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Original Article

Interaction between Overweight, Obesity and Smoking on the Risk of Pre-Diabetes and Type 2 Diabetes in Guangdong, China

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Abstract

Background: Pre-diabetes mellitus (PDM) is considered a precursor stage of type 2 diabetes mellitus (T2DM) and serves as an early warning sign for the disease. However, most studies only analyze the risk factors of T2DM, ignore the exploration of PDM.

Methods: Here 28,208 patients with T2DM were selected from 5 cities in the Pearl River Delta, Guangdong Province, China in 2017. Then a 1:1 matched case-control study was conducted according to the matching conditions. Finally, 28208 patients with PDM and 28208 patients with normal glucose tolerance (NGT) were matched, and when multiple subjects were matched, the same subjects in the region were preferredOrdered multiple logistic regression was used to analyze the influencing factors of T2DM and PDM. When analyzing the relationship between overweight, obesity, smoking, and T2DM, factors such as age, education level, exercise were adjusted.

Results: Overweight, obesity (OR=1.427, 95%CI:1.388~1.468; OR=1.829,95%*CI*:1.753~1.908) and smoking (OR=1.161,95%CI:1.113~1.212) were risk factors for the onset of T2DM by ordered multiple logistic regression. There was an additive interaction between overweight obesity and smoking in the developing of T2DM. Moreover, there were 0.196(0.051~0.341) relative excess risk due to the additive interaction, 9.1% (2.0%-16.1%) of T2DM exposed to both risk factors was attributable to the additive interaction, and the risk of T2DM in overweight and obese smokers was 1.203(1.004-1.402) times as high as the sum of risks in the participants exposed to a single risk factor too.

Conclusion: Overweight obesity and smoking are the risk factors for the onset of T2DM.

Keywords: Smoking; Overweight; Obesity; Type 2 diabetes mellitus; Pre-diabetes mellitus

Introduction

Pre-diabetes was defined as blood glucose concentrations higher than normal but not high enough to be classified as diabetes, which was the state between normal and diabetes, categorized into either impaired fasting glucose (IFG) or/and impaired glucose tolerance (IGT) (1,2) and was called impaired glucose Regulation (IGR). Pre-diabetes was an early warning signal of type 2 di-

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abetes mellitus. Several national or regional studies (1-3) have found that the prevalence of diabetes in China is on rise, and the prevalence of pre-diabetes is increasing. Overweight or obese patients have accounted for 70% of diabetic patients, and obesity has become the core pathogenic factor of diabetes (3). However, the risk factors and the mechanism of their interaction were not clear.

In 2014, China's obese population ranked first in the world (4). Smoking is another important risk factor for diabetes too. The risk of diabetes in smokers is 1.2 times higher than that in non-smokers (5). The occurrence of diabetes caused by overweight, obesity and smoking is related to insulin resistance (6,7). The reason may be related to abnormal adipose tissue function, inflammation activation, and accumulation of metabolic products. Therefore, there may be some synergistic effect in the mechanism leading to diabetes.

At present, most of the studies only analyze the risk factors of diabetes; ignore the exploration of risk factors of PDM. Hence, in this study, we aimed to explore the influence of overweight, obesity and smoking on incidence type 2 diabetes mellitus (T2DM), and the independent and comprehensive effects on Pre-diabetes mellitus and T2DM respectively.

Methods

Participants

The research objects of this study comes from the healthy screening population over 18 years of age in Pearl River Delta region of Guangdong Province from January to October 2017. Sampling was conducted on a community basis based on the population size of each city. 5 cities in Guangdong Province were selected, then 4 communities according to urban and rural area were selected from each city.

All residents aged 18 and above from the selected communities participated in the study. A questionnaire survey including general population characteristics, disease history, lifestyle and other factors will be conducted by uniformly trained researchers, and laboratory tests and physical measurements will be conducted by professionals.

Ethics Committee of the First Affiliated Hospital of Guangdong Pharmaceutical University agreed to the study (Guangzhou, China). Our research was performed in accordance with the declaration of Helsinki relevant and all subjects signed informed consent.

All subjects underwent blood sampling and epidemiological questionnaire survey. After glycemic, blood lipid, blood pressure and body weight measurements, combined with epidemiological history data, T2DM, PDM and normal controls were grouped. A1:1:1 case-control study was used in our research. According to the principle of same-gender, age difference less than 5 years, living in the same region, 28,208 patients with PDM and 28,208 NGT were matched with T2DM, respectively.

Inclusion criteria

Diabetes group

According to the "China T2DM Prevention and Treatment Guidelines (2017 Version)" standard grouping: fasting blood glucose value ≥7.0 mmol/L or 2h postprandial blood glucose value ≥11.1mmol/L or glycated hemoglobin HbA1c ≥6.5% or a previous history of diabetesor have typical symptoms of diabetes such asmultiple drinks, polyphagia, polyuriaand unexplained weight loss, with random blood glucose values ≥ 11.1 mmol/L.

PDM group

Impaired Fasting Glucose (IFG) is 6.1≤FPG＜ 7.0mmol/L, and Impaired Glucose Tolerance (IGF) is 7.8≤2hPG ＜11.1mmol / L.

Control group

Healthy people with fasting blood glucose value <7.0 mmol/L and random blood glucose value <11.1 mmol/L and 2 hours postprandial blood glucose value <11.1 mmol/L in the same sex and same area and 5 years old as diabetic patients were selected as the control group.

Exclusion criteria

Diabetes group and control group excluded patients with other types of diabetes such as type 1 diabetes, gestational diabetes, and patients with cerebral infarction, myocardial infarction, malignant tumors, and chronic inflammation.

Determination of blood glucose

The blood samples (5 ml for each subjects) from the vein were stored at −80 °C until analysis.

Fasting plasma glucose measurements

The subjects were fed fasting at 8:00 every day and performed by a specialist using a Beckman Coulter AU680 (Beckman Coulter, Cassina de' Pecchi, Italy) , by glucose oxidase method.

After fasting blood glucose was measured, the test of drinking 75g glucose water was carried out, and the blood glucose value was measured after 2 hours.

The HbA1c were measured by Pumen H9 automatic glycosylated hemoglobin analyzer (Shenzhen, China).

The random blood glucose values were measured by Beckman Coulter AU680 (Beckman Coulter, Cassina de' Pecchi, Italy).The intra batch coefficient of variation (CV) of AU680 is less than 1%, and the inter batch CV is less than 5%, which meets the quality requirements. Before daily testing, quality control calibration instruments were performed. Linear regression analysis showed that the detection results of AU680 were highly consistent with the theoretical values (R^2≈0.998-1.000), with a recovery rate between 97.5% and 99.1%, indicating good accuracy and linearity.

The questionnaire content

Our questionnaire was collected by surveyors with uniform training, who conducted a comprehensive questionnaire survey including general demographic characteristics, disease history, life style and other factors. The lipid and other biochemical parameters were performed by trained hospitals in Pearl River Delta region (Dongguan people's Hospital, Dongguan, Haizhu District People's Hospital, Guangzhou and Zhuhai People's Hospital, Zhuhai). Plasma cholesterol and TG were quantified by a standardized enzymatic assay. We used the standard mercury sphygmomanometer to measure the blood pressure. The staff must participate in the training of standard blood pressure measurement methods prior to the survey. The criterias of Overweight and Obesity were: Overweight: 24.0≤BMI＜28.0kg/m^2, Obesity: BMI≥28.0kg/m^2.

Statistical analysis

The development process of diabetes was an ordered categorical variable, so an ordered multiclass logistic regression model was used. NGT was used as the control group, PDM and T2DM were the case groups, and univariate analysis was performed first to incorporate the statistically significant variables into the multifactorial in the model. Then the unconditional logistic regression models of NGT-T2DM and NGT-PDM were established respectively to study the independent and comprehensive effects of smoking and overweight, obesity, and diabetes. When analyzing the relationship between overweight, obesity, smoking, and T2DM, factors such as age, education level, marriage, exercise, alcohol consumption, diet, and hypertension were adjusted by regression model. The multiplicative interaction was determined by *P* value less than 0.05, and the additive interaction was conducted by nonlinear mixed effect model by the relative excess risk ratio (RERI), attribution ratio (AP) and interaction index (S).

Results

Characteristics of study participants

A total of 84,624 subjects were enrolled, with 28,208 subjects in each group. There were statistical difference in age, education, marriage, occupation, smoking, drinking, exercise, diet and BMI among the three groups. By pairwise comparison, there were no difference in the distribution of education and marriage in the comparison NGT and PDM. In the comparison of NGT and T2DM, there were no significant difference in the distribution of occupations between the two groups too (Table 1).

Table 1: Basic situation of NGT, PDM, T2DM

Variables	NGT (n= 28208)	PDM (n= 28208)	T2DM (n= 28208)	P_a	P_b	P_c
Age(yr)				<0.001	<0.001	<0.001
18~43	5065(17.96)	3383(11.99)	3336(11.83)			
44~59	8322(29.5)	8613(30.53)	9548(33.85)			
≥60	14821(52.54)	16212(57.47)	15324(54.33)			
Education				<0.001	0.081	<0.001
Below primary school	4698(16.65)	4822(17.09)	5039(17.86)			
middle school	3625(12.85)	3450(12.23)	3453(12.24)			
Above high school	4168(14.78)	4110(14.57)	3917(13.89)			
Others	15717(55.72)	15826(56.1)	15799(56.01)			
Marriage				0.004	0.092	0.004
Unmar-ried/widowed/divorced	2079(7.37)	1910(6.77)	1903(6.75)			
Married	26129(92.63)	26298(93.23)	26305(93.25)			
Occupation				<0.001	<0.001	0.128
Mental workers	2620(9.29)	2804(9.94)	2609(9.25)			
Manual workers	6283(22.27)	5871(20.81)	6090(21.59)			
Other	19305(68.44)	19533(69.25)	19509(69.16)			
Smoking				<0.001	<0.001	
No	3052(10.82)	3721(13.19)	3736(13.24)			
Yes	25156(89.18)	24487(86.81)	24472(86.76)			
Drinking				<0.001	<0.001	<0.001
No	2193(7.77)	2527(8.96)	2510(8.9)			
Yes	26015(92.23)	25681(91.04)	25698(91.1)			
Fitness				<0.001	<0.001	<0.001
No	16878(59.83)	16980(64.13)	17758(62.95)			
Yes	11330(40.17)	9499(35.87)	10450(37.05)			
diet				<0.001	<0.001	<0.001
Vegetarian equilibrium	23125(81.98)	23003(81.55)	22980(81.47)			
Vegetarian imbalance	776(2.75)	1028(3.64)	992(3.52)			
Others	4307(15.27)	4177(14.81)	4236(15.02)			
BMI				<0.001	<0.001	<0.001
Normal	17214(61.03)	13418(47.57)	13424(47.59)			
Underweight	1505(5.34)	866(3.07)	1257(4.46)			
Overweight	7602(26.95)	10226(36.25)	9850(34.92)			
Obesity	1887(6.69)	3698(13.11)	3677(13.04)			
hypertension				<0.001	<0.001	<0.001
No	1575(5.58)	1836(6.51)	2007(7.12)			
Yes	26633(94.42)	26372(93.49)	26201(92.88)			

Note: a: represents the differences between the three groups of NGT, PDM, and T2DM, b: represents the differences between the two groups of NGT,PDM, and c: represents the differences between the two groups of NGT, T2DM

Biochemical indicators of NGT, PDM, T2DM

Table 2 shows the biochemical indicators between the three groups of NGT, PDM and T2DM. From the indicators, it might be found that HDL-C level decreased the risk to development PDM and T2DM, however, other indicators like TC, TG and SBP increase the risk of PDM and T2DM.

Table 2: Biochemical indicators of NGT, PDM, T2DM（ $\bar{\chi}$±s or M±Q）

Variables	NGT (n=28208)	PDM (n=28208)	T2DM (n=28208)	*F* or *H*	*P* value
Waistline(cm)	82.00±9.00	84.00±10.00	85.00±10.00	2155.033	<0.001
SBP(mmHg)	129.06±16.40	132.28±16.21	132.30±16.81	352.580	0.001
DBP(mmHg)	78.35±9.72	79.52±9.62	80.00±13.00	107.228	<0.001
TC(mol/L)	5.01±1.18	5.28±1.20	5.40±1.21	736.137	<0.001
TG(mol/L)	1.29±0.72	1.46±1.00	1.69±1.35	1665.199	<0.001
LDL-C(mol/L)	2.85±1.12	3.00±1.17	3.06±1.22	346.301	<0.001
HDL-C(mol/L)	1.37±0.44	1.33±0.47	1.30±0.47	325.210	<0.001

Analysis the risk factors of NGT, PDM, and T2DM by ordered Multi-Classification Logistic Results

NGT, PDM, T2DM were be regarded as dependent variables, and age, education, marriage, occupation, sports, alcohol, diet, BMI, hypertension and other factors were be regarded as risk factors, we utilized an orderly multi-class logistic regression analysis to find the risk factors of PDM and T2DM. Smoking and BMI have an impact on the development of diabetes. Adjusting factors such as age, education, marriage, exercise, alcohol, diet, hypertension, and other factors show that smoking also affects the development of diabetes (*P*<0.001, OR (95% CI) = 1.161 (1.113 ~ 1.212)), BMI were influential factors for the progression of diabetes too(P <0.05, $OR_{overweight}$ (95% CI) = 1.427 (1.388 ~ 1.468), $OR_{obesity}$(95% CI) = 1.829 (1.753 ~ 1.908)) (Table 3).

Unconditional Logistic Regression results between NGT-PDM and NGT-T2DM

Table 4 showed the results of unconditional logistic regression between NGT-PDM and NGT-T2DM. In the NGT-PDM group, adjusting for age, education and other confounding factors showed that smoking, obesity, and overweight were risk factors for PDM (*P*< 0.001), in the NGT-T2DM group, adjusting for mixed factors such as age and education showed that smoking, obesity and overweight were risk factors for T2DM (*P*<0.001).By comparing the two models, smoking and obesity affect the development both PDM and T2DM.

Table 3: Logistic regression analysis of T2DM risk factors

Variables	*β*	*sχ*	z	*P value*	Gross OR(95%CI)	Adjusted OR(95%CI)
Age(yr)						
18~43	1.000	-	-	-	-	-
44~59	0.3796	0.0210	326.4986	<0.001	1.564(1.503~1.628)	1.462(1.403~1.523)
≥60	0.3024	0.0201	225.1918	<0.001	1.443(1.39~1.498)	1.353(1.301~1.408)
Education						
Below primary school	1.000	-	-	-	-	-
Middle school	-0.0785	0.0242	10.5703	0.0011	0.914(0.873~0.957)	0.924(0.882~0.969)
Above high school	-0.0488	0.0235	4.2895	0.0383	0.906(0.867~0.947)	0.952(0.909~0.997)

Table 3: Continued…

Others	-0.0263	0.0182	2.0763	0.1496	0.952(0.92~0.985)	0.974(0.940~1.010)
Marriage						
Unmar-ried/widowed/ divorced/	1.000	-	-	-	-	-
Married	-0.0216	0.0255	0.7193	0.3964	1.075(1.024~1.128)	0.979(0.931~1.029)
Physical exer-cise						
No	1.000	-	-	-	-	-
Yes	0.0667	0.0140	22.6892	<.0001	1.106(1.078~1.135)	1.069(1.040~1.099)
Drinking						
No	1.000	-	-	-	-	-
Yes	-0.0011	0.0255	0.0019	0.9654	1.113(1.064~1.163)	0.999(0.950~1.050)
Diet						
Vegetarian equilibrium	1.000	-	-	-	-	-
Vegetarian imbalance	0.0951	0.0357	7.0801	0.0078	1.19(1.11~1.276)	1.100(1.025~1.180)
Others	-0.0473	0.0196	5.7965	0.0161	0.992(0.958~1.027)	0.954(0.918~0.991)
Smoking						
No	1.000	-	-	-	-	-
Yes	0.1496	0.0216	48.1665	<0.001	1.179(1.136~1.225)	1.161(1.113~1.212)
BMI						
Normal	1.000	-	-	-	-	-
Underweight	0.0601	0.0322	3.4807	0.0621	1.033(0.971~1.099)	1.062(0.997~1.131)
Overweight	0.3559	0.0144	611.6245	<.0001	1.459(1.419~1.5)	1.427(1.388~1.468)
Obesity	0.6037	0.0216	780.167	<.0001	1.851(1.776~1.93)	1.829(1.753~1.908)
Hypertension						
No	1.000	-	-	-	-	-
Yes	0.1132	0.0271	17.4629	<0.001	1.21(1.151~1.273)	1.12(1.062~1.181)

Table 4: Unconditional Logistic Results between NGT-PDM and NGT-T2DM

Variables	NGT-PDM					NGT-T2DM			
	β	*P value*	Crude OR (95%CI)	Regulated OR (95%CI)		*B*	*P值*	Crude OR (95%CI)	Regulated OR (95%CI)
Age(yr)									
18~43	1.000	-	-	-		1.000	-	-	-
44~59	0.329	<0.001	1.550 (1.47~1.634)	1.390 (1.315~1.469)		0.490	<0.001	1.742 (1.653~1.836)	1.633 (1.546~1.724)
≥60	0.364	<0.001	1.638 (1.56~1.72)	1.439 (1.364~1.517)		0.378	<0.001	1.57 (1.494~1.649)	1.459 (1.385~1.538)
Education									
Below	1.000	-	-	-		1.00	-	-	-

Table 4: Continued…

primary school						0			
middle school	-0.093	0.005	0.927 (0.872~0.986)	0.911 (0.854~0.972)		-0.112	0.001	0.888 (0.835~0.944)	0.895 (0.84~0.953)
Above high school	0.021	0.512	0.961 (0.906~1.019)	1.021 (0.959~1.088)		-0.072	0.023	0.876 (0.826~0.929)	0.931 (0.875~0.99)
others	-0.020	0.415	0.981 (0.937~1.027)	0.980 (0.933~1.029)		-0.033	0.174	0.937 (0.896~0.981)	0.967 (0.922~1.015)
Marriage									
Unmarried/ widowed/ divorced	1.000	-	-	-		1.000	-	-	-
married	-0.058	0.092	1.095 (1.027~1.168)	0.943 (0.881~1.01)		-0.021	0.535	1.100 (1.031~1.173)	0.979 (0.916~1.047)
Smoking									
No	1.000	-	-	-		1.000	-	-	-
Yes	0.195	<0.001	1.2503(1.19~1.318)	1.215 (1.146~1.288)		0.204	<0.001	1.258 (1.196~1.324)	1.226 (1.158~1.299)
Drinking									
No	1.000	-	-	-		1.000	-	-	-
Yes	-0.013	0.703	1.167 (1.099~1.239)	0.987 (0.921~1.057)		-0.007	0.837	1.158 (1.091~1.23)	0.993 (0.928~1.063)
Fitness									
No	1.000	-	-	-		1.000	-	-	-
Yes	0.20	<0.001	1.200 (1.159~1.242)	1.223 (1.178~1.27)		0.080	<0.001	1.141 (1.103~1.18)	1.083 (1.044~1.124)
Diet									
Vegetarian equilibrium	1.000	-	-	-		1.000	-	-	-
Vegetarian imbalance	0.174	0.001	1.332 (1.211~1.464)	1.190 (1.08~1.311)		0.155	0.002	1.286 (1.169~1.416)	1.168 (1.059~1.287)
Others	-0.651	<0.001	0.975 (0.931~1.021)	0.521 (0.493~0.552)		-0.061	0.016	0.99 (0.945~1.036)	0.941 (0.896~0.989)
BMI									
Normal	1.000	-	-	-		1.000	-	-	-

Table 4: Continued…

Under-weight	-0.181	<0.001	0.738 (0.677~0.805)	0.835 (0.763~0.913)		0.103	0.011	1.071 (0.99~1.158)	1.109 (1.024~1.2)
Over-weight	0.515	<0.001	1.726 (1.663~1.791)	1.674 (1.611~1.74)		0.477	<0.001	1.662 (1.6~1.725)	1.61 (1.551~1.672)
Obesity	0.902	<0.001	2.514 (2.368~2.669)	2.464 (2.318~2.62)		0.890	<0.001	2.499 (2.353~2.653)	2.434 (2.291~2.585)
Hyperten-sion									
No	1.000	-	-	-		1.000	-	-	-
Yes	0.068	0.074	1.177 (1.098~1.262)	1.070 (0.994~1.152)		0.145	<0.001	1.295 (1.21~1.387)	1.156 (1.077~1.242)

Results of multiplicative and additive interactions between NGT-PDM and NGT-T2DM

Table 4 showed that overweight and obesity were correlated with PDM and T2DM, and the risk had a dose-response relationship. While underweight was a protective factor of PDM in the NGT-PDM, but it was insignificance by comparison NGT-T2DM groups. Therefore, overweight and obesity were considered as risk group, and normal and underweight were considered as control group for additive interaction and multiplicative interaction model analysis.

Fig. 1 shows the multiplicative and additive interactions effects of obesity and smoking on PDM after stratification. The risk of PDM among overweight/ obesity and smokers was 2.262(2.091~2.448) times than that of non-overweight/non obesity and non-smokers. Overweight/ obese and smoking increased the risk of PDM than those exposed single risk factor alone. However, we did not find multiplicative and additive interactions between overweight/ obesity and smoking on PDM.

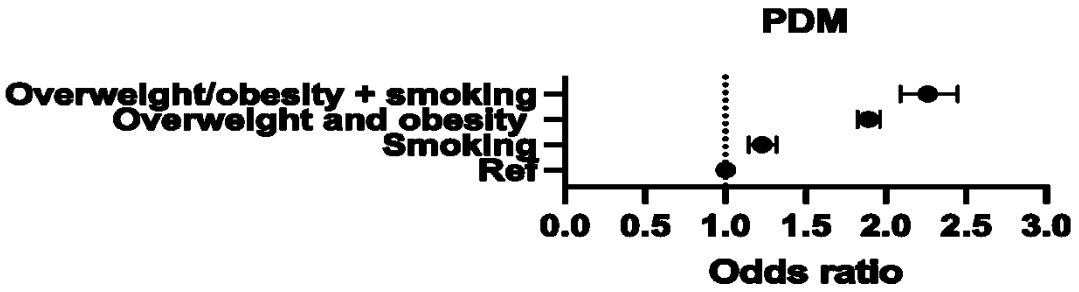

Fig. 1: Addition and multiplication of overweight/obesity and smoking in PDM after stratification
Note:P_{mult}=0.609,P_{add}=0.069,RERI(95%CI)=0.151(-0.012~0.314),AP(95%CI)=0.065 (-0.007~0.138),S(95%CI)=1.129(-0.962~1.295)

To found multiplicative and additive interactions of overweight/ obesity and smoking to develop T2DM, the risk of T2DM among overweight/obesity and smokers was 2.2(2.036~2.377) times than that of non-overweight /non-obesity and non-smokers. We found that subjects who were overweight/ obesity and smoking had greater risk to develop

T2DM than those exposed to a single risk factor alone did. However, there was no multiplicative interaction between smoking and overweight/obesity and T2DM, but an additive interaction was existence (Fig. 2).

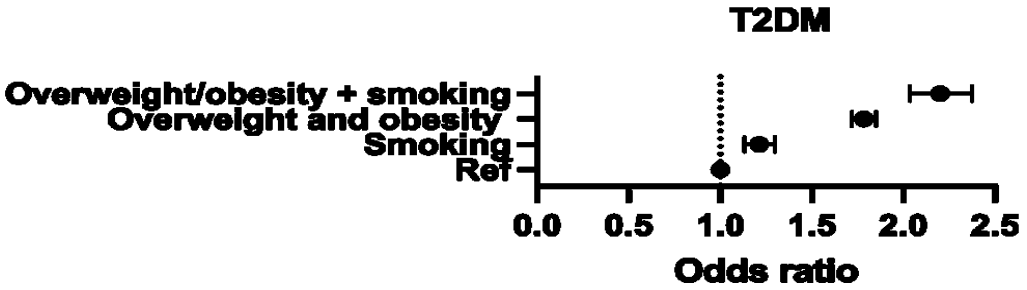

Fig. 2: Addition and multiplication of overweight and obesity and smoking in T2DM after stratification
Note:$P_{mult=}$0.757,$P_{add=}$0.008,RERI(95%CI)=0.196(0.051~0.341),AP(95%CI)=0.091 (0.020~0.161),S(95%CI)=1.203(1.004~1.402)

Discussion

Xiong et al. (8) had found that the incidence of PDM in the 40-70 age group was 38.9%, and another study found in the United States, the prevalence of PDM is 38.0% among adults over 18 years (9) ,which reveals that the prevention of PDM cannot be ignored. Nevertheless, there was less literature on the impact of smoking, overweight and obesity on the development of PDM. Fewer reports focus on the combined effects of smoking, overweight, impaired glucose tolerance and T2DM too. Our study found that smoking, overweight and obesity were independent factors of PDM and T2DM. Moreover, overweight/obesity and smoking might affect the development of T2DM too. The risk of abnormal glucose tolerance in overweight and obese people who smoke is 2.262 times higher than that in healthy and non-smoking people. There were many biological mechanisms could explain the link between overweight obesity, smoking in PDM and T2DM.

First, smoking affects the neuroendocrine system. Smoking directly act on the surrounding tissues (mainly mediated by catecholamines) and indirectly affect the neuroendocrine circuit in the central nervous system (10), reducing food intake by inhibiting the signal of hypothalamus appetite, and increasing energy consumption, thus reducing body weight. However, smoking increases the risk of central obesity by increasing the 2-hydroxylation of estradiol or by inducing an imbalance of androgen to estrogen activity in smokers (11).Smoking is associated with increased levels of anti-regulatory hormones and increased sympathetic activity, which may be the cause of impaired insulin sensitivity caused by smoking (12). Nicotine, a metabolic product of cigarettes in the blood, has the potential to induce pro-inflammatory metabolic state, which can impact insulin sensitivity and β-cell function (8).

Secondly, the insulin resistance of most obese patients (13) is related to the significantly increased level of free fatty acids in the blood (14). Smoking aggravates the insulin resistance of obese patients by increasing free fatty acids. Smoking has been associated with insulin resistance in non-diabetic (15) and T2DM(16), with long-term smokers having insulin resistance, hyperinsulinemia and dyslipidemia. Nicotine promotes adipo breakdown and transports free fatty acids to the liver and skeletal muscles, which are associated with the secretion of very low-density lipoprotein in the liver, lipid saturation in muscle cells, and peripheral insulin resistance (17). Smoking is associated with fat distribution leading to PDM, and some research had found smoking has severely impair insulin-stimulated glucose transport, increase free radical oxidative damage

and elicit oxidative stress response, and promote the progression of T2DM (18). Others found central obesity in the form of abdominal fat accumulation is closely related to insulin resistance and diabetes (19).

Our research also found that there is an additive interaction between smoking, overweight and obesity and diabetes. The proportion of diabetes caused by the interaction between smoking, obesity and overweight accounts for 9.1%. The proportion of overweight and obese people with smoking diabetes is 2.200 times higher than that of healthy controls. The result maybe relate to both smoking and obesity might affect mitochondrial function. Smoking increases oxidative stress and inflammation, thereby impairs endothelial function, leading to insulin resistance and diabetes (20). Furthermore, smoking is associated with carbon monoxide exposure (21). It had been reported that carbon monoxide exposure increases oxidative stress, leading to impaired mitochondrial function, inflammation, and endothelial function，inflammation plays a role in the development of T2DM. Visser et al. (22) found higher BMI was associated with a higher acute C - reactive protein (CRP) concentration, even in young people aged 17-39 years, this suggesting a low-grade systemic inflammatory state in overweight and obese people. Moreover, current smokers had significantly higher CRP levels (2.53 vs 1.35 mg/L) than those who had never smoked (23). Substantially, the double effects of overweight, obesity, and smoking increase chronic inflammatory responses then led to PDM or T2DM.

Although a study has found that central obesity and smoking jointly affect the occurrence of PDM (8), but the researchers conducted cross-sectional studies and only studied PDM, and without studying T2DM. The mechanisms by which overweight, obesity and smoking contribute to diabetes are still worth being investigated. Smoking is a risk factor for diabetes (24), however, there is few literatures on the influence of overweight/obesity and smoking on the progression of the disease, on whether overweight/obesity and smoking are risk factors for PDM. The combined effects of overweight and smoking on PDM and T2DM have been less well reported. Our study used a case-control study method and found that smoking and overweight and obesity affect the degree of disease development, which has improved the ability to verify the etiology.

Limitations

The limitation of this study was that the smoking status was collected through self-report of the respondents. Secondly, smoking intensity was not recorded. Third, the selection of The Pearl River Delta region in Guangdong had certain limitations, which might expand the sample to increase the representation of other Cities and regions in China.

Conclusion

The overweight/obesity and smoking are important influence factors of PDM and T2DM, which affect the degree of disease development. We found an interaction between overweight/obesity and smoking for T2DM. It is suggested that early weight control and active control is helpful to prevent and delay the onset of T2DM.This evidence collectively underscore the importance of intervening in cases of PDM as a vital measure to delay or impede its development into T2DM.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Data availability

All data generated or analysis during this study are included in this published article. However, for more data readers may contact with corresponding author.

Competing interests

The authors declare that they have no competing interests.

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