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Original Article

Association between BMI trajectory and the risk of diabetes mellitus: a prospective cohort study

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Abstract: The aim of this study was to investigate the quantitative association between body mass index (BMI) trajectory and the risk of diabetes mellitus. A prospective cohort study was performed among all residents in the Kailuan community in Tangshan, China, and a total of 39,321 participants were enrolled in the final analysis. A group-based trajectory model was used to determine BMI trajectories. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using Cox regression modeling to estimate the relationship between BMI trajectory and the risk of diabetes. During the 3.84-year follow-up, 2,577 cases of diabetes and 4,281 cases of impaired fasting glucose occurred. After adjustment for confounding factors, hazard regression analyses indicated that the upper-middle and high BMI trajectories had a statistically significant increase in the risk of diabetes [3.57 (95% CI 2.91-4.38) and 4.66 (95% CI 3.72-5.83), respectively] compared with the low BMI trajectory. Furthermore, the HRs (95% CI) of impaired fasting glucose were 1.92 (1.69-2.19) and 2.15 (1.83-2.53), respectively. The BMI trajectory of the general population is variable, with the high BMI trajectory associated with an increased risk of diabetes and impaired fasting glucose. Long-term trajectories in BMI may assist with more accurate identification of individuals with diabetes and impaired fasting glucose.

Keywords: Body mass index, trajectory, diabetes, impaired fasting glucose

Introduction

Obesity is a major threat to public health in economically developed countries, and its global prevalence more than doubled between 1980 and 2014 [1, 2]. The prevalence of patients who are overweight or obese in China has increased two to three times since the 1980s [3-6]. Previous studies have demonstrated that obesity is an independent risk factor for diabetes mellitus [6-10], hypertension [11], coronary disease [12-14], stroke [12, 15], and all-cause mortality [16]. A large study by Nagaya and colleagues [17] reported that an increase in body mass index (BMI) of 1 kg/m^2 may raise the risk of diabetes by around 25%.

Although studies have identified that being overweight or obese are risk factors for diabetes, previous studies have only investigated the impact of a single BMI measurement [11, 18, 19] or the change between two BMI measurements [20, 21] on new-onset diabetes, which may not accurately show the association between BMI and the onset of diabetes [22, 23].

Group-based trajectory modeling has the advantage of being data driven, and it can identify distinctive clusters of individual trajectories that follow similar developmental trajectories [23-27]. Trajectories track a measurement (for example, BMI) over time, and thus provide information on baseline BMI, on the changes between measurements, and on the overall BMI patterns that could be more informative than a single measurement such as initial BMI. To our knowledge, there is no large cohort study designed to investigate the quantitative association between BMI trajectories and the risk of

diabetes. Our study was based on data from the Kailuan study, an ongoing prospective population-based cohort study based on the functional and comprehensive data of all residents in the Kailuan community in Tangshan, China. This cohort provides an excellent opportunity to investigate the association between BMI trajectory and diabetes.

Materials and methods

Study participants

Participants from the Kailuan study were recruited from July 2006 to October 2007, July 2008 to October 2009, and July 2010 to October 2011. Subjects were excluded if (i) data on weight or height were missing (n = 5554), (ii) they had two consecutive measurements of BMI ≥35 kg/m^2 or ≤16 kg/m^2 (n = 454) to reduce the possibility of misrepresentation of data, (iii) they were pregnant (n = 100), (iv) they developed diabetes (n = 7838), (v) they had not attended the fourth and fifth medical examinations (July 2012 to October 2013 and July 2014 to October 2015, n = 4248), or (vi) they lacked data on fasting blood glucose (FBG) from the fourth and fifth medical examinations (n = 412). A total of 39,321 participants were included in the analysis and were followed up until the fifth medical examination. Data from all examinations were collected from 11 hospitals affiliated with the Kailuan Company. All participants provided written informed consent. The study was performed according to the guidelines of the Helsinki Declaration and approved by the Institutional Review Board and the Ethics Committee of the Kailuan General Hospital.

Data collection

General data collection: All participants received a biennial clinical examination and laboratory testing, and a biennial questionnaire including items on age, sex, smoking status, alcohol consumption, physical activity, educational level, working environment, and a history of hypertension, diabetes, myocardial infarction, stroke, and cancer. The epidemiological information and anthropometric and biochemical measurements have been described previously [28].

Body mass index measurement: Participants were asked to wear light clothing without shoes or hats during the assessment of height and weight by well-trained physicians and nurses following a standard protocol. Height was measured to the nearest 0.1 cm using a portable stadiometer and weight was measured to the nearest 0.1 kg using a digital weight scale. BMI was calculated as body weight in kilograms divided by the height in meters squared.

Biochemical measurements: Blood samples from the antecubital vein were collected in vacuum tubes containing EDTA between 7 and 9 in the morning after an overnight fasting period. The tubes were centrifuged at 3000 × g for 10 minutes to isolate the plasma. The measurement of the supernatant serum was performed within 4 hours. The FBG was measured by the hexokinase/glucose-6-phosphate dehydrogenase method. High-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels were measured enzymatically (Mind Bioengineering Co. Ltd, Shanghai, China). All biochemical variables were measured using an auto-analyzer (Hitachi 747; Hitachi, Tokyo, Japan).

Relevant definitions: Criteria for the diagnosis of diabetes were a fasting glucose level of 126 mg/dL (7.0 mmol/L) or greater, or the use of antihyperglycemic medications. Presence of impaired fasting glucose (IFG) was defined as a fasting glucose level between 110 mg/dL (6.1 mmol/L) and 126 mg/dL (7.0 mmol/L).

Statistical analysis

Statistical analyses were performed using SPSS 13.0 software (SPSS, Chicago, IL, USA) and SAS version 9.3 for UNIX (SAS Institute Inc, Cary, NC, USA). We used CNORM models to identify subgroups within the population that shared a similar underlying trajectory of BMI. These models were fit using SAS Proc Traj [20, 23-25, 29-30]. First, the number of trajectories was determined, and then the polynomial order of each trajectory was calculated. We used the Bayesian Information Criterion and average group posterior probability (AvePP) to select the ideal trajectory model and estimate the model fit. Five trajectories were observed with the polynomial order 2, 2, 2, 2, 2, respectively, which was the best model. Continuous variables were presented as means ± standard deviation, and categorical variables were expressed as frequencies and proportions. Continuous

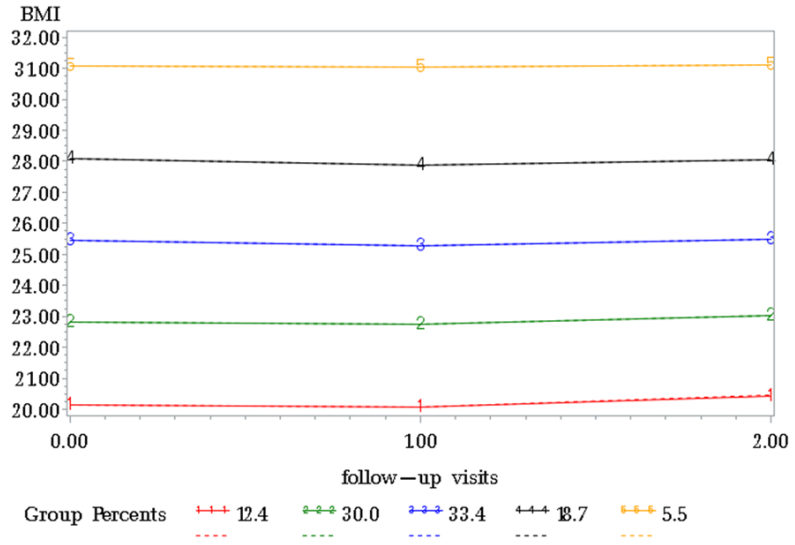

Figure 1. Trajectory of BMI in the follow-up visits.

variables were compared with a one-way analysis of variance followed by a least significant difference test for homogeneity of variance or Dunnett's test for variance heterogeneity. Data with a skewed distribution were converted by logarithmic transformation. The chi-square test was applied for the comparison of categorical variables.

The cumulative incidence of diabetes or IFG was calculated using a life-table method [31, and these values were compared using a log-rank test. Multivariable Cox proportional hazards models were used to determine the association between BMI trajectories and the development of diabetes and IFG. Hazard ratios (HRs) and 95% confidence intervals (CIs) were reported for each BMI trajectory after adjustment for covariates: Model 1 was a single-factor analysis model, Model 2 was adjusted for sex and age, and Model 3 was adjusted for covariates in Model 2 plus LDL-C, systolic blood pressure (SBP), physical activity, alcohol consumption, smoking status, family history of diabetes, and history of hypertension, myocardial infarction, and stroke. The models considered BMI trajectory, baseline BMI, and mean BMI separately and together.

Several sensitivity analyses were also performed, including censoring participants with a history of cardiovascular disease, hypertension, and antihypertensive or antihyperlipidemic medication use before the third medical examination to evaluate whether the associations between BMI trajectory and diabetes or IFG were influenced. Two-sided *P* values <0.05 were considered statistically significant.

Results

Baseline characteristics of participants

Of the 39,321 participants, 29,826 (75.9%) were men and 9,495 (24.1%) were women, with an age range of 17-94 years (mean 48.14 ± 11.68). Mean follow-up was 3.84 ± 0.97 years. Five discrete trajectories of BMI were identified (**Figure 1**) and all were maintained at a stable level: (i) Trajectory 1 included 12.4% of the participants in the low BMI group, (ii) Trajectory 2 had 30.0% in the lower-middle BMI group, (iii) Trajectory 3 had 33.4% in the middle BMI group, (iv) Trajectory 4 had 18.7% in the upper-middle BMI group, and (v) Trajectory 5 had 5.5% in the high BMI group.

Baseline characteristics of the patients in the BMI trajectories are presented in **Table 1**. Statistically significant differences among the trajectories were found for the following variables: sex, age, SBP, LDL-C, FBG, BMI, education, physical activity, alcohol consumption, and prevalent hypertension, myocardial infarction, and stroke (all with *P* values <0.01).

Incidence of diabetes and IFG in different trajectories

During a mean follow-up of 3.84 years, we documented 2577 cases of incident diabetes and 4281 cases of IFG. The incidence of diabetes among participants in the five BMI trajectories (1 through 5) was 2.4%, 4.2%, 7.0%, 10.2%, and 13.4%, respectively, and the incidence of IFG was 7.7%, 11.2%, 14.3%, 17.3%, and 19.2%, respectively, showing that the higher BMI trajectories had an increased incidence of diabetes and IFG. The log-rank test for the difference in the cumulative incidence rates of diabetes and IFG among the different BMI trajectories was statistically significant (χ^2 = 581

Table 1. Baseline participant characteristics and incidence of diabetes and IFG in different BMI trajectories

	Trajectory 1 (N = 4731)	Trajectory 2 (N = 11,886)	Trajectory 3 (N = 13,336)	Trajectory 4 (N = 7240)	Trajectory 5 (N = 2128)	Total (N = 39,321)	*P* value
Male, n (%)	3138 (66.3)	8698 (73.2)	10,545 (79.1)	5817 (80.3)	1628 (76.5)	29,826 (75.9)	<0.001
Age, years	45.78±12.91	48.08±11.58	48.89±11.30	48.49±11.34	47.77±12.22	48.14±11.68	<0.001
SBP, mm Hg	118.58±17.53	123.90±18.32	128.83±19.27	132.67±19.16	135.28±19.31	127.17±19.35	<0.001
First BMI, kg/m^2	20.02±1.32	22.76±1.39	25.48±1.46	28.18±1.52	31.17±1.62	24.81±3.25	<0.001
Second BMI, kg/m^2	19.95±1.28	22.68±1.31	25.29±1.42	27.98±1.50	31.13±1.57	24.67±3.20	<0.001
Third BMI, kg/m^2	20.33±1.36	22.99±1.42	25.50±1.48	28.15±1.55	31.21±1.64	24.92±3.16	<0.001
Mean BMI, kg/m^2	20.10±0.95	22.81±0.80	25.42±0.79	28.10±0.82	31.17±1.08	24.80±2.98	<0.001
LDL-C, mmol/L	4.89±0.63	4.98±0.65	5.04±0.66	5.09±0.66	5.08±0.64	5.02±0.65	<0.001
FBG, mmol/L	2.16±0.88	2.27±0.89	2.32±0.91	2.37±0.92	2.39±0.92	2.30±0.91	<0.001
Smoking status							0.08
Daily, n (%)	1424 (30.6)	3607 (31.0)	3996 (30.8)	2085 (29.5)	600 (28.8)	11,712 (30.5)	
Alcohol consumption							<0.001
Daily, n (%)	733 (15.8)	2109 (18.1)	2356 (18.1)	1228 (17.3)	310 (14.9)	6736 (17.5)	
Physical activity							<0.001
3 times/week, n (%)	573 (12.4)	1517 (13.1)	1873 (14.4)	1003 (14.2)	324 (15.6)	5290 (13.8)	
Hypertension, n (%)	897 (19.0)	3460 (29.1)	5319 (39.9)	3605 (49.8)	1193 (56.1)	14,474 (36.8)	<0.001
Stroke, n (%)	19 (0.4)	79 (0.7)	130 (1.0)	74 (1.0)	33 (1.6)	335 (0.9)	<0.001
Myocardial infarction, n (%)	34 (0.7)	132 (1.1)	169 (1.3)	109 (1.5)	36 (1.7)	480 (1.2)	<0.001
Family history of diabetes, n (%)	199 (4.2)	538 (4.5)	601 (4.5)	369 (5.1)	129 (6.1)	1836 (4.7)	0.003
Education, n (%)							<0.001
Illiteracy/primary	286 (6.1)	764 (6.6)	920 (7.1)	501 (7.1)	178 (8.5)	2649 (6.9)	
Middle school	3860 (83.0)	9952 (85.5)	11,113 (85.5)	6108 (86.3)	1757 (84.3)	32,790 (85.3)	
College/university	505 (10.9)	923 (7.9)	971 (7.5)	472 (6.7)	148 (7.1)	3019 (7.9)	
Income, n (%)							<0.001
<￥600/month	1254 (29.1)	3337 (30.8)	3803 (31.5)	2079 (31.5)	672 (34.4)	11,145 (31.1)	
￥600-1000/month	2689 (62.3)	6617 (61.1)	7223 (59.7)	3938 (59.7)	1101 (56.4)	21,568 (60.3)	
>￥1000/month	372 (8.6)	882 (8.1)	1059 (8.8)	584 (8.8)	179 (9.2)	3076 (8.6)	
Diabetes							
Participants, n	4731	11,886	13,336	7240	2128	39,321	
Cases of diabetes, n (%)	113 (2.4)	501 (4.2)	940 (7.0)	737 (10.2)	286 (13.4)	2577 (6.6)	<0.001
IFG							
Participants, n	4173	10,056	10,828	5609	1616	32,282	
Cases of IFG, n (%)	320 (7.7)	1125 (11.2)	1553 (14.3)	972 (17.3)	311 (19.2)	4281 (13.3)	<0.001

Note: BMI, body mass index; SBP, systolic blood pressure; LDL-C, low-density lipoprotein-cholesterol; FBG, fasting blood glucose; BMI, body mass index; First BMI, BMI at the first medical examination; Second BMI, BMI at the second examination; Third BMI, BMI at the third examination; Mean BMI, the BMI mean of all three medical examinations.

and 294, respectively, P<0.01) (**Table 1**). The cumulative incidence of diabetes and IFG is shown in **Figure 2**.

Hazard ratios for diabetes and IFG according to BMI trajectory

Table 2 shows the association between BMI trajectories and the risk of diabetes and IFG. After adjustment for age, sex, LDL-C, baseline SBP, smoking status, alcohol drinking status, physical activity, family history of diabetes, and history of hypertension, myocardial infarction, and stroke, the respective HRs for diabetes and IFG incidence were 1.55 (95% CI 1.26-1.91) and 1.30 (95% CI 1.15-1.48) for Trajectory 2, 2.50 (95% CI 2.05-3.06) and 1.64 (95% CI 1.45-1.86) for Trajectory 3,3.57 (95% CI 2.91-4.38) and 1.92 (95% CI 1.69-2.19) for Trajectory 4, and 4.66 (95% CI 3.72-5.83) and 2.15 (95% CI 1.83-2.53) for Trajectory 5, respectively. The higher trajectories had a significantly higher risk of diabetes and IFG compared with those in Trajectory 1.

Sensitivity analyses

In sensitivity analyses of the censored cases with cardiovascular disease (including myocardial infarction and stroke) and a history of anti-

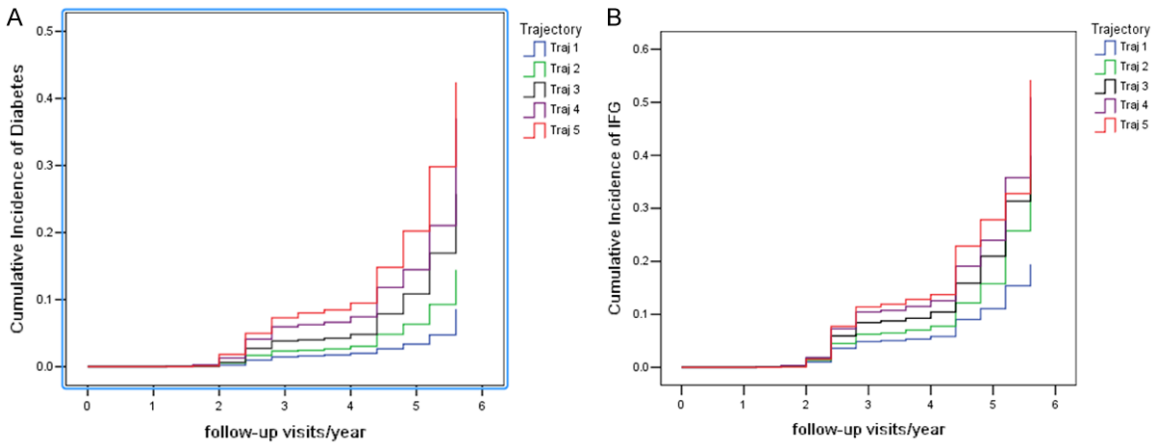

Figure 2. Cumulative incidence of diabetes (A) and IFG (B) by BMI trajectory.

Table 2. Associations of BMI trajectory, baseline BMI, and mean BMI (separately) with diabetes and IFG

	Hazard ratio (95% confidence interval) of diabetes			Hazard ratio (95% confidence interval) of IFG		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
BMI Trajectory						
Trajectory 1	1	1	1	1	1	1
Trajectory 2	1.78 (1.45-2.19)	1.69 (1.38-2.07)	1.55 (1.26-1.91)	1.48 (1.30-1.67)	1.39 (1.23-1.57)	1.30 (1.15-1.48)
Trajectory 3	3.06 (2.52-3.72)	2.84 (2.33-3.45)	2.50 (2.05-3.06)	1.95 (1.73-2.20)	1.81 (1.60-2.04)	1.64 (1.45-1.86)
Trajectory 4	4.51 (3.70-5.50)	4.21 (3.45-5.14)	3.57 (2.91-4.38)	2.38 (2.10-2.70)	2.22 (1.96-2.52)	1.92 (1.69-2.19)
Trajectory 5	6.00 (4.82-7.46)	5.68 (4.57-7.07)	4.66 (3.72-5.83)	2.67 (2.28-3.12)	2.55 (2.18-2.98)	2.15 (1.83-2.53)
Baseline BMI (kg/m^2)						
<18.5	1	1	1	1	1	1
18.5-24	1.64 (0.96-2.78)[a]	1.59 (0.93-2.69)[a]	1.57 (0.88-2.78)[a]	2.29 (1.54-3.41)	2.27 (1.53-3.37)	2.16 (1.43-3.27)
24-28	3.35 (1.98-5.67)	3.12 (1.84-5.29)	2.86 (1.62-5.05)	3.36 (2.26-4.98)	3.21 (2.16-4.76)	2.91 (1.92-4.39)
≥28	5.15 (3.04-8.74)	4.91 (2.89-8.33)	4.28 (2.41-7.59)	4.25 (2.86-6.32)	4.18 (2.81-6.22)	3.55 (2.34-5.38)
Mean BMI (kg/m^2)						
<18.5	1	1	1	1	1	1
18.5-24	2.13 (0.95-4.76)[a]	2.12 (0.95-4.74)[a]	1.75 (0.78-3.92)[a]	2.79 (1.58-4.93)	2.81 (1.59-4.97)	2.68 (1.48-4.85)
24-28	4.37 (1.96-9.75)	4.19 (1.88-9.34)	3.23 (1.45-7.21)	4.23 (2.40-7.46)	4.11 (2.33-7.25)	3.69 (2.04-6.68)
≥28	7.55 (3.38-16.86)	7.35 (3.29-16.42)	5.40 (2.41-12.08)	5.23 (2.96-9.25)	5.20 (2.94-9.20)	2.43 (2.43-7.99)

Note: [a]P >0.05. BMI, body mass index; IFG, impaired fasting glucose; Baseline BMI, BMI at the first medical examination; mean BMI, the mean BMI at all three medical examinations. Model 1: unadjusted, Model 2: adjusted for age and sex, Model 3: adjusted for age, sex, low-density lipoprotein cholesterol, baseline SBP, smoking status, alcohol drinking status, physical activity, family history of diabetes, and history of hypertension, myocardial infarction, and stroke.

hyperlipidemic agent use before the third medical examination, the association between higher BMI trajectory and the increased risk of diabetes and IFG remained unchanged. In addition, not carrying forward hypertension and the use of antihypertensive medication before the third medical examination did not substantially change the results (Table S1).

Comparison of predictive values of different indices on diabetes and IFG

In the models examining baseline BMI and mean BMI separately, we observed an influence of both factors on the risk of diabetes after adjusting for sex, age, LDL-C, SBP, physical exercise, smoking, drinking history, family history of diabetes, and history of hypertension, stroke, and myocardial infarction. With baseline BMIs as independent variables and the low BMI group (<18.5 kg/m^2) as the reference group, the HRs for normal weight (BMI 18.5-24 kg/m^2), overweight (BMI 24-28 kg/m^2), and obesity (BMI >28 kg/m^2) were 1.57 (95% CI 0.88-2.78), 2.86 (95% CI 1.62-5.05), and 4.28 (95% CI 2.41-7.59), respectively. With the BMI means as independent variables and the low BMI group as the reference group, the

Table 3. Associations of BMI trajectory, baseline BMI, and mean BMI (together) with diabetes and IFG

	Hazard ratio (95% confidence interval) of diabetes			Hazard ratio (95% confidence interval) of IFG		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
BMI Trajectory						
Trajectory 1	1	1	1	1	1	1
Trajectory 2	1.68 (1.37-2.06)	1.58 (1.29-1.95)	1.47 (1.19-1.82)	1.41 (1.24-1.60)	1.32 (1.16-1.50)	1.25 (1.10-1.42)
Trajectory 3	2.09 (1.63-2.67)	1.92 (1.50-2.46)	1.75 (1.36-2.25)	1.60 (1.34-1.90)	1.46 (1.23-1.74)	1.39 (1.16-1.65)
Trajectory 4	2.51 (1.84-3.42)	2.31 (1.70-3.15)	2.07 (1.51-2.83)	1.73 (1.38-2.19)	1.60 (1.27-2.01)	1.47 (1.17-1.86)
Trajectory 5	2.82 (1.95-4.09)	2.63 (1.81-3.80)	2.31 (1.58-3.37)	1.79 (1.34-2.40)	1.67 (1.25-2.24)	1.53 (1.14-2.06)
Baseline BMI (kg/m^2)						
<18.5	1	1	1	1	1	1
18.5-24	1.19 (0.70-2.02)[a]	1.15 (0.67-1.96)[a]	1.16 (0.65-2.06)[a]	2.01 (1.35-2.99)	2.00 (1.35-2.99)	1.95 (1.29-2.95)
24-28	1.51 (0.88-2.62)[a]	1.44 (0.83-2.48)[a]	1.38 (0.77-2.50)[a]	2.40 (1.59-3.61)	2.36 (1.56-3.56)	2.24 (1.46-3.44)
≥28	1.48 (0.83-2.64)[a]	1.45 (0.81-2.59)[a]	1.37 (0.74-2.55)[a]	2.50 (1.62-3.86)	2.58 (1.67-4.00)	2.36 (1.50-3.71)
Mean BMI (kg/m^2)						
<18.5	1	1	1	1	1	1
18.5-24	1.64 (0.73-6.38)[a]	1.63 (0.72-3.65)[a]	1.42 (0.63-3.20)[a]	2.22 (1.25-3.94)	2.23 (1.26-3.95)	2.23 (1.23-4.06)
24-28	2.20 (0.96-5.05)[a]	2.12 (0.93-4.87)[a]	1.87 (0.81-4.29)[a]	2.39 (1.33-4.32)	2.35 (1.30-4.24)	2.38 (1.28-4.41)
≥28	2.65 (1.12-6.30)	2.61 (1.10-6.21)	2.33 (0.98-5.57)[a]	2.21 (1.18-4.11)	2.22 (1.19-4.15)	2.26 (1.18-4.33)

Note: [a]P>0.05. BMI, body mass index; IFG, impaired fasting glucose; Baseline BMI, BMI at the first medical examination; mean BMI, the BMI mean at all three medical examinations. Model 1: unadjusted, Model 2: adjusted for age and sex, Model 3: adjusted for age, sex, low-density lipoprotein cholesterol, baseline SBP, smoking status, alcohol drinking status, physical activity, family history of diabetes, and history of hypertension, myocardial infarction, and stroke.

HRs for normal weight, overweight, and obesity were 1.75 (95% CI 0.78-3.92), 3.23 (95% CI 1.45-7.21), and 5.40 (95% CI 2.41-12.08), respectively. After adjusting for the above factors, the increasing trend of IFG risk with overweight and obesity persisted (**Table 2**).

The models examining BMI trajectories, baseline BMIs, and mean BMIs together are shown in **Table 3**. The HRs of the high BMI (Trajectory 5), baseline BMI, and mean BMI were significantly associated with an increased risk of IFG [1.53 (95% CI 1.14-2.06), 2.36 (95% CI 1.50-3.71), and 2.26 (95% CI 1.18-4.33), respectively]. However, no significant differences for diabetes risk were observed except for Trajectory 5 with high BMI values, which was independently associated with a significantly higher risk of diabetes [2.31 (95% CI 1.58-3.37)].

Discussion

In this large population-based cohort study of more than 39,000 participants in the Kailuan community, we examined the association between BMI trajectory and the risk of diabetes mellitus. The major finding was that a higher BMI trajectory was associated with a higher risk of diabetes and IFG.

Concerning the baseline BMI and mean BMI and their association with the outcomes (dependent variables), additional adjustments to include both baseline BMI and mean BMI were constructed to estimate the risk for diabetes and IFG (BMI trajectory as the independent variable). The estimates were attenuated but the result remained statistically significant. Our study demonstrated that a high BMI trajectory is a relevant risk factor for diabetes and IFG, independent of the degree of baseline BMI and mean BMI.

To compare the predictive values of different indicators for diabetes and IFG, baseline BMI and mean BMI were regarded separately as independent variables. The risk of diabetes and IFG in people who were obese or overweight was highly significant ($P<0.001$) with both baseline BMI or mean BMI as independent variables, which suggests an association between BMI and diabetes. In the models examining BMI trajectory and baseline and mean BMIs together, neither baseline nor mean BMIs as independent variables were significant. However, the high BMI trajectory was independently associated with a significantly higher risk of diabetes. These results suggest that using the BMI trajectory for obese and overweight individuals is a better predictor for exposing the risk of diabetes compared with using only a single or average BMI measurement [24].

Sensitivity analyses were conducted by excluding the participants with a history of cardiovascular disease, hypertension, antihypertensive

medication use, and antihyperlipidemic agent use before the third medical examination. These analyses did not change the conclusion, which indicated that high BMI is a risk factor for diabetes and IFG, regardless of the history of cardiovascular disease or hypertension.

The significance of our study was to observe the association between BMI trajectory and the risk of diabetes and IFG using a trajectory model, which highlighted changes in BMI. Our large prospective cohort study from China confirmed that with a higher BMI trajectory there is a greater risk of diabetes and IFG. In addition, the tendency for a change in the BMI trajectory, though small with an average slope of 0.05, may explain why in our study population the BMI change with age was not obvious. These results suggest that obese and overweight people should be advised as soon as possible to lose weight to reduce the risk of diabetes or IFG.

This study had limitations. First, there were more male than female individuals in the study cohort, although we did adjust for sex in the multivariable models to maintain the representativeness of the study. Second, our investigation used BMI as the obesity indicator for outcome observations, but as reported earlier, waist circumference and waist-to-hip ratio may be better indicators for the association between obesity and health status [29], which have now been confirmed as being strongly associated with diabetes risk [33]. Third, the mean follow-up time of 3.84 years may be insufficient to measure outcomes. Finally, because all participants were Chinese, it is unclear whether the results can be generalized to other ethnic groups.

The present study conclusively reveals that higher BMI trajectories were associated with an increased risk of diabetes and IFG, and long-term trajectories in BMI may assist in more accurate identification of individuals with diabetes and IFG.

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Disclosure of conflict of interest

None.

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Table S1. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) of diabetes and IFG according to BMI trajectory

	Hazard ratio (95% confidence interval)				
	Trajectory 1	Trajectory 2	Trajectory 3	Trajectory 4	Trajectory 5
Diabetes					
Sensitivity Analysis 1	1	1.58 (1.30-1.96)	2.52 (2.06-3.09)	3.53 (2.87-4.35)	4.75 (3.78-5.98)
Sensitivity Analysis 2	1	1.62 (1.17-2.24)	2.58 (1.88-3.56)	3.64 (2.57-5.16)	3.75 (2.29-6.15)
Sensitivity Analysis 3	1	1.48 (1.18-1.86)	2.47 (1.99-3.07)	3.47 (2.77-4.33)	4.67 (3.62-6.02)
Sensitivity Analysis 4	1	1.55 (1.25-1.91)	2.47 (2.02-3.02)	3.57 (2.90-4.38)	4.63 (3.69-5.82)
IFG					
Sensitivity Analysis 1	1	1.32 (1.16-1.50)	1.66 (1.47-1.89)	1.96 (1.71-2.24)	2.19 (1.85-2.58)
Sensitivity Analysis 2	1	1.40 (1.16-1.68)	1.61 (1.33-1.95)	2.26 (1.82-2.80)	1.99 (1.38-2.85)
Sensitivity Analysis 3	1	1.34 (1.17-1.53)	1.66 (1.45-1.89)	1.96 (1.70-2.27)	2.16 (1.78-2.61)
Sensitivity Analysis 4	1	1.31 (1.15-1.48)	1.64 (1.45-1.86)	1.92 (1.68-2.19)	2.15 (1.83-2.54)

Note: IFG, impaired fasting glucose; Sensitivity Analysis 1: adjusted for covariates in model 3 excluding the participants with a history of cardiovascular disease (N = 35,431 and 29,179); Sensitivity Analysis 2: adjusted for covariates in model 3 censoring the participants with a history of hypertension (N = 14,686 and 12,852); Sensitivity Analysis 3: adjusted for covariates in model 3 censoring the participants with a history of antihypertensive medication use (N = 29,553 and 24,677); Sensitivity Analysis 4: adjusted for covariates in model 3 censoring the participants with a history of antihyperlipidemic agent use (N = 35,838 and 29,509); Model 3: adjusted for age, sex, low-density lipoprotein-cholesterol, baseline SBP, smoking status, alcohol drinking status, physical activity, family history of diabetes, and history of hypertension, myocardial infarction, and stroke.