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## Retrospective Study

## Analysis of influencing factors and interaction of body weight and disease outcome in patients with prediabetes

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## Abstract

## BACKGROUND

The trend of prediabetes progressing to type 2 diabetes mellitus (T2DM) is prominent, and effective intervention can lead to a return to prediabetes. Exploring the factors influencing the outcome of prediabetes is helpful to guide clinical intervention. The weight change in patients with prediabetes has not attracted much attention.

## AIM

To explore the interaction between body weight and the factors affecting the progression of prediabetes to T2DM.

## METHODS

We performed a retrospective analysis of 236 patients with prediabetes and 50 with normal glucose tolerance (NGT), and collected clinical data and follow-up results of all patients. Based on natural blood glucose outcomes, we classified 66 patients with progression to T2DM into the disease progression (DP) group, and 170 patients without progression to T2DM into the disease outcome (DO) group. We analyzed the factors that influenced prediabetes outcome and the influence of body weight on prediabetes blood glucose outcome by unconditional logistic regression. A general linear model (univariate) was used to analyze the interaction between body weight and independent influencing factors.

## RESULTS

There were 98 cases of impaired fasting glucose (IFG), 90 cases of impaired glucose tolerance (IGT), and 48 cases of coexistent IFG and IGT. The body weight, waist circumference, body mass index, fasting blood glucose, and 2 h plasma glucose of patients with IFG, IGT, and coexistent IFG and IGT were higher than those in patients with NGT ( $P < 0.05$ ). Logistic regression analysis showed that body weight, glycosylated hemoglobin, uric acid, fasting insulin, and homeostatic model assessment for insulin resistance were independent factors affecting progression of prediabetes to T2DM ( $P < 0.05$ ). Receiver operating characteristic curve analysis showed that the area under the curve predicted by the above indicators combined was 0.905 [95% confidence interval (CI): 0.863-0.948], which was greater than that predicted by each indicator alone. Logistic regression analysis with baseline body weight as an independent variable showed that compared with body weight 1, the odds ratio (95%CI) of body weight 3 was 1.399 (1.142-2.126) ( $P = 0.033$ ). There was a multiplicative interaction between body weight and uric acid ( $\beta = 1.953$ ,  $P = 0.005$ ).

## CONCLUSION

High body weight in patients with prediabetes is an independent risk factor for progression to T2DM, and the risk of progression is increased when coexisting with high uric acid level.

**Key Words:** Prediabetes; Type 2 diabetes mellitus; Body weight; Disease outcome; Influencing factors; Interactions; Low-carbohydrate diet

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**Core Tip:** Progression of prediabetes to type 2 diabetes mellitus (T2DM) is severe, but effective interventions can delay or even reverse progression. High body weight is a common phenomenon in people with prediabetes. Unilateral weight-loss intervention may not be sufficient. We analyzed the interaction between body weight and the factors affecting prediabetes progression to T2DM and explored the influence of body weight and other factors, to better guide clinical intervention and reduce progression of prediabetes to T2DM.

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## INTRODUCTION

Diabetes is a serious threat to public health, and its prevention and treatment are increasingly challenging[1]. Type 2 diabetes mellitus (T2DM) and its complications are increasing worldwide. According to the latest data released by the International Diabetes Federation in 2017, there were 425 million patients worldwide, and this is expected to exceed 629 million by 2045[2]. The latest epidemiological data in China show that the prevalence of DM is 11.2%, and approximately 30% of nonendocrine inpatients have DM[3]. Prediabetes, also known as impaired glucose regulation, is a state of abnormal glucose metabolism between normal glucose metabolism and DM, including impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and three states of both, with an incidence of 35.7%[4]. Clinical practice has proved that blood glucose regulation in the prediabetes stage is reversible. Early intervention can prevent prediabetes from progressing to T2DM and delay its development, which can reduce the risk of progression by 58%[5,6]. At present, clinical intervention is mainly through dietary adjustment, weight control, moderate exercise, and other ways to delay the progression of prediabetes to T2DM, and its effectiveness has been confirmed[7]. Obesity [with body mass index (BMI) as an evaluation index] is an independent risk factor for the conversion of prediabetes to T2DM, and obese prediabetes patients can benefit from weight loss. However, whether weight and its influencing factors can lead to an increase in the risk of adverse outcomes of the disease under the combined influence of prediabetes with T2DM risk factors is currently unknown and has rarely been studied. In this study, by understanding the weight status of prediabetes patients, we analyzed the factors influencing disease outcome (DO) and their interaction to provide a basis for later intervention.

## MATERIALS AND METHODS

### Patients

In this retrospective analysis, we selected 236 patients with prediabetes admitted to the Department of General Practice of the First People's Hospital of Wenling City from February 2019 to January 2021. Based on natural blood glucose outcomes, we classified 66 patients with progression to T2DM into the disease progression (DP) group, and 170 patients



without progression to T2DM into the DO group. All patients met the diagnostic criteria for prediabetes in the Chinese Guidelines for Diabetes Prevention and Treatment[8]: (1) IFG: Fasting blood glucose (FBG) 6.1-6.9 mmol/L and oral glucose tolerance test (OGTT) 2h plasma glucose (PG) < 7.8 mmol/L; (2) IGT: FBG < 6.1 mmol/L and OGTT 2h PG 7.8-11.1 mmol/L; and (3) IFG and IGT coexistent: FBG 6.1-6.9 mmol/L and OGTT 2h PG 7.8-11.1 mmol/L.

Inclusion criteria: (1) FBG 5.6-6.9 mmol/L, with or without 2h PG 7.8-11.0 mmol/L; (2) No serious cardiovascular, liver, kidney, and lung diseases; and (3) Complete clinical and follow-up data. Exclusion criteria: (1) Combined with severe systemic diseases, such as heart, liver, kidney or lung disease, mental illness, connective tissue disease, and bone and joint injury; (2) Pregnancy, lactation or pregnancy preparation; and (3) Lack of follow-up data. Another 50 patients with normal glucose tolerance (NGT) were selected. NGT: FBG < 6.1 mmol/L with or without OGTT 2h PG < 7.8 mmol/L.

### Data collection

We consulted patients' electronic medical records, and collected clinical data and relevant test indicators at admission, including sex, age, blood glucose status, family history of DM, smoking, alcohol consumption, body weight, waist circumference, BMI, FBG, 2h PG, systolic blood pressure, diastolic blood pressure, glycosylated hemoglobin, total cholesterol (TC), triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), uric acid, anti-soluble liver antigen antibodies (SLA), fasting insulin (FINS), and homeostatic model assessment for insulin resistance (HOMA-IR).

### Definition and detection of relevant indicators

Body weight was measured by a general practitioner (GP) using a height and weight scale. Patients were measured with an empty stomach. They removed their shoes, wore thin clothing, stood upright, feet together, shoulders and hips close to the scale. The GP lowered the horizontal plate of the scale to the top of the patient's head to read the results of height and weight. Height readings were accurate to 0.5 cm and weight readings to 0.5 kg. BMI was calculated as weight (kg)/height (m<sup>2</sup>)[9].

Waist measurement was performed on patients with an empty stomach by a GP with an inelastic tape measure with a minimum scale of 0.1 cm. During the measurement, the patient remained upright with arms hanging down naturally and feet 25-30 cm apart. The tape measure was placed at the midpoint of the line between the anterior superior iliac spine and the line along the lower margin of the costal arch, and ran horizontally around the abdomen. The tape measure was close to the skin but not tight. The results were read at the end of the breath and were accurate to 0.1 cm.

Systolic and diastolic blood pressure was measured by a GP using a uniform mercury sphygmomanometer. Patients were prohibited from smoking and drinking coffee 30 min before the measurement and rested for 5-10 min in a quiet environment. Venous blood samples were collected in the fasting state in the morning (no intake of caloric food for at least 8 h). The blood glucose indices were determined by a HITACHI 7600-020 automatic biochemical analyzer. FPG, FINS, serum uric acid and blood lipids (TC, TG, HDL-C and LDL-C) were also measured. The homeostasis insulin resistance index (HOMA-IR) was calculated as follows[10]:  $HOMA-IR = (FPG \times FINS) / 22.5$ .

OGTT 2h PG: The patients took 75 g of anhydrous glucose dissolved in 250 mL water within 5 min. During the test, they did not drink any beverages, swallow, or perform strenuous exercise. The time was measured from the first mouthful of sugar water, and the venous blood was drawn 2 h after taking the sugar and was quickly examined by the hexokinase method. Glycosylated hemoglobin was determined by a Bole D-10 glycosylated swimming protein meter (high-pressure liquid chromatography).

### Grouping

T2DM[11]: FBG  $\geq$  7.0 mmol/L with or without OGTT 2h PG  $\geq$  11.1 mmol/L. According to the blood glucose outcomes of prediabetes patients after a 2-year follow-up, 66 patients with progression of T2DM were classified into the DP group, and 170 patients without progression of T2DM were classified into the DO group.

### Statistical analysis

Epidata3.0 software was used for double data entry and SPSS 21.0 statistical software was used for statistical analysis. The measurement data with normal distribution were expressed as mean  $\pm$  SD, and the least significant difference-*t* test was used for pairwise comparison between groups. Numerical data were represented by case number (percentage) and  $\chi^2$  tests. The factors influencing prediabetes DO and the influence of body weight on prediabetes blood glucose outcome were analyzed by unconditional logistic regression. The multiplication model was used to analyze the interaction between the two influencing factors. Beta level:  $\alpha = 0.05$ .

## RESULTS

### Weight of prediabetes patients with different blood glucose status

Among 236 patients with prediabetes, there were 98 cases of IFG, 90 of IGT, and 48 of coexistent IFG and IGT. The body weight, waist circumference, BMI, FBG, and 2h PG of patients with IFG, IGT and coexistent of IFG and IGT were higher than those of patients with NGT (all  $P < 0.05$ ) (Table 1).

### Univariate analysis of the outcome of prediabetes disease

Of 236 patients with prediabetes, 66 (27.97%) developed T2DM (DP group). There were no significant differences in

Table 1 Weight of prediabetes patients with different blood glucose status				
Index	NGT (50 cases)	IFG (98 cases)	IGT (90 cases)	IFG and IGT coexistent (48 cases)
Age (yr)	52.55 ± 14.67	54.68 ± 13.27 <sup>a</sup>	52.38 ± 11.62 <sup>a</sup>	57.75 ± 13.68 <sup>a</sup>
Weight (kg)	61.52 ± 12.13	66.38 ± 13.35 <sup>a</sup>	70.26 ± 10.62 <sup>a</sup>	72.26 ± 11.62 <sup>a</sup>
Waistline (cm)	90.37 ± 9.98	104.25 ± 12.23 <sup>a</sup>	100.22 ± 8.56 <sup>a</sup>	107.35 ± 11.07 <sup>a</sup>
BMI (kg/m2)	25.87 ± 5.46	31.57 ± 4.06 <sup>a</sup>	30.75 ± 3.39 <sup>a</sup>	32.27 ± 3.38 <sup>a</sup>
FBG (mmol/L)	4.46 ± 0.62	6.27 ± 0.75 <sup>a</sup>	5.58 ± 0.36 <sup>a</sup>	6.48 ± 0.82 <sup>a</sup>
2h PG (mmol/L)	5.16 ± 1.08	5.87 ± 0.77 <sup>a</sup>	8.82 ± 1.17 <sup>a</sup>	9.35 ± 1.12 <sup>a</sup>

<sup>a</sup>Indicates the same index compared with normal glucose tolerance,  $P < 0.05$ .  
NGT: Normal glucose tolerance; IFG: Impaired fasting glucose; IGT: Impaired glucose tolerance; BMI: Body mass index; FBG: Fasting blood glucose; 2h PG: 2h postprandial blood glucose.

gender, age, family history of diabetes, FBG, diastolic blood pressure, TC, HDL-C and LDL-C between the DP and DO groups ( $P > 0.05$ ). In addition, glucose status, history of smoking, drinking, body weight, waist circumference, BMI, 2h PG, systolic blood pressure, glycosylated hemoglobin, TG, uric acid, SLA, FINS, and HOMA-IR difference were statistically significant ( $P < 0.05$ ) (Table 2).

Multivariate analysis of DOs in patients with prediabetes

We took whether to progress to T2DM as the dependent variable and the index of  $P > 0.05$  in the above single-factor analysis as the independent variable, which were inserted into the logistic regression model for analysis. Table 3 shows the assignment of the data in the model. Body weight, glycosylated hemoglobin, uric acid, FINS, and HOMA-IR were independent factors affecting progression of prediabetes to T2DM ( $P < 0.05$ ) (Table 4). Receiver operating characteristic (ROC) curve analysis of body weight, glycosylated hemoglobin, uric acid, FINS, and HOMA-IR predicted prediabetes progression to T2DM, and showed that the area under the curve (AUC) predicted by the above indices combined was 0.905 [95% confidence interval (CI): 0.863-0.948], which was higher than predicted by each index separately (Figure 1, Table 5).

Analysis of the influence of body weight on DO in patients with prediabetes

Whether progressed to T2DM was used as the dependent variable, and baseline body weight [body weight 1 (35-60 kg), body weight 2 (60-80 kg), body weight 3 (80-100 kg)] was the independent variable. Logistic regression analysis was performed by adjusting blood glucose status, smoking history, drinking history, waist circumference, BMI, 2h PG, systolic blood pressure, glycosylated hemoglobin, triglycerides, uric acid, SLA, FINS and HOMA-IR. Body weight was a risk factor for prediabetes progression to T2DM. Compared with body weight 1, the odds ratio (OR) (95%CI) of body weight 3 was 1.399 (0.142-1.126) ( $P = 0.083$ ) (Table 6).

Analysis of interaction between body weight and independent influencing factors

Taking the best cut-off value of each index as the boundary, we converted the data of body weight, glycosylated hemoglobin, uric acid, FINS and HOMA-IR into binary variables. Whether progressed to T2DM was used as the dependent variable and weight by glycosylated hemoglobin, weight by uric acid, weight by FINS, and weight by HOMA-IR as the fixed factors, the interaction analysis showed that there was a multiplicative interaction between weight and uric acid ( $\beta = 1.953$ ,  $P = 0.005$ ) (Table 7).

DISCUSSION

There has been significant progression of prediabetes to T2DM in recent years[12]. According to our study, 27.97% of prediabetes patients developed T2DM. The progression to T2DM was highest in patients with coexistent IFG and IGT, which is consistent with the findings of Wu *et al*[13]. We found that most patients with prediabetes had IFG or IGT, and coexistent IFG and IGT accounted for 20%. Further analysis showed that body weight, waist circumference, BMI, FBG and 2h PG were higher in patients with IFG, IGT, and coexistent IFG and IGT than in patients with NGT, which is similar to previous results[14].

Our logistic regression analysis showed that body weight ( $> 71.75$  kg), glycosylated hemoglobin ( $> 6.25\%$ ), uric acid ( $> 289.5$  mmol/L), FINS ( $> 6.25$  mL/mL) and HOMA-IR ( $> 1.35$ ) were independent risk factors for prediabetes progression to T2DM ( $P < 0.05$ ). ROC curve analysis showed that the AUC predicted by combination of the above indicators was 0.905 (95%CI: 0.863-0.948), which was greater than that predicted by each indicator alone, indicating that the above indicators had high efficacy in predicting the progression of prediabetes to T2DM, suggesting that high levels of these indicators increase the risk of prediabetes progression to T2DM. Our logistic regression analysis, with T2DM progression as the dependent variable and baseline body weight as the independent variable, showed that the OR (95%CI) of those with



Table 2 Univariate analysis of the outcome of prediabetes disease

Data	DP group (n = 66)	DO group (n = 170)	$t/\chi^2/Z$	P value
Gender			0.143	0.705
Male	39 (59.09)	105 (61.76)		
Female	27 (40.91)	65 (38.24)		
Age			< 0.001	0.988
< 60 yr	42 (63.64)	108 (63.53)		
≥ 60 yr	24 (36.36)	62 (36.47)		
Blood glucose status			14.639	0.001
IFG	16 (24.24)	82 (48.24)		
IGT	28 (42.42)	62 (36.47)		
IFG and IGT coexistent	22 (33.33)	26 (15.29)		
Family history of diabetes			0.279	0.598
Yes	6 (9.09)	12 (7.06)		
No	60 (90.91)	158 (92.94)		
Smoking history			4.561	0.033
Yes	20 (30.30)	30 (17.65)		
No	46 (69.70)	140 (82.35)		
Drinking history			5.457	0.019
Yes	26 (39.39)	41 (24.12)		
No	40 (60.61)	129 (75.88)		
Weight, kg (mean ± SD)	74.59 ± 11.19	66.91 ± 11.86	4.535	< 0.001
Waist circumference, cm (mean ± SD)	106.84 ± 10.31	101.98 ± 10.95	3.110	0.002
BMI, kg/m <sup>2</sup> (mean ± SD)	32.37 ± 3.58	30.41 ± 3.75	0.074	0.941
FBG, mmol/L (mean ± SD)	5.98 ± 0.73	6.08 ± 0.75	0.926	0.355
2h PG, mmol/L (mean ± SD)	8.12 ± 1.83	7.54 ± 1.84	2.177	0.031
Systolic blood pressure (mmHg)	128 ± 21	122 ± 20	2.040	0.043
Diastolic blood pressure (mmHg)	81 ± 11	80 ± 10	0.670	0.503
Glycosylated hemoglobin (%)	6.28 ± 0.53	5.89 ± 0.33	6.794	< 0.001
TC (mmol/L)	4.76 ± 1.17	4.64 ± 1.06	0.758	0.449
TG (mmol/L)	1.58 ± 0.32	1.42 ± 0.47	2.544	0.012
HDL-C (mmol/L)	1.25 ± 0.27	1.21 ± 0.32	0.899	0.370
LDL-C (mmol/L)	1.88 ± 0.53	1.85 ± 0.41	0.463	0.644
Uric acid (μmol/L)	3.43 ± 0.76	3.20 ± 0.87	2.067	0.040
SLA (μmol/L)	325.10 ± 75.04	300.22 ± 80.23	2.176	0.031
FINS (μU/mL)	5.96 ± 1.57	5.11 ± 1.19	6.016	< 0.001
HOMA-IR	1.67 ± 0.45	1.21 ± 0.39	7.782	< 0.001

Results presented as *n* (%), unless indicated otherwise. DP: Disease progression; DO: Disease outcome; IFG: Impaired fasting glucose; IGT: Impaired glucose tolerance; BMI: Body mass index; FBG: Fasting blood glucose; 2h PG: 2h postprandial blood glucose; TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SLA: Anti-soluble liver antigen antibodies; FINS: Fasting insulin; HOMA-IR: Homeostatic model assessment for insulin resistance.

**Table 3 Assignment table**

Independent variable	Assignment
Blood glucose status	1 = IFG, 2 = IGT, 3 = IFG and IGT coexist
Smoking history	1 = Yes, 2 = No
Drinking history	1 = Yes, 2 = No
Weight	Measured value
Waist circumference	Measured value
BMI	Measured value
2h PG	Measured value
Systolic blood pressure	Measured value
Glycosylated hemoglobin	Measured value
TG	Measured value
Uric acid	Measured value
SLA	Measured value
FINS	Measured value
HOMA-IR	Measured value

IFG: Impaired fasting glucose; IGT: Impaired glucose tolerance; BMI: Body mass index; 2h PG: 2h postprandial blood glucose; TG: Triglycerides; SLA: Anti-soluble liver antigen antibodies; FINS: Fasting insulin; HOMA-IR: Homeostatic model assessment for insulin resistance.

**Table 4 Logistic regression analysis of disease outcomes in prediabetes patients**

Independent variable	$\beta$	SE	Wals	P value	OR	95%CI
Blood glucose status			1.138	0.566		
Blood glucose status (1)	0.034	0.958	0.001	0.972	1.035	0.158-6.771
Blood glucose status (2)	0.588	0.648	0.825	0.364	1.801	0.506-6.415
Smoking history	0.916	0.486	3.553	0.059	2.499	0.964-6.479
Drinking history	0.341	0.457	0.555	0.456	1.406	0.574-3.445
Weight	0.066	0.020	11.128	0.001	1.068	1.028-1.110
Waist circumference	0.041	0.022	3.427	0.064	1.042	0.998-1.089
BMI	0.006	0.060	0.010	0.920	1.006	0.895-1.131
2h PG	0.150	0.204	0.538	0.463	1.162	0.778-1.734
Systolic blood pressure	0.015	0.010	2.213	0.137	1.016	0.995-1.036
Glycosylated hemoglobin	2.542	0.599	18.014	< 0.001	12.705	3.928-41.092
TG	0.527	0.528	0.997	0.318	1.694	0.602-4.772
Uric acid	0.007	0.003	7.217	0.007	1.007	1.002-1.012
SLA	0.001	0.003	0.226	0.635	1.001	0.996-1.007
FINS	0.503	0.169	8.872	0.003	1.653	1.188-2.301
HOMA-IR	2.224	0.547	16.561	< 0.001	9.245	3.167-26.984
Constant (quantity)	-38.654	6.686	33.420	< 0.001	< 0.001	-

BMI: Body mass index; 2h PG: 2h postprandial blood glucose; TG: Triglycerides; SLA: Anti-soluble liver antigen antibodies; FINS: Fasting insulin; HOMA-IR: Homeostatic model assessment for insulin resistance; OR: Odds ratio; CI: Confidence interval.

**Table 5 Receiver operating characteristic curve analysis of weight, glycosylated hemoglobin, uric acid, fasting insulin, homeostatic model assessment for insulin resistance in predicting progression of prediabetes to type 2 diabetes mellitus**

Independent variable	AUC	95%CI	Specificity	Sensitivity	Optimum break value
Weight	0.699	0.620-0.778	0.729	0.758	71.75
Glycosylated hemoglobin	0.726	0.645-0.806	0.882	0.515	6.25
Uric acid	0.590	0.512-0.668	0.424	0.788	289.5
FINS	0.666	0.583-0.750	0.835	0.500	6.25
HOMA-IR	0.798	0.736-0.859	0.647	0.818	1.35
Collaborative forecasting	0.905	0.863-0.948	-	-	

AUC: Area under the curve; FINS: Fasting insulin; HOMA-IR: Homeostatic model assessment for insulin resistance; CI: Confidence interval.

**Table 6 Analysis of the influence of weight on disease outcome in patients with prediabetes**

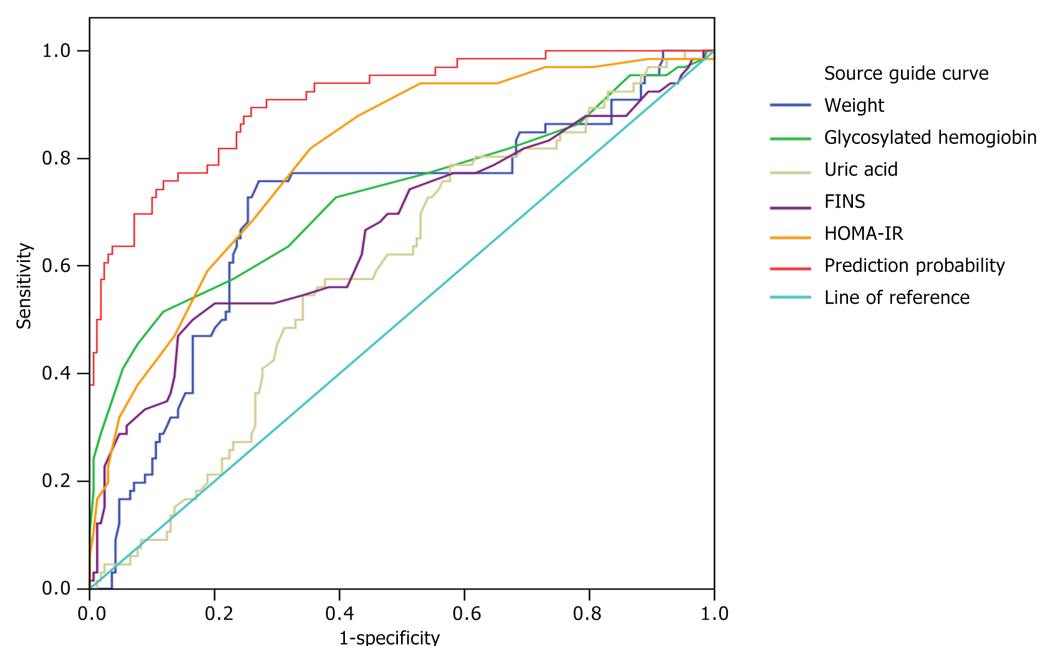
Model	Weight 1	Weight 2	Weight 3		
		OR (95%CI)	P value	OR (95%CI)	P value
Model 1	1	1.210 (1.082-2.532)	0.001	1.366 (1.180-2.743)	0.005
Model 2	1	1.233 (1.085-2.640)	0.005	1.357 (1.166-3.768)	0.008
Model 3	1	1.164 (1.041-1.662)	0.011	1.399 (1.142-2.126)	0.033

No variable adjusted in model 1; model 2 adjusted blood glucose status, smoking history, drinking history, waist circumference and body mass index (BMI); model 3 adjusted blood glucose status, smoking history, drinking history, waist circumference, BMI, 2h postprandial blood glucose, systolic blood pressure, glycosylated hemoglobin, triglycerides, uric acid, anti-soluble liver antigen antibodies, fasting insulin, homeostatic model assessment for insulin resistance; weight 1 is 35-60 kg, weight 2 60-80 kg, and weight 3 is 80-100 kg. OR: Odds ratio; CI: Confidence interval.

**Table 7 Analysis of the interaction between body weight and independent influencing factors**

Independent variable	$\beta$	SE	Wals	P value	OR	95%CI
Weight	2.664	0.52	26.23	< 0.001	14.356	5.179-39.795
Glycosylated hemoglobin	2.772	0.606	20.948	< 0.001	15.987	4.878-52.390
Weight by glycosylated hemoglobin	-0.828	0.82	1.021	0.312	0.437	0.088-2.178
Constant	-3.082	0.457	45.408	< 0.001	0.046	-
Weight	2.453	0.565	18.86	< 0.001	11.625	3.842-35.174
Uric acid	1.887	0.578	10.664	0.001	6.6	2.127-20.484
Weight by uric acid	1.953	0.719	1.758	0.005	0.386	0.094-1.577
Constant	-2.923	0.459	40.545	0	0.054	-
Weight	2.883	0.565	26.066	< 0.001	17.86	5.906-54.009
FINS	2.578	0.622	17.189	< 0.001	13.174	3.894-44.570
Weight by FINS	-0.797	0.833	0.916	0.339	0.451	0.088-2.305
Constant	-3.229	0.51	40.113	< 0.001	0.04	-
Weight	3.31	1.08	9.39	0.002	27.375	3.296-227.343
HOMA-IR	3.067	1.049	8.55	0.003	21.471	2.749-167.718
Weight by HOMA-IR	-1.463	1.15	1.619	0.203	0.231	0.024-2.205
Constant	-4.29	1.007	18.159	< 0.001	0.014	-

FINS: Fasting insulin; HOMA-IR: Homeostatic model assessment for insulin resistance; OR: Odds ratio; CI: Confidence interval.



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**Figure 1** Receiver operating characteristic curves of body weight, glycosylated hemoglobin, uric acid, fasting insulin, and homeostatic model assessment for insulin resistance predict progression of prediabetes to type 2 diabetes mellitus. FINS: fasting insulin; HOMA-IR: Homeostatic model assessment for insulin resistance.

weight 80-100 kg was 1.399 (1.142-2.126) ( $P = 0.033$ ), compared with those with weight ranging from 35 to 60 kg. The risk of prediabetes progression to T2DM was increased by 1.399 times with high body weight based on low body weight.

Prediabetes is an early stage of glucose metabolism disorder, in which glucose regulation function is impaired, accompanied by insulin resistance and lipid metabolism disorder[15]. Being overweight or obese increases the risk of diabetes, and our study did not show the risk effect of BMI on progression to T2DM, which may be because BMI did not reflect the actual content and distribution of body fat. Although BMI may be normal, the body may have ectopic fat deposition and metabolic disorders[16]. Being overweight or obese is an important factor in predicting self-underestimation of body mass in prediabetes, and overweight people tend to underestimate self-body mass[17]. Only 10% of overweight DM patients judged their body weight correctly[18]. High body weight in prediabetes patients with improper control of body mass increases the risk of progression to T2DM. Obesity is associated with metabolic dysfunction and overnutrition. Weight gain often means increased BMI, which is closely related to changes in adipocyte secretion, release of inflammatory mediators, chronic inflammation, and insulin resistance[19]. For patients with DM, 5%-10% weight loss can improve their health status, reduce the level of glycosylated hemoglobin, improve cardiovascular disease risk factors, and reduce the use of antidiabetic, antihypertensive and lipid-regulating drugs[20].

The progression of prediabetes is reversible, and effective intervention is important for the outcome of patients with prediabetes[21]. Weight loss can reduce or even reverse ectopic deposition and reduce progression of prediabetes to T2DM. At present, the main clinical intervention for prediabetes is lifestyle intervention, supplemented by drug intervention. Lifestyle intervention mainly includes diet, exercise, body mass, and dietary intervention is divided into diet control and nutritional supplementation[22]. Through long-term control of total dietary calories and restriction of various types of energy intake, such as fat and sugar, weight loss can be achieved and postprandial hyperglycemia can be reduced, thus reducing the burden on pancreatic islet beta cells, improving the function of beta cells, and improving HOMA- $\beta$ , to correct the disorder of glucose metabolism[11]. In recent years, many patients with DM in western countries have been affected by various dietary programs, such as low-carbohydrate diet, a very low-carbohydrate diet, and a Mediterranean diet to reduce weight and improve blood sugar. In particular, a low-carbohydrate diet has the most obvious effect on weight loss, which has been widely confirmed in some clinical experiments, including obesity, metabolic disorders, and risk of cardiovascular events[23]. There are also many domestic and foreign studies on low-carbon diets, and it has been preliminarily confirmed that a low-carbon diet can reduce body weight and the level of glycosylated hemoglobin[24]. Griauzde *et al*[18] showed that carbohydrate-restricted diets benefit patients with obesity and T2DM and can be used as a potential tool to support individual patients' weight loss and metabolic health. Therefore, we suggest that dietary intervention programs represented by a low-carbon diet can reduce body weight and body fat accumulation in prediabetes patients with high body weight. At the same time, regular monitoring of blood glucose and adjustment of the program are conducive to better weight loss, and to delay or even reverse the course of prediabetes. However, it should be noted that weight loss intervention is not appropriate in patients with severe organ diseases, malnutrition, and age > 55 years.

Our interaction analysis showed that there was a multiplying interaction between body weight and uric acid, but no interaction between body weight and glycosylated hemoglobin, FINS and HOMA-IR, suggesting that for prediabetes

patients with T2DM, the higher the body weight, the higher the uric acid level. The levels of glycosylated hemoglobin, FINS and HOMA-IR were not related to body weight. Obesity is a condition in which body weight exceeds the normal standard and body fat is accumulated excessively or distributed abnormally. Obesity is associated with elevated blood uric acid, and hyperuricemia is associated with obesity[25]. Obesity caused by high body weight is related to genetic and environmental factors. Such people often have an unreasonable diet and lack of exercise, resulting in accumulation of body fat, which can be accompanied by disorders of purine metabolism or uric acid excretion, increasing uric acid levels, the end product of purine metabolism. In addition, regular intake of too much high-purine food, such as seafood, animal viscera, or long-term drinking of beer, may lead to increased purine metabolism in the body, resulting in increased uric acid level, and thus manifested as disorders of uric acid metabolism[26]. Uric acid is associated with obesity[27]. Therefore, we suggest that prediabetes patients with high body weight can undertake comprehensive treatment through behavior, diet, and exercise, adopt a healthy lifestyle and reasonable eating habits, to reduce weight, avoid elevated uric acid, and reduce the possibility of prediabetes progressing to T2DM. However, this study has its limitations, that is, the sample size in this study is insufficient, and there may be selective bias leading to biased research results. In addition, we selected the study sample from a single center, and the research results can only reflect the population of this center. It is unknown whether it is widely applicable to the population of other centers. Therefore, multi-center and larger sample size studies are needed to further verify these findings.

## CONCLUSION

High body weight in patients with prediabetes is an independent risk factor for progression to T2DM, and high body weight coexisting with high uric acid level increases the risk of T2DM progression. Clinically, patients with high body weight and high uric acid should be vigilant, and timely clinical intervention measures should be taken to reduce the risk of prediabetes progressing to T2DM.

## ARTICLE HIGHLIGHTS

### Research background

The high incidence of diabetes mellitus (DM) is a serious threat to public health. There have been many reports on its influencing factors, but few studies on the influence of body weight on the progression from prediabetes to type 2 diabetes mellitus (T2DM), and the interaction between body weight and various influencing factors has not been reported.

### Research motivation

The phenomenon of high weight, waist circumference, and body mass index is common in prediabetes patients, and there are many factors affecting the progression of prediabetes to T2DM. Unilateral weight control cannot reduce this risk, and it is necessary to understand the interaction between weight and other factors.

### Research objectives

The purpose of this study was to explore the weight status of patients with prediabetes and analyze the interaction between weight and other disease outcome (DO) factors, so as to guide clinical intervention and reduce the risk of prediabetes progressing to T2DM.

### Research methods

A retrospective analysis of 236 patients with prediabetes and 50 patients with normal glucose control was performed. Clinical data and follow-up results of all patients were collected. The influencing factors (including body weight) of prediabetes DO were analyzed by logistic regression, and the interaction between body weight and independent influencing factors was analyzed by a general linear model (univariate).

### Research results

Body weight, glycosylated hemoglobin, uric acid, fasting insulin (FINS), and homeostatic model assessment for insulin resistance (HOMA-IR) were independent factors affecting the progression of prediabetes to T2DM ( $P < 0.05$ ). There was a multiplicative interaction between weight and uric acid ( $\beta = 1.953$ ,  $P = 0.005$ ).

### Research conclusions

Body weight has a significant effect on prediabetes progression to T2DM, and coexistent high body weight and high uric acid increase the risk of progression to T2DM.

### Research perspectives

From the perspective of high body weight as a risk factor for prediabetes progression to T2DM, the interaction between body weight and other risk factors (including glycosylated hemoglobin, uric acid, FINS and HOMA-IR) was discussed, and low carbon diet and weight loss were proposed to reduce the risk of progression and guide clinical intervention.

## FOOTNOTES

**Author contributions:** Li YY designed and performed the research and wrote the paper; Lin XY designed the research and supervised the report; Tong LP, Wu XD, Lin D, and Lin Y provided clinical advice.

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