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Association between body mass index and cardio-metabolic risk factors among subjects in Wuhan, China

A cross-sectional study

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Abstract

The aim of this study is to evaluate the association between body mass index (BMI) and cardio-metabolic risk factors and to determine the optimal BMI cut-off values in male and female subjects in Wuhan, China.

We conducted a retrospective cross-sectional analysis of 20218 adult subjects (aged 18–85 years, 12717 men of them) who had health examinations at the health management center of Tongji Hospital of Wuhan in 2017. Multivariate logistic regression analysis was preformed to calculate the odds ratios (ORs) of cardio-metabolic risk factors. Receiver operating characteristic curve was used to determine the area under the receiver operating characteristic curve and optimal cut-off values for BMI predictive of cardio-metabolic risk factors.

Of the 20218 participants, the percentage of males with overweight and obesity was as twice as that of females and the prevalence of hypertension, diabetes mellitus (DM), dyslipidemia, and hyperuricemia was significantly higher in males than females (27.18% vs 17.69%, 7.88% vs 4.16%, 41.97% vs 15.20%, and 34.50% vs 9.93%, respectively). Multivariate logistic regression analysis showed that higher BMI was a significant risk factor for hypertension (OR:1.27, 95% confidence intervals [CI]: 1.25–1.29), DM (OR:1.25, 95% CI:1.22–1.28), dyslipidemia (OR:1.26, 95% CI:1.25–1.28), and hyperuricemia (OR:1.25, 95% CI:1.23–1.27) after adjusting for age in both sexes. But in overweight or obesity status, females had higher ORs for hypertension and DM, and lower ORs for dyslipidemia than that in males. The optimal cut-off values of BMI for the presence of cardio-metabolic risk factors were among 24.25 to 25.35 kg/m^2 in males, which were higher than in females among 22.85 to 23.45 kg/m^2.

The association between BMI and cardio-metabolic risk factors is different by gender. It is necessary to determine appropriate threshold for overweight status in men and women separately.

Abbreviations: AUC = the area under ROC curve, BMI = body mass index, CIs = confidence intervals, DM = diabetes mellitus, eGFR = estimated glomerular filtration rate, HDL = high density lipoprotein, LDL = low density lipoprotein, ORs = odds ratios, ROC = the receiver operating characteristic, TC = total cholesterol.

Keywords: body mass index, diabetes mellitus, dyslipidemia, hypertension, hyperuricemia

1. Introduction

In recent years, excess bodyweight has become a major public health concern worldwide.[1] From 1975 to 2014, the global age-standardized prevalence of obesity increased from 3.2% to 10.8% in men, and from 6.4% to 14.9% in women.[2] Similarly, the prevalence of obesity in China has also been on the rise.[3] Overweight and obesity are the abnormal or excessive fat accumulation that results from chronic positive energy balance

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and whose reasons include the overconsumption of energy-dense, nutrient-poor foods and the lack of physical activity.[4–6] Excess bodyweight is an important risk factor for hypertension, diabetes mellitus (DM), dyslipidemia, and hyperuricemia which are the major cardio-metabolic risk factors.[7,8]

WHO recommended that body mass index (BMI) 25 to 29.9 kg/m^2 was defined as overweight, and BMI ≥ 30 kg/m^2 was defined as obesity.[9] But evidence indicates that the definition of the WHO may not apply to Asians.[10] Compared with western countries, the same BMI among Asians may have a higher percentage of body fat.[11] It can be concluded that the BMI threshold for overweight and obesity does not apply to all population. Moreover, there are some essential differences between men and women, for example the unhealthy lifestyles, sex hormone levels, and underlying genetic predisposition,[12–14] so the association of BMI and cardio-metabolic risk factors in male and female population may be different. Few studies assessed the discriminatory power for BMI predictive of cardio-metabolic risk factors between genders in our population,[15,16] so it is necessary to conduct a large-scale cross-sectional study to compare the optimal BMI cut-off points for cardio-metabolic risk factors in our male and female population. Wuhan is located in central China, with developed economy and dense population, and is the representative city of China. Therefore, the objective of this study is to evaluate the association between BMI and hypertension, DM, dyslipidemia, and hyperuricemia and to determine the optimal cut-off values for BMI predictive of cardio-metabolic risk factors in male and female subjects in Wuhan, China.

2. Material and methods

2.1. Study participants

This retrospective cross-sectional study was conducted at the health management center of Tongji Hospital, the top high-quality hospital in Wuhan (China), receiving more than 100000 medical examinations per year. People who were outpatients chose to have medical examinations according to personal wishes which was not obligatory. These people include all age groups, which can represent the general population of Wuhan to some extent. If a person has multiple medical examinations in 1 year, we will only randomly select 1 record from them. The medical records of subjects (18–85 years) in this study, who underwent annual medical examination at this center during the year 2017, were analyzed. All subjects underwent the routine anthropometric and laboratory measurements, and at the same time, we collected information about their medical history. The exclusion criteria included self-reported pregnancy, cancer patients, cachectic patients, chronic kidney disease (defined as estimated glomerular filtration rate [eGFR] <60 mL/min/1.73m^2), and subjects with incomplete data. As a consequence, a total of 20218 participants (12717 men and 7501 women) were included in this study (Fig. 1). Written informed consent was signed from all participants. The study was approvaled by the Ethics Committee of Tongji Hospital, Huazhong University of Science and Technology (TJ-C20160115).

2.2. Definition of the cardio-metabolic risk factors

Hypertension was defined as systolic blood pressure ≥140 mm Hg and/or a diastolic blood pressure ≥90 mmHg or taking antihypertensive medications.

DM was defined as taking medications for diabetes (insulin and oral anti-diabetic agent) or a glycated hemoglobin concentration of ≥6.5%.[8]

The definition of dyslipidemia depended on the Chinese guideline for the management of dyslipidemia in adults (2016 version)[17]: hypercholesterolemia: total cholesterol (TC) ≥6.2 mmol/L; hypertriglyceridemia: triglyceride ≥2.3mmol/L; hyper-low density lipoprotein (LDL): LDL ≥4.1 mmol/L; low-high density lipoprotein (HDL): HDL < 1.0 mmol/L.

Hyperuricemia was defined as serum uric acid levels ≥416 μmol/L (7.0 mg/dL) in male and ≥357 μmol/L (6.0 mg/dL) in female.[18,19] eGFR was estimated according to the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation: $eGFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female] × 1.159 [if black], where Scr is serum creatinine, black is black person, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.[20]

2.3. Anthropometric measurements

The blood pressure was measured in the right arm using electronic sphygmomanometer (HBP-9020; OMRON, Dalian, China), and the height of the right arm corresponded to the level of the heart, with sitting position, keeping quiet and rest for at least 10 minutes before measurement, and each participant was measured twice, at least 3 minutes apart. The mean value of the 2 measurements was used as final result of blood pressure. Body weight and height were measured by the specially designated nurses. Body mass index (BMI) was calculated as the participant's body weight (kg) divided by the square of the participant's height (m^2).

According to the Chinese adult obesity standard, we used the BMI to define underweight (<18.5 kg/m^2), normal weight (18.5–23.9 kg/m^2), overweight (24–27.9 kg/m^2) and obesity (≥28 kg/m^2).[10,21]

2.4. Assessment of covariates

The data of age, sex and medical history were self-reported in detail. Fasting blood samples were collected for biochemical variables in the morning after at least 12 h of fasting for all participants. Fasting plasma glucose, glycated hemoglobin, TC, triglyceride, LDL, HDL, uric acid, creatinine, urea nitrogen, urine protein, aspartate transaminase, and alanine transaminase were detected at the department of clinical laboratories of Tongji Hospital.

2.5. Statistical analysis

The statistical analyses were performed using software SPSS (version 11.0, SPSS Inc., Chicago, IL, USA). Statistical significance was defined as $p < .05$, and all statistical analyses were 2-sided. The continuous variables were expressed as mean ± standard deviation and categorical variables were frequencies by percentage (%). Comparisons between 2 groups were conducted by Student's t test for normally distributed data and χ^2 test analyses for categorical data. The odds ratios (ORs) and 95% confidence intervals (CIs) from logistic regression models were used to assess the association between BMI and the prevalence of hypertension, DM, dyslipidemia, and hyperuricemia in males or females after adjusting for age (and sex if including both genders

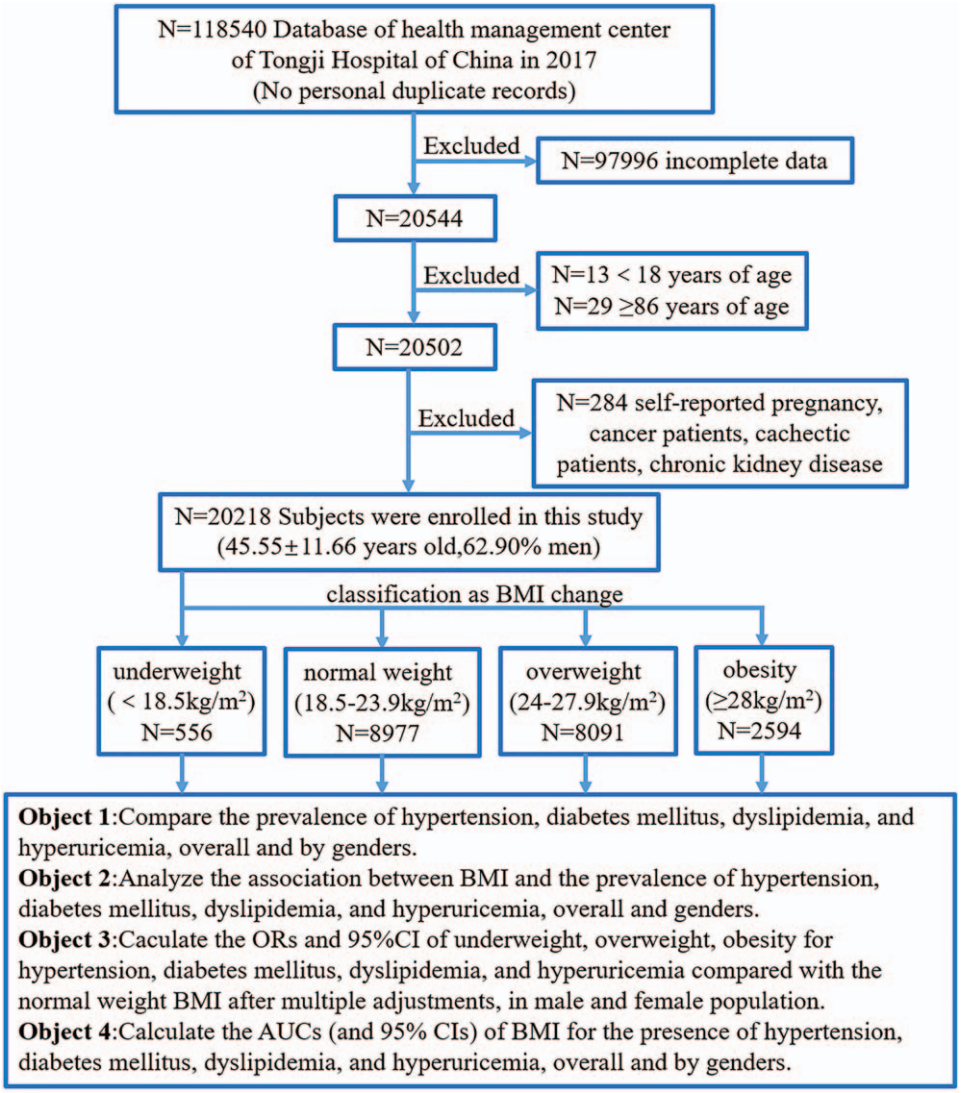

Figure 1. Flow diagram of study design.

in the same model). The cut-off values of BMI for the presence of cardio-metabolic risk factors were determined by the receiver operating characteristic (ROC) curve, which was quantified by the area under ROC curve (AUC). We calculated the optimal cut-off points of BMI by the Youden index (sensitivity+specificity-1). The process of statistical analysis is as shown in Figure 1.

3. Results

3.1. General characteristics of participants

A total number of 20218 participants (12717 males, accounting for 62.90%; 7501 females, accounting for 37.10%; median age: 46.00 years, range: 18–85 years) were included in the present cross-sectional study. According to the classification of BMI recommended by experts of China, overweight status was observed among 6085 (47.85%) males participants, and the males with obesity were 2115 (16.63%). Among the female subjects, the prevalence of normal BMI, overweight and obesity was 61.83%, 26.74%, and 6.39%, respectively. Table 1 shows the demographic, anthropometric, and biochemical characteristics of the 20218 participants. Males had a higher incidence of proteinuria, and higher levels of creatinine, urea nitrogen, alanine transaminase and aspartate transaminase than women (P for trend $<.001$). The age and TC levels were not different in both genders. In this study, the overall prevalence of hypertension, DM, dyslipidemia, hyperuricemia was 23.66%, 6.50%, 32.04%, and 25.39%, respectively. As compared with females, males had a higher prevalence of hypertension, DM, dyslipidemia, and hyperuricemia (27.18% vs 17.69%, 7.88% vs 4.16%, 41.97% vs 15.20%, and 34.50% vs 9.93%, respectively).

3.2. The prevalence of cardio-metabolic risk factors in relation to BMI and age

The prevalence of hypertension, DM, dyslipidemia, and hyperuricemia for each level of BMI in all participants is shown in Figure 2A. The overall prevalence of hypertension, DM, dyslipidemia, and hyperuricemia in China was 23.2%,[22] 10.9%,[23] 40.4%,[17] and 13.3%,[24] respectively. The incidence

Table 1

Characteristics of study participants between male and female subjects.

	Male	Female	Total	*P*-value
No. of participants	12717	7501	20218	
Age (r)	45.49 ± 11.24	45.65 ± 12.35	45.55 ± 11.66	.38
Hypertension, n (%)	3456 (27.18%)	1327 (17.69%)	4783 (23.66%)	<.001
Systolic blood pressure (mmHg)	128.19 ± 17.66	121.25 ± 19.41	125.61 ± 18.63	<.001
Diastolic blood pressure (mmHg)	80.02 ± 12.11	72.71 ± 11.93	77.31 ± 12.55	<.001
Diabetes mellitus, n (%)	1002 (7.88%)	312 (4.16%)	1314 (6.50%)	<.001
Fasting plasma glucose (mmol/L)	5.56 ± 1.40	5.27 ± 1.10	5.46 ± 1.31	<.001
Glycated hemoglobin	5.68 ± 0.82	5.55 ± 0.65	5.63 ± 0.76	<.001
Dyslipidemia, n (%)	5337 (41.97%)	1140 (15.20%)	6477 (32.04%)	<.001
Total cholesterol (mmol/L)	4.63 ± 0.88	4.62 ± 0.88	4.63 ± 0.88	.56
Triglycerides (mmol/L)	1.83 ± 1.61	1.21 ± 0.95	1.60 ± 1.44	<.001
Low-density lipoprotein (mmol/L)	2.81 ± 0.75	2.72 ± 0.75	2.78 ± 0.75	<.001
High-density lipoprotein (mmol/L)	1.15 ± 0.25	1.42 ± 0.30	1.25 ± 0.30	<.001
Hyperuricemia, n (%)	4388 (34.50%)	745 (9.93%)	5133 (25.39%)	<.001
Uric Acid (umol/L)	391.32 ± 83.90	276.09 ± 63.13	348.57 ± 94.89	<.001
Creatinine (umol/L)	83.03 ± 11.03	60.09 ± 8.48	74.52 ± 15.04	<.001
Blood urea nitrogen (mmol/L)	5.11 ± 1.19	4.57 ± 1.18	4.91 ± 1.22	<.001
Proteinuria, n (%)	1647 (12.95%)	514 (6.85%)	2161 (10.69%)	<.001
Aspartate transaminase (U/L)	28.61 ± 22.34	17.96 ± 16.94	24.67 ± 21.14	<.001
Alanine transaminase (U/L)	23.68 ± 12.31	20.50 ± 11.48	22.50 ± 12.11	<.001

Data are mean ± SD or percentages.

of dyslipidemia was highest among these risk factors in each level of BMI. The prevalence of cardio-metabolic risk factors parallelly increased with BMI increasing. Moreover, we further evaluated the prevalence of cardio-metabolic risk factors between males and females, as shown in Figure 2B. From the general trend, lower BMI associated with a lower prevalence of hypertension, DM, dyslipidemia, and hyperuricemia both in males and females. As compared with women, men had a higher prevalence of dyslipidemia and hyperuricemia almost in each level of BMI ($P < .05$). But for hypertension, when the BMI ranged from 20.1 to 22.0 and 25.1 to 26.0 kg/m^2, the prevalence of hypertension was higher in men than in women. In the population of overweight and obesity, there was no significant difference of the prevalence of DM between in men and in women. In the same time, we found that the prevalence of hypertension and DM increased with age. Instead, the prevalence of hyperuricemia decreased with age. The dyslipidemia was most common in the group aged 45–59 years old (Supplementary Figure 1, http://links.lww.com/MD/F436).

3.3. Association between BMI and the prevalence of hypertension, diabetes mellitus, dyslipidemia, and hyperuricemia, overall and by gender

Table 2 shows the ORs and 95% CI for hypertension, DM, dyslipidemia, and hyperuricemia according to the BMI that increased per 1 kg/m^2. We could see that higher BMI was an independent risk factor for hypertension (OR: 1.27, 95% CI: 1.25–1.29 in males; OR: 1.25, 95% CI: 1.22–1.28 in females), DM (OR: 1.23 in males, 1.29 in females), dyslipidemia (OR: 1.27 in males, 1.21 in females), and hyperuricemia (OR: 1.24 in males, 1.25 in females) in all participants.

As shown in Figure 3, underweight males population had lower risk for hypertension (OR: 0.31, 95% CI: 0.16–0.60, $P = .001$), DM (OR: 0.23, 95% CI: 0.06–0.94, $P = .04$), dyslipidemia (OR: 0.22, 95% CI: 0.13–0.40, $P < .001$), and hyperuricemia (OR: 0.28; 95% CI: 0.16–0.48, $P < .001$) than the normal weight males population. Moreover, the underweight females also had lower risk for hypertension (OR: 0.58, 95% CI: 0.35–0.97, $P = .04$), dyslipidemia (OR: 0.53, 95% CI: 0.33–0.86, $P = .01$), and hyperuricemia (OR: 0.49; 95% CI: 0.27–0.89, $P = .02$), but no difference for DM ($P = .46$) compared with the normal weight females. Overweight and obesity were the significantly risk factors for hypertension, DM, dyslipidemia, and hyperuricemia in males and females compared with the respective normal weight BMI after adjusting with age ($P < .001$). What was more, the females population had higher ORs for hypertension (OR: 2.08, 4.71 in males, 2.16, 4.80 in females) and DM (OR: 1.94, 3.76 in males, 2.66, 6.07 in females), but lower ORs for dyslipidemia (OR: 2.59, 4.49 in males, 2.14, 3.30 in females) compared with the males population in both overweight and obesity status, respectively. However, for the hyperuricemia, overweight males had a higher ORs than overweight females (OR: 2.17 in males, 2.12 in females), but in obesity status, the ORs of hyperuricemia in males was lower than in females (OR: 3.90 in males, 5.21 in females).

3.4. The AUCs and optimal cut-off values of BMI for the presence of cardio-metabolic risk factors

In addition, we drew the ROC curve according to BMI and the presence of hypertension, DM, dyslipidemia and hyperuricemia. The AUCs and optimal cut-off values of BMI for the presence of hypertension, DM, dyslipidemia, hyperuricemia, overall and by gender, are displayed in Table 3. The AUCs varied from 0.64 to 0.67 in men, and 0.68 to 0.75 in women. The optimal BMI cut-off values varied from 24.25 to 25.35 kg/m^2 in men, and 22.85 to 23.45 kg/m^2 in women. The optimal BMI cut-off values were mostly higher for men compared with for women.

4. Discussion

In this study, we demonstrated that males had 1.54-fold higher prevalence of hypertension, 1.89-fold higher prevalence of DM,

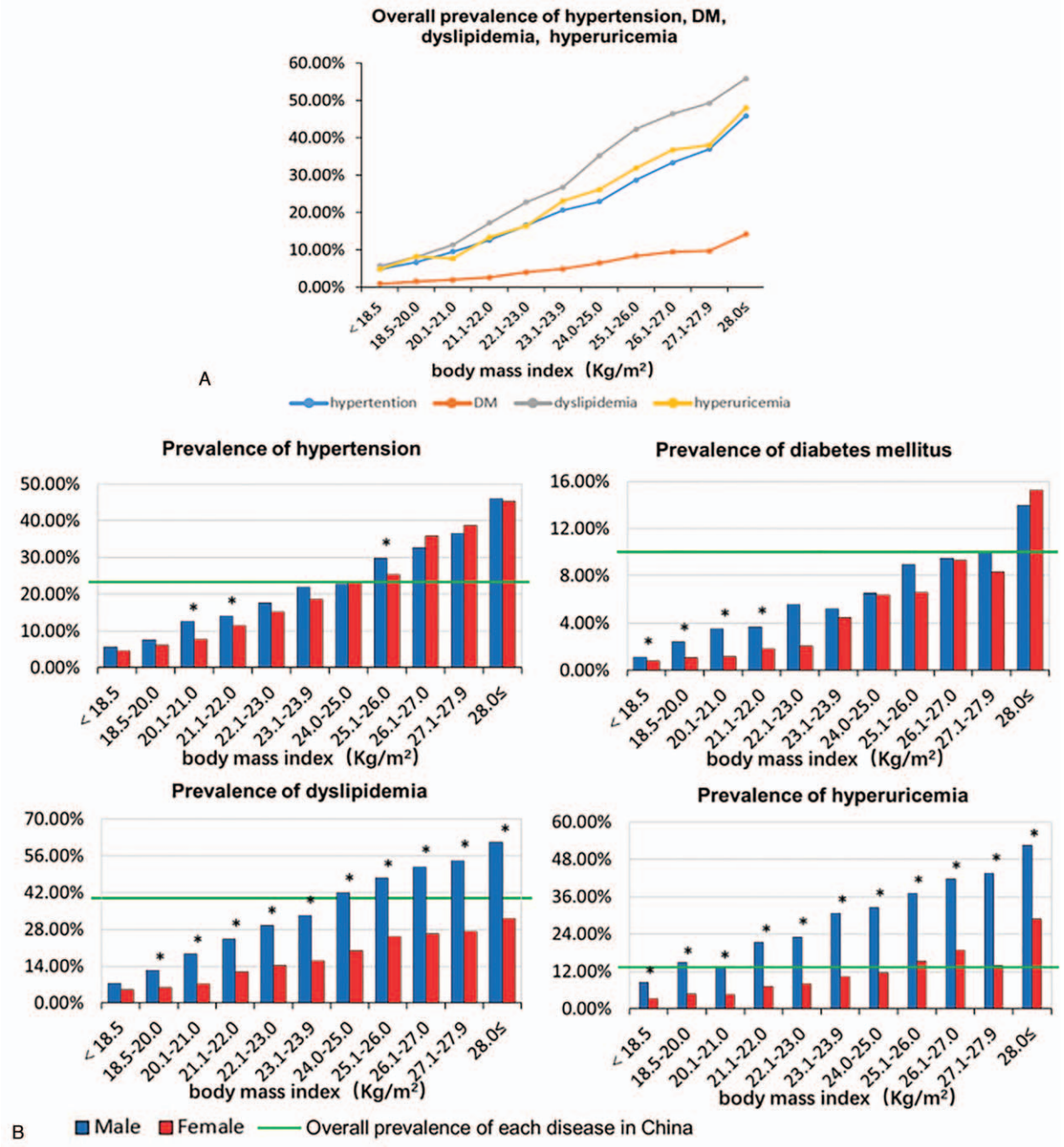

Figure 2. The prevalence of cardio-metabolic risk factors in each level of BMI, overall and by gender. (A) The overall prevalence of hypertension, DM, dyslipidemia, and hyperuricemia. (B) The prevalence of hypertension, DM, dyslipidemia, and hyperuricemia between males and females. Green solid lines showed mean prevalence of each disease in China. * indicated $P < .05$ compared between males and females in the same BMI.

2.76-fold higher prevalence of dyslipidemia, and 3.47-fold higher prevalence of hyperuricemia compared to the females. In particular, overweight and obesity status were independent risk factors for hypertension, DM, dyslipidemia and hyperuricemia both in males and females population after adjusting with age. The difference was that females had higher ORs for hypertension and DM, but lower ORs for dyslipidemia compared with males in both overweight and obesity status. The optimal cut-off values of BMI predictive of cardio-metabolic risk factors were higher for men compared with women. The overall direction of results showed trends that the association between BMI and cardio-metabolic risk factors differed by gender.

Worldwide, there was a difference in the prevalence of cardio-metabolic risk factors between men and women.[25–27] For instance, Zhang et al. reported that men had a higher incidence of hypertension compared with women in young adults.[25] Regitz-Zagrosek and Dearden et al. revealed that the metabolic syndrome, including DM, dyslipidemia, and hyperuricemia, was more prevalent in men than in women.[26,27] Consistent with this, our study found that the total prevalence of hypertension,

Table 2

Body mass index as a risk for hypertension, diabetes, dyslipidemia, and hyperuricemia.

	All		Male		Female	
	OR and 95%CI	P-value	OR and 95%CI	P-value	OR and 95%CI	*P*-value
Hypertension BMI per 1 kg/m^2 increased	1.27 (1.25–1.29)	<.001	1.27 (1.25–1.29)	<.001	1.25 (1.22–1.28)	<.001
Diabetes mellitus BMI per 1 kg/m^2 increased	1.25 (1.22–1.28)	<.001	1.23 (1.19–1.26)	<.001	1.29 (1.23–1.35)	<.001
Dyslipidemia BMI per 1 kg/m^2 increased	1.26 (1.25–1.28)	<.001	1.27 (1.25–1.29)	<.001	1.21 (1.18–1.24)	<.001
Hyperuricemia BMI per 1 kg/m^2 increased.	1.25 (1.23–1.27)	<.001	1.24 (1.22–1.26)	<.001	1.25 (1.21–1.29)	<.001

95% CI = 95% confidence interval, OR = odds ratio. Data was adjusted with age in male subjects or female subjects, and with age and sex in all subjects.

DM, dyslipidemia, and hyperuricemia was significantly higher in males than females. The reason might be the differences of sex hormone levels[28,29] and underlying genetic predisposition[13] between the genders and the higher percentage of smoking[12] and drinking[14] in men. Particularly, in our study men had a higher prevalence of dyslipidemia and hyperuricemia than in women almost in each level of BMI. But for the prevalence of hypertension and DM, there was no difference between males and females in group of overweight and obesity population. These results suggest that the males are more likely to suffer from dyslipidemia and hyperuricemia than females in the same level of BMI. Compared with females, males should be more active to control their weight, or, it suggests that the classification standard of BMI cut-off value in men should be higher, to some extent.

Consistent with previous studies, we found that overweight and obesity were significant risk factors for hypertension, DM, dyslipidemia, and hyperuricemia both in men and women.[7,30,31] Even so, since the percentage of men with overweight and obesity was as twice as that of women, the overall prevalence of cardio-metabolic risk factors was significant higher in men than women. So for a better prevention of cardio-metabolic risk factors, it is necessary to develop appropriate strategies for prevention and intervention of overweight and obesity based on gender, especially in male population.

The WGOC (Working Group on Obesity in China) recommends the BMI cut-off value of 24 kg/m^2 for overweight status in the general Chinese population.[32] Consistent with this, Feng et al and Yu et al reported that the optimal BMI cut-off value of metabolic syndrome was near 24 kg/m^2 in both sexes in northern China and northeast China, separately.[33,34] However, in our study, the optimal BMI cut-off values for cardio-metabolic risk factors varied from 24.25 to 25.35 kg/m^2 in men, and from 22.85 to 23.45 kg/m^2 in women. The BMI cut-off values were significantly higher in males than in females. These findings directly showed that BMI cut-off value of males in our study was a little higher than the criteria of WGOC, but, BMI cut-off value

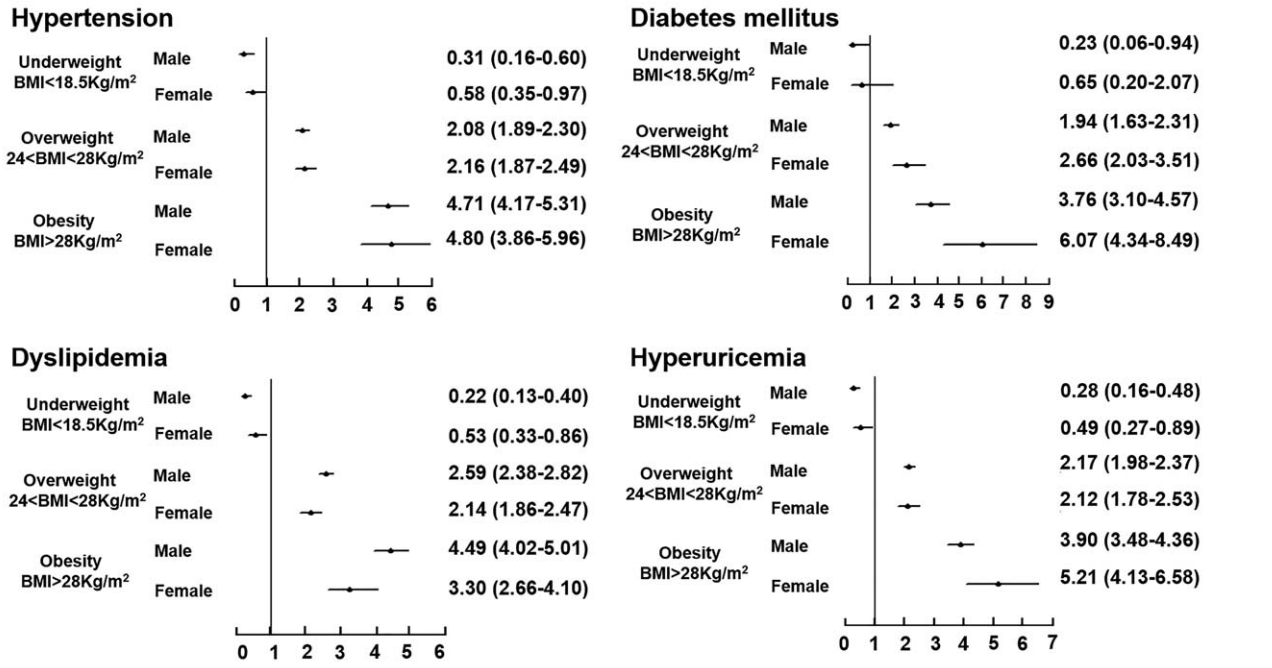

Figure 3. ORs and 95% CI of underweight, overweight, obesity for each disease compared with normal weight (18.5 ≤ BMI < 24 kg/m^2). Data were adjusted for age.

Table 3

The area under the receiver operating characteristic curve and optimal cut-offs for body mass index predictive of cardio-metabolic risk factors in both genders.

Variables	AUC (95%CI)	Cut-off	Sen	Spe	YI	*P* value
hypertension	0.69 (0.69–0.70)	24.85	0.628	0.652	0.28	<.001
DM	0.69 (0.67–0.70)	25.35	0.607	0.666	0.273	<.001
dyslipidemia	0.71 (0.70–0.72)	24.15	0.709	0.608	0.317	<.001
hyperuricemia	0.70 (0.69–0.71)	24.45	0.683	0.614	0.297	<.001
men						
hypertension	0.66 (0.65–0.68)	25.05	0.656	0.585	0.241	<.001
DM	0.64 (0.62–0.66)	25.35	0.641	0.569	0.21	<.001
dyslipidemia	0.67 (0.66–0.68)	24.25	0.745	0.508	0.253	<.001
hyperuricemia	0.65 (0.64–0.66)	24.95	0.653	0.563	0.216	<.001
women						
hypertension	0.71 (0.70–0.73)	23.15	0.675	0.643	0.318	<.001
DM	0.75 (0.72–0.78)	23.05	0.795	0.592	0.387	<.001
dyslipidemia	0.68 (0.66–0.69)	22.85	0.687	0.577	0.264	<.001
hyperuricemia	0.68 (0.66–0.70)	23.45	0.616	0.647	0.263	<.001

Sen = sensitivity, Spe = specificity, YI = Youden's index.

of females was a little lower than the criteria. Similarly, Zhang et al also reported that the optimal BMI cut-off values for hypertension, DM, dyslipidemia, hyperuricemia were higher for men compared with women in Shanghai, China.[16] By the BMI cut-off value of 24 kg/m^2 to define overweight status in Wuhan, some men with normal weight were mistaken for overweight, and some women of overweight were mistaken for normal weight. The difference of the prevalence of hypertension, DM, dyslipidemia, and hyperuricemia between men and women was increased. Therefore, it is necessary to re-determine appropriate threshold of overweight status in men and women in the central region of China, separately. Through analyzing the BMI thresholds of men and women, the overweight status should be re-defined more timely and rationally, which will help subsequent interventions to achieve better results.

Strengths of our study include a large sample size and abundant cardio-metabolic risk factors data available for study participants. Based on gender differences, we compared the optimal cut-off values and evaluated the association between BMI and cardio-metabolic risk factors. This study also has some limitations. First, this is a retrospective cross-sectional study. The nature of the retrospective study has a limitation to reach final conclusions. Second, smoking, drinking, dietary factors, stress, socioeconomic status and other confounders of obesity are not taken into consideration because we have not collected such information in advance.

In conclusion, the overweight and obesity status were significant risk factors for hypertension, DM, dyslipidemia, and hyperuricemia in both sexes, but the association between BMI and cardio-metabolic risk factors differed by gender. The optimal cut-off values of BMI for the presence of cardio-metabolic risk factors were higher in males compared with in females. Thus, it is necessary to determine appropriate threshold for overweight status in men and women separately.

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Author contributions

Qingquan Liu and Yongman Lv contributed to the conception and design of the research. Yongman Lv and Zhengce Wan acquired the data from the database of the health management center of Tongji Hospital in China. Shijie Zhang, Fei Huang and Ranran Xu performed statistical analyses. Shijie Zhang, Fei Huang and Anying Cheng drafted the manuscript. All authors critically revised the article and approved the final version of the manuscript.

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