The Relationship Between Body Mass Index and Incident Diabetes Mellitus in Chinese Aged Population: A Cohort Study

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Research

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Abstract

Background

Previous studies reported that aged population with overweight had a lower mortality after cardiovascular diseases attack, indicating being thinner might not be better. However, the debate is ongoing what is optimal range of body mass index (BMI) for aged population. We aimed to evaluate the association between BMI and incident diabetes mellitus (DM) in Chinese elderly people.

Methods

6,489 Chinese elderly people (3,828 men and 2,661 women) with medium age of 69 years (interquartile range: 67-74 years) were included in this cohort study. BMI was measured at baseline (2014). All the participants were further classified into eight groups based on baseline BMI with 2.0 kg/m^2 interval: ≤17.9 kg/m^2, 18.0-19.9 kg/m^2, 20.0-21.9 kg/m^2, 22.0-23.9 kg/m^2, 24.0-25.9 kg/m^2, 26.0-27.9 kg/m^2, 28.0-29.9 kg/m^2, and ≥30.0 kg/m^2. Fasting blood glucose (FBG) and glycated hemoglobin A1c (HbA1c) were annually measured during follow-up (2014-2019). DM was confirmed if either FBG ≥7.0 mmol/L or HbA1c ≥6.5%. We used the Cox proportional hazards regression model to evaluate the association between BMI and incident DM.

Results

Comparing individuals with a BMI range of 20.0~21.9 kg/m^2 (reference), the hazards ratio for incident DM was 2.07 (95% CI: 1.33, 3.22), 2.07 (95% CI: 1.33, 3.23), 2.18 (95% CI: 1.37, 3.47), 2.68 (95% CI: 1.61, 4.46), and 2.26 (95% CI: 1.17, 4.37) for the group with a BMI range of 22.0-23.9 kg/m^2, 24.0-25.9 kg/m^2, 26.0-27.9 kg/m^2, 28.0-29.9 kg/m^2, and ≥30.0 kg/m^2 after adjusting baseline age, sex, blood pressure, lipid profiles, and eGFR. Each unit increase of BMI (=1.0 kg/m^2) was associated with a high risk of 9% (HR=1.09, 95% CI: 1.05, 1.14, P for trend<0.001) after adjusting for above-mentioned confounders.

Conclusions

High BMI was associated with high risk of developing DM in Chinese aged population. To lower the incidence of DM, it is better to be thinner than heavier.

Introduction

China has become a leading country with a dramatic number of aged people. According to data from National Bureau of Statistics of the People's Republic of China, there were 170 million people over 65 years by the end of 2019. The aggravating trend of aged population results in deep impacts on social old-age system's sustainable development.

Diabetes mellitus (DM) is a non-communicable disease affecting approximately one-quarter of people over the age of 65 years (1), which significantly increases mortality and disability (2), thus in turn increases both direct and indirect medical costs (3). DM and obesity share the same originality (4). Obesity has been confirmed to be associated with insulin resistance and decreased insulin sensitivity in aged population with newly diagnosed type 2 DM in a case-control study (5) and a predictor of incident type 2 DM in a cohort study (6). A healthy body index mass (BMI) is believed to be helpful to decrease the prevalence of DM in adults. One WHO panel reported that Asian populations have a lower BMI cut-off point for type 2 diabetes mellitus and cardiovascular disease risk than the WHO criteria of BMI 25.0 kg/m^2 (7). A cohort study, including different ethnic participants, reported that Chinese have lower BMI cutoff points than black and white individuals (25.0 vs. 26.0 vs. 30.0 kg/m^2 respectively), thus supporting the point that lower BMI is better for DM prevention in nonwhite populations (8). However, evidences are not enough to generate the optimal BMI range for aged population. Another retrospective study with 88,305 Japanese aged population has reported that the optimal BMI cut-off for prediction of DM of 23.6 kg/m^2 (9). Further, existed evidences have reported that the association between BMI and all-cause mortality follows a "U" (10, 11) or "J" curve (12, 13) indicating that aged population with overweight (BMI≈25.0~29.9 kg/m^2) might be better for aged population (11, 14). It is not clear that the association between BMI and DM in aged population follows the same pattern. Therefore, we aim to evaluate the association between BMI and incident DM in 6,489 Chinese aged population and followed them for 5 years. We hypothesis that a relatively lower BMI is better to prevent the development of DM than a higher BMI.

Methods

Study population

All the participants (≥65 y) were recruited from local communities who have taken healthy check-up at Health Management Center, Ren Ji Hospital from January 1, 2014 to May 31, 2019. A total number of 9,902 Chinese aged population were eligible for the study. BMI was measured at baseline (2014). Fasting blood glucose (FBG) and glycated hemoglobinA1c (HbA1c) were measured annually during follow-up (2014-2019). We first excluded the extremist values (>99^{th} percentile or <1^{st} percentile) (n=1,930) at baseline. Then, we excluded participants whose FBG ≥ 7.0mmol/L, or HbA1c ≥ 6.5mmol/L, or with self-reporting DM at baseline (n=1,471). Finally, we excluded those who were lost during follow up (n=12), a total number of 6,489 Chinese aged population [3,828 men and 2,661 women, aged 69 (interquartile range: 67, 74) years] were included in the study **(Supplementary Figure 1)**. Compared with those out of the study, the participants included in the study were with similar level of BMI and with lower level of FBG and HbA1c **(Supplementary Table 1)**. The study protocol was approved by the Ethical Committee of Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University (Reference Number: KY-2019-112). As a re-identified study, the signed consent was waived by the Ethical Committee.

Exposures (BMI)

Body weight and height were measured in light clothes with no shoes at baseline, and BMI was calculated by body weight in kilogram divided by square of height in meter. All the participants were further classified into eight groups based on baseline BMI with 2.0 kg/m^2 interval: ≤17.9 kg/m^2, 18.0-19.9 kg/m^2, 20.0-21.9 kg/m^2, 22.0-23.9 kg/m^2, 24.0-25.9 kg/m^2, 26.0-27.9 kg/m^2, 28.0-29.9 kg/m^2, and ≥30.0 kg/m^2. The BMI was also used as a continuous variable with interval of 1.0 kg/m^2.

Outcomes (incident DM)

Venous blood samples were drawn and transfused into vacuum tubes containing EDTA in the morning after participants were fasted overnight for eight hours. FBG was measured by enzyme linked immunosorbent assay (Roche 701 Bioanalyzer, Roche, UK). HbA1c were measured by a high-performance liquid chromatography method (Variant II automatic glycosylated hemoglobin analyzer, Bio-Rad, America). DM was confirmed if either FBG ≥ 7.0 mmol/L or HbA1c ≥ 6.5% (15).

Assessment of other confounders

Blood pressure was measured twice using an automatic blood-pressure meter [HBP-9020, OMRON (China) Co., Ltd.] after participants were seated for at least 10 mins. **The average of two measurements was recorded for further analysis.** Total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, were measured as well. The estimating glomerular filtration (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration 2-level race equation(16). All the biochemical measurements were completed in the Clinical Laboratory of our hospital.

Statistical analysis

We completed all statistical analysis by SAS version 9.4 (SAS Institute, Inc, Cary, NC). Formal hypothesis testing will be Wilcoxon test for rank sum with a significant level of 0.05.

In the current study, we used the Cox proportional hazards regression model to evaluate the association between BMI and incident DM in whole group. The person-time of follow-up for each participant was determined from the baseline to (January 1, 2014) to either the onset date of DM, loss to follow up, or the end of follow-up (May 31, 2019), whichever came first.

With the analysis of dose-response trend, more specifically, the continuous variable of the change in BMI was used to fit into a restricted cubic spline model (17) and to obtain a smooth representation of the hazard ratio as a function of the change in BMI adjusted by potential confounders. We used 5 knots defined at the 5^{th}, 27.5^{th}, 50^{th}, 72.5^{th}, and 95^{th} percentiles to divide continuous change in BMI into 5 intervals.

We adjusted for potential confounders in different models: **model 1**, adjusting for age (y) and sex; **model 2**, adjusting for variables in model 1, and systolic blood pressure (mmHg), diastolic blood pressure (mmHg), total cholesterol (mmol/L), triglyceride (mmol/L), low density lipoprotein cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L), eGFR (mL/min per 1.73 m^2); **model 3,** adjusting age (y), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), total cholesterol (mmol/L), triglyceride (mmol/L), low density lipoprotein cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L), eGFR (mL/min per 1.73 m^2); **model 4,** adjusting sex, systolic blood pressure (mmHg), diastolic blood pressure (mmHg), total cholesterol (mmol/L), triglyceride (mmol/L), low density lipoprotein cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L), eGFR (mL/min per 1.73 m^2).

The interaction between continuous BMI and sex, age groups was tested by adding the cross-product terms in the multivariable model**.** To test the robustness of the results obtained from the main analysis, we conducted three sensitivity analyses: excluding participants with high blood pressure (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg (18)) , with abnormal lipid metabolism (total cholesterol ≥ 5.7mmol/L or triglyceride ≥ 1.7mmol/L or low density lipoprotein cholesterol ≥ 3.4mmol/L or high density lipoprotein cholesterol < 1.0 mmol/L for man or high density lipoprotein cholesterol < 0.9 mmol/L for female) (19), or with decreased eGFR (≤ 60 mL/min per 1.73 m^2) (16).

Results

A total number of 6,489 Chinese elderly people [3,828 men and 2,661 women, aged 69 (interquartile range: 67-74) years] were included in the study. The medium of BMI was 24.4 (interquartile range: 22.4-26.4) kg/m^2. BMI was associated with all the characteristics at baseline **(Table 1)**.

During five years of follow up, we identified 335 new cases of DM. The incidence of DM was 30.0/1000 person-year. Comparing with participants whose BMI range was between 20.0 and 21.9 kg/m^2 (**Reference group**), the hazard ratios for incident DM was 2.07 (95% CI: 1.33, 3.22), 2.07 (95% CI: 1.33, 3.23), 2.18 (95% CI: 1.37, 3.47), 2.68 (95% CI: 1.61, 4.46), and 2.26 (95% CI: 1.17, 4.37) for the group with a BMI range of 22.0-23.9 kg/m^2, 24.0-25.9 kg/m^2, 26.0-27.9 kg/m^2, 28.0-29.9 kg/m^2, and ≥30.0 kg/m^2 after adjusting for baseline age, sex, blood pressure, lipid profiles, and eGFR **(Table 2, Model 2)**. One unit increase of BMI (=1.0 kg/m^2) was associated with a high risk of 9% (HR=1.09, 95% CI: 1.05, 1.14, P for trend<0.001) **(Table 2, Model 2)**. The association between BMI and the risk of DM demonstrated a “straight line” curve **(Figure 1** Hazard ratio for diabetes mellitus based on continuous change in based BMI in 2014. Model was adjusted for baseline age, sex, blood pressure, lipid profiles, and eGFR). Data were fitted by a restricted cubic spline Cox proportional hazards model. The 95% confidence intervals are indicated by the dashed line**).**

We did not find the interactions between continuous BMI and sex, and age in relation to the risk of incident diabetes (both p for interaction >0.05). Men (HR=1.11, 95% CI: 1.05, 1.66) tended to have a stronger association between BMI and DM than women (HR=1.08, 95% CI: 1.01, 1.15]. Older aged population (≥75 years, HR=1.10, 95% CI: 1.03, 1.18) had a stronger association than younger aged population (<75 years, HR=1.08, 95% CI: 1.03, 1.14) **(Table 3)**.

Excluding participants with high blood pressure (n=3,499), with abnormal lipid profiles (n=3,475), and with decreased eGFR (n=324) at baseline, generated similar results with prospective analysis **(Table 4)**.

Discussion

In the current cohort study with 6,489 Chinese aged population, we found that high BMI was associated with high risk of developing DM after adjusting conventional risk factors for DM such as blood pressure, lipid profiles and renal function.

Existed evidences have pointed out that the association between BMI and all-cause mortality follows a “U” (10, 11) or “J” curve (12, 13). However, the optimal BMI range was based on the relationship between BMI and mortality not for BMI-DM association, according to our study, we found the association between BMI and the risk of DM demonstrated a “straight line” curve, similar to Hu et al’s (20), indicating that the relationship between BMI and DM might follow the different pattern. It is better to be thinner even BMI was in normal range. The hazards ratio was 2.07 (95% CI: 1.33, 3.22) for those participants whose BMI was between 22.0 and 23.9 kg/m^2 compared to those whose BMI was between 20.0 and 21.9 kg/m^2. The results of the current study were similar to that of Hu et al. (20) They performed a perspective cohort study in a relatively low risk middle-aged and elderly Chinese population, found that when BMI was above 22.0 kg/m^2 (HR=1.49, 95% CI: 1.00-2.22) can predict diabetes risk, and participants with BMI ≥22.0 kg/m^2 (HR=1.09, 95%CI: 1.09-2.32) had significantly elevated diabetic risk. Chen et al., (21) also found the age-adjusted HR for incident diabetes was 2.51 (95% CI: 2.33- 2.70) in overweight individuals with a BMI of 24.0-27.9 kg/m^2 and 5.58 (95% CI: 5.13-6.07) in obese individuals with a BMI of ≥28.0 kg/m^2, compared with normal weight individuals with a BMI of 18.5 to <24.0 kg/m^2 in a retrospective cohort study in 211,833 Chinese adults (20–30, 30–40, 40–50, 50–60, 60–70 and ≥70 years old) in 11 cities. Most epidemiological studies in Europe (22, 23), the U.S.A (24), and Asia (9) were consistent to the results. These studies, however, focused on the risks associated with overweight or obesity and were less concerned about the risks associated with a BMI at the lower end of the normal weight range. Moreover, some proposed an additional breakdown for the normal BMI category, 18.5-19.9 kg/m^2, 20.0-22.9 kg/m^2, and 23.0-24.9 kg/m^2 (25), therefore in order to avoid preconceptions related to what should be normal or abnormal, the BMI categories in our study were differ from those defined by the National Institutes of Health and World Health Organization (26), and found that the incident DM with a BMI in upper limit of normal range was higher than that with lower limit of normal range. To our knowledge, there are no guidelines that define optimal BMI cut-offs for aged population. Future studies are needed to determine optimal BMI range for aged population.

In contrast, in a longitudinal study cohort of 1,501 Harbin aged population (aged 60-74 years) for a mean follow-up of 6 years. Comparing with participants whose BMI range was between 22.5-24.9 kg/m^2, the hazards risk of incident DM was no significant difference from the group with a BMI range of 18.5-22.4 kg/m^2 (HR=0.78, 95%CI:0.37-1.20), 25.0-27.4 kg/m^2 (HR=0.76, 95%CI:0.47-1.19), 27.5-29.9 kg/m^2 (HR=0.87, 95%CI:0.58-1.28), and ≥30.0 kg/m^2 (HR=0.49, 95%CI:0.21-1.15) after adjusting for sex, age, systolic blood pressure, alcohol use, smoking history, education, regular exercise, family history of diabetes and prediabetes status at baseline, and follow-up years (27). The reasons for the inconsistent conclusion may lie in difference in BMI categories, diagnosis of DM and sample size.

The ethnicity might be another reason for the differences in optimal BMI cutoff for aged population. Accumulating evidences have suggested that the relationship between BMI and body fat deposit differs between ethnic populations (28) and Asians have a higher risk of DM than other ethnic groups even they were at the same BMI levels (29, 30). The possible explanation was that Asians have more visceral adiposity than Caucasians, which is more metabolically adverse, and contributes to lip-toxicity and insulin resistance at any given BMI (28, 31). Thus, in the Diabetes Prevention Program (DPP) (32), a BMI value of 22.0 kg/m^2 was selected as the eligibility BMI for Asians and BMI≥ 23.0 kg/m^2 was a risk factor for insulin resistance and diabetes in Japanese people (9). The above studies might suggest a lower BMI range for Asians compared to Caucasians. The results were consistent with ours. Furthermore, eating habits (33), dietary inflammatory index (34), income status (35), education level (36), significant heterogeneity in critical metabolic factors (32) might modify the relationship between BMI and DM.

Strengthens and Limitations

The strengthens of the study were a large number of sample size, deliberately adjustment of a series of conventional risk factors, and cohort study design. However, some limitations need to be addressed. Firstly, despite considering many possible confounders and performing multivariate analysis, there is a lack of investigation for the correlation of several other risk factors (alcohol consumption, cigarette smoking status, eating habit, and exercise) to BMI and DM. Secondly, we did not collect information on anti-diabetes medications during follow-up, which could result in the loss of new DM case. Thirdly, DM was confirmed by either FGB or HbA1c, but had not further been assessed by OGTT, which might lead to misclassification of DM status. We excluded participants with self-reported DM in the follow-up, but we cannot exclude the possibility that some of the participants with diabetes mellitus were still included in the study due to undiagnosed DM (37). Finally, we did not consider history of diseases in elderly that might affect the incidence of DM.

Conclusions And Implications

Increased BMI was associated with the risk of DM in Chinese aged population. Thus, it is recommended that aged population need to maintain their body weight within a reasonable range to prevent chronic diseases.

Abbreviations

BMI, body mass index

DM, diabetes mellitus

FBG, fasting blood glucose

HbA1c, Glycated hemoglobinA1c

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethical Committee of Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University (Reference Number: KY-2019-112). As a re-identified study, the signed consent was waived by the Ethical Committee.

Consent for publication

Not applicable.

Availability of data and materials

All the data and SAS code for the analyses were available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Molian Tang conceived, designed, and drafted the study; Molian Tang, Yiquan Zhou, and Jialu Wang collected and analyzed the data; Yanping Wan conceived the study concept; Renying Xu finally proved the paper.

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Not applicable

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Tables

Due to technical limitations, table 1, 2, 3 and 4 is only available as a download in the Supplemental Files section.

Figures

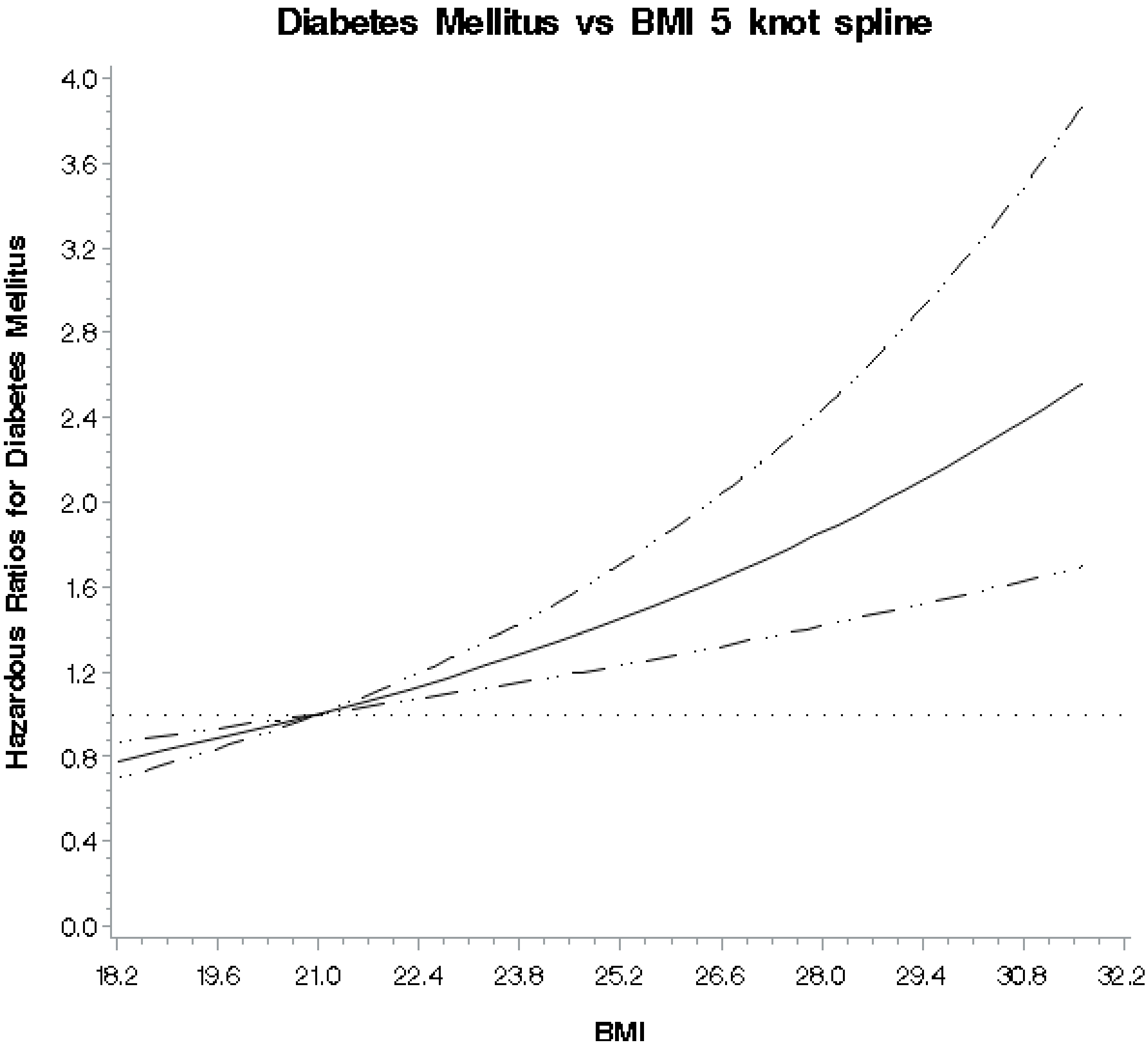

Figure 1

Hazard ratio for diabetes mellitus based on continuous change in based BMI in 2014. Model was adjusted for baseline age, sex, blood pressure, lipid profiles, and eGFR

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterial.doc
- Table1.xls
- Table2.xls
- Table3.xls
- Table4.xls