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Correlation between C-peptide and diabetic retinopathy in patients with type 2 diabetes mellitus: a cross-sectional study

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This study aimed to investigate the relationship between C-peptide levels, specifically 180-min postprandial C-peptide levels, and diabetic retinopathy (DR) in individuals with type 2 diabetes. This cross-sectional study involved 1545 participants divided into two groups: one with diabetic retinopathy (742 individuals) and one without (803 individuals). To assess the connection between C-peptide levels and DR, multivariate logistic regression and Spearman correlation analysis were performed, including subgroup analyses to ensure robustness of the results. Compared with individuals without DR, individuals with DR had significantly lower postprandial C-peptide levels. Additionally, these postprandial C-peptide levels were inversely correlated with Haemoglobin A1c (HbA1c), fasting blood glucose, and duration of diabetes but positively correlated with body mass index (BMI) and triglyceride levels. Logistic regression analysis revealed a strong inverse association between postprandial 180-min C-peptide levels and the risk of DR. Specifically, higher C-peptide levels were linked to a lower prevalence of DR, a relationship that persisted even after adjusting for potential confounding factors. Furthermore, when different subgroups were analyzed based on sex, age, BMI, and HbA1c levels, individuals without DR consistently had higher C-peptide levels than those with DR. A stratified analysis further confirmed that the inverse relationship between C-peptide levels and DR risk was consistent across most subgroups. In conclusion, the results of this study suggest that higher postprandial 180-min C-peptide levels are inversely related to the risk of diabetic retinopathy, implying that elevated C-peptide levels could offer some protection against the retinal damage associated with diabetes.

Keywords Type 2 diabetes mellitus, Complications, Diabetic retinopathy, C-peptide, Cross-sectional study

Diabetes has become one of the major issues threatening human health. According to a 2021 report by the International Diabetes Federation (IDF), approximately 536.6 million people aged 20–79 years have type 2 diabetes mellitus worldwide, and this figure is expected to increase to 783.2 million by 2045[1]. Diabetes not only reduces quality of life and life expectancy but also serves as a leading cause of various microvascular and macrovascular complications, including blindness, kidney failure, and stroke[2]. Among these complications, diabetic retinopathy (DR) is a common complication in type 2 diabetes patients[3] and is among the leading causes of vision impairment and blindness globally[4]. With the increasing incidence of diabetes and the increasing lifespan of patients, the prevalence of DR and its associated vision impairment are also increasing[5].

Currently, in clinical practice, DR screening primarily relies on imaging technologies. For example, fundus fluorescein angiography, optical coherence tomography angiography, and fluorescence lifetime imaging ophthalmoscopy (FLIO) are novel noninvasive imaging technologies[6]. To some extent, these technologies have improved the sensitivity and accuracy of diagnosis. However, imaging detection is already at the stage of DR onset. The key lies in how to predict DR early, identify risk factors, and intervene in advance before its occurrence.

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Biochemical markers could serve as valuable tools for detecting earlier stages of DR, identifying patients at high risk of retinal disease progression, and monitoring therapeutic efficacy[7]. Many studies based on clinical data have revealed associations between amino acids[8] cholesterol[9] and serum albumin[10] and the development and progression of DR, indicating their potential as predictive biomarkers for this condition. Additionally, studies have shown that a decrease in fasting C-peptide levels is a risk factor for DR[11,12] but the relationship between postprandial late-phase C-peptide levels and DR progression still needs further investigation.

Compared with insulin, C-peptide has a longer circulatory half-life and prevents first-pass metabolism in the liver; thus, it serves as a reliable indicator of β-cell function[13,14]. Moreover, C-peptide exhibits anti-angiogenic properties, reducing retinal neovascularization[15]. Research indicates that C-peptide serves not only as a predictor of whether type 2 diabetes patients need insulin therapy[16–18] but also as a potential treatment for long-term complications of type 2 diabetes, such as DR[19]. However, fasting C-peptide levels mainly represent the basal secretion of pancreatic β-cells, whereas postprandial C-peptide can more accurately assess the function of pancreatic β-cells and the condition of diabetes patients[20,21]. Previous studies have confirmed that the occurrence of DR is closely associated with islet cell function[22]. Nevertheless, the connection between postprandial C-peptide levels and chronic complications such as DR remains debatable[13] especially the link between 180-min post-load C-peptide (C-peptide-180) levels and DR, which is still unclear.

Thus, the present study aims to explore the correlation between C-peptide-180 levels and DR through a cross-sectional study involving 1545 patients with type 2 diabetes.

Results

Participant characterization description

Participants were categorized based on the presence or absence of DR (Table 1). Among the 1,545 participants, 803 (51.97%) had no DR, whereas 742 (48.03%) were diagnosed with DR. DR patients were older (53 years vs. 48 years, $P<0.01$) and had a longer diabetes duration (8 years vs. 3 years, $P<0.0001$) than NDR patients. Additionally, DR patients had lower postprandial C-peptide (PCP) and insulin levels than NDR patients. Significant differences in body mass index (BMI) ($P=0.012$), (triglycerides) TG ($P=0.003$), (high-density lipoprotein cholesterol) HDL-C ($P=0.003$), and FCP levels ($P<0.0001$) were also detected. No significant

	DR ($n=742$)	No DR ($n=803$)	P value
Gender (males), n (%)	482(64.96)	578(71.98)	0.004
Age, years	53(46–60)	48 (39–56)	< 0.0001
Diabetes course, years	8 (3–14)	3 (0.5-8)	< 0.0001
BMI, kg/m^2	25.1 (23.06–27.68)	25.95 (23.5-28.12)	0.012
Smoking, n (%)	174 (23.45)	209 (26.03)	0.266
Dringking, n (%)	200 (26.95)	254 (31.63)	0.050
Fatty liver disease, n (%)	505 (68.06)	540 (67.25)	0.775
hyperuricemia, n (%)	15 (2.02)	38 (4.73)	0.005
HbA1c, %	8.7 (7.4–10.3)	8.52 (7.2–10.3)	0.133
FBG, mmol/L	7.69(6.07–10.07)	7.705(6.31–10.1)	0.792
Fasting Insulin,μU/mL	5.08(2.55–9.47)	5.655(2.85–10.11)	0.123
30-minute PPI, μU/mL	7.17(2.86–14.02)	9.295(3.82–17.3)	0.006
60-minute PPI, μU/mL	11.06(4.88–20.41)	13.38(5.35–26.79)	0.015
120-minute PPI,μU/mL	13.25(5.84–24.36)	16.55(8.4-32.59)	0.0001
180-minute PPI,μU/mL	11.48(4.66–21.62)	14.97(7.33–23.69)	0.005
TC, mmol/L	4.31(3.56–5.12)	4.38(3.68–5.03)	0.383
TG, mmol/L	1.54(1.06–2.37)	1.72(1.13–2.77)	0.003
HDL-C, mmol/L	1.055(0.87–1.27)	1.01(0.84–1.22)	0.003
LDL-C, mmol/L	2.5(1.86–3.2)	2.54(1.98–3.2)	0.458
FCP, ng/mL	1.53(0.99–2.21)	1.85(1.17–2.68)	< 0.0001
30-minute PCP, ng/mL	1.89(1.31–2.64)	2.23(1.49–3.24)	< 0.0001
60-minute PCP, ng/mL	2.49(1.68–3.55)	3.14(1.99–4.56)	< 0.0001
120-minute PCP, ng/mL	3.56(2.49–4.91)	4.585(3.08–6.68)	< 0.0001
180-minute PCP, ng/mL	3.64(2.63–5.18)	4.63(3.23–6.6)	< 0.0001
SBP, mmHg	133(124–144)	131(122–142)	0.005
DBP, mmHg	83(76–89)	83(76–90)	0.332

Table 1. Characteristics of the participants according to the presence of DR. FBG, fasting blood glucose; FCP, fasting C-peptide; PCP, postprandial C-peptide; PPI, postprandial insulin; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; HbA1c, glycated hemoglobin A1c.

Variable-1	Variable-2	*r*	*P* value
0-minute PCP, ng/mL	DR	−0.1540708	< 0.0001
30-minute PCP, ng/mL		−0.168383117	< 0.0001
60-minute PCP, ng/mL		−0.175052718	< 0.0001
120-minute PCP, ng/mL		−0.216773408	< 0.0001
180-minute PCP, ng/mL		−0.195184201	< 0.0001
BMI, kg/m^2	180-minute PCP, ng/mL	0.279	< 0.0001
HbA1c, %		−0.369	< 0.0001
FBG, mmol/L		−0.218	< 0.0001
TC, mmol/L		−0.057	0.05
TG, mmol/L		0.129	< 0.0001
HDL-C, mmol/L		−0.193	< 0.0001
LDL-C, mmol/L		−0.125	< 0.0001
Diabetic duration(years)		−0.217	< 0.0001

Table 2. Correlation between C-peptide and other parameters.

	OR (95% CI)	*P* value
Non-adjusted model	0.70 (0.62, 0.80)	< 0.0001
Adjust model 1	0.74 (0.64, 0.84)	< 0.0001
Adjust model 2	0.79 (0.69, 0.90)	0.0002
Adjust model 3	0.69 (0.59, 0.80)	< 0.0001

Table 3. Relationship between 180-minute postprandial C-peptide levels and DR. model 1 was adjusted for age, sex, and BMI; model 2 was adjusted for age, sex, BMI, hypertension, smoking status, drinking status, diabetes duration, and fatty liver; and model 3 was adjusted for all variables in model 2 plus HbA-1c, TC, TG, HDL-C, LDL-C, and FBG.

differences were observed in Haemoglobin A1c (HbA1c), (fasting blood glucose) FBG, fasting insulin, (total cholesterol) TC, (low-density lipoprotein cholesterol) LDL-C, and DBP between groups.

Correlation of C-peptide with DR and other variables

Spearman's correlation coefficient was used to evaluate the relationships between C-peptide and DR, as well as 180-minute postprandial C-peptide and other parameters (Table 2). Postprandial C-peptide was significantly negatively correlated with DR. 180-min postprandial C-peptide was significantly negatively correlated with HbA1c ($r = -0.369$, $p < 0.0001$), FBG ($r = -0.218$, $p < 0.0001$), HDL-C ($r = -0.193$, $p < 0.0001$), LDL-C ($r = -0.125$, $p < 0.0001$), and diabetes duration ($r = -0.217$, $p < 0.0001$) but significantly positively correlated with BMI ($r = 0.279$, $p < 0.0001$) and TG ($r = 0.129$, $p < 0.0001$).

Associations between 180-minute postprandial C-peptide and DR risk

After adjusting for potential confounders, we assessed the associations using multivariate logistic regression analysis. As shown in Table 3, the risk of DR significantly decreased with increasing 180-minute postprandial C-peptide levels. The unadjusted model showed that the OR for 180-minute postprandial C-peptide was 0.70 (95% CI 0.62–0.80; $P < 0.0001$). After adjusting for age, sex, and BMI in adjusted Model I, the OR for 180-minute postprandial C-peptide was 0.74 (95% CI 0.64–0.84, $P < 0.0001$). In Model 2, with further adjustments for hypertension, smoking status, drinking status, diabetes duration, and fatty liver, the corresponding OR was 0.79 (95% CI 0.69–0.90; $P = 0.0002$). In adjusted Model 3, after further adjustments, the association remained significant (OR, 0.69; 95% CI 0.59–0.80; $P < 0.0001$). Moreover, we performed ROC curve analysis to assess the predictive value of 180-minute postprandial C-peptide levels for diabetic retinopathy (DR). Model 2 showed the best performance (AUC = 0.69, 95% CI 0.66–0.72), with an optimal cutoff of 0.44 (sensitivity 67.3%, specificity 63.9%) according to the Youden index (Figure S1).

Comparison of C-peptide levels within various subgroups of DR categorized by sex, age, HbA1c level, and BMI

We grouped the participants based on sex, age, BMI, and HbA1c levels and compared the differences in C-peptide levels between those with and without DR in each group (Fig. 1). The results showed significant differences in C-peptide levels across all subgroups. Across all subgroups, C-peptide levels were significantly higher in patients without DR than in those with DR, suggesting that higher C-peptide levels may offer some degree of protection against diabetes-related retinal damage.

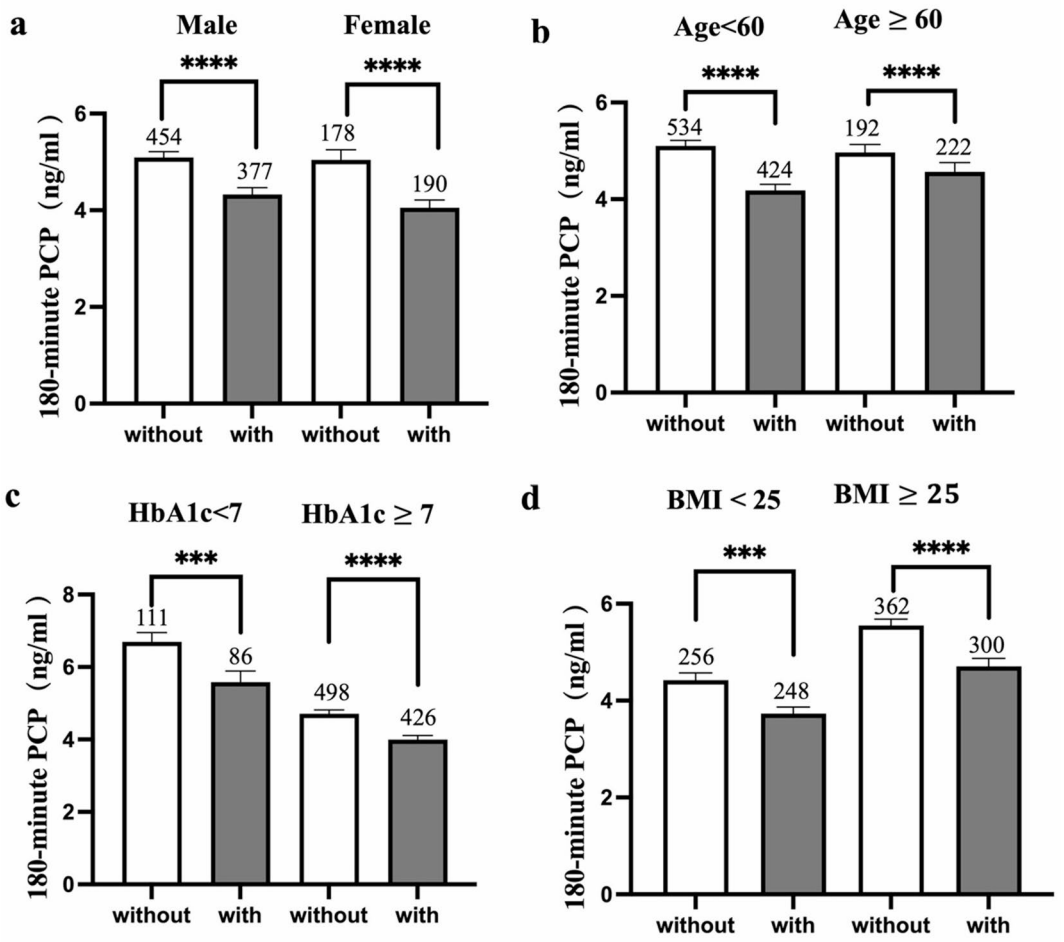

Fig. 1. 180-Minute Postprandial C-Peptide Levels in T2DM Patients with and without Diabetic Retinopathy. Comparison between males and females (**a**), older age (≥ 60) and younger age (< 60) (**b**), higher HbA1c levels (< 7%) and lower HbA1c levels (≥ 7%) (**c**), and higher BMI (≥ 25 kg/m^2) and lower BMI (< 25 kg/m^2) (**d**). Sample sizes for each subgroup are indicated above the corresponding bars. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

Stratified analysis of 180-minute postprandial C-peptide and the risk of diabetic retinopathy

As shown in Table 4, subsequent stratified analyses were conducted considering variables such as age, sex, BMI, diabetes duration, smoking status, FBG, HbA1c, and fatty liver. In most subgroup analyses, the association between 180-minute postprandial C-peptide and the risk of DR remained significant. This consistency highlights the significant association between 180-minute postprandial C-peptide levels and DR across various conditions and demographic characteristics. For patients aged ≥ 60 years and with a duration of diabetes > 10.0 years, the correlation was not significant. Additionally, in the subgroup analysis, the interaction effects of 180-minute postprandial C-peptide with diabetes duration (*P* value for interaction < 0.0001), smoking (*P*value for interaction < 0.0001), and fatty liver (*P*value for interaction 0.0002) on DR were significant.

Discussion

This cross-sectional study revealed that among 1545 type 2 diabetes patients, those with DR had lower postprandial C-peptide levels. Furthermore, 180-minute postprandial C-peptide levels were significantly negatively correlated with DR. After adjusting for major confounding factors, this correlation remained significant. Therefore, based on these observations, the 180-minute postprandial C-peptide level can serve as an effective predictive marker for assessing DR risk in individuals with type 2 diabetes.

Previous studies have shown significant variability in the prevalence of DR among diabetic patients. A study conducted in the UK revealed that among 46,962 type 2 diabetes patients, the prevalence of any form of DR was 38.0% in European whites, 52.4% in African/African-Caribbean individuals, and 42.3% in South Asians[23]. Another meta-analysis conducted in mainland China indicated that the prevalence of DR, nonproliferative diabetic retinopathy (NPDR), and proliferative diabetic retinopathy (PDR) among diabetic patients was 23%, 19.1%, and 2.8%, respectively[24]. A recent cross-sectional study conducted in the endocrinology department of Qingdao University Affiliated Hospital reported that 41.24% of patients had DR[10]. Based on data from this study, the prevalence of DR among type 2 diabetes patients was 48.03%. In studies involving hospitalized patients, the

	Stratified Group	OR(95%Cl)	*P* value	*P* for interaction
Age, (years)	< 60	0.86(0.81–0.91)	< 0.0001	0.303
	≥ 60	0.92(0.827–1.01)	0.094	
Sex	Female	0.86(0.78–0.93)	0.0003	0.237
	Male	0.89(0.83–0.94)	< 0.0001	
BMI (kg/m^2)	< 25	0.88(0.81–0.95)	0.001	0.606
	≥ 25	0.88(0.82–0.94)	0.0001	
Diabetic duration (years)	< 5.0	0.89(0.83–0.96)	0.002	< 0.0001
	5.0–10.0	0.88(0.80–0.96)	0.007	
	> 10.0	0.98(0.89–1.09)	0.741	
Smoking history	No	0.88(0.83–0.93)	< 0.0001	< 0.0001
	Yes	0.85(0.77–0.94)	0.003	
FBG (mmol/L)	< 7	0.86(0.80–0.92)	< 0.0001	0.007
	≥ 7	0.88(0.82–0.94)	0.0001	
HbA1c (%)	< 7	0.85(0.76–0.95)	0.006	0.085
	≥ 7	0.88(0.83–0.93)	< 0.0001	
Fatty liver disease	No	0.84(0.76–0.92)	0.0002	0.0002
	Yes	0.89(0.84–0.94)	< 0.0001	

Table 4. Subgroup analysis of the association between 180-minute postprandial C-peptide and DR.

prevalence of DR was higher among type 2 diabetes patients, possibly because of poor glycemic control and a greater number of complications in this population.

The relationship between C-peptide levels and DR in type 2 diabetes patients remains controversial. Some previous studies have shown that fasting C-peptide, 30-minute postprandial C-peptide, and 2-hour postprandial C-peptide are negatively correlated with DR in type 2 diabetes patients[25–27]. A study from Korea found that lower quartiles of fasting and 2-hour postprandial serum C-peptide levels were associated with increased severity of retinopathy[28]. A European cohort study demonstrated that after adjusting for multiple confounding factors, the highest quartile of baseline C-peptide levels was negatively associated with the risk of retinopathy[29]. The above studies did not include 180-minute postprandial C-peptide, possibly because its level at this time point is relatively low, with smaller variations, making it difficult to obtain sufficient data to support its clinical relevance in practice. The 180-minute postprandial C-peptide reflects the functional state of the pancreas during the later postprandial phase (when blood glucose levels gradually decline), including pancreatic reserve function and delayed insulin secretion. C-peptide captures the dynamic changes during the recovery phase of postprandial blood glucose[30,31]. Additionally, it can accurately assess the impact of prolonged high blood glucose exposure on the retina and the relationship between chronic metabolic imbalance and DR, helping to identify high-risk patients at an early stage. However, our analysis of data from 1,545 patients indicates a negative correlation between 180-minute postprandial C-peptide levels and DR in patients with type 2 diabetes. A decline in insulin secretion capacity is typically accompanied by poor glycemic control, which increases the risk of DR. Adequate insulin secretion and early intervention can help delay the progression of DR, making 180-minute postprandial C-peptide a potential clinical marker for predicting DR risk. Additionally, our study employed standard diagnostic methods for DR and type 2 diabetes, with a relatively large sample size, enhancing its generalizability.

The results of the present study offer a simpler and more cost-effective indicator for clinical application. However, some studies have not found such an association. A study conducted in India involving 195 type 2 diabetes patients reported no association between serum C-peptide levels and retinopathy or diabetes duration[32]. A study from the United States involving 1,007 type 2 diabetes patients indicated that glycemic control, rather than C-peptide, was associated with the incidence and progression of DR. These findings might have resulted from small sample sizes, random errors, or the use of less accurate biomarker measurement methods two decades ago, which may have led to biased data. Taken together, our present data suggested a negative correlation between C-peptide levels and the occurrence of DR.

Moreover, we conducted a stratified analysis of the association between 180-minute postprandial C-peptide and DR. In most subgroup analyses, the association remained significant. However, it is noteworthy that no significant association was observed in individuals aged ≥ 60 years or those with a diabetes duration of more than 10 years. As shown in Table 1, the differences in age and diabetes duration between the DR and NDR groups were significant. These findings align with those of established consensus and research[33,34] confirming that advanced age and long diabetes duration are critical risk factors for DR. These factors may entirely overshadow the influence of C-peptide on DR. Nonetheless, even after adjusting for confounding factors, the risk of DR remained significantly associated with 180-minute postprandial C-peptide levels.

Neovascularization in DR is a multifactorial process involving microvascular endothelial damage caused by hyperglycemia, exacerbation of oxidative stress, and the expression of pro-angiogenic factors[35–37]. C-peptide, a biologically active polypeptide, has been shown to reduce reactive oxygen species (ROS) production in endothelial cells and mitigate apoptosis[38,39]. In diabetic mice, C-peptide supplementation improved retinal neurodegeneration and inhibited VEGF-induced pathological changes[40]. Additionally, C-peptide acts as an anti-angiogenic agent, reducing retinal neovascularization by mitigating oxidative stress, vascular leakage, and

inflammation[15,41]. In summary, C-peptide appears to protect retinal blood vessels by suppressing hyperglycemia-induced oxidative stress, reducing endothelial cell injury, and minimizing neovascular formation.

This study has certain limitations. First, due to the cross-sectional design, a causal relationship between C-peptide and diabetic vascular complications could not be established; further prospective studies are needed to confirm these effects. Second, the patients included in this study were from a single center, and the sample may not represent the entire population. Additionally, confounding factors such as dietary habits, genetics, and osteoporosis may have been present.

Conclusion

Based on the results from this hospitalized population, 180-minute postprandial C-peptide was negatively correlated with the risk of DR. Even after accounting for confounding factors, this correlation persisted. Our findings not only add to the current evidence but also suggest that maintaining optimal C-peptide levels may reduce the risk of DR. As research progresses, we aim to identify the clinical utility of monitoring and modulating C-peptide levels to inform future diabetes care strategies.

Methods

Study design and patients

This cross-sectional study included patients aged 18 years and older who were diagnosed with type 2 diabetes. Data were collected from hospitalized patients at the First Affiliated Hospital of Zhengzhou University between January 2018 and December 2020. Person data were extracted from the hospital's electronic medical records system. The exclusion criteria were as follows: (1) special types of diabetes or gestational diabetes; (2) severe systemic diseases (hematologic diseases, rheumatic diseases, or malignancies); (3) severe ocular conditions such as uveitis, glaucoma, or vitreous hemorrhage; (4) history of intraocular surgery; (5) incomplete or inconsistent clinical and laboratory data; and (6) renal insufficiency (serum creatinine ≥ 115 μmol/L) or hepatic dysfunction (alanine aminotransferase ≥ 97.5 U/L and/or aspartate aminotransferase ≥ 55.5 U/L). A total of 1545 patients, including 1060 men, were included in the final analysis. The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the ethics committee of the First Affiliated Hospital of Zhengzhou University.

Anthropometric and biochemical measurements

After overnight fasting, venous blood samples were collected in the morning to measure FBG, fasting C-peptide, fasting insulin, TC, TG, LDL-C, and HDL-C levels. Fasting C-peptide levels were measured using the Elecsys C-Peptide assay (Roche Diagnostics) on a cobas e 801 analyzer. Intra- and inter-assay CVs were 0.9–2.9% and 2.3–3.6% respectively, validated across clinical concentrations with human serum and quality controls. Patients subsequently underwent an oral glucose tolerance test (OGTT), during which blood samples were collected again at 30, 60, 120, and 180 min to measure postprandial C-peptide and insulin levels. The above measurements were performed using a chemiluminescence assay on an automated analyzer. HbA1c concentrations were quantified using high-performance liquid chromatography (HPLC). At baseline, weight and height were measured, and BMI was calculated as weight (kg) divided by height squared (m^2). After resting for at least 10 min, blood pressure was measured using an automated sphygmomanometer, and the average of three readings was recorded. Hypertension was defined as a blood pressure ≥ 140/90 mmHg or the use of antihypertensive medication. Obesity was defined according to the Asia-Pacific criteria as a BMI ≥ 25 kg/m^2[42] and fatty liver was diagnosed by ultrasound.

Assessment of diabetic retinopathy

A standardized clinical ophthalmic evaluation was administered to all participants by board-certified endocrinologists or ophthalmologists with a minimum of 10 years of clinical experience. Protocol components included a comprehensive ophthalmologic history, visual acuity assessment, slit lamp biomicroscopy, and dilated fundoscopic examination. Subsequent to pharmacological mydriasis, two-field (macular and optic disc) 45° digital fundus photography was executed per a standardized protocol utilizing a digital retinal camera (Carl Zeiss Meditec AG). DR was diagnosed per Early Treatment Diabetic Retinopathy Study (ETDRS) criteria, defined by the presence of at least one microaneurysm or blot hemorrhage, with or without additional findings such as exudates (hard/soft), intraretinal microvascular abnormalities, venous beading, neovascularization (disc/elsewhere), or vitreous hemorrhage.

Statistical analyses

Normality tests were conducted, with continuous variables expressed as medians with interquartile ranges or means with standard deviations and categorical variables expressed as percentages. To evaluate differences between DR and NDR subjects, we used the Mann–Whitney U test for continuous variables via the wilcox.test function in R and the chi-square test for categorical variables using the chisq.test function. The correlation between C-peptide and DR, as well as other parameters, were assessed using Spearman's correlation coefficients. Multivariate binary logistic regression was further employed to determine the association between postprandial 180-minute C-peptide levels and DR. A receiver operating characteristic (ROC) curve (AUC) was constructed to evaluate the discrimination of different models for DR. The maximum Youden index was used to determine the optimal cutoff point. Binary logistic regression was used to perform subgroup analysis of different clinical parameters and their interactions. Statistical significance was defined as $P < 0.05$. All analyses were conducted using R software version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org).

Data availability

The data presented in this study can be obtained from the corresponding author upon reasonable request.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics statement

Research involving human participants was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University. All participants provided informed consent during the study.

Additional information

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