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Interaction of smoking and obesity on type 2 diabetes risk in a Chinese cohort

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HIGHLIGHTS

- The first study to examine the combined effects of current smoking and abdominal obesity
- Independent effects of current smoking on type 2 diabetes

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ABSTRACT

The aim of this study was to examine the independent and combined effects of current smoking and obesity on risk of type 2 diabetes (T2DM) in a Chinese cohort. We analyzed the data from a population-based prospective cohort of 3598 participants aged 35–74 years from Jiangsu, China. A Cox proportional hazards regression model was used to calculate the hazard ratio (HR) of T2DM and corresponding 95% confidence interval (CI), and to examine the interaction between current smoking and obesity on risk of T2DM. Compared with non-smokers, the hazard ratio of T2DM for current smokers was 4.16 (2.77–6.24). There was a significant interaction between current smoking and abdominal obesity on T2DM. RERI = 2.84 (0.02–5.67), suggesting that there would be 2.84 relative excess risk due to the additive interaction; AP = 0.48 (0.20–0.76), indicating that 48% of T2DM exposed to both risk factors was attributable to the additive interaction; and SI was 2.36 (1.15–4.87), suggesting that the risk of T2DM in obese smokers was 2.36 times as high as the sum of risks in the participants exposed to a single risk factor alone. We did not find a significant interaction between smoking and overall obesity on T2DM, but the incidence of T2DM in overall obese smokers was also highest. Both current smoking and abdominal obesity are strong risk factors of T2DM in the Chinese population. This study further demonstrates an additive interaction of current smoking and abdominal obesity on T2DM risk.

1. Introduction

Type 2 diabetes (T2DM) is a global public health crisis that threatens the economies of all nations, particularly developing countries; in China, a rapid increase in the prevalence of T2DM has been reported, and a total of 92.4 million adults were affected [1]. Several factors contribute to the accelerated epidemic of diabetes in China, including obesity. Obesity increases the risk of a number of health conditions including hypertension and type 2 diabetes, and has become a growing global health problem. There are approximately 937 million and 396 million obese and overweight adults worldwide, respectively [2]. The prevalence of overweight and obesity was high in urban Chinese adults, although China is a developing country.

Smoking has long been known to worsen the prognosis of patients with diabetes. In the study published in 1990 [3], subsequent systematic reviews have strengthened these conclusions while adding evidence that smoking increases insulin resistance, worsens diabetes control, and may even induce the disease [4,5]. Some studies also have shown that current smokers have 1.2- to 2.6-times higher risk of type 2 diabetes than nonsmokers [6–9]. As two important risk factors of type 2 diabetes, however, few studies focus on the combined effects of smoking and obesity on incident type 2 diabetes. Hence, in this study, we aimed to examine the independent and combined effects of current smoking and obesity on incident type 2 diabetes in a population-based Chinese cohort.

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2. Material and methods

2.1. Study cohort

The Prevention of MS and Multi-metabolic Disorders in Jiangsu Province of China Study (PMMJS) is an ongoing prospective cohort study aimed to estimate the prevalence of MS and the incidence of CVD and type 2 diabetes in Jiangsu Province, China. The detailed design of this study has been described elsewhere [10]. Briefly, the cohort was established between 2000 and 2004 in Jiangsu, China. Overall, 6400 participants aged 35–74 years were randomly selected based on a multi-stage sampling method. In the first survey, 5888 participants (92%) returned a completed questionnaire with information on diet, education, occupation, lifestyle factors, and medical history. The protocol was approved by the Ethical Committee of Soochow University.

In the second survey between 2006 and 2008, 4582 participants who had been followed for at least 5 years in this cohort were investigated. A total of 4083 participants completed the follow-up survey, with a follow-up rate of 89.1%. The characteristics of non-participants, such as age, sex, and metabolic variables, were similar to those who participated in the follow-up survey.

For this analysis, we excluded participants with diabetes (n = 289), CVD (n = 36), and missing data (n = 133) at baseline. We also excluded participants with BMI < 18.5 kg/m^2 (n = 27), leaving 3598 eligible participants (1451 males and 2147 females) for final analysis.

2.2. Exposure assessment

Current smokers were defined as those who have smoked for at least 100 cigarettes and still smoked at the time of the interview, and individuals with no history of cigarette smoking were considered as never smokers [11,12]. The cutoff values of waist circumference for abdominal obesity were 90 cm for male and 80 cm for female, which were in agreement with modification for Asian populations [13], and overweight was defined as BMI ≥ 24 kg/m^2 [14].

2.3. End point ascertainment

For this study, the criteria [15] for the diagnosis of T2DM included a fasting glucose level of ≥126 mg/dl (7.0 mmol/l), and hypoglycemic therapy (oral agents or insulin) that had been started in the interim.

2.4. Covariate measurement

Data on demographic characteristics, lifestyle risk factors, personal medical history and family history of T2DM for all participants were obtained using a standard questionnaire administered by trained staff. Three sitting blood pressure (BP) measurements were taken at 30-second intervals by trained observers using a standard mercury sphygmomanometer after the subjects had been resting for 5 min according to a standard protocol. The first and fifth Korotkoff sounds were recorded as the SBP and DBP, respectively. The mean of the three BP measurements was used in the analysis. Body weight and height were measured using standard methods, and the BMI was calculated as the weight in kilograms divided by the square of the height in meters. The WC was measured two times at 1 cm above the umbilicus at minimal respiration by trained observers; the mean of the two WC measurements was utilized in the analysis.

Blood samples were collected in the morning after at least 8 h of fasting. All plasma and serum samples were frozen at −80 °C until laboratory testing was performed. Plasma glucose was measured using an oxidase enzymatic method. The concentrations of HDL cholesterol and triglycerides were assessed enzymatically using an automatic biochemistry analyzer (Hitachi Inc., Tokyo, Japan) and commercial reagents. All analyses were performed by the same lab.

All of the participants signed the informed consent form. The study was approved by the Soochow University Ethics Committee.

2.5. Statistical analysis

The baseline continuous variables of participants were calculated as mean with standard deviation or median with interquartile range according to their distribution, and the categorical variables were presented as percentage. Baseline characteristics were compared according to BMI and WC using a chi-square test for categorical variables and ANOVA test for continuous variables. A Cox proportional hazards regression model was used to calculate the hazard ratio (HR) of T2DM and corresponding 95% confidence interval (CI). The multivariable HR was further adjusted for sex, age, family history of T2DM, and alcohol consumption. We next examined the interaction between smoking and overall obesity (defined by BMI) or abdominal obesity (defined by WC) on risk of T2DM, by dividing the participants into 4 groups according to smoking and obesity status. We then tested an interaction on an additive scale by calculating the relative excess risk due to interaction ($RERI = RR_{11} - RR_{10} - RR_{01} + 1$), the attributable proportion due to interaction ($AP = RERI / RR_{11}$), and the synergy index [$SI = (RR_{11} - 1) / (RR_{01} - 1) + (RR_{10} - 1)$] based on the methods proposed by Andersson et al. [16]. Both the point estimation and the 95% CI of RERI, AP, and SI were assessed using a method accounting for the asymmetric distribution of confidence limits for risk ratio [17]. All statistical analyses were performed using the SPSS statistical software system for Windows version 16.0 (SPSS Inc., Chicago, USA).

Table 1
Baseline characteristics of 3598 participants with abdominal and overall obesity.

Variables	Non-abdominal obesity	Abdominal obesity	Non-overall obesity	Overall obesity
Sex (males %)	47.5	17.8*	42.9	33.5*
Age (years)	49.75 ± 9.91	51.76 ± 9.99*	50.27 ± 10.05	50.04 ± 9.70
TC (mmol/l)	4.50 ± 0.94	4.73 ± 0.89*	4.48 ± 0.93	4.76 ± 0.91*
HDL-C (mmol/l)	1.29 ± 0.36	1.16 ± 0.31*	1.30 ± 0.35	1.16 ± 0.33*
LDL-C (mmol/l)	2.53 ± 0.76	2.70 ± 0.76*	2.53 ± 0.77	2.71 ± 0.74*
FPG (mmol/l)	5.09 ± 0.62	5.33 ± 0.66*	5.12 ± 0.62	5.24 ± 0.66*
TG (mmol/l)	1.50 (0.94–1.71)	1.99 (1.22–2.33)*	1.45 (0.93–1.68)	2.12 (1.23–2.42)*
Smoke (%)	25.6	14.0*	23.7	20.7
Alcohol (%)	25.2	13.9*	23.1	21.0
WC (cm)	73.1 ± 6.8	87.8 ± 6.5*	73.5 ± 7.3	85.8 ± 8.1*
BMI (kg/m^2)	22.0 ± 2.6	26.3 ± 2.9*	21.6 ± 2.1	27.3 ± 2.1*
Family history of T2DM (%)	4.5	7.5*	4.6	7.1*

BMI, body mass index; WC, waist circumference; TC, total cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein; FPG, fast plasma glucose; TG, triglyceride; T2DM, type 2 diabetes. Note: median and inter-quartile for TG; means ± standard deviation for age, TC, HDL-C, LDL-C, FPG, BMI, and WC.
* $P < 0.05$.