Normal body weight with central obesity increases newly onset cardiovascular disease in adults from rural Northeast China

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Research

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Abstract

Background
Cumulative evidence indicates that normal weight with central obesity (NWCO) is associated with cardiovascular diseases risk factors like hypertension, diabetes, dyslipidemia. However, the possible predictive effect of NWCO on newly onset cardiovascular diseases (CVD) including coronary heart disease (CHD) and stroke has not been studied in detail.

Methods
Participants underwent physical examination at 2012–2013 and followed-up at 2015–2017 who previously diagnosed CVD were excluded. Body mass index (BMI) ≥ 25 kg/m² defined obesity, waist-to-height ratio ≥ 0.5 defined central obesity. Four groups: Normal weight without (NW) or NWCO, obesity without (OB) or with central obesity (OBCO).

Results
In total, 9439 participants (5006 men and 4433 women). The prevalence of different types of obesity were 39.6% for NW, 16.1% for NWCO, 4.1% for OB and 40.2% for OBCO. NWCO [HR = 1.565, 95%CI = 1.195, 2.051] and OBCO [HR = 1.845, 95%CI = 1.480, 2.300] were significantly associated with increasing risk of newly onset CVD. Besides, NWCO [HR = 2.337, 95%CI = 1.257, 4.344], OB [HR = 3.22, 95%CI = 1.166, 8.905] and OBCO [HR = 2.449, 95%CI = 1.386, 4.326] were all correlated with newly onset CHD but none of them had relationship with newly onset stroke.

Conclusions
We found that NWCO and OBCO were associated with newly onset CVD in rural Northeast Chinese adults. This underscored the effect of central obesity on CVD and suggested that even in individual with normal BMI, it is still necessary to prevent, monitor and control of central obesity.

Introduction
Cardiometabolic diseases such as cardiovascular disease (CVD), diabetes and their major risk factors are prevalent around the world. Cumulative evidence indicated that CVD was responsible for a higher cardiovascular mortality and all-cause mortality [1]. Therefore, many effective strategies had been taken in order to prevent CVD which testified by the decreasing CVD mortality in high-income countries [2]. However, in the low-/middle income countries or rural areas, there was still increased trend of CVD mortality [3]. Hence, it is necessary to figure out the possible risk factors that might promote CVD and establish specific strategies to control them.
Obesity had been well proved to be relevant to diabetes, dyslipidemia, CVD and cerebrovascular disease and resulted in higher all caused mortality [4]. Subjects who were diagnosed obesity would gain more concern due to its higher likelihood to develop CVD. Normal weight with central obesity (NWCO) defined by body mass index (BMI) and waist-to-height ratio (WHtR) was often overlooked by subject due to its normal weight. However, there were many previous studies reported the association between NWCO and the CVD risk factors such as hypertension, dyslipidemia and diabetes [5–7]. However, relationships between NWCO and newly onset CVD remain obscure.

We aimed to figure out the possible predictive effect of NWCO on newly onset CVD among rural Northeast general population. We postulated that rural subjects are at higher risk for CVD when they have NWCO at baseline.

**Methods**

**Data source and study subjects**

The design and inclusion criteria of the community-based prospective cohort study, named the Northeast China Rural Cardiovascular Health Study (NCRCHS), have been described previously [8, 9]. In all, 11,956 participants older than thirty-five years were enrolled from three countries in LiaoNing Province (Dawa, Zhangwu and Liaoyang) between 2012 and 2013. The Ethics Committee of China Medical University approved this study (Shenyang, China AF-SDP-07-1, 0-01). During 2015 and 2017, we invited participants at baseline to attend the follow-up study. In total, 1,256 out of 11,956 subjects were excluded due to a lack of contact information. Ultimately, 86.6% of the participants (10,349) finished the follow-up visits (median 4.66 follow-up years). All participants signed the written informed consent. We consider covariables that have complete information from the baseline visit in the present analysis. We excluded those participants who already were diagnosed CVD (n=821) and who were lack of experiment data (n=89). In the present study, 9439 participants were included.

**Study variables**

At baseline, participants were asked to finish a standardized questionnaire that contained detailed information about socioeconomic factors, lifestyle, demographic characteristics, and chronic disease history. Regular exercise was defined as yes or no. Self-reported history of cerebrovascular diseases, such as ischemic stroke, hemorrhagic stroke, and cardiovascular diseases, such as coronary heart disease and chronic heart failure at baseline, was recorded and confirmed by their medical records. Educational level included ≤ primary school, middle school, and ≥ high school. Annual income of the family was categorized into ≤ 5000 CNY/year, 5000-20000 CNY/year and >20000 CNY/year. Waist circumference was measured as previously described (8). Obesity was defined using BMI criteria with the cutoff ≥25 kg/m² [BMI = weight (kg)/height (m)²]. Blood pressure was measured automatically followed the standard criteria using an electronic sphygmomanometer (HEM-907; Omron, Tokyo, Japan). After fasting for at least 12 hours, participants were gathered together to take blood samples by trained nurses.
Fasting plasma glucose (FPG) and lipid profiles, such as low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol and triglyceride, were analyzed enzymatically. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was performed to calculate estimated glomerular filtration rate (eGFR) [10].

**Diagnosis of CVD**

The median follow-up was 4.66 years. In the present study, an incident cardiovascular disease was defined as a composite of new onset stroke or CHD during follow-up period. The specific incidences of stroke and CHD were also determined. For all participants reporting possible diagnoses or death, all available clinical information was collected including medical records and death certificates. All materials were independently reviewed and adjudicated by the end-point assessment committee. Stroke was defined according to the WHO Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) criteria [11, 12], as rapidly developing signs of focal or global disturbance of cerebral function, lasting more than 24 hours (unless interrupted by surgery or death) with no apparent non-vascular causes. Hemorrhagic stroke was defined as stroke cases with diagnosis of subarachnoid hemorrhage or intracerebral hemorrhage and ischemic stroke was defined as stroke cases with diagnosis of thrombosis or embolism. Transient ischemic attack and chronic cerebral vascular disease were excluded. CHD was defined as a diagnosis of hospitalized angina, hospitalized myocardial infarction, CHD death or any revascularization procedure [13].

**Statistical analysis**

Mean values ± standard deviations were used to describe continuous variables, and categorical variables were reported as numbers together with percentages. ANOVA, t-test, nonparametric test or the χ²-test were performed to evaluate differences among categories as appropriate. Cox proportional hazards models were used to identify the associations of obesity categories with the risk of newly onset CHD, stroke and CVD incidence with hazard ratios (HRs) and 95% confidence intervals (CIs) calculated. Multivariable hazard ratio was adjusted for gender, age, ethnicity, educational status, marriage status, annual income, physical activity, cigarette smoking status, alcohol intake status, family history of stroke, family history of CHD, family history of hypertension, antihypertension medication, SBP, DBP, TC, TG, HDL-C, LDL-C, eGFR, FPG. SPSS version 17.0 software was used to calculate all the statistical analyses, and statistical significance was defined as P≤0.05.

**Results**

Table 1 shows the characteristics of study subjects with mean age of 52.7 and 53.7 years for women and men, respectively. Men at baseline had significantly higher value of SBP, DBP, TG, FPG, and eGFR compared to women. Meanwhile, men had higher rates of current smoking and drinking whereas women had higher prevalence of family history of coronary heart disease, hypertension and antihypertensive medication than men. The proportions of NWCO among men and women were 11.9% and 19.8%,
respectively (Fig. 1A). As shown in Fig. 1B, with aged increased, the prevalence of NWCO increased significantly (35–45 years: 10.2%; 45–55: 13.6%; 55–65: 19.3%; >65: 26.3%; P for trend < 0.001).
Table 1
Demographic, anthropometric and plasma biochemical characteristics of subjects at baseline.

| Characteristics                                | Female (n = 5006) | Male (n = 4433) | P value |
|------------------------------------------------|-------------------|-----------------|---------|
| Age (years)                                    | 52.71 ± 10.12     | 53.70 ± 10.59   | < 0.001 |
| Ethnicity                                      |                   |                 | 0.370   |
| Han                                            | 4717(94.2)        | 4169(94.0)      |         |
| Others *                                       | 289(5.8)          | 264(6.0)        |         |
| Education status                               |                   |                 | < 0.001 |
| Primary school or below                        | 2810(56.1)        | 1807(40.8)      |         |
| Middle school                                  | 1788(35.7)        | 2096(47.3)      |         |
| High school or above                           | 408(8.2)          | 530(12.0)       |         |
| Marriage status                                |                   |                 | < 0.001 |
| Married                                        | 4519(91.9)        | 4106(92.7)      |         |
| Single or divorced                             | 32(0.6)           | 129(2.9)        |         |
| Widowed                                        | 375(7.5)          | 194(4.4)        |         |
| Physical activity                              |                   |                 | < 0.001 |
| Light                                          | 2014(40.6)        | 1172(26.7)      |         |
| Moderate                                       | 953(19.2)         | 822(18.7)       |         |
| Severe                                         | 1996(40.2)        | 2401(54.6)      |         |
| Annual income (CNY/year)                       |                   |                 | 0.127   |
| ≤ 5000                                        | 524(10.5)         | 522 (11.8)      |         |
| 5000–20000                                     | 2777(55.5)        | 2415(54.5)      |         |
| > 20000                                       | 1703(34.0)        | 1494(33.7)      |         |
| Current smoking status                         | 817(16.3)         | 2575(58.1)      | < 0.001 |
| Current drinking status                        | 156(3.1)          | 2079(46.9)      | < 0.001 |
| Family history of stroke                       | 837(16.7)         | 691(15.6)       | 0.072   |
| Family history of coronary heart disease       | 741(14.8)         | 552(12.5)       | 0.001   |
| Family history of hypertension                 | 1175(23.5)        | 937(21.1)       | 0.004   |
| Antihypertension medication in 2 weeks         | 711(31.6)         | 465(20.4)       | < 0.001 |
| Characteristics | Female (n = 5006) | Male (n = 4433) | P value |
|-----------------|------------------|----------------|---------|
| BMI (kg/m²)     | 24.80 ± 3.80     | 24.73 ± 3.45   | 0.322   |
| SBP (mmHg)      | 139.32 ± 23.38   | 143.24 ± 22.08 | < 0.001 |
| DBP (mmHg)      | 80.39 ± 11.37    | 83.72 ± 11.78  | < 0.001 |
| WC (cm)         | 80.68 ± 9.65     | 83.57 ± 9.59   | < 0.001 |
| TC (mmol/L)     | 5.28 ± 1.11      | 5.17 ± 1.03    | < 0.001 |
| TG (mmol/L)     | 1.53 ± 1.24      | 1.62 ± 1.62    | 0.005   |
| LDL-C (mmol/L)  | 2.98 ± 0.85      | 2.89 ± 0.79    | < 0.001 |
| HDL-C (mmol/L)  | 1.42 ± 0.35      | 1.43 ± 0.43    | 0.743   |
| FPG (mmol/L)    | 5.81 ± 1.54      | 5.90 ± 1.56    | 0.006   |
| eGFR (ml/min per 1.73 mm²) | 93.31 ± 15.64 | 95.12 ± 14.44 | < 0.001 |

* Including some ethnic minorities in China, such as Mongol and Manchu. BMI body mass index, WC waist circumference, CNY China Yuan (1CNY = 0.161 USD), SBP systolic blood pressure, DBP diastolic blood pressure, TG triglyceride, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, FPG fasting plasma glucose. NW: normal weight without central obesity; NWCO: normal weight with central obesity; OB: obesity without central obesity; OBCO: obesity with central obesity.

Table 2 shows the characters of subjects according to different obese status. Subjects had NWCO were significantly older than the other three groups. OBCO and NWCO had relatively high value of SBP, TC, TG, and FPG whereas lower value of eGFR than the other two groups (all P < 0.001).
| Characteristics                  | NW (n = 3736) | NWCO (n = 1517) | OB (n = 388) | OBCO (n = 3798) | P value |
|---------------------------------|---------------|-----------------|--------------|-----------------|---------|
| Gender (male)                   |               |                 |              |                 | < 0.001 |
|                                 | 1972(52.8)    | 526(34.7)       | 226(58.2)    | 1709(45.0)      |         |
| Age (years)                     | 52.29 ± 10.31 | 56.76 ± 10.86   | 49.76 ± 9.03 | 52.96 ± 9.97    | < 0.001 |
| Ethnicity                       |               |                 |              |                 | 0.025   |
| Han                             | 3550(95.0)    | 1425(93.9)      | 361(93.0)    | 3550(93.5)      |         |
| Others *                        | 186(5.0)      | 92(6.1)         | 27(7.0)      | 248(6.5)        |         |
| Education status                |               |                 |              |                 | < 0.001 |
| Primary school or below         | 1701(45.5)    | 896(59.1)       | 154(39.7)    | 1866(49.1)      |         |
| Middle school                   | 1666(44.6)    | 498(32.8)       | 172(44.3)    | 1548(40.8)      |         |
| High school or above            | 369(9.9)      | 123(8.1)        | 62(16.0)     | 384(10.1)       |         |
| Marriage status                 |               |                 |              |                 | < 0.001 |
| Married                         | 3470(92.9)    | 1335(88.2)      | 371(95.9)    | 3521(92.9)      |         |
| Single or divorced              | 78(2.1)       | 23(1.5)         | 5(1.3)       | 55(1.5)         |         |
| Widowed                         | 186(5.0)      | 156(10.3)       | 11(2.8)      | 216(5.7)        |         |
| Physical activity               |               |                 |              |                 | < 0.001 |
| Light                           | 1147(31.0)    | 567(37.7)       | 108(28.1)    | 1364(36.2)      |         |
| Moderate                        | 675(18.2)     | 290(19.3)       | 83(21.6)     | 727(19.3)       |         |
| Severe                          | 1882(50.8)    | 648(43.1)       | 194(50.4)    | 1673(44.4)      |         |
| Annual income (CNY/year)        |               |                 |              |                 | < 0.001 |
| ≤ 5000                          | 391(10.5)     | 250(16.5)       | 29(7.5)      | 376(9.9)        |         |
| 5000–20000                      | 2062(55.2)    | 827(54.5)       | 204(52.6)    | 2100(55.3)      |         |
| > 20000                         | 1282(34.3)    | 440(29.0)       | 155(39.9)    | 1320(34.8)      |         |
| Current smoking status          | 1611(43.1)    | 487(32.1)       | 141(36.3)    | 1153(30.4)      | < 0.001 |
| Characteristics                                      | NW (n = 3736) | NWCO (n = 1517) | OB (n = 388) | OBCO (n = 3798) | P value  |
|------------------------------------------------------|---------------|----------------|-------------|----------------|----------|
| Current drinking status                              | 979(26.2)     | 303(20.0)      | 94(24.2)    | 859(22.6)      | < 0.001  |
| Family history of stroke                             | 496(13.3)     | 305(20.1)      | 57(14.7)    | 670(17.6)      | < 0.001  |
| Family history of coronary heart disease              | 473(12.7)     | 208(13.7)      | 54(13.9)    | 558(14.7)      | 0.086    |
| Family history of hypertension                        | 715(19.1)     | 335(22.1)      | 86(22.2)    | 976(25.7)      | < 0.001  |
| Antihypertension medication in 2 weeks                | 218(17.0)     | 189(23.4)      | 32(19.3)    | 737(32.5)      | < 0.001  |
| BMI (kg/m²)                                          | 21.79 ± 1.87  | 23.34 ± 1.43   | 26.20 ± 1.61| 28.11 ± 2.75   | < 0.001  |
| SBP (mmHg)                                           | 134.66 ± 20.88| 143.58 ± 23.21| 139.26 ± 20.43| 146.79 ± 23.16| < 0.001  |
| DBP (mmHg)                                           | 79.14 ± 10.96 | 81.37 ± 11.98  | 81.82 ± 11.10| 84.97 ± 11.58  | < 0.001  |
| WC (cm)                                              | 73.64 ± 5.60  | 83.39 ± 5.12   | 77.93 ± 6.22| 90.17 ± 7.21   | < 0.001  |
| TC (mmol/L)                                          | 5.05 ± 1.00   | 5.29 ± 1.12    | 5.13 ± 1.00 | 5.39 ± 1.11    | < 0.001  |
| TG (mmol/L)                                          | 1.19 ± 0.92   | 1.64 ± 1.64    | 1.38 ± 0.86 | 1.95 ± 1.68    | < 0.001  |
| LDL-C (mmol/L)                                       | 2.72 ± 0.74   | 2.96 ± 0.82    | 2.92 ± 0.76 | 3.13 ± 0.86    | < 0.001  |
| HDL-C (mmol/L)                                       | 1.52 ± 0.41   | 1.44 ± 0.40    | 1.42 ± 0.36 | 1.32 ± 0.34    | < 0.001  |
| FPG (mmol/L)                                         | 5.61 ± 1.19   | 5.94 ± 1.70    | 5.69 ± 1.13 | 6.07 ± 1.80    | < 0.001  |
| eGFR (ml/min per 1.73 mm²)                            | 95.57 ± 14.68 | 91.52 ± 16.01  | 96.39 ± 13.72| 93.60 ± 15.13  | < 0.001  |

* Including some ethnic minorities in China, such as Mongol and Manchu. BMI body mass index, WC waist circumference, CNY China Yuan (1CNY = 0.161 USD), SBP systolic blood pressure, DBP diastolic blood pressure, TG triglyceride, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, FPG fasting plasma glucose. NW: normal weight without central obesity; NWCO: normal weight with central obesity; OB: obesity without central obesity; OBCO: obesity with central obesity;
Table 3 shows the age- and gender- adjusted and multivariable adjusted associations between obese categories and CVD, CHD or stroke. In the age- and gender- adjusted model, NWCO (HR: 1.565, 95%CI: 1.195, 2.051) and OBCO (HR: 1.845, 95%CI: 1.480, 2.300) were associated with newly onset CVD in study participants. After adjusted the possible confounders such as ethnicity, educational status, marriage status, annual income, physical activity, cigarette smoking status, alcohol intake status, family history of stroke, family history of CHD, family history of hypertension, antihypertension medications, SBP, DBP, TC, TG, HDL-C, LDL-C, eGFR, FPG, NWCO [HR: 1.468, 95%CI: 1.048, 2.056] and OBCO [HR: 1.482, 95%CI: 1.098, 2.000] were still significantly correlated with newly onset CVD in study participants. Besides, NWCO [Adjusted for age and gender: HR: 1.643, 95%CI: 1.023, 2.638; Adjusted for all possible confounders: HR: 2.337, 95%CI: 1.257, 4.344], OB [Adjusted for age and gender: HR: 2.347, 95%CI: 1.044, 5.275; Adjusted for all possible confounders: HR: 3.22, 95%CI: 1.166, 8.905] and OBCO [Adjusted for age and gender: HR: 2.306, 95%CI: 1.579, 3.367; Adjusted for all possible confounders: HR: 2.449, 95%CI: 1.386, 4.326] were all associated with increased risk no matter adjusted for age- and gender- or further possible confounders. As for newly onset stroke, only OBCO was significantly associated with higher risk when adjusted for age and gender but becoming insignificant when adjusted for all possible confounders.
### Table 3
Age, gender-adjusted and multivariable hazard ratio (HRs, 95%CI) of CVD, CHD, or stroke according to classification of obesity.

|                | NW | NWCO | OB  | OBCO | P value for trend |
|----------------|----|------|-----|------|-------------------|
| **No. at risk**| 3736 | 1517 | 388 | 3798 |                   |
| **CVD**        |     |      |     |      |                   |
| No. of events  | 125 | 99   | 17  | 225  |                   |
| Age- and gender-adjusted HR (95%CI) | 1.00 | 1.565 | 1.603 | 1.845 | <0.001 |
|                | (1.195, 2.051) | (0.965, 2.664) | (1.480, 2.300) |         |       |
| Multivariable HR (95%CI) | 1.00 | 1.468 | 1.737 | 1.482 | 0.021 |
|                | (1.048, 2.056) | (0.936, 3.221) | (1.098, 2.000) |         |       |
| **CHD**        |     |      |     |      |                   |
| No. of events  | 39  | 34   | 7   | 94   |                   |
| Age- and gender-adjusted HR (95%CI) | 1.00 | 1.643 | 2.347 | 2.306 | <0.001 |
|                | (1.023, 2.638) | (1.044, 5.275) | (1.579, 3.367) |         |       |
| Multivariable HR (95%CI) | 1.00 | 2.337 | 3.22  | 2.449  | 0.001 |
|                | (1.257, 4.344) | (1.166, 8.905) | (1.386, 4.326) |         |       |
| **Stroke**     |     |      |     |      |                   |
| No. of events  | 99  | 72   | 11  | 157  |                   |
| Age- and gender-adjusted HR (95%CI) | 1.00 | 1.480 | 1.365 | 1.614 | 0.001 |
|                | (1.084, 2.020) | (0.731, 2.548) | (1.252, 2.080) |         |       |
| Multivariable HR (95%CI) | 1.00 | 1.227 | 1.509 | 1.251 | 0.401 |
|                | (0.830, 1.814) | (0.716, 3.180) | (0.891, 1.758) |         |       |
Multivariable hazard ratio adjusted for gender, age, ethnicity, educational status, marriage status, annual income, physical activity, cigarette smoking status, alcohol intake status, family history of stroke, family history of CHD, family history of hypertension, antihypertension medication in 2 weeks, systolic blood pressure, diastolic blood pressure, serum total cholesterol, serum triglycerides, HDL-C, LDL-C, estimated glomerular filtration rate, fasting plasma glucose.

CHD: coronary heart disease; CVD: cardiovascular disease. NW: normal weight without central obesity; NWCO: normal weight with central obesity; OB: obesity without central obesity; OBCO: obesity with central obesity;

### Discussion

The present study estimated the relationships between NWCO and newly onset CVD in rural Northeast Chinese adults. We found that newly onset CVD, or CHD was significantly associated with NWCO and OBCO, compared with subjects of NW.

Obesity is a chronic multifaceted disease and increases risk of CVD risk factors, such as hypertension, diabetes, and dyslipidemia. However, it does not mean those risk can occur only among subjects with increased body weight [14]. In China, there is 6.5–8.0% subjects in the face of normal BMI suffered from type 2 diabetes [15]. Similarly, 40% of newly onset type2 diabetes in Japan occurred in subjects with normal BMI [16]. A relatively recently introduced NWCO describes a phenomenon when subjects are found to have normal weight as indicated by BMI but have central obesity defined by WHtR. Data from the central European Urban female population of Brno, Czech Republic said that 14% of the women were found to be NWCO whereas among Korean adults, 25.7% of men and 33.4% of women were diagnosed NWCO [17, 18]. In the present study, the rate of NWCO was 19.8% among rural women and 11.9% among rural men which were relatively lower than other developed areas. Previous studies had confirmed that NWCO individuals faced a higher risk of developing metabolic syndrome, cardiovascular dysfunction and have higher mortality [18]. Cumulative evidence showed that NWCO had close relationship with CVD risk factors, such as hypertension, dyslipidemia, and diabetes, compared with NW, regardless of sex [19]. Furthermore, Yangbo Sun and colleagues also confirmed that NWCO in women was associated with excess risk of mortality, similar to that of women with OBCO [20]. One clinic review analyzed prospective cohort studies concluded that a waist-to-height ratio exceeding 0.5 at normal BMI identified elevated mortality risk for cardiometabolic disease and this risk might be equitant to or even exceed that of OBCO [21]. Similar, in our study, NWCO subjects had significantly higher risk of newly onset CVD. The mechanisms responsible for the development of central obesity in normal weight subjects are not entirely clear. However, there was evidence suggested that older age played an important role for the development of central obesity and metabolic disease in the absence of obesity [22]. Data in our study also showed that subjects with NWCO had the oldest age compared to the rest groups.

In recent years, cumulative evidence indicated that individual with metabolic unhealthy normal weight (MUNW) had an adverse cardiometabolic risk factor profiles in the absence of excess body weight, and
increased risk of diabetes and CVD. As they analysis in detail, they found that these subjects had a preferential accumulation of fat in the upper body (abdominal subcutaneous and visceral adipose tissue) and liver which suggested that abdominal obesity were prevalent among this subjects. In our study, subjects with NWCO had significantly higher value of SBP, TC, TG, LDL-C, and FPG than NW or OB. Therefore, it is difficult to determine whether central obesity or metabolic unhealthy that finally resulted in CVD. However, they both share one possible mechanism-insulin resistance. NWCO or MUNW both had increased visceral adipose tissue, the accumulation of fat in liver and pancreas which were more prone to cause insulin resistance [23, 24]. Besides, there were other mechanisms correlated with the central obesity inducing CVD in normal weight subjects, such as inflammation, impairments in iron homeostasis and oxidative stress [25, 26].

Except for NWCO in the present study that correlated with higher risk of newly onset CVD, current smoking at baseline also increased the risk of CVD (HR: 1.381, 95%CI: 1.071, 1.780). Unlike previous study reported that exercise and eating pattern changes could produce cardiometabolic and mortality benefit in NWCO subjects [21]. Physical activity in the present study did not show significant effect on newly onset CVD among rural Chinese. However, sedative lift style and unhealthy habit, such as drinking and smoking should be avoid in order to maintain healthy.

There are some limitations in the present study. First, other potential confounding factors that might affect our finding were not determined in this study, such as diet. Second, there were some participant loss contact in the follow-up which might cause bias in the predictive effect of NWCO on CHD, stroke or CVD. Third, HDL-C, LDL-C, triglyceride, fasting plasma glucose were measured only once, which might be imprecise and resulted in random errors.

**Conclusion**

The present study showed that even among normal weight, central obesity was associate with newly onset CVD among rural Northeast Chinese. These findings indicated that physical health screening in rural areas should combine BMI and WHtR. More emphasis should be put on those people with central obesity even though with normal weight.

**Abbreviations**

NWCO: normal weight with central obesity; CVD: cardiovascular diseases; CHD:coronary heart disease; WHtR:waist-to-height ratio; NW:Normal weight without; OB:obesity without central obesity; OBCO:obesity with central obesity; BMI:body mass index; FPG:Fasting plasma glucose; LDL-C:low-density lipoprotein cholesterol; HDL-C:high-density lipoprotein cholesterol;

**Declarations**

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Authors’ contributions

SSY contributed to the data collection, analysis and interpretation. XFG and HMY contributed to data collection. GXL and SSY contributed to the data analysis. YXS contributed to the study conception and design. All authors read and approved the final version of the manuscript.

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No

Availability of data and materials

Enquiries regarding the availability of primary data should be directed to the principal investigator Professor Yingxian Sun (sunyingxiancmu1h@163.com).

Ethics approval and Consent to participate

The study was approved by the Ethics Committee of China Medical University (Shenyang, China AF-SDP-07-1, 0-01). All procedures were performed in accordance with ethical standards. Written consent was obtained from all participants after they had been informed of the objectives, benefits, medical items and confidentiality agreement regarding their personal information.

Consent for publication

All the participants gave consent for direct quotes from their interviews to be used in this manuscript.

Competing interests

The authors declare that they have no competing interests.

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