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Does body mass index and adult height influence cancer incidence among Chinese living with incident type 2 diabetes?

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ABSTRACT

Background: We investigated the site-specific cancer incidence risks among participants living with newly diagnosed type 2 diabetes (T2D) in relation to body mass index (BMI) and height.
Methods: The sample consisted of 25,130 participants living in Ningbo (China) who were newly diagnosed with T2D between 01/01/2006 and 12/31/2007 but without cardiovascular disease or cancer diagnoses at baseline. Follow-up of the sample was from 01/01/2008 to 12/31/2014. Cancer incidence stratified by BMI categories and quartiles of height were analyzed using standardized incidence ratios (SIR; the ratio of observed to the expected number of diagnosed cases) with 95% confidence intervals (95%CI).
Results: Follow-up included 22,795 participants, 155,845 person-years and 1063 cancer diagnoses. Compared with the general population of Ningbo, SIRs of all-cancer were 2.19 (95% CI: 2.01–2.37) for males and 1.80 (95% CI: 1.64–1.96) for females. The all-cancer SIRs for participants in the normal BMI category was 1.13 (95% CI: 1.00–1.38). By comparison, the SIRs for the overweight and obese groups were 0.62 (95% CI: 0.26–0.95) and 0.35 (95% CI: 0.03–0.71), respectively. Besides, higher participants had higher all-cancer SIRs. For males, SIRs were 1.08 (95% CI: 0.88–1.27) and 2.41 (95% CI: 2.05–2.78) in the lowest and highest quartiles of height, respectively. For females, SIRs were 1.03 (95% CI: 0.72–1.35) and 2.01 (95% CI: 1.66–2.58) in the lowest and highest quartiles of height, respectively.
Conclusion: In this sample of participants living with newly diagnosed T2D, cancer incidence was higher among those who were taller, but also lower among those with higher BMI.

1. Introduction

Type 2 diabetes (T2D) is a severe global health burden [1]. The prevalence of T2D in China is 9.1% overall, 9.9% among males and 11.6% for females [2]. Cancer is also a major public health issue. The age-standardized incidence and mortality rates of all-cancer in China were 201.1 and 126.9 per 100,000 in 2015, respectively [3]. Also, both T2D and cancer are significant causes of morbidity and mortality globally [4].

T2D care often involves a reduction in body mass index (BMI) to help prevent complications and co-morbidities [5]. However, some studies reported a higher risk of cancer mortality with lower BMI among people living with T2D [6,7]. This observation had been referred to as an "obesity paradox" [8]. Besides, association between T2D status and cancer incidence had been previously explored in European samples [9–12]. However, only a few studies have examined specific cancer incidence among people living with T2D across different BMI and height categories in Asians [13,14], and the results are controversy, thus warranting to be verified in larger sample size.

In European samples, higher cancer risk has been observed among taller males and females [15,16]. A cohort study conducted in South Korea also found that an increase of 5 cm in height was related to 5%

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(male) and 7% (female) increases in cancer risk after adjustment for age, BMI, and behavioral and socioeconomic factors [17]. Rapid urbanization and economic development in China in recent decades has contributed to substantial mean increases in height and weight, as well as major (often adverse) changes in diet, resulting in substantial social and spatial inequities in obesity risk across China [18–20]. Therefore, the paucity of studies examining cancer risk among people living with T2D in relation to BMI and height in China is an important gap in knowledge.

In this study, we aimed to investigate associations between cancer incidence risks with BMI and height among a sample of Chinese people living with T2D. In line with prior evidence from other countries, we hypothesized that people living with T2D with normal BMI and/or taller heights would experience higher cancer incidence risks than those with overweight or obesity.

2. Methods

2.1. Study population

Ningbo is an economic center of Zhejiang Province, which is also a coastal city with population over than 7 million, with a high level of economic development comparing to the general situation of China (GDP per capita in 2014: 16,112$ vs 7065$) [21,22]. The mean age of the whole population is 62.33 ± 12.78 years with 88.32% Han nationality in 2015 [23].

The included participants were obtained from the Chronic Disease Surveillance System (CDSS) of Ningbo. The CDSS was established based on 11 monitoring sites, which comprehensively representative the whole Ningbo. The system was founded in 2002, with the purpose for the collection, evaluation, and publication of chronic diseases (diabetes mellitus, cardiovascular disease (CVD) and cancer), all residents who lived in Ningbo at least for more than five years were included in the CDSS [24]. The Cancer Registry System of Ningbo, part of the CDSS, was also founded in 2002 with the purpose for the collection, evaluation, and publication of cancer data. The International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes were assigned to each cancer case by the type of cancers since 2011 (ICD-10: C00.0–C97) [25]. The proportion of morphologic verification (MV%), the percentage of cancer cases identified with death certification only (DCO%), the mortality(M) to incidence (I) ratio (M/I), and the percentage of uncertified cancer (UB%) were 74.72%, 0.34%, 0.66 and 7.08%, respectively [26].

The baseline sample consisted of 25,130 participants selected via four criteria. First, all participants had been recently diagnosed with T2D, with diagnoses occurring between 01/01/2006 and 12/31/2007. T2D diagnoses were defined in line with the American Diabetes Association (certificated by health practitioners) [27], whereas we did not obey to the HbA_{1C} guideline because this measurement had not been used widespread across China due to lack of standardized instruments and methods [28]. Second, all participants did not have CVD or cancer at the time of the T2D diagnoses, because subjects with CVD were reported to have higher cancer risks [29]. Third, all participants had lived in the city of Ningbo (China) since birth. Fourth, each participant had health records available in the CDSS of Ningbo [24]. The study was approved by the institutional review board of Ningbo Municipal Center for Disease Prevention and Control. All of the participants provided written informed consent.

2.2. Outcome: cancer incidence

The baseline sample was linked to cancer diagnosis records (certificated by health practitioners) from 01/01/2008 to 12/31/2014 in the Cancer Registry System, through each participant's full name, personal ID and gender. The ICD-10 codes were assigned to each cancer case by the type of cancers such as Stomach (C16), Liver (C22), Pancreas (C25), Lung (C33-C34), and Bladder (C67). This linkage was verified by Ningbo Municipal Center for Disease Prevention and Control. Approximately 10.3% (N = 2335) of the sample were lost to follow-up because they had either moved their registered residence out of Ningbo or could not be contacted after three attempts.

2.3. Key exposures: BMI categories and height

BMI was calculated as kg/m^2 based on participants' height and weight measured by a registered nurse practitioner during the participants' baseline visit. Weight was measured without shoes and in light clothing to the nearest 0.1 kg using a calibrated beam scale and height of participants was measured without shoes to the nearest 0.2 cm using a portable stadiometer [30]. The National Health and Family Planning Commission of China defined BMI of 24.0 kg/m^2 and 28.0 kg/m^2 as the ideal cut-off points for overweight and obesity, which were based on previous study [31]. Accordingly, the Chinese Diabetes Association used these recommended cut-off points as a treatment goal; therefore, the participants in the present study were divided into three group: normal BMI group (18.5–24.0 kg/m^2), overweight group (24.0–28.0 kg/m^2) and obesity group (≥28.0 kg/m^2), respectively [31]. For height, each participant was allocated to one of four quartiles: ≤160 cm (quartile 1), 160–165 cm (quartile 2), 166–170 cm (quartile 3) and ≥171 cm (quartile 4) in males; ≤155 cm (quartile 1), 156–160 cm (quartile 2), 161–165 cm (quartile 3) and ≥166 cm (quartile 4) in females.

2.4. Covariates

Demographic and clinical data were obtained from medical records for each participant. Demographics included age, gender, and education level. Clinical measurements included fasting blood glucose (FBG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and glycated hemoglobin (HbA_{1C}). Blood glucose levels were measured by modified hexokinase enzymatic method. TC and HDL-C were analyzed enzymatically using commercial reagents, and LDL-C levels were calculated using the Fried Ewald equation. HbA_{1C} was measured by ion-exchange HPLC on a Biorad Variant II instrument [32]. We also divided the participants into different groups according to FBG and HbA_{1C} levels [33].

2.5. Statistical analysis

Continuous variables were presented as means ± SD and categorical variables as absolute and relative frequencies (percentage). Baseline characteristics were summarized across BMI categories and height quartiles. Comparisons of demographic and clinical variables between male and female participants were performed using *t*-tests and χ^2 tests, as appropriate. The number of person-years of follow-up was calculated from the baseline date to the diagnosis of cancer, death, loss to follow-up, or 12/31/2014, whichever occurred first [25,34]. We excluded the underweight subjects (≤18.5 kg/m^2) in our study as lower body weight tended to be in the existence of obesity-related metabolic disorders which was reported to be an possible indication reflecting potential illness predisposes to cancer [35]. The main analyses were focused on cancer incidence across different BMI categories and height quartiles. Crude incidence rate (CIR) for cancers were calculated by the number of newly diagnosed cancers divided by the number of observed person-years. Standardized incidence ratios (SIRs) and its 95% confidence interval (CI) were calculated as the ratio of the observed to the expected number of newly diagnosed cancer cases with the Poisson regression model, in which sex (male or female) and education level (illiteracy, below college, or above college) were entered as categorical variable (male or female), and factors such as age, FBG, TC, HDL-C, LDL-C, and TG as continuous variables. The expected number of cases was calculated by applying the age-specific cancer incidence rates in