Diabetes, Metabolic Syndrome and Obesity

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ORIGINAL RESEARCH

Association of Metabolically Healthy Obesity and Risk of Cardiovascular Disease Among Adults in China: A Retrospective Cohort Study

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Purpose: Previous studies have shown that metabolically healthy obesity (MHO) and changes in its status are connected to an increased incidence of cardiovascular disease (CVD). Yet, fewer studies have been conducted in China, especially for the middle-aged and elderly population, a high-risk group. The purpose of the study was to investigate the association between metabolic health status and CVD events.

Patients and Methods: A total of 46,055 participants were categorized into 6 subgroups with different metabolic states according to the existence of metabolic syndrome and body mass index (BMI). The changes in obesity and metabolic health status were defined from baseline to follow-up outcomes with a combination of overweight and obesity. Cox proportional hazards models estimated the association of CVD events and each BMI–metabolic groups.

Results: MHO and metabolic abnormality normal weight (MANW) subjects had a higher HR of CVD, 1.62 (95% CI, 1.36–1.92) and 1.24 (95% CI, 1.07–1.44), respectively, than their metabolically healthy normal weight (MHNW) counterparts. Then, more than 50% and 30% of the metabolically healthy overweight or obesity (MHOO) populations maintained their status and converted to a metabolically unhealthy state, respectively. Stable MANW, MHOO and metabolically abnormal obesity (MAO) were associated with a higher risk for CVD, 1.68 (95% CI, 1.37–2.05),1.26 (95% CI, 1.08–1.47) and 1.65 (95% CI, 1.45–1.88), respectively, than stable MHNW.

Conclusion: Despite being of normal weight, MANW status is in fact a risk factor for CVD, as well as MHO, especially for the Chinese middle-aged and elderly population. Furthermore, metabolic health is a transient state for partial middle-aged and elderly Chinese individuals, and MAO has the highest risk of CVD, including coronary heart disease (CHD) and stroke.

Keywords: metabolic health, obesity, heterogeneity, metabolically healthy obesity, cardiovascular disease, retrospective study

Introduction

With a rapidly aging global population and epidemiologic changes in disorders, CVD is still the leading cause of both morbidity and mortality globally, especially for middle-aged and older adults.[1,2] Several risk factors associated with metabolic syndrome, such as obesity, hypercholesterolemia, hypertension, and diabetes, have been proven to be primary risk factors for CVD globally, including the Chinese population.[3–5] In fact, obesity has become a component or even a necessary component of metabolic syndrome even under different definitions.[6] As for the definition of metabolic syndrome, the worldwide accepted standard was published as early as 2009, while it emphasized that suitable cut-off points should be adopted for study populations of specific ethnicity and gender.[7] Based on the combinations of BMI categories (normal weight, overweight and obesity) and metabolic health states (metabolically healthy and metabolically abnormal), most studies, including this one, have classified into 6 groups: "metabolically healthy normal weight" (MHNW); "metabolically healthy overweight" (MHOW); "metabolically healthy obesity" (MHO); "metabolically abnormal normal weight" (MANW); "metabolically abnormal overweight" (MAOW) and "metabolically abnormal obesity" (MAO). In addition, we defined transitions (stable MHNW, MHNW to metabolically healthy

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overweight or obesity (MHOO), stable MHOO, MHOO to metabolically abnormal overweight or obesity (MAOO)) from baseline to the follow-up outcomes, with a combination of overweight and obesity sample.

However, due to the heterogeneity in the metabolic factors of the obesity, there are some subjects with obesity who do not suffer from metabolic disorders that are usually considered to be MHO.[8,9] Previous findings have documented that MHO individuals had a heightened risk for CVD, including CHD and stroke, compared to their counterparts with MHNW, even though that was significantly lower than MAO individuals.[3,10–12] This reminds us that MAO may be the final state of metabolic health status while MHO is a transitional state.

However, compared to Westerners, with a lower BMI while bearing relatively higher body and visceral fat and lower fat-free mass, Chinese individuals may be more likely to have metabolic syndrome under the same BMI levels.[13–15] At the same time, compared with younger adults, the middle-aged and elderly people were at a heightened risk of developing comorbidities and chronic diseases, and it might elevate the risk of CVD.[16] Nevertheless, the majority of these researches were performed in Western people, while there have been scarce results from Asia, and very few in a representative cohort of Chinese middle-aged and elderly individuals. Exploring the cardiovascular hazards of obesity-related phenotypes and various metabolic health states' transformations during follow-up is of great public health significance to the self-management of obesity and the primary prevention of CVD.

Hence, the purpose of the present study was to evaluate the association between BMI groups and metabolic health status and the risk of CVD and explore the interconversion among various metabolic health statuses based on a retrospective cohort.

Materials and Methods

Participants

The study was based on an annual health screening dataset from the Electronic Health Management Center of Jinshui District, Zhengzhou City, Henan Province, China. The screening program, including the questionnaire survey and anthropometric and laboratory measurements, is an important part of the National Basic Public Health Service Program, organized by Jinshui Municipal Health Committee and collected by professional medical fellows.

In total, 131,179 individuals aged 45 and older were admitted to the study between January 2016 and December 2021, and data were analyzed from January 2016 to September 2021. From the 131,179 individuals, at first, 75,784 participants were excluded because of the lack of laboratory data. We then excluded participants with CVD at baseline (n=5,273), or with incomplete baseline data on smoking, drinking, physical activity (n=3,331), or BMI <18.5 kg/m^2 at baseline (n=729) and excluded the abnormal data where the date of death was before the date of medical screening (n=7). Ultimately, a total of 46,055 participants were eligible for inclusion in our study (Figure S1).

Data Collection

Data were collected through standardized questionnaires, physical examinations and laboratory tests. Standardized questionnaire of the National Norms for Basic Public Health Services (Third Edition), which included their sociodemographic characteristics (age, sex), medical history (type two diabetes, hypertension, coronary heart disease and stroke), smoking, drinking, and physical activity, were administered by trained research staff. Based on self-reported smoking, drinking and physical activity status, participants were divided into two categories: never or former/current levels.

Standing height and weight were measured to the nearest 0.1 cm and 0.1kg with the participant standing erect on bare feet, and the results were recorded by the mean of two replicate measurements. Waist circumference was measured to the nearest 0.1 cm at the midpoint between the lowest rib margin and the iliac crest following a standard protocol. BMI was calculated using weight in kilograms divided by height in meters squared, and the waist–height ratio was determined by WC (cm) divided by height (cm). Blood pressure was measured at least twice using an automatic sphygmomanometer (OMRON HEM-7125, Kyoto, Japan), and the average of the two qualified results of the measurements were taken in the analysis. After an 8-hour overnight fast, blood samples for laboratory were obtained to assess levels of fasting plasma glucose (FPG) using an automatic biochemical analyzer (DIRUI CS380, Changchun, China).[17] Biochemical indicators, including FPG, high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were assessed in this study.

Determination of Risk Exposure and Disease Outcome

Subjects were divided into BMI classes based on the Working Group on Obesity in China (WGOC): normal weight (BMI 18.5–23.9 kg/m^2), overweight (BMI 24.0–27.9 kg/m^2), and obese (BMI ≥28 kg/m^2).[18] Metabolic health was defined according to the Joint Interim Statement (JIS) criterion where a person had metabolic abnormality if he or she met ≥3 of the following criteria: 1) a waist circumference of ≥85 cm for men and ≥80 cm for women; 2) an FPG of ≥100 mg/dl, or previously diagnosed diabetes; 3) an SBP of ≥130 mm Hg, a DBP of ≥85 mm Hg, or previously diagnosed hypertension; 4) a fasting triglyceride level of ≥1.7 mmol/L; and 5) an HDL-C of <1.0 mmol/L for men and <1.3 mmol/L for women.[7]

The date of incidence was obtained from the Electronic Health Management Center, and the diagnosis of CVD was made during follow-up for those who had CHD or stroke according to the International Classification of Diseases, 10th Edition (ICD-10). CVD events were obtained from a self-reported questionnaire with clinical diagnosis certificates, and the first new CVD event was considered in the analyses.

Statistical Analysis

Continuous variables are described as the mean ± standard deviation and categorical variables are expressed as numbers and proportions. The analysis of continuous and categorical variables to estimate variance among the six phenotypes was performed by one-way ANOVA or the χ^2 test. The person-time of the follow-up was calculated from the date at baseline to the resurvey which had a report of a cardiovascular disease event, or the end of the follow-up. The proportional hazard assumption was examined by Schoenfeld test, and the Cox regression model was used to evaluate the hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of BMI-metabolic status and CVD incidence. Two multivariate-adjusted models were as follows: Model 1: Adjusted for age and sex; Model 2: Adjusted for age, sex, exercise, and smoking status. The missing data were imputed by multivariate multiple imputation (50 cycles).

Besides the primary analysis above, we also performed some sensitivity analyses. First, we adopted the CDS 2017 as the new criteria to identify metabolic status. Second, we used waist–height ratio to replace WC in sensitivity analysis. Third, we used the inverse probability of treatment weighting (IPTW) to correct for possible selection bias caused by the exclusion of missing data. Finally, the population with a follow-up time longer than the median follow-up time was examined.

$P < 0.05$ for a two-sided test was regarded as statistically significant. All analyses were performed using R version 4.1.3 (R Foundation for Statistical Computing).

Results

Baseline Characteristics

Out of totally 46,055 participants from the cohort, the mean age was 67.86 years (SD, 7.29 years), and 59.18% were women. At baseline, 46.34% (n = 21,343) of the subjects were metabolically abnormal, and 15.85% (n = 7,299) had obesity. Overall, 4.98% of the subjects investigated were MHO, and they accounted for 31.43% of the subjects with obesity. The sex-specific and age-specific prevalence of metabolic health status can be seen in Figures S2 and S3. Table 1 shows the baseline characteristics based on the metabolic health statuses. We compared analyzed data with missing data and found statistically significant differences in all variables except high-density lipoprotein cholesterol (Table S1). The significant differences were presented in age, BMI, waist circumference, FBS, SBP, DBP, TG, HDL-C, sex, smoking, drinking and physical activity status among the participants in the six metabolic health phenotypes (all P values <0.001). By analyzing the data after multiple imputation, we find that the results were generally consistent with the primary analysis (Table S2).

Associations of Metabolic Health Statuses with Risk of CVD Events

After a median follow-up of 1.91 years, 2,502 CVD cases were identified, including 1,982 CHDs and 575 strokes. The results presented that the highest risk of CVDs was associated with MAO, with an HR of 1.72 (95% CI, 1.50–1.96), followed by MHO, with an HR of 1.62 (95% CI, 1.36–1.92), compared with MHNW subjects. For the subtypes of CVD, similar results were found for the subgroups in CHD. The adjusted HRs for the MHO and MAO individuals were 1.76 (95% CI, 1.46–2.13) and 1.76 (95% CI, 1.52–2.04), respectively, while no meaningful differences were observed in MHO in stroke; the adjusted HRs for the MHO and MAO individuals were 1.12 (95% CI, 0.74–1.69) and 1.64 (95% CI, 1.24–2.18), respectively (Table 2).

Table 1 Baseline Characteristics of the Study Population

Variables	Overall	MHNW	MHOW	MHO	MANW	MAOW	MAO	P
Num	46,055	12,717	9,701	2,294	5,424	10,914	5,005	
Age (years)	67.86±7.29	68.36±7.30	67.80±7.26	67.12±6.93	68.50±7.35	67.53±7.32	67.05±7.22	<0.001
BMI (kg/m^2)	25.04±3.05	22.08±1.38	25.59±1.09	29.92±1.89	22.55±1.14	25.86±1.12	30.16±2.08	<0.001
WC (cm)	84.77±9.00	79.01±7.19	84.34±8.20	91.27±10.30	82.92±6.93	87.39±6.91	93.57±8.90	<0.001
FPG (mmol/L)	5.93±1.76	5.44±1.41	5.43±1.21	5.40±1.19	6.49±2.27	6.49±1.90	6.57±1.96	<0.001
TG (mmol/L)	1.62±1.05	1.25±0.61	1.30±0.58	1.32±0.66	1.99±1.32	2.02±1.29	2.05±1.24	<0.001
HDL-C (mmol/L)	1.44±1.37	1.55±1.99	1.48±1.22	1.46±0.37	1.36±0.47	1.34±0.45	1.34±1.85	<0.001
SBP (mm Hg)	136.53±16.66	131.02±15.89	133.21±16.16	135.78±17.49	139.20±14.88	141.28±15.69	144.01±16.73	<0.001
DBP (mm Hg)	79.88±9.96	77.27±9.54	78.95±9.87	80.42±10.38	80.25±9.39	81.79±9.74	83.49±10.06	<0.001
WHR	0.52±0.06	0.49±0.04	0.52±0.05	0.57±0.06	0.51±0.04	0.54±0.04	0.58±0.06	<0.001
Gender (%)								<0.001
Woman	27,254(59.18)	7,084(55.70)	4,752(48.98)	1,237(53.92)	3,967(73.14)	6,978(63.94)	3,236(64.66)	
Man	18,801(40.82)	5,633(44.30)	4,949(51.02)	1,057(46.08)	1,457(26.86)	3,936(36.06)	1,769(35.34)	
Smoking status (%)								<0.001
Never	42,942(93.24)	11,888(93.48)	9,011(92.89)	2,107(91.85)	5,170(95.32)	10,133(92.84)	4,633(92.57)	
Current and former	3,113(6.76)	829(6.52)	690(7.11)	187(8.15)	254(4.68)	781(7.16)	372(7.43)	
Drinking status (%)								<0.001
Never	42,554(92.40)	11,914(93.69)	8,893(91.67)	2,070(90.24)	5,151(94.97)	9,985(91.49)	4,541(90.73)	
Current and former	3,501(7.60)	803(6.31)	808(8.33)	224(9.76)	273(5.03)	929(8.51)	464(9.27)	
Exercise status (%)								<0.001
Never	15,216(33.04)	4,284(33.69)	3,077(31.72)	788(34.35)	1,837(33.87)	3,472(31.81)	1,758(35.12)	
Current	30,839(66.96)	8,433(66.31)	6,624(68.28)	1,506(65.65)	3,587(66.13)	7,442(68.19)	3,247(64.88)	

Abbreviations: MHNW, metabolically healthy normal weight; MHOW, metabolically healthy overweight; MHO, metabolically healthy obesity; MANW, metabolic abnormality normal weight; MAOW, metabolically unhealthy overweight; MAO, metabolically abnormal obesity; BMI, body mass index; WC, waist circumference; FPG, fasting plasma glucose; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; WHR, waist–height ratio.

Table 2 Incidence and Adjusted HRs for CVDs by BMI-Metabolic Health Status at Baseline

Variables	MHNW	MHOW	MHO	MANW	MAOW	MAO
Cardiovascular disease						
Incident cases	542	489	172	277	642	380
Person-years of follow-up	25,969.30	20,545.07	5,093.42	11,173.23	23,286.82	11,034.16
Incidence rate (per 1000 person-years)	20.87	23.80	33.77	24.79	27.57	34.44
HR (95% CI) Model 1	Ref	1.13(0.99–1.27)	1.63(1.37–1.93)*	1.24(1.08–1.44)*	1.37(1.22–1.54)*	1.73(1.52–1.97)*
HR (95% CI) Model 2	Ref	1.13(1.01–1.28)*	1.62(1.36–1.92)*	1.24(1.07–1.44)*	1.37(1.22–1.54)*	1.72(1.50–1.96)*
Coronary heart disease						
Incident cases	429	395	148	211	490	309
Person-years of follow-up	25,969.30	20,545.07	5,093.42	11,173.23	23,286.82	11,034.16
Incidence rate (per 1000 person-years)	16.52	19.23	29.06	18.88	21.04	28.00
HR (95% CI) Model 1	Ref	1.16(1.01–1.32)*	1.77(1.47–2.14)*	1.19(1.01–1.40)*	1.32(1.16–1.50)*	1.77(1.53–2.05)*
HR (95% CI) Model 2	Ref	1.16(1.01–1.33)*	1.76(1.46–2.13)*	1.19(1.01–1.40)*	1.32(1.16–1.51)*	1.76(1.52–2.04)*
Stroke						
Incident cases	124	102	27	72	167	83
Person-years of follow-up	25,969.30	20,545.07	5,093.42	11,173.23	23,286.82	11,034.16
Incidence rate (per 1000 person-years)	4.77	4.96	5.30	6.44	7.17	7.52
HR (95% CI) Model 1	Ref	1.02(0.78–1.32)	1.12(0.74–1.70)	1.46(1.09–1.95)*	1.58(1.25–2.00)*	1.68(1.27–2.22)*
HR (95% CI) Model 2	Ref	1.03(0.79–1.34)	1.12(0.74–1.69)	1.45(1.08–1.94)*	1.56(1.24–1.98)*	1.64(1.24–2.18)*

Notes: *P<0.05. Model 1: adjusted for age and sex. Model 2: adjusted for age, sex, exercise, and smoking.
Abbreviations: MHNW, metabolically healthy normal weight; MHOW, metabolically healthy overweight; MHO, metabolically healthy obesity; MANW, metabolic abnormality normal weight; MAOW, metabolically unhealthy overweight; MAO, metabolically abnormal obesity; HR, hazard ratio; CI, confidential interval.

The incidence trends of CVD in the participants with different metabolic health statuses are presented in Figure 1. In addition, the connection between the number of abnormal metabolic components and the risk of CVDs is shown in Figure S4. Among the four sensitivity analyses, we found that the results of the study remained robust without significant differences (Table S3).

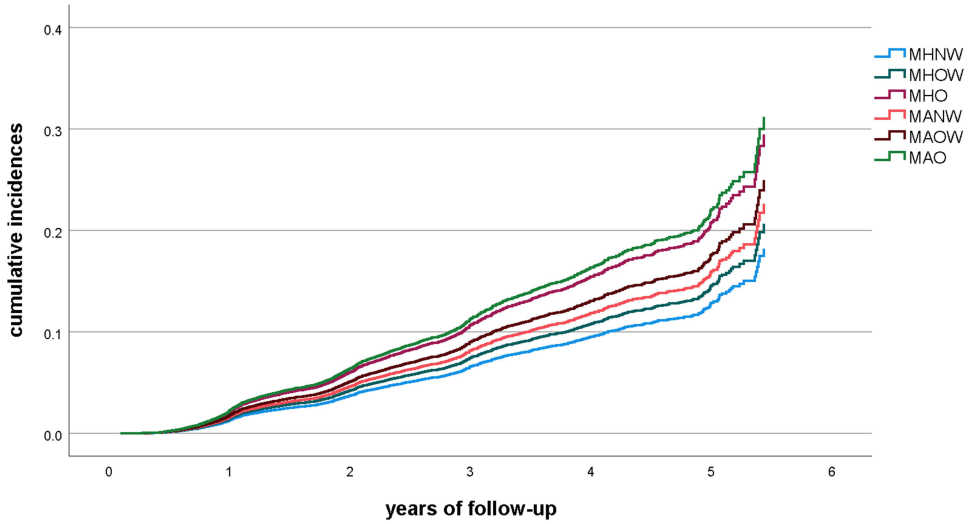

Figure 1 The cumulative incidence trends of CVD in the participants with different metabolic health statuses. The subjects with MAO had the highest incidences of CVD, followed by MHO, MAOW, MANW and MHOW. MHNW had relatively lower risks.

Association of Metabolic Transition Statuses with Risk of CVD Events

The study focused on the interconversion among all metabolic health status categories and investigated the connection with CVD in the populations above. Of the subjects with MHNW at baseline, 67.19% remained in the original state and 11.21% converted to MHOO in the follow-up outcomes. Second, among participants with MHOO, 50.33% were unconverted and 34.01% converted to MAO, while 21.97% of MAO people converted to MHOO at the same time (Table S4). The association between the subjects in each transition group and the HRs of CVDs is presented in Figure 2. The cumulative incidence of CVD for participants who remained in the MAOO state (HR 1.65, 95% CI 1.45–1.88) was

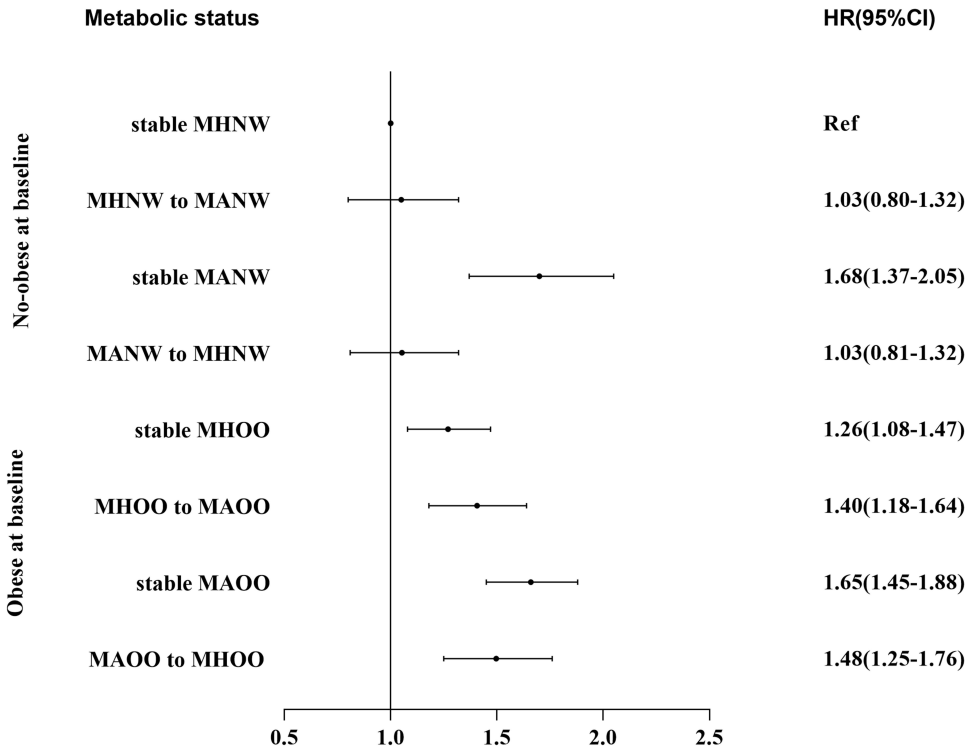

Figure 2 The hazard ratios (HRs) and 95% confidence intervals (CIs) between the subjects in each transition group and cardiovascular disease. HRs (95% CIs) were adjusted for age, sex, exercise, and smoking status.

much higher than that for the group who changed from MHOO (HR 1.40, 95% CI 1.18–1.64), whereas no significant association was observed in the groups correlated to MHNW status.

Discussion

In this retrospective cohort study, it was founded that metabolic abnormalities significantly elevated the risk of developing CVD across BMI categories among middle-aged and elderly adults in central China. Furthermore, our study tested whether metabolic health status changes over time irrespective of obesity levels and explored heterogeneous components of metabolic abnormal among subjects with metabolic abnormalities converted from metabolically healthy. In particular, participants with stable MANW were observed to have the highest risk for CVD, followed by the group that had stable MAOO and the group converted to metabolic health in participants with obesity.

Although the existing studies in this regard remain controversial, our findings support the latest advances that MHO individuals are at much higher risk of CVD. Two systematic reviews in the West and Asia found that participants with MHO were at a 45% and 61% increased risk of CVD, respectively, than their MHNW counterparts.[19,20] Several long-term studies have found that MHO, as a transient status, conferred an increased risk of diabetes mellitus, stroke and some early stages of CVD, such as subclinical atherosclerosis, in different populations.[21–24] In fact, there are scarce cohort studies with a large sample in Asian populations, including China, calling for more reliable evidence to examine the previous findings. A recent respective study from Japan found that only when abdominal obesity existed did MHO individuals have a significantly higher risk of CVD. The primary reason for this discrepancy lies in the definition of "metabolic health", which demands no metabolic syndrome manifestations presented according to their diagnostic criteria, while most international standards require less than 2.[6,25,26]

More recently, the China Kadoorie Biobank and the China XinJiang cohort study, including 458,246 and 5,059 Chinese adults, respectively, showed that MHO individuals were at an increased risk of CVD (HR 1.54, 95% CI 1.49–1.60 and HR 2.60, 95% CI 1.93–3.49) than their MHNW counterparts.[3,27] On the basis of these studies, the strength of our study was that the cohort was well characterized, the laboratory data were complete at baseline and follow-up and the uniform definition was defined according to the Joint Interim Statement (JIS). Our findings not only examined whether MHO individuals had higher risk of CVD but also investigated the effects on MANW populations (HR 1.24, 95% CI 1.07–1.44). As nearly one-third of normal-weight individuals were reported before as MANW, of equal concern were these individuals and they had higher risks of CVD than their MHNW counterparts.[28] Therefore, due to their normal BMI level, they are easily neglected for screening, thus delaying diagnosis.[29]

Previous evidence of the majority of metabolically healthy participants would gradually transform into unhealthy obesity indicated that MHO was a transitional status for the phenotype, which was consistent with ours.[3,19] This has been proven by studies with a follow-up period of approximately 10 years, which suggested that the rates varied between 30% and 50% of the MHO individuals converted to MAO status.[3,23,30,31] Only several studies with a follow-up of more than 10 years found that more than 50% of the participants with MHO would be converted to an unhealthy phenotype.[30,32] To our knowledge, however, it is still unclear whether such a transition would affect the risk of CHD and stroke in Chinese adults, especially among middle-aged and elderly population. As the long-term CVD risk in middle-aged and elderly population may not be predicted well by cross-sectional surveys, our findings found that 34.01% of the subjects with metabolic healthy obesity converted to unhealthy obesity were observed. A higher conversion rate from metabolic health to metabolically unhealthy status in overweight and obesity compared with normal-weight counterparts was observed from our results, which indicated that prolonged exposure to obesity may have a higher likelihood of developing metabolic abnormality. Additionally, we found that normal-weight subjects, regardless of the direction converted between metabolic health and metabolic abnormality, had no significant association with CVD compared with their stable metabolic health counterparts. Conversely, overweight, and participants with obesity, no matter how the metabolic status changed, were always at significant risk of CVD, although slightly smaller than that of individuals who remained stable metabolic abnormal.

What we found was that MAO status was at a higher risk for CVD than MHO, whether in individuals at baseline or in the transitional period, and previous research may provide some clues to explain the difference in CVD risk. Affected by changes in food habits and food availability, the Chinese consume many processed carbohydrate foods, which are

connected to the risk of obesity and CVD.[33] Hence, at similar BMIs, they have relatively higher body and atherogenic visceral fat and lower subcutaneous fat than Westerners.[34,35] Furthermore, visceral fat has been proven to be a higher risk of metabolic risk than subcutaneous fat for the association with greater vascularization, pro-inflammatory cytokines, macrophage infiltration, and more thrombogenic proteins.[34] Then, compared with MAO individuals, MHO subjects have less visceral fat mass, more subcutaneous adipose tissue and lower ectopic fat deposition in the liver, which have been demonstrated to be a lower risk for metabolic abnormalities and CVD.[36–42] The transition from metabolically healthy to unhealthy status has been proven to be related to higher BMI, WC and to a longer period of obesity.[43–45] Our findings suggest that it is difficult for the Chinese middle-aged and elderly population to maintain the ideal health status of MHNW for a long time to prevent CVD. Our results highlight that prolonged exposure to obesity or metabolic abnormalities increases the risk of CVD and that the management of metabolic health should not be neglected among normal weight participants. Additionally, in terms of the components of metabolic syndrome, it would be more important to pay attention to blood pressure, blood glucose and triglyceride status.

This study has several strengths, including complete anthropometric and biochemical measurements collected by professionals, a relatively large sample size and adjustments for known risk factors for CVD. Another strength of this study is that it examines the risk of CVD related to the transformations in metabolic health status during follow-up, which is a rare cohort study conducted in the middle-aged and elderly Chinese population. Finally, three sensitivity analyses demonstrated the reliability of the study results. On the other hand, several limitations of the study are worth mentioning for future improvements. First, the study was conducted among middle-aged and elderly Chinese individuals with an average age of approximately 67 years, making it difficult to generalize to all populations. Second, due to the lack of laboratory data on visceral fat as a better measure, obesity categories based on BMI may be controversial by misclassifying the persons with short stature or a muscular build. Third, the study used FPG to assess metabolic health status rather than random plasma glucose (RPG), a better biochemical indicator, which may also lead to some potential biases. Then, for assessing the risk of CVD from transitions in metabolic health and obesity over time, a longer follow-up duration may improve the accuracy of the risk estimates. Finally, although we have adjusted for some confounders as far as possible, the possibility of bias still existed, such as the use of antidiabetic, antihypertension drugs and other medications, dietary factors, genetic factors, and unavoidable recall bias.

Conclusion

Our study shows that obesity remains a significant risk factor for CVD events in Chinese population. The MHO and MANW populations have a higher risk of CVD than their MHNW counterparts. Furthermore, the results show that for most middle-aged and elderly adults, metabolic health is a transient state and that prolonged exposure to MHO and MAO status increases the risk of CVD.

Data Sharing Statement

Due to third-party requirements for confidentiality, the raw data in the study are not currently available to the public but can be requested from the corresponding authors upon reasonable request.

Ethics Approval

Study procedures were performed in accordance with the Declaration of Helsinki ethical principles for medical research involving human subjects.

The study was approved by the Ethics Committee of Zhengzhou University, and written informed consent was obtained from all participants (Reference Number: ZZUIRB2019-019).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. All authors acknowledge that all those entitled to authorship are listed as authors.

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Disclosure

The authors declare that they have no competing interests in this work.

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