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Overweight, obesity, and their associations with insulin resistance and β-cell function among Chinese: a cross-sectional study in China

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Abstract

The aim of this study was to evaluate the associations of body mass index (BMI) with insulin resistance and β-cell function in subjects with normal glucose tolerance. A cross-sectional study was carried out in Fujian province by multistratified sampling from July 2007 to May 2008. The sample consisted of 2931 subjects aged from 20 to 79 years. The questionnaires, physical examinations, and laboratory tests were obtained from all the participants. The homeostasis model assessment of insulin resistance (HOMA-IR) index was used to estimate insulin sensitivity, insulin secretion was assessed using the HOMA-β index, and β-cell function was quantified as the ratio of the incremental insulin to glucose responses over the first 30 minutes during the oral glucose tolerance test (ΔI30/ΔG30). Another measure was adjusted for insulin sensitivity as it modulates β-cell function ([ΔI30/ΔG30]/HOMA-IR). Associations of BMI with morbidities were estimated using multiple logistic regression analysis. Relationships of BMI to insulin resistance and β-cell function were assessed using multiple linear regression analysis and analysis of covariance. The age- and sex-adjusted prevalence of overweight and obesity was 23.04% (27.44% in men and 18.40% in women) and 2.65% (2.75% in men and 2.55% in women), respectively. After adjustment for covariables, BMI was independently associated with morbidity conditions; and there were increasing trend for odds ratios of morbidities across the BMI categories. There were independent differences for HOMA-IR, HOMA-β, and ΔI30/ΔG30 between the normal-weight, overweight, and obese groups except for (ΔI30/ΔG30)/HOMA-IR. Body mass index was significantly and independently associated with HOMA-IR, HOMA-β, and ΔI30/ΔG30 in the multiple linear regression analysis. Body mass index was an independent risk factor for hypertension, type 2 diabetes mellitus, dyslipidemia, metabolic syndrome, as well as the indexes of insulin resistance and β-cell function. It is imperative that the whole society pay more attention to the identification and intervention of overweight and obesity to prevent obesity-related diseases at the very early stage.

1. Introduction

The prevalence of overweight and obesity is increasing to epidemic proportions at an alarming rate around the world [1,2]. It is estimated that more than 1 billion adults worldwide are overweight and more than 300 million adults worldwide are obese (based on the World Health Organization [WHO] criterion of overweight and obesity) [1].

Developing countries are increasingly vulnerable to the worldwide epidemic of obesity, which affects all segments of the population, including men, women, and now children [3,4]. Compared with populations in industrialized countries, those in the developing world appear to be at greater risk of the obesity-related diseases such as cardiovascular disease (CVD), which has become the leading cause of disability and death in many developing countries [5-7]. Studies [8-10] have shown that obesity is an independent risk factor for dyslipidemia, hypertension, and CVD, and affects physical and social functioning and quality of life [11,12].

Previous studies [13,14] have reported that the risk of developing type 2 diabetes mellitus (T2DM) increases in a dose-dependent manner as body mass index (BMI) increases. The prevalence of T2DM in obese adults is 3 to 7 times than that in normal-weight adults, and those with a BMI of at least 35 kg/m^2 are 20 times as likely to develop diabetes compared with those with a BMI between 18.5 and

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24.9 kg/m^2 [15,16]. Obesity also complicates the management of T2DM by increasing insulin resistance (IR) and blood glucose concentration [17].

Because excess body weight plays such an important role in the development and management of diabetes, it is important to evaluate the insulin sensitivity and β-cell function in overweight and obese subjects with normal glucose tolerance (NGT), as the intervention at this stage is likely to be more successful rather than that after the development of impaired glucose tolerance or overt T2DM [18].

Fujian province, in coastal southeastern China, is one of the provinces with the fastest economic development over the past 2 decades. As a result, the prevalence of overweight and obesity has significantly increased because of the economic growth, rapid urbanization, and subsequent lifestyle changes [19]. The aims of this cross-sectional study were to examine the prevalence of overweight and obesity in this province and its risk factors, and to access the risk associations between BMI, cardiovascular risk factors, and morbidity conditions. Most importantly, we evaluated the relationships of BMI to insulin sensitivity and β-cell function in those with NGT.

2. Subjects and methods

2.1. Subjects

Subjects registered were permanent residents in Fujian province from July 2007 to May 2008. A multistage, stratified, cluster random sampling method was used. The sampling frame was based on the 2000 National Bureau of Statistics of China.

In the first stage, the whole province was stratified into urban and rural areas. Three sample points from urban areas and 3 from rural areas were selected to be representative of the geographic and economic characteristics in their regions. In the second stage of sampling, each sample point provided 2 kinds of smaller sample units (one from plenty and one from poor parts in the selected sample point) according to average income RMB per capita as reference bulletined by government economic reporting in the locality. Basic sample units (6 from city regions and 6 from rural counties) were street districts in urban and hamlets in rural sample points. In the third stage, the first individual was randomly selected from a randomly selected household in the basic sample unit. Subjects were then registered by door-to-door canvas in proportion to local population age-specific parameters until the sufficient sample size was gotten. Simple random sampling methods were used at each stage. A total sample size of 3960 was registered. Subsample size was allocated according to the proportion of each layer in integer. All investigators received special training before the investigation, and all subjects signed informed consent authorized by the Diabetes Branch of the Chinese Medical Association.

2.2. Questionnaires

1. The questionnaires were completed by trained investigators as they interviewed each participant. Content included age, sex, smoking status (past or present smoker, number of cigarettes smoked daily, and years smoking), history of diabetes, history of CVD (ie, myocardial infarction, coronary artery bypass graft, coronary intervention therapy, heart failure, stroke, amputation history, hypertension, and whether under drug treatment), family history of hypertension, myocardial infarction, stroke, or diabetes.

2. Physical examinations: Height and weight were measured without shoes and in light clothing after overnight fasting. Body mass index was calculated by dividing weight (in kilograms) by height (in meters) squared. Waist circumference (WC) was measured as the minimum circumference between the umbilicus and xiphoid process. Blood pressure was measured twice, in the sitting position, using a manual sphygmomanometer in the right arm; and the mean of the 2 readings was used for analysis. Resting 12-lead electrocardiography (ECG) was performed by professional investigators and then coded according to Minnesota code criteria [20] by one well-trained coder blinded to the rest of subjects' data.

3. Laboratory tests were taken from 5 mL of blood with and without anticoagulant (sodium fluoride + potassium oxalate 1:3) drawn from subjects who had fasted for at least 10 hours. From these, standard laboratory tests determined fasting blood glucose, insulin concentration, and lipid profile, including total cholesterol (TC), triglycerides (TGs), high-density lipoprotein (HDL), and low-density lipoprotein (LDL). All subjects except those previously diagnosed with diabetes were subjected to a 75-g oral glucose tolerance test (OGTT). For Chinese medical ethics, diabetes subjects accepted 100-g steamed-bread test (a kind of standardized mixed meal test) as surrogate, which equally contains 75 g carbohydrate and was linearly related to those measured 2 hours after OGTT [21]. After 30 and 120 minutes, 5 mL of blood with anticoagulant was drawn from subjects. Levels of blood glucose, insulin concentration, TC, TG, and HDL were tested using the glucose oxidase method, the Phadebas Insulin Test (Pharmacia, Uppsala, Sweden), colorimetric enzyme assays, glycerol phosphate enzymatic oxidation assay, and end point colorimetry, respectively. Low-density lipoprotein was calculated by the formula of Friedewald et al [22].

2.3. Definitions

2.3.1. Assessment of household income and educational levels

Annual household income was classified into 3 levels: (1) low income (<10 000 yuan RMB), (2) medium income (10 000-30 000 yuan RMB), and (3) high income (>30 000 yuan RMB). The educational levels were categorized into 3 groups: (1) low education (illiteracy, primary education, <6 years of schooling), (2) medium education (middle

school education, 6-12 years of schooling), and (3) high education (college or university education and above, >12 years of schooling).

2.3.2. Assessment of smoking and alcohol consumption

Smokers included current smokers and ex-smokers; current smokers were those who smoked at least 1 cigarette per day lasting for at least 1 year; ex-smokers were those who had regularly smoked in the past, but had quit for at least half a year.

The subjects were divided into 2 groups (nondrinkers and drinkers) according to the frequency, quantity, and the types of alcohol beverages. Nondrinkers were those who never or only occasionally drank, and drinkers were those who drank 6 g or more of alcohol per day on average for at least 1 year.

2.3.3. Assessment of exercise

Exercisers were defined as those who regularly exercise, with the total time for exercising no less than 3 hours per week.

2.3.4. Diagnosis criteria

Obesity was defined as BMI of at least 30 kg/m^2, and *overweight* was defined as 25 ≤ BMI < 30 kg/m^2 according to 1997 WHO criterion [23]. *Type 2 diabetes mellitus* was defined as a fasting plasma glucose (FPG) of at least 7.0 mmol/L, a 2-hour postprandial glucose loading PG level of at least 11.1 mmol/L, or with diagnosed T2DM using the WHO 1999 criterion [24]. For impaired glucose regulation (IGR), subjects with 6.1 ≤ FPG < 7.0 mmol/L and/or 7.8 ≤ 2-hour PG < 11.1 mmol/L were identified. Diagnosis of hypertension was based on the criteria of the WHO 1999 or "The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure" recommendation of systolic blood pressure (SBP) of at least 140 mm Hg, diastolic blood pressure (DBP) of at least 90 mm Hg, diagnosis of hypertension, or treatment with antihypertension drugs [24,25]. Subjects with one or more of the following results were considered as dyslipidemic: TC greater than 6.2 mmol/L, TG greater than 2.3 mmol/L, LDL greater than 4.1 mmol/L, HDL less than 0.91 mmol/L, or TC/HDL greater than 5 [26]. The presence of *metabolic syndrome* was defined according to National Cholesterol Education Program Adult Treatment Panel III criteria [27], which require the presence of 3 or more of the following 5 factors: (*a*) abdominal obesity: WC greater than 88 cm for women or greater than 102 cm for men, (*b*) plasma level of TGs of at least 150 mg/dL, (*c*) plasma level of HDL lower than 40 mg/dL for men or 50 mg/dL for women, (*d*) SBP of at least 130 mm Hg or DBP of at least 85 mm Hg, and (*e*) FPG of at least 110 mg/dL.

2.3.5. Definition of ECG abnormality

Resting 12-lead ECG was coded with the Minnesota code criteria [20]. According to the Pooling Project classification [28], major changes in Minnesota ECG codes, such as obvious Minnesota code Q wave (1-1,1-2), ST-segment depression (4-1,4-2), T-wave inversion code (5-1,5-2), II atrioventricular block (6-1,6-2), bundle-branch block code (7-1,7-2,7-4), and arrhythmia (8-1,8-3) were listed as major abnormal ECG (MA-ECG); others were considered non-major abnormality.

2.3.6. Assessment of IR and β-cell function

For the quantification of IR, the homeostasis model assessment of IR (HOMA-IR) index of Matthews et al [29] was calculated as fasting plasma insulin (FIN) × FPG/22.5. Insulin secretion was assessed using the HOMA-β index (20 × FIN/[FPG − 3.5]) [29] and the ratio of the incremental insulin to glucose responses over the first 30 minutes during the OGTT (ΔI30/ΔG30) [30], which is correlated with criterion standard measures of insulin secretion (first phase insulin secretion on intravenous glucose tolerance testing) and has been shown to predict the development of T2DM [31]. Another measure of β-cell function was defined as insulinogenic index divided by HOMA-IR ([ΔI30/ΔG30]/HOMA-IR).

2.4. Statistical analysis

Of 3960 people selected from July 2007 to May 2008 by multistage stratified sampling, 3294 completed the survey and examination; the response rate was 88.8%. Among the 3294 participants, the following were excluded from the current analyses: 33 for being outside of the 20- to 79-year age range, 326 for missing laboratory data, and an additional of 4 for missing BMI and blood pressure data. Therefore, data from 2931 participants were used in the current analyses. Moreover, the subjects with T2DM or IGR were excluded for the evaluation of the associations of BMI with insulin sensitivity and β-cell function; so a subsample of 2152 subjects with NGT was used for the further study.

EpiData software (The EpiData Association, Odense, Denmark) was used to establish the database, and all survey data were checked twice. All analyses were performed using the Statistical Package for Social Sciences (SPSS for Windows, version 16.0; Chicago, IL). Age and sex standardization was performed by using the direct method with the 2000 China census data. We used P-P plot to test the normality of the numerical variables. Serum TG, PG, and insulin, as well as all the indexes for insulin sensitivity and β-cell function, were log-transformed owing to skewed distributions (nontransformed values displayed for ease of interpretation). The significant differences of univariate between 2 groups were assessed by Student *t* tests or χ^2, tests and data were expressed as means ± SD or percentage (number of cases) as appropriate. Besides, Mantel-Haenszel χ^2 test was used to compare the categorical variables. The analysis of variance or analysis of covariance, and R × C χ^2 test for the trend were used to determine the significance of trends of continuous variables and frequency, respectively, across the BMI categories (<19.0, 19.0-20.9, 21.0-22.9, 23.0-24.9, 25.0-26.9, 27.0-28.9, and ≥29.0 kg/m^2); data were expressed as means ± SE or percentage (number of

cases). Variables found to be significant difference in the univariate analyses were included in multivariate logistic regression models. The forward LR method was used. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. The associations of BMI with indexes of IR and β-cell function were assessed using the multiple linear regression analysis and analysis of covariance. Partial correlation analysis between BMI and indexes of IR and β-cell function was conducted in the linear regression models. All P values were 2-sided, and values < .05 were considered statistically significant.

3. Results

3.1. Baseline characteristics

The sex-specific baseline clinical characteristics were shown in Table 1. There were no differences in means of the age and the prevalence of obesity, hypertension, IGR, metabolic syndrome, and major Minnesota codes abnormality between the male and female participants. Men had more smokers, drinkers, and exercisers; higher prevalence of overweight, diabetes, and dyslipidemia; as well as higher education and income than women. Table 2 displays the metabolic characteristics of the study participants. The levels of BMI, WC, SBP, DBP, FPG, 30-minute PG, and TG were higher in men than women, whereas higher levels of 30-minute insulin, HDL, and LDL were found in women.

Table 1
Sex-stratified baseline clinical characteristics of all the participants in the survey

Categorical variables	Men (n = 1167)	Women (n = 1764)	P value
Age (y)	45.18 ± 15.97	46.06 ± 13.55	NS
Smokers (% [n])	55.10 (634)	0.85 (15)	<.001
Drinkers (% [n])	49.96 (583)	11.17 (197)	<.001
Exercisers (% [n])	57.33 (669)	53.85 (950)	.005
Education (% [n])			
College or above	29.2 (341)	16.0 (283)	<.001
Middle school	58.4 (681)	57.0 (1005)	
Primary or below	12.4 (145)	27.0 (476)	
Income (% [n])			
Low	33.3 (389)	43.9 (775)	<.001
Middle	44.0 (514)	42.5 (750)	
High	22.6 (264)	13.5 (239)	
Overweight (% [n])	27.44 (354)	18.40 (405)	<.001
Obesity (% [n])	2.75 (35)	2.55 (64)	NS
Hypertension (% [n])	29.79 (419)	25.04 (609)	NS
T2DM (% [n])	11.03 (175)	8.48 (208)	.008
IGR (% [n])	14.20 (204)	13.21 (298)	NS
Dyslipidemia (% [n])	40.36 (517)	29.15 (642)	<.001
Metabolic syndrome (% [n])	17.3 (201)	15.8 (277)	NS
MA-ECG (% [n])	13.11 (153)	15.65 (276)	NS

Data were expressed as means ± SD or percentage(number of cases)in continuous and categorical variables. Between-groups comparisons were conducted using Student t tests or χ^2 tests. Comparisons of percentages were based on the Mantel-Haenszel χ^2 test stratified by age group (every 10 years). NS indicates not significant.

Table 2
Sex-stratified metabolic characteristics of all the participants in the survey

Categorical variables	Men (n = 1167)	Women (n = 1764)	P value
BMI (kg/m^2)	23.61 ± 3.37	23.14 ± 3.36	<.001
WC (cm)	82.67 ± 9.89	77.20 ± 9. 23	<.001
SBP (mm Hg)	124.78 ± 17.52	119.67 ± 19.90	<.001
DBP (mm Hg)	79.33 ± 11.36	76.61 ± 11.19	<.001
FPG (mmol/L)	5.13 ± 1.23	5.01 ± 1.26	.019
30-min PG (mmol/L)	9.20 ± 2.50	8.65 ± 2.63	<.001
2-h PG (mmol/L)	6.17 ± 1.55	6.31 ± 1.51	NS
0-min plasma insulin (μU/mL)	7.59 ± 1.78	7.24 ± 1.78	NS
30-min plasma insulin (μU/mL)	37.15 ± 2.19	40.74 ± 2.09	.006
TC (mmol/L)	4.80 ± 1.04	4.84 ± 1.10	NS
TG (mmol/L)	1.45 ± 1.91	1.12 ± 1.74	<.001
HDL (mmol/L)	1.21 ± 0.33	1.34 ± 0.34	<.001
LDL (mmol/L)	2.77 ± 0.93	2.90 ± 0.99	<.001

Data were expressed as means ± SD. Between-groups comparisons were conducted using Student t tests. Log-transformed values for abnormally distributed continuous variables were used for analysis; nontransformed values displayed for ease of interpretation.

No significant differences were found in 2-hour PG, FIN, and TC between male and female participants.

3.2. The prevalence of overweight and obesity and their risk factors

The age- and sex-adjusted prevalence of overweight and obesity was 23.04% and 2.65%, respectively. The age-adjusted prevalence of overweight and obesity was 27.44% and 2.75% for men and 18.40% and 2.55% for women, respectively. The prevalence of overweight was higher in men, whereas there was no difference in the prevalence of obesity between male and female participants. The sex-specific prevalence of overweight and obesity across age categories (unit of 10) is shown in Fig. 1. As we can see from Fig. 1A, before the age of 60 years, men had a higher prevalence of overweight than women at the corresponding age, whereas women reached their highest prevalence of overweight at 60 to 69 years of age. Both men and women had an increased prevalence of overweight with increased age; and after 60 years of age, the prevalence for men dropped slightly. From Fig. 1B, we can learn that women had a higher prevalence of obesity than men except for the 20- to 29-, 30- to 39-, and 60- to 69-year-old groups; and the prevalence increased rapidly from the 40- to 49-year-old group. Logistic regression analysis was carried out to explore the associations between excess body weight (including overweight and obesity) and risk factors such as age, education, income, smoking, alcohol consumption, exercise, hypertension, diabetes, and dyslipidemia. Old age, low education, lack of exercise, diabetes, hypertension, and dyslipidemia were independent risk factors for men, whereas old age, low education, alcohol consumption, diabetes, hypertension, and dyslipidemia were independent risk factors for women.

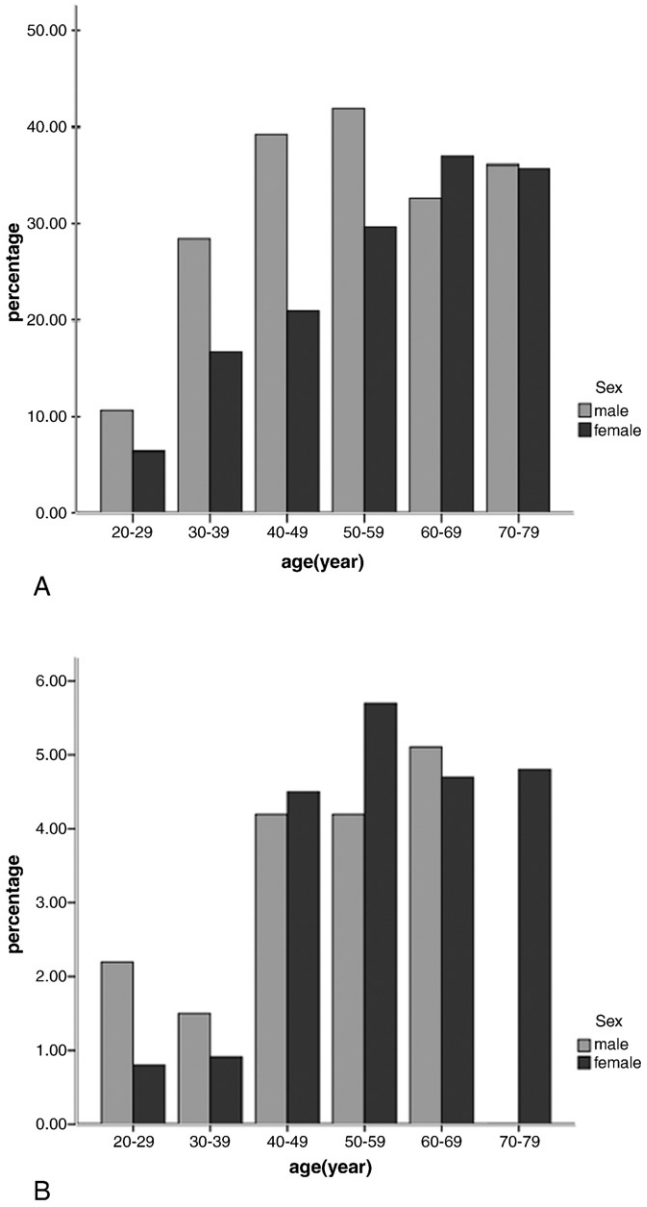

Fig. 1. Sex- and age-stratified prevalence of overweight and obesity of all participants.

3.3. Comparisons between subjects with different ranges of BMI

Age-standardized means for continuous risk factors across BMI categories were compared with analysis of covariance (Table 3). There were increasingly adverse risk levels of WC, blood pressure, PG, plasma insulin concentration, and plasma lipid levels with increasing levels of BMI (all P values for the trend were < .001, except for the LDL that was .003 but also with statistically significant difference). There was also increasing prevalence of morbidities with increasing categories of BMI (in all analyses, P values for trend were < .001). However, we did not find significant difference in major ECG abnormalities across the different ranges of BMI.

3.4. ORs of morbidities across BMI categories

Logistic regression analysis was conducted again to explore the associations of obesity-related morbidities with factors such as age, sex, education, income, smoking, alcohol consumption, and BMI categories. Because the BMI range of less than 19 kg/m^2 shows the lowest prevalence of all of the morbidities, we choose this BMI category as the reference (OR = 1.00). Body mass index was independently associated with all the morbidities, and there were increasing trends for all the morbidities across increasing degrees of BMI (Table 4). The ORs of hypertension, diabetes, dyslipidemia, and metabolic syndrome for subjects in the BMI range of 25 to 27 kg/m^2 were 2.8, 6.1, 5.1, and 5.7, respectively, compared with those within the reference level. The ORs further increased to 4.6, 10.5, 9.8, and 14.4 when the BMI increased from 25 to at least 29 kg/m^2, respectively.

3.5. Comparisons of different indexes of insulin sensitivity and β-cell function across different degrees of BMI

Age-adjusted means of different indexes of insulin sensitivity and β-cell function between different BMI groups (normal weight, overweight, and obese) are shown in Table 5. The HOMA-IR, HOMA-β, and ΔI30/ΔG30 tended to increase across BMI categories (all P values for trend were < .001). There were also statistical differences between any 2 of the BMI groups except the overweight group vs the obese group for HOMA-β (P = .122). There were no differences among 3 different BMI categories for the (ΔI30/ΔG30)/HOMA-IR (P value for trend was .211).

3.6. Associations of BMI with IR and β-cell function in multiple linear regression models

Table 6 shows the linear relationships of BMI to different indexes of IR and β-cell function after adjustment for age, sex, smoking, alcohol consumption, exercise, blood pressure, and lipid profiles. Body mass index was independently and significantly associated with HOMA-IR, HOMA-β, and ΔI30/ΔG30; the standardized β coefficients were 0.195, 0.090, and 0.126 for HOMA-IR, HOMA-β, and ΔI30/ΔG30, respectively. The partial correlation coefficients of BMI with the 3 indexes were 0.183, 0.083, and 0.114, respectively (all the P values ≤ .001). No statistically significant relationship of BMI to (ΔI30/ΔG30)/HOMA-IR was found in our study.

4. Discussion

In our study population, the means of BMI were 23.61 ± 3.37 kg/m^2 for men and 23.14 ± 3.36 kg/m^2 for women; and the overall prevalences of overweight and obesity were

Table 3
Comparisons of clinical characteristics and prevalence of obesity-related morbidities across BMI categories

	BMI categories (kg/m^2)							
	<19	<21	<23	<25	<27	<29	≥29	*P* value
WC (cm)	67.12 ± 0.40	72.14 ± 0.29	76.19 ± 0.25	80.87 ± 0.27	85.69 ± 0.31	89.75 ± 0.46	94.64 ± 0.70	<.001
SBP (mm Hg)	108.56 ± 0.85	115.27 ± 0.77	119.56 ± 0.68	123.76 ± 0.75	126.93 ± 0.86	130.92 ± 1.28	133.65 ± 1.49	<.001
DBP (mm Hg)	69.84 ± 0.56	73 ± 0.45	76.08 ± 0.40	79.06 ± 0.41	81.66 ± 0.50	83.35 ± 0.76	85.75 ± 0.96	<.001
FPG (mmol/L)	4.72 ± 1.01	4.86 ± 1.01	4.95 ± 1.01	5.11 ± 1.01	5.24 ± 1.01	5.20 ± 1.01	5.50 ± 1.02	<.001
30-min PG (mmol/L)	8.68 ± 0.17	8.60 ± 0.11	8.53 ± 0.10	8.92 ± 0.10	9.22 ± 0.12	9.16 ± 0.17	9.74 ± 0.19	<.001
2-h PG (mmol/L)	5.19 ± 1.02	5.53 ± 1.02	5.93 ± 1.01	6.49 ± 1.02	6.97 ± 1.02	7.06 ± 1.03	7.59 ± 1.03	<.001
FIN (μU/mL)	6.26 ± 1.04	6.41 ± 1.03	6.92 ± 1.02	7.29 ± 1.02	8.28 ± 1.03	9.20 ± 1.04	10.21 ± 1.04	<.001
30-min insulin (μU/mL)	33.11 ± 1.05	34.43 ± 1.04	37.33 ± 1.03	43.05 ± 1.03	46.05 ± 1.04	51.29 ± 1.05	50.93 ± 1.06	<.001
TC (mmol/L)	4.32 ± 0.05	4.58 ± 0.05	4.78 ± 0.04	4.93 ± 0.04	5.02 ± 0.05	5.15 ± 0.07	5.12 ± 0.08	<.001
TG (mmol/L)	0.82 ± 1.03	0.96 ± 1.02	1.16 ± 1.02	1.34 ± 1.02	1.54 ± 1.03	1.69 ± 1.04	1.80 ± 1.05	<.001
HDL (mmol/L)	1.43 ± 0.02	1.38 ± 0.02	1.32 ± 0.01	1.26 ± 0.01	1.19 ± 0.02	1.17 ± 0.02	1.15 ± 0.03	<.001
LDL (mmol/L)	2.66 ± 0.06	2.76 ± 0.04	2.86 ± 0.04	2.87 ± 0.04	2.90 ± 0.04	2.96 ± 0.06	2.95 ± 0.07	.003
Hypertension (% [n])	10.5 (25)	23.2 (116)	30.1 (207)	42.3 (274)	42.9 (201)	51.3 (116)	54.3 (89)	<.001
Diabetes (% [n])	1.7 (4)	7.0 (35)	9.6 (66)	15.0 (97)	20.7 (97)	15.5 (35)	29.9 (49)	<.001
Dyslipidemia (% [n])	11.4 (27)	23.2 (116)	34.3 (235)	48.0 (309)	52.1 (244)	51.8 (117)	67.7 (111)	<.001
Metabolic syndrome (% [n])	1.3 (3)	5.0 (25)	11.0 (75)	16.2 (104)	25.8 (120)	31.3 (70)	50.0 (81)	<.001
MA-ECG (% [n])	14.7 (35)	12.8 (64)	14.7 (101)	16.4 (106)	14.1 (66)	15.9 (36)	12.8 (21)	NS

Data were expressed as means ± SE or percentage (number of cases).Comparisons across BMI categories were made using analysis of covariance adjusting for age in numerical variables and χ^2 for the trend in categorical variables. Log-transformed values for abnormally distributed continuous variables were used for analysis; nontransformed values displayed for ease of interpretation.

23.04% and 2.65% (27.44% and 2.75% in men and 18.40% and 2.55% in women, respectively). In agreement with other Asian data [32,33], our findings confirmed that Chinese population exhibited lower prevalence of overweight and obesity than those seen in Western countries [34,35]. Report from Klumbiene et al [35] showed that the prevalence of obesity among men and women was 10% and 15% in Estonia, 11% and 10% in Finland, and 10% and 18% in Lithuania, respectively. When the combined prevalence of overweight and obese people (BMI >24.99 kg/m^2) was examined, more than half of the male respondents from Finland and more than 45% of men from Estonia and Lithuania were overweight. This was also the case for 38% of Finnish women, 42% of Latvian women, and 48% of Lithuanian women. The study by Zhou et al [36] from 14 populations of different geographical regions of China reported a prevalence for overweight and obesity of 20.7% and 1.5% in men and 27% and 3.9% in women, respectively. Our results showed much higher prevalence of overweight and obesity in men, although the prevalence was much lower in women than that in the report from Zhou et al [36]. The decrease in the prevalence of overweight and obesity for women may be due to women of all age segments in modern society paying more and more attention to maintaining good shape and the beauty of appearance.

The shared risk factors of overweight and obesity for both sexes were old age, low education, diabetes, hypertension, and dyslipidemia conditions. Our results confirmed the inverse associations that had been found between age, education, and obesity in both sexes in previous studies [37-40]. Except for the shared risk factors, an additional risk factor for developing overweight and obesity was lack of exercise for men and alcohol consumption for women. Over the last few decades in the industrialized nations, a transition

Table 4
Multiple logistic regression analysis of the associations between BMI degrees and morbidities

BMI categories (kg/m^2)	Hypertension		T2DM		Dyslipidemia		Metabolic syndrome	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
<19	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
<21	1.91	(1.17-3.12)	3.01	(1.04-8.74)	1.92	(1.22-3.05)	1.63	(0.47-5.68)
<23	2.30	(1.44-3.69)	3.55	(1.26-10.04)	3.11	(2.00-4.82)	2.99	(0.90-9.94)
<25	3.10	(1.93-4.96)	4.35	(1.55-12.23)	4.65	(2.99-7.22)	3.14	(0.95-10.37)
<27	2.84	(1.75-4.61)	6.11	(2.17-17.19)	5.09	(3.24-8.01)	5.67	(1.71-18.76)
<29	4.16	(2.47-7.01)	3.98	(1.36-11.69)	4.91	(2.99-8.03)	8.09	(2.40-27.30)
≥29	4.59	(2.65-7.98)	10.52	(3.61-30.7)	9.79	(5.75-16.65)	14.39	(4.23-48.9)

Data were expressed as ORs and 95% CIs. Odds ratios were in relation to BMI degrees for hypertension, T2DM, dyslipidemia, and metabolic syndrome after adjustment for age, sex, smoking, alcohol consumption, education, occupation, income, blood pressure, PG, and lipid profiles as appropriate.

Table 5
Analysis of covariance examining differences of IR and β-cell function between normal-weight, overweight, and obese groups

	Normal weight	Overweight	Obese	*P*1	*P*2	*P*3
HOMA-IR	1.36 ± 1.01	1.73 ± 1.02	2.37 ± 1.08	<.001	<.001	<.001
HOMA-β	113.8 ± 1.02	133.35 ± 1.03	157.04 ± 1.11	<.001	.002	NS
ΔI30/ΔG30	11.07 ± 1.02	13.06 ± 1.04	17.66 ± 1.15	<.001	.001	.039
(ΔI30/ΔG30)/HOMA-IR	8.22 ± 1.02	7.55 ± 1.05	7.45 ± 1.16	NS	NS	NS

Data were expressed as means ± SE using analysis of covariance adjusted for age. *P*1 = overweight vs normal weight *P*2 = obese vs normal weight; *P*3 = obese vs overweight. Log-transformed values for abnormally distributed continuous variables were used for analysis; nontransformed values displayed for ease of interpretation.

from a positive to a negative association had been found between household income and obesity [41,42]. In this study, the negative association in both sexes was found in univariate models but not found in multivariate models. One possible reason was that education and income were correlated with each other and education was more strongly associated with the risk of overweight and obesity than income in this population. Lower risk of overweight and obesity among smokers had been reported in other studies [39,43], but was not found in our present study. The protective effect of smoking on overweight and obesity may due to the fact that smoking subjects were at increased risk of developing chronic diseases such as respiratory disease and cancer that may decrease the body weight. We did not detect the comprehensive associations between smoking, chronic diseases, and obesity in the present study.

Despite the lower means of BMI and prevalence of overweight and obesity than Western populations, there were clear relationships of BMI to multiple cardiovascular risk factors and obesity-related morbidities. Our findings were in line with reports from lots of previous studies [8-10,13-16] that an increased risk of obesity-related morbidities was accompanied by the increase of BMI. In our study, we found the lowest rates of morbidities (such as hypertension, diabetes, dyslipidemia, and metabolic syndrome) in the lowest BMI categories. These findings were discordant with the previous study with Hong Kong Chinese [44] that reported that the low BMI or low normal BMI was also a risk factor for developing various morbidities. Whereas the association between BMI and all-cause mortality from lots of prospective cohort studies was more controversial, a direct association or a J-shaped or U-shaped relationship has been reported [45-51]. From our study, BMI was independently associated with all the morbidities; and there were increasing trends for all the morbidities across increasing degrees of BMI. The ORs for subjects in the BMI category of 25 to 27 kg/m^2 for having any of the morbidities had the most significant increase, whereas there were also a gradual increase in the lower BMI categories compared with the reference group. In agreement with other South Asian and Chinese data [36,37,44], our findings confirmed that subjects were already at risk state with normal BMI (defined by the WHO criteria) and that when the BMI reached 25 kg/m^2, the risk of developing obesity-related morbidities was very high. So our study supports to use the lower cutoff values for Chinese population to define overweight and obesity to guide health-promotion strategies [52]. Although there were significant independent associations between BMI and cardiovascular risk factors, we did not find a difference in major Minnesota codes abnormality across BMI categories. There was also no independent association between BMI and the presence of major Minnesota codes abnormality in logistic regression analysis. The WHO recommended the Minnesota code for measuring the CVDs in 1968. It has since become a unified index for ECG diagnosis and evaluation of cardiovascular epidemiology and has demonstrated the strongest risk factors for CVDs [20,28]. It seems unreasonable that BMI had no effect on the presence of major Minnesota codes abnormality in our data. Maybe our limited sample size can explain this contradiction.

In our subsample population with NGT evaluated for the differences of IR and β-cell function between the normal-weight, overweight, and obese groups after adjusting for age, we found that both the HOMA-IR and ΔI30/ΔG30 increased with the BMI degrees and that significant differences existed between any 2 of the 3 groups. There was also increasing trend for HOMA-β across BMI categories, but there was no significant difference between the overweight and obese groups. In our present study, we found that there was a slightly decreased trend in (ΔI30/ΔG30)/HOMA-IR across the BMI ranges but with no significant difference. The (ΔI30/ΔG30)/HOMA-IR represents the ability of β-cell to compensate for IR and to maintain the glucose homeostasis.

Table 6
Full multiple linear regression models examining associations of BMI with IR and β-cell function

	Standardized β coefficient	*t*	*P* value	Partial correlation coefficient
HOMA-IR	0.195	8.234	<.001	0.183
HOMA-β	0.090	3.706	<.001	0.083
ΔI30/ΔG30	0.126	5.120	<.001	0.114
(ΔI30/ΔG 30)/ HOMA-IR	0.012	0.489	.625	0.011

Linear regression models adjusted for age, sex, smoking, alcohol consumption, exercise, blood pressure, and lipid profiles. All the independent variables entered the models with the stepwise method (criteria: probability of F to enter ≤0.05, probability of F to remove ≥0.10). Log-transformed values for abnormally distributed continuous variables were used for analysis; nontransformed values displayed for ease of interpretation.

Our result indicated that β-cell can completely compensate for IR and maintain the homeostasis of blood glucose in overweight and obese subjects with NGT. Our findings were in line with the reports from Kissebah et al [53] and Ferrannini et al [54] that hyperinsulinemia is a characteristic of obesity. Insulin hypersecretion as a compensation for IR to keep the glucose concentration at a normal level existed at the early stage of the overweight or obese subjects with NGT. A recent study [55] indicated the concept that the insulin hypersecretion of obesity is in part primary (ie, independent of IR). The notion that primary insulin hypersecretion is an inherent feature of obesity was also put forward in previous studies [56,57].

Also in the multiple linear regression models, after adjustment for a broad spectrum of covariates, BMI was shown to be significant predictor of HOMA-IR, HOMA-β, and ΔI30/ΔG30 with the standardized β coefficient of 0.195, 0.09, and 0.126, respectively. Body mass index correlated with all the 3 indexes significantly after adjusting for other variables. A report from Ferrannini et al [58] also indicates that both fasting insulin secretion and total insulin response to oral glucose increase with BMI in an approximately linear fashion in the nondiabetic subjects. It is clear that body weight plays a very important role in the development of IR and the subsequent IGR or even diabetes. Camastra et al [55] demonstrated that although severe uncomplicated obesity is characterized by gross insulin hypersecretion and IR, the dynamic aspects of β-cell function are intact. Lots of other studies [59,60] also reported that the dynamic properties of β-cell function are not substantially altered by the presence of obesity or IR as long as glucose tolerance is normal. Camastra et al [55] also reported that malabsorptive bariatric surgery corrects both the insulin hypersecretion and the IR at a time when BMI is still high. With continued weight loss over a 2-year period, moderately obese subjects become supersensitive to insulin and, correspondingly, insulin hyposecretion. In Pima Indians with NGT, spontaneous long-term (~2.5 years) changes in body weight have been found to be linearly associated with changes in insulin action (as measured by the euglycemic clamp technique) in a reciprocal manner [61]. However, whether the ability of an essentially normal β-cell to cope with extreme demands would be eventually compromised with long duration of obesity (ie, whether bona fide exhaustion would ever occur) remains an untested possibility. Besides, in our study, the IGR-to-diabetes ratio was 1.3, indicating a large pool of prediabetic subjects. A recent study [62] demonstrated that both insulin sensitivity and β-cell function predict conversion to diabetes in different ethnic groups and varying states of glucose tolerance, family history of diabetes, and obesity. The prevention of T2DM should focus on interventions that improve both IR and insulin secretion. All of our findings highlight the importance of weight control in overweight or obese subjects with NGT to reverse the IR and insulin hypersecretion. Interventions such as lifestyle modification including diet and exercise are necessary and effective at the early stage.

5. Limitations

The present study has a number of limitations. First, the response rate was higher in women than men because, in such a developing country, lots of men work far away from their home for a better salary. Second, our study is cross-sectional and thus does not allow us to establish a cause-effect relationship. Although the nature of our study is cross-sectional, clear associations between BMI and cardiovascular risk factors, morbidity conditions, IR, and β-cell function were confirmed. Undoubtedly, people at overweight or obese state are at high risk of developing morbidity conditions and already have IR and β-cell dysfunction even if they are NGT at present. Third, our study does not explore the associations of diseases with the potential risk factors such as depression, anxiety, and stress from all aspects of their lives and the modern society. They may be both cause and effect of the diseases and be likely to confound the associations of BMI with diseases or prediseases state.

6. Conclusion

Our present study confirmed the significant independent associations of BMI with CVD risk factors, morbidity conditions, IR, and β-cell function. The CVD risk factors and indexes of IR and β-cell function increased in a stepwise manner across BMI categories. Given that the developing world appears to be at greater risk of the diseases associated with overweight, that CVD has become the leading cause of disability and death in many developing countries [5-7], and that the risk of developing T2DM increases with BMI values in a dose-dependent manner [13,14], it is imperative that the identification and treatment of overweight and obesity in Chinese people become a key focus of the Chinese health care community. Health education such as lifestyle modification and regular health examination should be enhanced to form a patient-centered model of prevention of obesity and obesity-related morbidity conditions at the very early stage.

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