

Relationship Between Fasting C-Peptide to Diabetes Duration Ratio (FCP/DD) and Diabetic Peripheral Neuropathy

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Purpose: To explore the correlation between fasting C-peptide to diabetes duration ratio (FCP/DD) and diabetic peripheral neuropathy (DPN).

Methods: The study was conducted on 816 patients with type 2 diabetes (T2DM). Subjects were classified into a diabetic peripheral neuropathy group (DPN, n=408) and a non-diabetic peripheral neuropathy group (NDPN, n=408) depending on the presence of DPN. Collected patients' baseline data, calculated the FCP/DD ratio, and analyzed the correlation between FCP/DD and DPN.

Results: A comparative analysis of general characteristics revealed that the DPN group exhibited higher values for age, DD, proportion of hypertension, proportion of DN, and proportion of DR compared to the NDPN group. Conversely, the DPN group demonstrated lower proportions of eGFR, FCP/DD, FCP, and fatty liver relative to the NDPN group, with all differences achieving statistical significance ($P < 0.05$). Compared to the high FCP/DD group, the low FCP/DD group exhibited higher values in age, DD, the proportion of DPN, DN, DR, and hypertension, as well as elevated levels of HDL-C and NEUT ($P < 0.05$). Conversely, the low FCP/DD group demonstrated a lower proportion of patients who smoked and those with fatty liver, along with reduced BMI, ALB, FBG, UA, eGFR, TC, TG, and LDL-C levels ($P < 0.05$). In patients with T2DM, after adjusting for confounding factors, high levels of FCP/DD were found to be a protective factor for DPN ($P < 0.05$). The area under the curve of the FCP/DD Model predicting DPN (AUC=0.737) was higher than that of single FCP (AUC=0.587), DD (AUC=0.665).

Conclusion: The high FCP/DD ratio was a protective factor for T2DM with DPN. Additionally, the FCP/DD ratio was found to be a better predictor for the occurrence of DPN in T2DM compared to FCP and DD alone.

Keywords: Diabetic peripheral neuropathy, type 2 diabetes, FCP/DD

Introduction

Diabetes is still one of the most significant public health concerns today, with 451 million people globally living with diabetes in 2017. This number is expected to increase to as many as 693 million by 2045.¹ The high prevalence of chronic complications of diabetes significantly impacts the quality of life and longevity of patients.² Diabetic peripheral neuropathy (DPN) is one of the common complications affecting approximately 50% of patients with diabetes (type 1 diabetes and type 2 diabetes).³

Diabetic Peripheral Neuropathy (DPN) can result in numbness and pain in the lower extremities, foot ulcers, and potentially necessitate amputation, thereby markedly diminishing patients' quality of life. The onset of DPN is often insidious, with up to 50% of affected individuals remaining asymptomatic during the initial stages, which frequently leads to neglect and delayed diagnosis. Therefore, early prevention and detection of diabetic peripheral neuropathy are of paramount importance.⁴ The pathogenesis of Diabetic Peripheral Neuropathy (DPN) is multifaceted, encompassing

oxidative stress, inflammatory responses, neurotrophic dysregulation and various other contributing factors.^{5–7} Wahren et al⁸ showed that compared with the placebo group, injected C-peptide analogues can increase the vibration perception thresholds; This indicates that C-peptide replacement therapy may enhance neurological function in patients with diabetic peripheral neuropathy (DPN). C-peptide, a byproduct of glucagon, is more stable than insulin. C-peptide levels and release profiles are commonly used to assess islet function.⁹ Umaid Potaliya et al¹⁰ demonstrated that lower serum C-peptide levels are linked to diabetic peripheral neuropathy (DPN) in people with type 2 diabetes, they also found that the risk of DPN increases with longer duration of diabetes.¹¹ Some studies have shown that C-peptide at physiological concentrations has anti-inflammatory, immunomodulatory, and neurotrophic effects, C-peptide and its analogs have been found to lower blood glucose and alleviate the complications of diabetes.¹² At present, no studies have examined the relationship between FCP/DD and type 2 diabetes mellitus in conjunction with DPN. Therefore, this study aims to explore the correlation between the FCP/DD ratio and type 2 diabetes combined with peripheral neuropathy. The objective is to establish a new clinical indicator for the early detection and prediction of DPN.

Methods

Subjects

816 patients with type 2 diabetes who were hospitalized at Hebei Provincial People's Hospital in 2022 were selected for the study. Inclusion criteria: T2DM was diagnosed according to the diagnostic criteria of 1999 World Health Organization (WHO); Exclusion criteria: (1) type 1 diabetes mellitus, gestational diabetes mellitus, and special types of diabetes mellitus; (2) age <18 years old or age >80 years old; (3) admitted to the hospital with acute diabetes mellitus complications including ketoacidosis, hyperosmolar-hyperglycemic syndrome, and hypoglycemic coma; (4) history of type B history of viral hepatitis, cirrhosis, hepatic encephalopathy, and liver surgery; (5) recent comorbidities of severe renal disease, cardiovascular disease, acute and chronic infections, stress, tumors, or hematological disorders; (6) pregnancy and breastfeeding; (7) other lesions or drug-induced neuropathy; and (8) drug-induced neurotoxicity. Neurological symptoms included burning, numbness, tingling, fatigue, cramping or aching, and neurological signs included vibration sense, pain, temperature sensation and ankle reflex. The symptoms and signs abnormalities assessed for DPN were in a glove/stocking distribution. Evaluating DPN using the Toronto Clinical Scoring System (TCSS) and neurophysiological examination as the gold standard has high diagnostic value for DPN.¹³ As follows: (1) non-DPN, all neurological symptoms/signs and NCV were normal; (2) clinical DPN, at least two abnormal results among neurological symptoms/signs, or ankle reflex in accordance with a distal symmetrical polyneuropathy and normal NCV; (3) confirmed DPN, at least one abnormal nerve parameter (of NCV, amplitude, latency, and F-wave) in two or more nerves among the median, peroneal, and sural nerves, regardless of neurological signs and symptoms. This study received approval from the Ethics Committee of Hebei Provincial People's Hospital, and the patient's information was anonymous and confidential, so the signed informed consent was exempted.

Data Collection and Laboratory Analysis

General and biochemical data were collected: gender, age, diabetes duration, smoking history, drinking history, medication history, hypertension history, fatty liver history, diabetic nephropathy history, diabetic retinopathy history, etc; height and weight were measured, and body mass index(BMI) was calculated; blood samples were collected early in the morning of the following day after 8–10 hours of fasting after admission to the hospital, and the white blood cell count (WBC), percentage of neutrophils (NEUT), albumin (ALB), fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), blood creatinine (Cr), blood uric acid (UA), glomerular filtration rate (eGFR), erythrocyte sedimentation rate (ESR), fasting C-peptide (FCP) and other indexes were measured; using flow cytometry to detect routine blood indexes, using automatic biochemical analyzer to detect biochemical indexes, using high-performance liquid-contrast cation-exchange chromatography to determine the glycosylated hemoglobin, and electrochemiluminescence to determine fasting C-peptide, and so on. Our laboratory doctors perform all of these laboratory tests.

Calculation of Ratio and Grouping

Fasting C-peptide/diabetes duration (FCP/DD) was calculated by dividing fasting C-peptide by diabetes duration; its median was calculated statistically, and the median of this ratio was 0.25, according to which the patients were divided into two groups: the Low FCP/DD group ($FCP/DD \leq 0.25$, $n=408$) and the High FCP/DD group ($FCP/DD > 0.25$, $n=408$). Patients with type 2 diabetes mellitus (T2DM) were divided into two groups: the DPN group ($n=455$) and the NDPN group ($n=361$), based on the presence of diabetic peripheral neuropathy (DPN).

Statistical Methods

Statistical SPSS 25.0 statistical software was used to analyze the collected data. Measurement data that conformed to a normal distribution were expressed as mean \pm standard deviation, with group comparisons performed using two independent samples t-tests. Non-normally distributed measurement data were expressed as the median and quantile spacing [M(P25%, P75%)], with group comparisons performed using the Mann–Whitney *U*-test. Categorical variables were expressed as percentages, and the chi-square test was used for between-group comparisons. Pearson's correlation analysis was used when continuous variables in the two groups conformed to normal distribution, and Spearman's rank correlation analysis was used to explore the correlation between DPN and the general information of the study population if any of the continuous variables in the two groups did not obey normal distribution. A binary logistic regression analysis was conducted to investigate the determinants of diabetic peripheral neuropathy (DPN). The predictive value of fasting C-peptide (FCP), diabetes duration (DD) and fasting C-peptide/diabetes duration (FCP/DD) in patients with DPN was assessed by Receiver Operating Characteristic (ROC) curve analysis, including the calculation of the area under the curve (AUC). The DeLong test was used for AUC comparison. Statistical significance was established at $P < 0.05$ for all analyses.

Results

Comparison of General Data and Laboratory-Related Indicators in All Patients

A total of 816 patients with T2DM were included in this study, including 455 patients (55.76%) with DPN and 361 patients (44.24%) with NDPN. The differences in age, diabetes duration, the proportion of history of combined fatty liver, FCP/DD, GFR, and fasting C-peptide were statistically significant between the two groups of study subjects ($P < 0.05$): the age, diabetes duration, the proportion of history of combined hypertension, the proportion of history of combined diabetic nephropathy, and the proportion of history of combined diabetic retinopathy were higher in the DPN group than those in the NDPN group; and the proportion of history of combined fatty liver, GFR, FCP/DD, and fasting C-peptide were lower than those in the NDPN group. But the differences in the smoking history, drinking history, BMI, ALB, FBG, Cr, UA, TC, TG, HDL-C, LDL-C, HbA1c, ESR, were not statistically significant ($P > 0.05$) (Table 1).

Comparison of General Data and Laboratory-Related Indicators on Study Participants from Different FCP/DD Subgroups

The age, diabetes duration, the proportion of history of combined hypertension, proportion of combined diabetic peripheral neuropathy, proportion of combined diabetic nephropathy, and proportion of combined diabetic retinopathy, HDL-C, and NEUT in the High FCP/DD group were lower than those in the Low FCP/DD group ($P < 0.05$), and the proportion of history of combined fatty liver, proportion of smoking history, BMI, ALB, FBG, UA, eGFR, TC, TG, and LDL-C were higher than those in the Low FCP/DD group ($P < 0.05$). Comparison of gender, drinking history, HbA1c, ESR, Cr, and WBC between the two study groups was not statistically significant (Table 2).

Correlation Analysis Between FCP/DD and Indicators

The indicators of general data were included in Spearman's rank correlation analysis, which showed that FCP/DD was negatively correlated with age, NEUT, HDL-C ($P < 0.05$), positively correlated with BMI, ALB, TC, TG, LDL-C, GFR, UA, FBG ($P < 0.05$), and WBC, Cr, HbA1c, ESR levels were not significantly correlated (Table 3).

Table 1 Comparison of General Data and Laboratory-Related Indicators in All Patients

Variable	DPN	NDPN	Z (χ^2)	P
n	455	361	–	–
Age (years)	59 (52,68)	56 (43,66)	–4.271	<0.001
Sex (male/female)	290/164	224/137	0.246 ^a	0.620
DD (years)	11 (5,20)	4 (1,12)	–8.129	<0.001
BMI (kg/m ²)	25.92 (23.80,28.18)	26.18 (23.78,28.87)	–1.239	0.215
Smoking (n%)	122 (26.81%)	96 (26.59%)	0.005 ^a	0.994
Drinking (n%)	104 (22.86%)	85 (23.55%)	0.054 ^a	0.817
Hypertension (n%)	253 (55.60%)	174 (48.20%)	4.425 ^a	0.035
Fatty liver (n%)	233 (51.21%)	214 (59.28%)	5.293 ^a	0.021
DN (n%)	115 (25.27%)	32 (8.86%)	36.703 ^a	<0.001
DR (n%)	204 (44.84%)	43 (11.91%)	103.376 ^a	<0.001
WBC ($\times 10^9$ /L)	6.37 (5.37,8.07)	6.27 (5.18, 7.62)	–1.445	0.148
NEUT (%)	63.80(57.10,70.50)	62.70(56.30,70.85)	–1.357	0.175
ALB (g/l)	39.75(36.93,42.78)	40.40(37.40,43.30)	–1.939	0.053
FBG (mmol/l)	8.03 (5.97,11.00)	7.96 (6.08,10.67)	–0.019	0.985
Cr (umol/L)	66.50 (55.93,79.83)	65.25 (55.40,76.32)	–1.333	0.182
UA (umol/L)	317.65 (258.15,388.68)	331.15 (270.50,399.40)	–1.396	0.163
eGFR (mL/min)	96.73(82.49,106.25)	99.95 (87.32,111.43)	–3.38	0.001
TC (mmol/l)	4.71 (3.90,5.57)	4.70 (3.97,5.65)	–0.792	0.429
TG (mmol/l)	1.37 (0.90,2.09)	1.50 (0.99,2.21)	–1.752	0.08
HDL-C (mmol/l)	1.09 (0.90,1.30)	1.05 (0.92,1.22)	–1.147	0.251
LDL-C (mmol/l)	2.94 (2.37,3.57)	2.96 (2.43,3.64)	–0.865	0.387
HbA _{1c} (%)	8.70 (7.38,10.50)	8.40 (6.90,10.30)	–1.552	0.121
ESR (mm/h)	10.50 (5.00,21.00)	10.00 (5.00,20.75)	–0.313	0.754
FCP (nmol/l)	1.83 (1.19,2.71)	2.28 (1.43,3.21)	–3.882	<0.001
FCP/DD	0.18 (0.08,0.45)	0.45 (0.16,2.23)	–8.316	<0.001

Note: ^aindicates χ^2 value. Significance at a P value of <0.05.

Abbreviations: DPN, diabetic peripheral neuropathy; NDPN, non-diabetic peripheral neuropathy; DN, diabetic nephropathy; DR, diabetic retinopathy; DD, diabetes duration; BMI, body mass index; WBC, white blood cell count; NEUT, percentage of neutrophils; HbA_{1c}, glycated hemoglobin; FBG, fasting blood glucose; ALB, albumin; Cr, blood creatinine; UA, blood uric acid; eGFR, Glomerular filtration rate; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; FCP, fasting C-peptide; FCP/DD, fasting C-peptide/ diabetes duration.

Table 2 Comparison of General Data and Laboratory-Related Indicators on Study Participants from Different FCP/DD Subgroups

Variable	Low FCP/DD	High FCP/DD	Z (χ^2)	P
n	408	408	–	–
Age (years)	63 (56,70)	53 (42,62)	–11.416	<0.001
Sex (male/female)	246/162	269/139	2.544 ^a	0.111
DD (years)	17.00 (11.00,20.00)	3.00 (1.00,6.00)	–22.139	<0.001
BMI (kg/m ²)	25.60 (23.41,27.71)	26.39 (24.29,29.55)	–4.402	<0.001
Smoking (n %)	94 (23.04%)	124 (30.39%)	5.644 ^a	0.018
Drinking (n %)	86 (21.08%)	103 (25.25%)	1.990 ^a	0.158
Hypertension (n%)	237 (58.23%)	190 (46.57%)	10.825 ^a	0.001
Fatty liver (n%)	180 (44.12%)	267 (65.44%)	37.445 ^a	<0.001
DN (n%)	97 (23.77%)	50 (12.25%)	18.329 ^a	<0.001
DR (n%)	179 (43.87%)	68 (16.67%)	71.536 ^a	<0.001
DPN (n %)	275 (67.40%)	180 (44.12%)	44.835 ^a	<0.001

(Continued)

Table 2 (Continued).

Variable	Low FCP/DD	High FCP/DD	Z (χ^2)	P
ESR (mm/h)	10.00 (5.00,23.00)	10.00 (5.00,18.00)	-1.263	0.206
ALB (g/l)	38.90 (35.95,41.55)	41.30 (38.20, 44.40)	-7.629	<0.001
FBG (mmol/l)	7.67 (5.71,10.50)	8.17 (6.39,11.17)	-2.69	0.007
Cr (μ mol/L)	66.25 (56.10,78.50)	65.40 (55.08,77.30)	-0.746	0.456
UA (μ mol/L)	309.10 (250.00,381.10)	338.30 (277.00,404.20)	-3.529	<0.001
eGFR (mL/min)	93.90 (80.77, 103.26)	101.95 (89.64, 112.44)	-6.64	<0.001
TC (mmol/l)	4.57 (3.75, 5.49)	4.86 (4.01, 5.66)	-2.827	0.005
TG (mmol/l)	1.21 (0.84,1.82)	1.62 (1.12,2.56)	-6.956	<0.001
HDL-C (mmol/l)	1.09 (0.93,1.30)	1.05 (0.90,3.66)	-2.208	0.027
LDL-C (mmol/l)	2.89 (2.27,3.55)	3.08 (2.46,3.66)	-2.923	0.003
HbA _{1c} (%)	8.70 (7.50,10.40)	8.40 (6.90,10.40)	-1.696	0.090
WBC ($\times 10^9$ /L)	6.37 (5.25,7.98)	6.28 (5.29,7.73)	-0.687	0.492
NEUT (%)	65.40 (57.60,72.80)	61.30 (55.80,68.70)	-4.334	<0.001

Note: ^aindicates χ^2 value. Significance at a P value of <0.05.

Abbreviations: DPN, diabetic peripheral neuropathy; DN, diabetic nephropathy;DR, diabetic retinopathy; DD, diabetes duration; BMI, body mass index; HbA_{1c}, glycated hemoglobin; FBG, fasting blood glucose; ALB, albumin;Cr, blood creatinine; UA, blood uric acid; eGFR, Glomerular filtration rate; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate;WBC, white blood cell count;NEUT, percentage of neutrophils.

Table 3 Correlation Analysis Between FCP/DD and Indicators (R_s Value)

Variable	r_s	P	Variable	r_s	P
Age	-0.434	<0.001	TC	0.138	<0.001
BMI	0.225	<0.001	TG	0.315	<0.001
ALB	0.288	<0.001	HDL-C	-0.104	0.004
NEUT	-0.177	<0.001	LDL-C	0.146	<0.001
WBC	-0.018	0.613	FBG	0.162	<0.001
UA	0.145	<0.001	Cr	-0.035	0.325
ESR	-0.07	0.091	eGFR	0.269	<0.001
HbA _{1c}	-0.02	0.596			

Note: Significance at a P value of <0.05.

Abbreviations: BMI, body mass index; WBC, white blood cell count; NEUT, percentage of neutrophils;HbA_{1c}, glycated hemoglobin; FBG, fasting blood glucose; ALB, albumin; Cr, blood creatinine; UA, blood uric acid; eGFR, Glomerular filtration rate; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate.

Multifactor Logistic Regression Analysis of FCP/DD on DPN

Whether T2DM was combined with DPN as the dependent variable, clinical data and biochemical indicators were screened for independent variables, FCP and DD covariates were excluded, and the independent indicators were included in binary Logistics regression analysis. As shown in Table 4, after adjusting for potential confounders, a high ratio of FCP/DD was found to be a protective factor for DPN (Table 4).

Evaluate the Predictive Value of FCP, DD, and the FCP/DD Model for T2DM with DPN and Compare Using the DeLong Test

The regression equation for the FCP/DD Model: $\text{logit}(P)=1.148+0.081\times\text{sex}-0.097\times\text{smoking}+0.013\times\text{drinking}+0.052\times\text{Hypertension}+0.127\times\text{fatty liver}-0.844\times\text{DN}-1.458\times\text{DR}+0.017\times\text{Age}-0.018\times\text{BMI}+0.02\times\text{FBG}+0.028\times\text{ALB}-0.01\times\text{NEUT}$

Table 4 Multifactor Logistic Regression Analysis of FCP/DD on DPN

	Model 1		Model 2		Model 3	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
FCP/DD						
Low	2.619 (1.970, 3.482)	<0.001	1.470 (1.045, 2.068)	0.027	1.554 (1.073, 2.251)	0.02
High	Ref		Ref		Ref	

Notes: Significance at a P value of <0.05. Model 1: no adjustment for confounders; Model 2: adjusted for age, sex, smoking history, drinking history, hypertension history, fatty liver history, diabetic nephropathy history, diabetic retinopathy history based on Model 1; Model 3: further adjusted for BMI, ALB, NEUT, UA, eGFR, TC, TG, FBG, LDL-C, HDL-C based on Model 2.
Abbreviation: FCP/DD, fasting C-peptide/ diabetes duration.

Table 5 ROC Curves of FCP, DD, and FCP/DD Model

Variable	Cut-off	AUC (95% CI)	Sensitivity	Specificity
FCP	2.667	0.587 (0.546, 0.629)	0.733	0.427
DD	6.500	0.665 (0.624, 0.704)	0.700	0.554
FCP/DD Model	0.609	0.737 (0.701, 0.773)	0.557	0.816

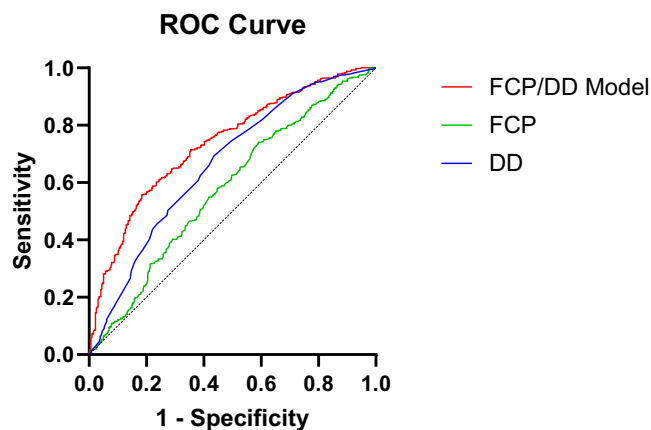
Note:Significance at a P value of <0.05.

Abbreviations: FCP, fasting C-peptide; DD, diabetes duration; FCP/DD Model, fasting C-peptide/ diabetes duration Model; AUC, the area under the subject's operating characteristic curve.

$0.001 \times UA + 0.002 \times eGFR + 0.375 \times TC - 0.111 \times TG - 0.464 \times LDL-C - 0.554 \times HDL-C + 0.441 \times FCP/DD$, and compared with FCP and DD, which showed that the AUC of the FCP/DD Model was 0.737, which was greater than that of the FCP ($Z=6.000$, $P<0.01$) and DD ($Z=4.099$, $P<0.01$) (Table 5 and Figure 1).

Discussion

Diabetic peripheral neuropathy (DPN) is a common complication associated with diabetes mellitus. Early detection of DPN is often challenging due to the difficulty in identifying small fibrotic lesions, which may result in a delayed diagnosis until the condition becomes symptomatic. This delay can lead to severe complications, including the development of ulcers and an increased risk of foot amputation, ultimately resulting in irreversible neuropathy.¹⁴ Therefore, early detection or prediction of DPN is of paramount importance, as the current treatment options are frequently inadequate, significantly impairing the patient's quality of life.

**Figure 1** ROC curves for FCP, DD, and FCP/DD Model suggest the risk of type 2 diabetes combined with DPN.

Abbreviation: FCP, fasting C-peptide; DD, diabetes duration; FCP/DD Model, fasting C-peptide/ diabetes duration Model.

In our study, patients with DPN had higher age, longer diabetes duration, a higher proportion of hypertension, a higher proportion of fatty liver and diabetic complications, and lower blood FCP and eGFR levels, which is consistent with Wang et al.⁴ And some studies have also shown a correlation between the development of DPN and both a history of diabetic nephropathy and diabetic retinopathy.¹⁵ While fasting blood glucose and glycated hemoglobin did not show statistically significant differences, this was observed in the subgroup of patients with type 2 diabetes mellitus with or without comorbid DPN. This finding may be attributable to the critical role of blood glucose management in the selected population, all of whom were administered standardized glucose-lowering medications. Regarding gender, one study claimed that there was no statistically significant association between gender and DPN ($p = 0.966$), which is consistent with our findings.¹⁶

C-peptide, a cleavage product of proinsulin, exhibits greater stability than insulin and remains unaffected by exogenous insulin administration. Consequently, it is frequently utilized in clinical settings to evaluate pancreatic islet function.⁹ In a study involving Chinese patients with type 2 diabetes, C-peptide demonstrated a potential protective effect against the progression of type 2 diabetes when administered in conjunction with diabetic peripheral neuropathy (DPN);¹⁷ a retrospective cohort study showed that higher C-peptide levels (OR: 0.39; 95% CI:0.25–0.61) were negatively associated with the risk of developing neuropathy.¹⁸ Zhao et al¹⁹ found that the C-peptide area under the curve [AUC (C-pep)] was negatively associated with the prevalence of diabetic peripheral neuropathy. In addition to this, exogenous C-peptide replacement therapy was able to delay and improve diabetic peripheral neuropathy.²⁰ Research has confirmed that the duration of diabetes mellitus is a risk factor for DPN. As the duration of the disease increases, the islet function of diabetic patients gradually decreases, leading to a decrease in serum C-peptide and insulin secretion, and an increase in the prevalence of DPN; In their study, Lian et al¹⁴ established a risk factor and risk model for DPN, they found a high correlation between age and duration of diabetes mellitus and DPN, indicating that age and duration of diabetes mellitus are risk factors; Wang et al⁴ in studying the prevalence and risk factors of DPN showed that DPN was negatively correlated with FCP and positively correlated with diabetes duration. Our findings indicated that FCP levels were lower in DPN patients compared to NDPN patients, and there was a negative correlation. Additionally, the duration of diabetes in DPN patients was longer than in NDPN patients, and there was a positive correlation. These results align with the previous findings. Elafros et al²¹ conducted a study on DPN prevention and found that diabetes duration strongly influences DPN.

For the first time in this study, FCP (fasting C-peptide) and DD (diabetes duration) are combined to analyze the relationship between the FCP/DD ratio and DPN (diabetic peripheral neuropathy). In this study, there were 816 patients with T2DM with 455 patients (about 55.76%) with combined DPN and 361 patients (about 44.24%) without combined DPN. The FCP levels of patients with DPN were lower than those without DPN, while the DD levels were higher in patients with DPN, consistent with previous studies.⁴ Upon further analysis of the study, it was found that as the FCP/DD decreased, the incidence of DPN increased. There is a negative correlation between FCP/DD and DPN. Even after adjusting for confounding factors, a high level of FCP/DD was still found to be a protective factor for DPN. This suggests that FCP/DD has the potential to be a predictor of DPN risk.

We analyzed whether the ratio of FCP/DD could be a better predictor of DPN. We plotted the ROC curve and found that FCP/DD had a greater predictive value for the development of DPN in patients with type 2 diabetes than FCP and DD alone, with an AUC of 0.737 (0.701, 0.773). This was superior to FCP and DD alone, suggesting that the FCP/DD ratio is a better clinical predictor of DPN risk.

Chronic inflammation is thought to be closely associated with the onset and progression of DPN, and some studies have shown that neutrophil counts are higher in patients with DPN;²² In our study, we found that there were no statistically significant differences in erythrocyte sedimentation rate, white blood cell count, and percentage of neutrophils between the subgroup of patients with DPN and those without DPN. However, in the subgroup of FCP/DD ratios by the median, we observed that the percentage of neutrophils was higher in patients with a low FCP/DD ratio. This finding aligns with previous research on the topic. Ban et al²³ showed that the albumin ratio was lower in patients with DPN than in patients with NDPN, and our study showed that albumin was lower in patients in the low-ratio FCP/DD group, which is consistent with the Ban et al.²³ Therefore, patients with type 2 diabetes need to maintain adequate nutritional levels to reduce the risk of DPN.

This study has some limitations that should be taken into account. Firstly, because it's a retrospective study, it cannot establish a cause-and-effect relationship. Secondly, the study has a small sample size from a single center, which could lead to inaccurate results. Therefore, further validation of the results would require a larger sample size and a more diverse study population. Additionally, conducting a long-term follow-up or a case-control study would help to validate the reliability of the results.

Conclusion

In conclusion, a high FCP/DD ratio is a protective factor for type 2 diabetes combined with DPN. The FCP/DD model has good predictive value for determining whether type 2 diabetes is combined with DPN, and its predictive ability is better than that of FCP and DD alone.

Ethics Statement

The study followed the principles in the Declaration of Helsinki and was approved by the Ethical Committees of Hebei General Hospital (No.2024-LW-145). In addition, this study was a retrospective non-interventional study, and the patient's information was anonymous and confidential, so the signed informed consent was exempted.

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Disclosure

The authors report no conflicts of interest in this work.

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