FAZ area and RT, while markedly increasing MCD compared with conventional insulin treatment. These findings are consistent with previous studies [16, 17] demonstrating that metabolic and pharmacologic interventions may improve retinal microcirculation in diabetic patients. The potential mechanism underlying these effects may be multifactorial. Chronic hyperglycemia promotes excessive production of reactive oxygen species and accumulation of advanced glycation end-products, which synergistically contribute to endothelial dysfunction, increased vascular permeability, and impaired microcirculatory homeostasis [18, 19]. In addition, CSII may attenuate these pathological processes by rapidly stabilizing blood glucose levels and reducing glucose variability, thereby alleviating oxidative stress-mediated endothelial injury. Furthermore, improved insulin sensitivity may help normalize vascular endothelial growth factor expression, thus supporting capillary regeneration and perfusion [20]. Compared with conventional insulin injection, CSII also mitigates endothelial injury caused by excessive glycemic fluctuations, facilitating macular microvascular recovery [21].

Table 7. Univariate logistic regression analysis of factors influencing glycemic control outcomes

Factors	β	StdError	Wald x^2	P	OR	95% CI	
						Lower	Upper
FAZ ≥0.305 mm^2	2.894	0.409	49.985	<0.001	18.069	8.100	40.308
MCD <25.185 mm/mm^2	2.452	0.395	38.539	<0.001	11.611	5.354	25.182
RT ≥241.825 μm	2.378	0.368	41.825	<0.001	10.787	5.247	22.179
HbA1c ≥8.26%	2.260	0.363	36.684	<0.001	9.581	4.700	19.528

Notes: FAZ: foveal avascular zone; MCD: macular capillary density; RT: and retinal thickness; HbA1c: glycated hemoglobin.

Table 8. Multivariate logistic regression analysis of factors influencing glycemic control outcomes

Factors	β	StdError	Wald x^2	P	OR	95% CI	
						Lower	Upper
FAZ ≥0.305 mm^2	1.788	0.545	10.775	0.001	5.980	2.056	17.395
MCD <25.185 mm/mm^2	2.300	0.487	22.297	<0.001	9.970	3.838	25.895
RT ≥241.825 μm	1.141	0.503	5.144	0.023	3.131	1.168	8.394
HbA1c ≥8.26%	1.197	0.514	5.424	0.020	3.310	1.209	9.063

Notes: FAZ: foveal avascular zone; MCD: macular capillary density; RT: and retinal thickness; HbA1c: glycated hemoglobin.

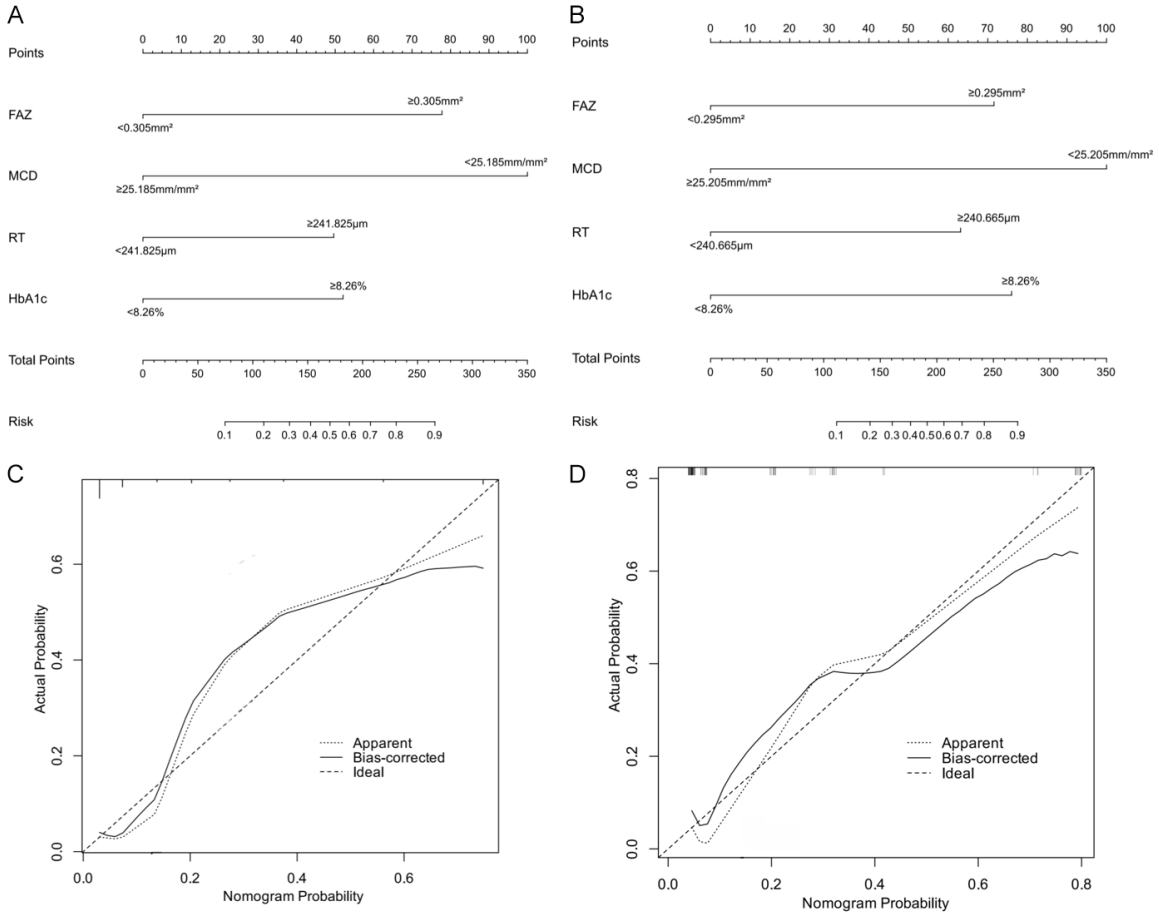


Figure 2. Construction and predictive performance evaluation of the Nomogram model. A. Nomogram in the training set; B. Nomogram in the validation set; C. Calibration curve for the Nomogram in the training set; D. Calibration curve for the Nomogram in the validation set.

Table 9. ROC curve analysis of risk factors for glycemic control outcomes

Group	Factor	AUC	P	95% CI	Sensitivity	Specificity	Youden index	Cut-off value
Training set	FAZ	0.815	<0.001	0.741-0.889	0.592	0.926	0.518	0.305 mm^2
	MCD	0.829	<0.001	0.766-0.892	0.749	0.796	0.545	25.185 mm/mm^2
	RT	0.832	<0.001	0.768-0.896	0.653	0.851	0.504	241.825 μm
	HbA1c	0.826	<0.001	0.758-0.894	0.673	0.823	0.496	8.26%
	Combine	0.905	<0.001	0.853-0.957	0.796	0.897	0.693	-
Validation set	FAZ	0.805	<0.001	0.652-0.958	0.722	0.897	0.619	0.295 mm^2
	MCD	0.830	<0.001	0.717-0.943	0.795	0.833	0.628	25.205 mm/mm^2
	RT	0.821	<0.001	0.707-0.934	0.778	0.821	0.599	240.665 μm
	HbA1c	0.834	<0.001	0.716-0.952	0.778	0.846	0.624	8.26%
	Combine	0.960	<0.001	0.921-0.998	0.889	0.885	0.774	

Notes: FAZ: foveal avascular zone; MCD: macular capillary density; RT: and retinal thickness; HbA1c: glycated hemoglobin.

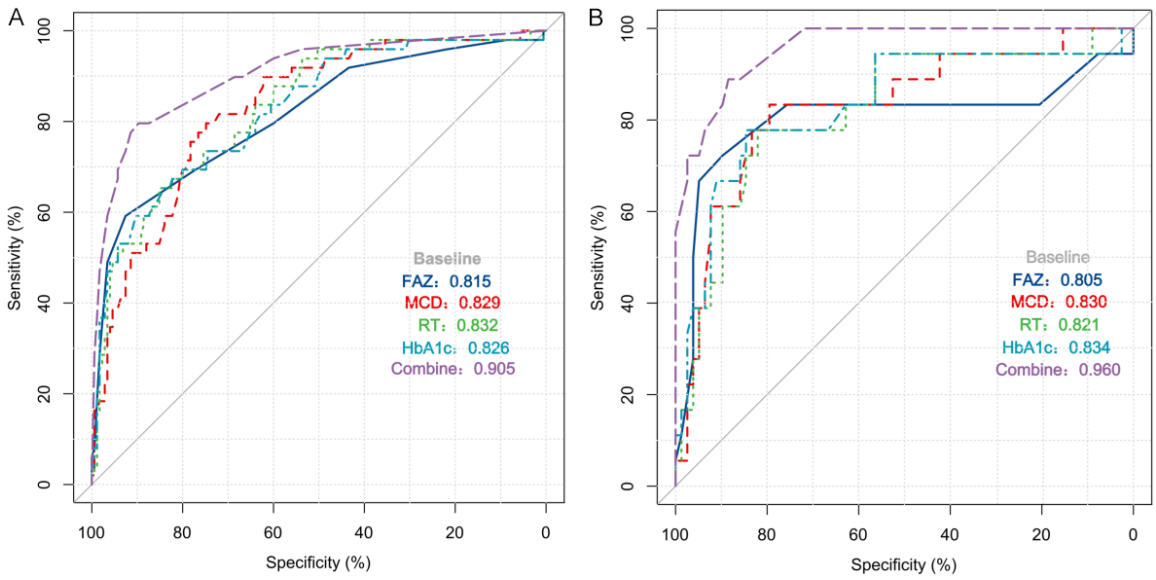


Figure 3. ROC curves of risk factors in predicting glycemic control outcomes. A. Training set; B. Validation set.

Univariate and multivariate logistic regression analyses revealed that FAZ ≥0.305 mm^2, MCD <25.185 mm/mm^2, RT ≥241.825 μm, and HbA1c ≥8.26% were independent risk factors for poor glycemic control. These results are consistent with the findings of Atlı et al. [5], supporting a close link between systemic metabolic abnormalities in diabetes and retinal microcirculatory disturbance. As the most metabolically active zone of the retina, the macula is extremely vulnerable to metabolic dysfunction. An enlarged FAZ indicates capillary dropout or hypoperfusion in the fovea, whereas reduced MCD reflects decreased microvascular density. Both defects impair oxygen and nutrient delivery in retinal tissue and further disrupt glucose metabolism [22, 23]. Increased RT is associated with elevated microvascular permeability and intraretinal edema, representing a key biomarker for early microvascular impairment [24]. HbA1c reflects the mean blood glucose level over the preceding 2-3 months and indicates the severity of long-term metabolic dysregulation in diabetes [25, 26].

ROC curve analyses from both the training and validation sets demonstrated that the combined predictive model achieved significantly better predictive performance than any single indicator alone. HbA1c enables the assessment of short-term glycemic control trends but

cannot reflect real-time changes in the retinal microvasculature [27]. In contrast, macular microvascular parameters derived from OCTA are noninvasive, quantitative, and sensitive in detecting subclinical microvascular damage. However, these parameters alone cannot directly illustrate the impact of glycemic fluctuations on microvascular integrity [28, 29]. Taken together, our findings indicate that in clinical practice, the integrated model can be used to rapidly estimate the risk of poor glycemic control by inputting individual patient parameters, thus providing a straightforward and objective tool to support clinical decision-making.

This study has several limitations. First, as a single-center study with a relatively modest sample size, potential selection bias may exist, and the generalizability of our model needs to be further validated in large-scale, multicenter cohorts. Second, the follow-up duration was limited to 3 months; thus, the long-term impacts of short-term intensive glycemic control on macular microvascular parameters and DR incidence could not be evaluated. Future prospective, multicenter, and long-term follow-up studies are warranted to clarify the association between changes in macular microvascular parameters and DR risk, as well as to verify the long-term predictive value of the model.

Conclusion

Short-term intensive glycemic control using CSII effectively improves macular microvascular perfusion and reduces the risk of poor glycemic control in patients with T2DM but without DR. The combined predictive model incorporating FAZ, MCD, RT, and HbA1c exhibits favorable predictive efficacy and stability, which may provide a novel clinical strategy for reducing the incidence of DR and improving visual outcomes in this population.

Disclosure of conflict of interest

None.

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References

[1] Zhou Z, Xu M, Xiong P, Yuan J, Zheng D and Piao S. Prognosis and outcome of latent autoimmune diabetes in adults: T1DM or T2DM? Diabetol Metab Syndr 2024; 16: 242.

[2] Lin R, Hsu CL, Shih MC, Chien KL and Wu HY. Comparison of the renal outcomes of novel antidiabetic agents in patients with type 2 diabetes with chronic kidney disease: a systematic review and network meta-analysis of randomized controlled trials. Diabetes Obes Metab 2026; 28: 518-528.

[3] Kour V, Swain J, Singh J, Singh H and Kour H. A review on diabetic retinopathy. Curr Diabetes Rev 2024; 20: e201023222418.

[4] Dorweiler TF, Singh A, Ganju A, Lydic TA, Glazer LC, Kolesnick RN and Busik JV. Diabetic retinopathy is a ceramidopathy reversible by anti-ceramide immunotherapy. Cell Metab 2024; 36: 1521-1533, e1525.

[5] Atlı H, Onalan E, Yakar B, Kaymaz T, Duzenci D, Karakulak K, Dönder E, Gürsu MF and Dayanan R. The relationship of serum asprosin level with diabetic and non-diabetic retinopathy. Eur Rev Med Pharmacol Sci 2022; 26: 2117-2123.

[6] O'Meara M, Mateus Acuña JC and Uribe A. Long-term benefits of an integrated continuous glucose monitoring and insulin pump system for emergency admissions, hospitalization, and metabolic control in a cohort of people with diabetes: retrospective cohort study. JMIR Diabetes 2023; 8: e46880.

[7] Li Z, Luo D and Li Z. Effectiveness of internet-based management in newly diagnosed young adults with type 2 diabetes: a prospective comparative study. Endocr Connect 2025; 14: e240576.

[8] Nair RM, Chawla S, Mentias A, Saleem T, Vural A, Ko T, Rampersad P, Cremer P and Menon V. Glycemic patterns and impact of early hyperglycaemia in patients with cardiogenic shock on mechanical circulatory support. Eur Heart J Acute Cardiovasc Care 2023; 12: 328-335.

[9] Fung TH, Patel B, Wilmot EG and Amoaku WM. Diabetic retinopathy for the non-ophthalmologist. Clin Med (Lond) 2022; 22: 112-116.

[10] Seo H, Park SJ and Song M. Diabetic retinopathy (DR): mechanisms, current therapies, and emerging strategies. Cells 2025; 14: 376.

[11] Sivaprasad S and Pearce E. The unmet need for better risk stratification of non-proliferative diabetic retinopathy. Diabet Med 2019; 36: 424-433.

[12] Ba-Ali S, Larsen M, Andersen HU and Lund-Andersen H. Full-field and multifocal electroretinogram in non-diabetic controls and diabetics with and without retinopathy. Acta Ophthalmol 2022; 100: e1719-e1728.

[13] Li Y, Gui X, Weng Y, Xun L, Yu W, Xiang C, Qi X, Wang X and Bai F. Effect of short-term intensive insulin pump therapy on serum endotrophin levels in patients with newly diagnosed type 2 diabetes. Front Endocrinol (Lausanne) 2025; 16: 1658272.
[14] Li X, Xie J, Zhang L, Cui Y, Zhang G, Chen X, Wang J, Zhang A, Huang T and Meng Q. Identifying microvascular and neural parameters related to the severity of diabetic retinopathy using optical coherence tomography angiography. Invest Ophthalmol Vis Sci 2020; 61: 39.
[15] Gulyesil FF, Inan S, Gobeka HH, Sabaner MC and Alizada A. Retinal ultrastructural, electrophysiological, and microvascular morphological outcomes in diabetic macular edema treated with intravitreal bevacizumab. Ir J Med Sci 2023; 192: 149-159.
[16] Ceylan A, Dogan ME, Demircan A and Akar Y. Evaluation of macular vascular density and foveal avascular zone changes by optical coherence tomography angiography (OCT-A) after intravitreal dexamethasone implant in diabetic macular edema resistant to Anti-VEGF treatment. Int Ophthalmol 2022; 42: 3579-3588.
[17] Kato F, Nozaki M, Kato A and Yasukawa T. Retinal microvascular changes after intravitreal triamcinolone acetonide in diabetic macular edema. J Clin Med 2023; 12: 3475.
[18] Doğan ME and Erkan Pota Ç. Investigation of the effects of gestational diabetes and hypertension on retinal and choroidal microvascular circulation using swept-source optical coherence tomography angiography. Microvasc Res 2024; 152: 104622.
[19] Borel AL, Lablanche S, Waterlot C, Joffray E, Barra C, Arnol N, Amougay H and Benhamou PY. Closed-loop insulin therapy for people with type 2 diabetes treated with an insulin pump: a 12-week multicenter, open-label randomized, controlled, crossover trial. Diabetes Care 2024; 47: 1778-1786.
[20] Huang X, Jiang J, Liu L, Lin Y, Zhang F, Ling X, Wei H, Huang G, Ye J, Huang C, Huang J, Tao W and Zou X. Diabetes remission in newly diagnosed type 2 diabetes mellitus through short-term continuous subcutaneous insulin infusion intensive therapy combined with low-carbohydrate diet treatment. J Diabetes Investig 2025; 16: 426-433.
[21] Ke W, Liu L, Zhang P, Yan L, Zhang Q, Zhang F, Xu X, Liu J, Xu L, Wan X, Li H, Cao X, Xiao H, Putman MS and Li Y. Effects of short-term intensive insulin therapy combined with oral hypoglycemic agents for inducing remission in newly diagnosed type 2 diabetes mellitus: a randomized clinical trial. J Diabetes 2026; 18: e70187.
[22] Guan L, Yang L, Sun J, Liu Y, Lu Z, Feng R, Liu H, Zhang Z and Li S. Choroidal vascular alterations in diabetic retinopathy and their association with macular microvascular parameters. Sci Rep 2025; 15: 29381.
[23] Zhang J, Yu Y, Zhou XM, Liao X, Hu JY, Ling Q, Zou J, Chen C, He LQ, Wei H, Chen X, Wang YX, Shao Y and Li RM. Changes in retinal capillary density in female with type 2 diabetes and gestational diabetes-an analysis based on OCTA technology. Int J Ophthalmol 2025; 18: 435-448.
[24] Chen Q, Song K, Cun Q, Yang W, Tao Y, Zhong H, Lv S and Qian C. Differences in macular structure and microvasculature between high myopia and non-high myopia. Front Med (Lausanne) 2025; 12: 1645015.
[25] Zhao T, Laotaweerungsawat S, Chen Y, Liu X, Liu D and Stewart JM. Right versus left eye asymmetry of microvasculature in diabetes revealed by optical coherence tomography angiography. Sci Rep 2023; 13: 9332.
[26] Kim J, Park IW and Kwon S. Factors predicting final visual outcome in quiescent proliferative diabetic retinopathy. Sci Rep 2020; 10: 17233.
[27] Figueras-Roca M, Molins B, Sala-Puigdollers A, Matas J, Vinagre I, Ríos J and Adán A. Peripheral blood metabolic and inflammatory factors as biomarkers to ocular findings in diabetic macular edema. PLoS One 2017; 12: e0173865.
[28] Chen Y, Xu Z, Liang A, Chen R, Wang Z, Chen X, Zheng K, Lu P, Liang H, Cao D and Zhang L. Comprehensive assessment of ocular parameters for identifying diagnostic indicators of diabetic peripheral neuropathy. Acta Diabetol 2024; 61: 1283-1291.
[29] Zagst AJ, Smith JD, Wang R and Harrison WW. Foveal avascular zone size and mfERG metrics in diabetes and prediabetes: a pilot study of the relationship between structure and function. Doc Ophthalmol 2023; 147: 99-107.