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Weight loss before a diagnosis of type 2 diabetes mellitus is a risk factor for diabetes complications

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Abstract

Our goal was to investigate the relationship between weight loss before a diagnosis of type 2 diabetes mellitus (T2DM) and diabetic complications among hospitalized patients with T2DM.

We conducted a cross-sectional study and evaluated 347 and 642 hospitalized patients with T2DM who experienced and did not experienced weight loss before T2DM diagnosis, respectively. We used propensity score matching to reduce the confounding bias between the groups. In addition, a logistic regression analysis of the matched data was performed to evaluate the risk of diabetic complications.

A total of 339 patients who experienced weight loss were matched to 339 patients who did not experience weight loss. After adjusting for age, gender, origin, occupation, smoking history, alcohol use, and duration of diabetes, the logistic regression analysis showed that compared with patients who did not experience weight loss, patients who lost ≤5 kg had a higher risk of diabetic nephropathy (DN) (odds ratio [OR]: 2.05, 95% confidence interval [CI]: 1.35–3.10) and diabetic retinopathy (OR: 1.79, 95% CI: 1.11–2.87). However, we did not observe a dose–response relationship in terms of weight loss.

We found that weight loss before a diagnosis of T2DM might serve as a risk factor for DN and diabetic retinopathy. Our findings demonstrate that we should strengthen the management and prevention of complications in patients who experience weight loss of ≤5 kg prior to a T2DM diagnosis, particularly those who are centrally obese.

Abbreviations: CI = confidence interval, DM = diabetes mellitus, DN = diabetic nephropathy, FBG = fasting blood glucose, OR = odds ratio, PSM = propensity score matching, T2DM = type 2 diabetes mellitus.

Keywords: Chinese, diabetic complications, T2DM, weight loss

1. Introduction

The prevalence of diabetes mellitus (DM) has increased rapidly over the past 2 decades.[1,2] In 2015, a total of 415 million adults worldwide had diabetes, and by 2040, this figure is expected to increase to 642 million.[3] China has the most patients with DM (92.4 million) of any country in the world.[4] As a result, DM has caused more than 10 million disability-adjusted life years and was the 8th major cause of death in China in 2012; thus, DM represents a major public health problem in China.[5] Type 2 diabetes mellitus (T2DM) is the most common type of DM in China, and a substantial proportion of patients with T2DM are at risk for diabetic complications.[6] Diabetic complications are linked with disability and even death in patients with T2DM and thus constitute the main disease burden of T2DM. Therefore, identifying patients at a high risk of developing complications is important.

To the best of our knowledge, clinical trials have generally focused on the association between diabetic complications and blood pressure and the levels of blood glucose and blood lipids. Furthermore, previous studies on weight loss have typically studied the benefits of intrusive body weight control for the control of diabetes complications.[7,8] Along with increased drinking, eating, and urinating, weight loss in the absence of intentional dieting, diuretic therapy or exercise prior to the diagnosis of T2DM is generally identified as a symptom of T2DM[9]; however, few studies have investigated the relationship between weight loss prior to the T2DM diagnosis and diabetic complications.

Thus, we designed an observational study to investigate the relationship between weight loss prior to the T2DM diagnosis and diabetic complications in hospitalized patients with T2DM, which is the population with the highest proportion of diabetic complications. To increase the comparability between the 2 groups (patients who experience and who do not experience weight loss before the diagnosis of T2DM) and to reduce the influence of confounding factors, we used propensity score matching (PSM).[10]

2. Design and methods

2.1. Study sample

We used clinical data from the Department of Nephrology and Endocrinology at the PLA 148th Hospital. Among the 1025 inpatients (recruited from January 2010 to December 2012), we

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excluded 25 type 1 DM inpatients and 11 latent autoimmune diabetes in adult inpatients and therefore recruited a total of 989 (507 men and 482 women) participants in this study.

Based on the inclusion criteria, the included participants were inpatients of the Department of Nephrology and Endocrinology at the PLA 148th Hospital from January 2010 to December 2012 who were diagnosed with T2DM, had no history of cancer and tumors, were not pregnant, and agreed to participate in this study. The exclusion criteria were the following: non-Chinese nationality, pregnant women, a history of cancer and tumors, and lack of consent to participate in this study.

We collected information regarding the participant's gender, age, occupation, region, alcohol consumption, smoking history, diabetes duration, weight loss, and diabetes complications status (acute and chronic complications).

2.2. Measurement

T2DM was defined according to the American Diabetes Association criteria. Diabetic complications comprise acute and chronic complications, and the acute complications included diabetic ketoacidosis, hyperglycemia hyperosmolar state, and diabetes lactic acidosis.[9] The chronic diabetic complications included cardiovascular and cerebrovascular diseases (diagnosed after T2DM), diabetic nephropathy (DN), diabetic retinopathy, diabetic peripheral neuropathy, and diabetic lower limb angiopathy. All diabetic complications were diagnosed by 2 physicians according to the diagnostic criteria provided by the Chinese Diabetes Society.

Weight loss was defined as a decrease of at least 5% body weight within 6 months before the diagnosis of T2DM in the absence of intentional dieting and diuretic therapies. This information was collected by the primary nurse, and to ensure the accuracy of the information, the weight loss was confirmed with the patients and their relatives. Central obesity was defined as a waist circumference >90 cm for men or >80 cm for women.[11] In addition, we used 5 kg as the threshold for weight loss because previous studies showed that a weight loss of at least 5 kg was the standard value defining significant weight loss in patients with obesity[12] and weight loss >5 kg during the course of 1 year is an independent risk factor for 6-month mortality of nursing home residents. Furthermore, we included continuous loss of weight (kg) in the logistic analysis to determine the odds ratios [ORs] of weight loss (kg).

2.3. Statistical analysis

SPSS version 19.0 (Serial No. 5076595) was used for the data analyses. The significance level for all tests was set to a 2-tailed α value of 0.05. The differences in means and proportions were evaluated using Student *t* test and Chi-squared tests, respectively. Logistic regression models were used to identify the risk of weight loss (grouped and continuous).

PSM[13] was used for matching between the weight-loss group and the no-weight-loss groups. Gender, age, origin, occupation, smoking history, alcohol use, and duration of T2DM were included as covariates. We used nearest-neighbor matching to match former smokers to current smokers at a 1:1 ratio with a caliper width of 0.02.[14]

2.4. Ethical considerations

The Committee for Medical Ethics of the Chinese PLA General Hospital examined and approved our study. Before completing the questionnaire, each involved participant signed an informed consent form.

3. Results

A total of 989 (507 men and 482 women) inpatients were included in our study prior to PSM. The average age of the participants was 56.8±11.6 years (range: 14–93 years). The average ages of the patients in the weight-loss and no-weight-loss groups were 54.7±11.3 years (19–93 years) and 58.0±11.6 years (14–87 years), respectively. The general characteristics (age, gender, origin, occupation, smoking history, and alcohol use) of the participants are shown in Table 1. Compared with the patients in the weight-loss group, those in the no-weight-loss

Table 1

Demographic characteristics of the participants according to weight loss before and after PSM.

		Weight loss before PSM			Weight loss after PSM		
Group	**Total (N=989), n (%)**	**Yes (n=347)**	**None (n=642)**	***P***	**Yes (n=339)**	**None (n=339)**	***P***
Age, y				<0.001			0.374
≤40	83 (8.4)	35 (10.1)	48 (7.5)		29 (8.6)	40 (11.8)	
60–69	538 (54.4)	212 (61.1)	326 (50.8)		210 (61.9)	204 (60.2)	
≥70	368 (37.2)	100 (28.8)	268 (41.7)		100 (29.5)	95 (28.0)	
Gender				0.011			0.700
Male	507 (51.3)	197 (56.8)	310 (48.3)		189 (55.8)	184 (54.3)	
Female	482 (48.7)	150 (43.2)	332 (51.7)		150 (44.2)	155 (45.7)	
Occupation				0.301			0.654
White collar	104 (10.5)	30 (8.6)	74 (11.5)		30 (8.8)	34 (10.0)	
Light physical labor	117 (11.8)	45 (13.0)	72 (11.2)		41 (12.1)	47 (13.9)	
Hard physical labor	768 (77.7)	272 (78.4)	496 (77.3)		268 (79.1)	258 (76.1)	
Region				0.473			0.485
Shandong province	958 (96.9)	338 (97.4)	620 (96.6)		331 (97.6)	328 (96.8)	
Other province	31 (3.1)	9 (2.6)	22 (3.4)		8 (2.4)	11 (3.2)	
Smoker				0.699			0.922
Yes	186 (18.8)	63 (18.2)	123 (19.2)		63 (18.6)	64 (18.9)	
No	803 (81.2)	284 (81.8)	519 (80.8)		276 (81.4)	275 (81.1)	
Alcohol use				0.269			0.821
Yes	142 (14.4)	44 (12.7)	98 (15.3)		44 (13.0)	46 (13.6)	
No	847 (85.6)	303 (87.3)	544 (84.7)		295 (87.0)	293 (86.4)	
Age, mean±SD		54.7±11.3	58.0±11.6	<0.001	55.2±10.9	53.8±10.9	0.093
Duration of diabetes, mean±SD		6.0±5.8	7.8±6.2	<0.001	6.1±5.8	6.2±5.7	0.297
FBG, mean±SD		13.2±4.9	11.0±4.5	<0.001	13.1±4.6	12.6±4.6	0.108

FBG = fasting blood glucose, PSM = propensity score matching, SD = standard deviation.

Table 2

OR (95% CI) of diabetic complications according to weight loss among participants.

		N (%)	Model A* OR (95% CI)	Model B† OR (95% CI)	Model C‡ OR (95% CI)
Acute complication					
Loss of weight	None (reference)	26 (7.7)	1	1	1
	≤5 kg	9 (4.7)	0.60 (0.27–1.30)	0.59 (0.27–1.30)	0.61 (0.28–1.36)
	>5 kg	12 (8.1)	1.06 (0.52–2.17)	1.14 (0.55–2.34)	1.15 (0.55–2.40)
	P for trend		0.973	0.995	0.958
Chronic complication					
Cardio-cerebrovascular disease					
Loss of weight	None (reference)	91 (26.8)	1	1	1
	≤5 kg	48 (25.1)	0.55 (0.39–0.80)	0.67 (0.45–1.00)	0.79 (0.50–1.24)
	>5 kg	39 (26.4)	0.58 (0.39–0.86)	0.71 (0.46–1.10)	0.84 (0.51–1.36)
	P for trend		<0.001	0.045	0.372
Diabetic nephropathy					
Loss of weight	None (reference)	217 (64.0)	1	1	1
	≤5 kg	150 (78.5)	1.80 (1.23–2.63)	1.83 (1.25–2.69)	1.93 (1.35–3.10)
	>5 kg	99 (66.9)	1.00 (0.68–1.44)	1.01 (0.69–1.48)	1.14 (0.73–1.69)
	P for trend		0.325	0.290	0.199
Diabetic retinopathy					
Loss of weight	None (reference)	255 (75.2)	1	1	1
	≤5 kg	161 (84.3)	1.77 (1.12–2.80)	1.72 (1.08–2.75)	1.79 (1.11–2.87)
	>5 kg	112 (75.7)	1.03 (0.65–1.61)	1.03 (0.65–1.64)	1.11 (0.69–1.78)
	P for trend		0.506	0.514	0.330
Diabetic peripheral neuropathy					
Loss of weight	None (reference)	239 (70.5)	1	1	1
	≤5 kg	149 (78.0)	1.48 (0.98–2.25)	1.45 (0.95–2.20)	1.51 (0.99–2.31)
	>5 kg	99 (66.9)	0.85 (0.56–1.28)	0.85 (0.55–1.29)	0.86 (0.56–1.32)
	P for trend		0.764	0.752	0.863
Diabetic lower limb angiopathy					
Loss of weight	None (reference)	56 (16.5)	1	1	1
	≤5 kg	32 (16.8)	1.02 (0.63–1.64)	0.96 (0.59–1.56)	1.00 (0.61–1.64)
	>5 kg	22 (14.9)	0.88 (0.52–1.51)	0.79 (0.46–1.37)	0.76 (0.43–1.34)
	P for trend		0.695	0.433	0.400

CI = confidence interval, FBG = fasting blood glucose, OR = odds ratio.

* Crude model.

† Adjusted for age, gender, origin, and occupation.

‡ Adjusted for age, gender, origin, occupation, smoking history, alcohol use, duration of diabetes, and FBG.

group were older, included a higher proportion of females, experienced a longer duration of T2DM and had a lower fasting blood glucose (FBG) level.

After PSM, a total of 392 participant pairs were matched, and the weight-loss and no-weight-loss groups were balanced in terms of age, gender, duration of diabetes, and FBG (Table 1).

After adjusting for age, gender, origin, occupation, smoking history, alcohol use, duration of diabetes, and FBG, the logistic regression analysis revealed that compared with the no-weight-loss group, the group of patients who experienced a weight loss of ≤5 kg had a higher risk of DN (OR: 2.05, 95% confidence interval [CI]: 1.35–3.10) and diabetic retinopathy (OR: 1.79, 95% CI: 1.11–2.87); however, we did not observe a dose–-response relationship based on the weight loss (Table 2). Furthermore, we included continuous loss of weight (kg) in the logistic analysis to determine the ORs of weight loss (continuous, kg) and obtained similar but not significant results (Table 3).

As shown in Table 4, among centrally obese participants, the weight-loss group (≤5 kg) was found to have a higher risk of DN (OR: 2.12, 95% CI: 1.26–3.58) and diabetic retinopathy (OR: 1.96, 95% CI: 1.07–3.59) after adjusting for age, gender, origin, occupation, smoking history, alcohol use, duration of diabetes, and FBG (Table 4). Among nonobese participants, this relationship was not significant (Supplementary Table S1, http://links.lww.com/MD/B445).

4. Discussion

Weight loss without intentional dieting, diuretic therapy, or excise before a diagnosis of T2DM is a classic symptom of T2DM, although few studies have focused on the relationship between weight loss before a T2DM diagnosis and diabetic complications. Thus, we designed this study to observe this relationship among patients with T2DM in the PLA 148th Hospital. To the best of our knowledge, this study constitutes the first investigation of this association. The major strength of our study was the comprehensive control of and adjustment for a wide range of potential confounders using PSM. The similar results between the matched groups demonstrate the robustness of the results. Moreover, because weight loss prior to the T2DM diagnosis occurred before the onset of diabetic complications, the problem of reverse causality, one of the major limitations of cross-sectional studies, was not a major concern in our study.

After matching, we observed a significant association between an involuntary weight loss ≤5 kg before the diagnosis of T2DM and diabetic complications (DN and diabetic retinopathy). Previous studies have generally focused on the association

Table 3

OR (95% CI) of diabetic complications for loss of weight in participants (continuous variable).

	Model A*	Model B†	Model C‡
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Acute complication			
Loss of weight			
Continuous	0.99 (0.92–1.05)	0.99 (0.93–1.06)	0.99 (0.93–1.06)
P for trend	0.665	0.992	0.784
Chronic complications			
Loss of weight (cardio-cerebrovascular disease)			
Continuous	0.98 (0.95–1.02)	0.98 (0.94–1.02)	0.98 (0.93–1.01)
P for trend	0.343	0.226	0.198
Loss of weight (diabetic nephropathy)	1.03 (1.00–1.07)	1.03 (1.00–1.07)	1.03 (1.00–1.07)
Continuous			
P for trend	0.051	0.056	0.052
Loss of weight (diabetic retinopathy)	1.01 (0.97–1.05)	1.01 (0.97–1.05)	1.02 (0.98–1.06)
Continuous			
P for trend	0.630	0.516	0.306
Loss of weight (diabetic peripheral neuropathy)	1.00 (0.97–1.04)	1.01 (0.97–1.04)	1.01 (0.97–1.04)
Continuous			
P for trend	0.921	0.788	0.734
Loss of weight (diabetic lower limb angiopathy)	0.99 (0.95–1.04)	0.99 (0.94–1.03)	0.98 (0.94–1.03)
Continuous			
P for trend	0.663	0.985	0.418

CI = confidence interval, FBG = fasting blood glucose, OR = odds ratio.

* Crude model.

† Adjusted for age, gender, origin, and occupation.

‡ Adjusted for age, gender, origin, occupation, smoking history, alcohol use, duration of diabetes, and FBG.

Table 4

OR (95% CI) of diabetic complications according to weight loss among obese participants.

			Model A*	Model B†	Model C‡
		N (%)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Acute complication					
Loss of weight	None (reference)	12 (6.3)	1	1	1
	≤5 kg	4 (3.2)	0.48 (0.15–1.54)	0.49 (0.15–1.61)	0.55 (0.16–1.85)
	>5 kg	5 (6.1)	0.96 (0.33–2.81)	1.05 (0.34–3.23)	1.09 (0.33–3.59)
	P for trend		0.701	0.827	0.959
Chronic complication					
Cardio-cerebrovascular disease					
Loss of weight	None (reference)	51 (27.0)	1	1	1
	≤5 kg	35 (27.8)	1.04 (0.63–1.73)	0.90 (0.52–1.56)	0.90 (0.52–1.58)
	>5 kg	26 (31.7)	1.26 (0.71–2.21)	0.93 (0.50–1.72)	0.92 (0.49–1.72)
	P for trend		0.459	0.956	0.750
Diabetic nephropathy					
Loss of weight	None (reference)	118 (62.4)	1	1	1
	≤5 kg	98 (77.8)	2.11 (1.26–3.52)	2.12 (1.26–3.56)	2.12 (1.26–3.58)
	>5 kg	55 (67.1)	1.23 (0.71–2.12)	1.19 (0.68–2.08)	1.15 (0.65–2.03)
	P for trend		0.167	0.198	0.254
Diabetic retinopathy					
Loss of weight	None (reference)	143 (75.7)	1	1	1
	≤5 kg	106 (84.1)	1.71 (0.95–3.05)	1.82 (1.00–3.31)	1.96 (1.07–3.59)
	>5 kg	63 (76.8)	1.07 (0.58–1.97)	1.04 (0.55–1.96)	1.14 (0.59–2.19)
	P for trend		0.522	0.545	0.369
Diabetic peripheral neuropathy					
Loss of weight	None (reference)	134 (70.9)	1	1	1
	≤5 kg	95 (75.4)	1.26 (0.75–2.10)	1.32 (0.78–2.22)	1.42 (0.83–2.43)
	>5 kg	56 (68.3)	0.88 (0.50–1.55)	0.87 (0.49–1.56)	0.89 (0.49–1.61)
	P for trend		0.865	0.874	0.966
Diabetic lower limb angiopathy					
Loss of weight	None (reference)	32 (16.9)	1	1	1
	≤5 kg	23 (18.3)	1.10 (0.61–1.98)	1.02 (0.56–1.88)	1.15 (0.62–2.15)
	>5 kg	16 (19.5)	1.19 (0.61–2.31)	0.98 (0.49–1.95)	1.00 (0.48–2.05)
	P for trend		0.599	0.965	0.935

CI = confidence interval, FBG = fasting blood glucose, OR = odds ratio.

* Crude model.

† Adjusted for age, gender, origin, and occupation.

‡ Adjusted for age, gender, origin, occupation, smoking history, alcohol use, duration of diabetes, and FBG.

between weight loss after a T2DM diagnosis (usually with an intervention, such as diet control, physical exercise, and even weight reduction surgery) and the developmental tendency of T2DM.[7,8] This intervention weight loss with lifestyle change is beneficial for controlling the patient's blood glucose and blood lipids[15,16]; furthermore, postdiagnosis weight loss might impact the patient's psychological state and therefore improve their health-related quality of life.[17] Regarding diabetic complications, the effect of intervention weight loss is confused or null; a cohort study showed weight loss due to gastric banding has no unfavorable effect on kidney function and retinopathy and no effect on the prevention of arterial hypertension or cardiovascular disease.[18] A meta-analysis on glycemic control and weight loss in patients with T2DM showed that exercise training reduces hemoglobin A1c by an amount that should decrease the risk of diabetic complications, but no significant effect on weight loss was found.[19] Different from intervention weight loss, we focused on weight lost without lifestyle changes or other interventions before the diagnosis of T2DM. This type of weight loss is usually identified as a symptom of T2DM, and in our study, we found that it might also be a risk factor for the development of diabetic complications (i.e., DN and diabetic retinopathy). Prediagnosis weight loss might be caused by osmotic diuresis under high blood glucose conditions. Moreover, compared with patients who do not experience weight loss, patients who experience weight loss may have a higher blood glucose when diagnosed with T2DM, which likely places a heavier burden on the kidney and microvascular system and thereby predisposes these individuals to a higher risk of developing DN and diabetic retinopathy. However, we did not observe a dose–response relationship with weight loss, which might reveal that the effect of weight loss on diabetic complications is not linear or that the mechanism differs when the amount of weight lost is >5 kg.

Our study further showed that among centrally obese patients, the weight-loss group had a higher risk of developing DN and diabetic retinopathy, but this risk was not significant among patients without central obesity. Indeed, studies have linked obesity with increased circulating hormone levels (including estrogens, androgens, insulin, and IGF-I), and central obesity is the manifestation of impaired glucose tolerance and insulin resistance.[20,21] Thus, the effect of weight loss in patients with T2DM with central obesity might be more significant.

This study had several limitations. Because the weight-loss information was based on recall, recall bias cannot be fully ruled out; however, the information was confirmed with patients and their relatives to ensure accuracy. Second, our sample might not be completely representative of patients with T2DM in China because our hospital is one of the best hospitals in Zibo and the inpatients at our hospital show a higher frequency of diabetic complications; however, the representativeness of our sample should not substantially affect the internal validity of the study. Finally, we could not examine the hazard ratio of weight loss with diabetic complications due to the lack of detailed information on the onset time of diabetic complications.

In summary, our study provides the first examination of the association of weight loss prior to a diagnosis of T2DM with diabetic complications among T2DM inpatients. We increased the comparability of the weight-loss and no-weight-loss groups using the PSM method and found that weight loss before a diagnosis of T2DM might be a risk factor for DN and diabetic retinopathy development; however, further cohort studies should be conducted to verify this causal relationship. Our findings further demonstrate that we should strengthen the management and prevention of complications in patients with weight loss ≤ 5 kg before their T2DM diagnosis, particularly those with central obesity.

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