Gender discrepancy in the predictive effect of metabolic syndrome and its components on newly onset cardiovascular disease in elderly from rural China

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Abstract

Background

To evaluate the possible predictive effect of metabolic syndrome (MetS) and its components on cardiovascular disease (CVD) in a longitudinal analysis according to different criteria of MetS among rural Chinese elderly.

Method

A population-based sample of 2486 rural elderly Chinese residents aged ≥ 60 years at baseline were followed up from 2012–2013 to 2015–2017. CVD included stroke, coronary heart disease (CHD) diagnosed by clinicians were self-reported and were confirmed by medical records. MetS was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) and the international Diabetes Federation (IDF) criterion respectively.

Result

Hazard ratio adjusting for CHD, Stroke and CVD in those with MetS using NCEP ATP III criteria in female were 1.27 (95%CI 0.73, 2.21), 1.54 (95%CI 0.99, 2.40) and 1.45 (95%CI 1.00, 2.10); 1.33 (95%CI 0.77, 2.32), 1.44 (95%CI 0.92, 2.25) and 1.36 (95%CI 0.94, 1.97) with the AHA/NHLBI criteria; and 1.10 (95%CI 0.89,1.36), 1.62 (95%CI 1.03, 2.55) and 1.36 (95%CI 0.93, 1.97) with IDF criteria. Besides, abdominal obesity using the AHA/NHLBI criteria was significantly associated with the incidence of stroke (HR: 1.60; 95%CI 1.01, 2.52). However, among rural male elderly, neither MetS nor its components were capable of predicting newly onset CVD.

Conclusion

MetS is significantly associated with high incidence of CVD among rural female elderly only, and the incidence of CVD was evident only when MetS was defined using NCEP ATP III criterion. In order to reduce CVD among elderly in rural China, effective strategies to prevent, diagnose, and treating MetS should be made in time, especially among female.

Background

Noncommunicable disease (NCDs), like cardiometabolic diseases such as cardiovascular diseases (CVD), stroke and diabetes, and their major risk factors have become prevalent especially among elderly around the world. Cardiovascular diseases (CVD) is responsible for higher cardiovascular
mortality and all-cause mortality especially among older subjects [1]. However, in the past recent decades, CVD mortality declined in high-income countries whereas increased in low- and middle-income countries. The reasons contributing to this discrepancy area varied and are affected by environmental, social, and commercial determinants of health [2]. With the improvement of preventing, diagnosis and treatment of cardiovascular risk factors, the CVD mortality began to fall in developed countries [2]. Nevertheless, in recent years, as metabolic disorder like obesity, hypertension, diabetes, and dyslipidemia became prevalent in rural China, the CVD mortality increased synchronously [5–7]. The Metabolic syndrome (MetS) is a cluster of cardio-metabolic risk factors and comorbidities conveying high risk of both CVD and cerebrovascular disease [8]. Both of MetS and CVD are responsible for huge socio-economic costs with their resulting morbidity and mortality around the world.

Previous studies confirmed the relationship between MetS on the risk of CVD in different population with controversial conclusions among the elderly. Some claimed that MetS and its components were lack of association with CVD in elderly whereas others insisted that MetS significantly increased the risk of fatal and non-fatal CVD [9, 10]. Besides, there was research reported a gender discrepancy in the association between MetS and CVD [11]. As far as we know, there is an obvious paucity of study estimate the predictive effect of MetS and its components on CVD in rural elderly. Most of the studies to date is limited by small sample sizes and cross-sectional design. To the best of our knowledge, there is no population cohort study investigated the prospective relationship between MetS and CVD in elderly from rural areas.

In the present study, we aimed to evaluate whether MetS and its components at baseline can be an effective predictor of CVD among elderly subjects from rural China. Whether there is gender discrepancy in the association between MetS and CVD. Besides, due to the variation of MetS criteria, we adopted three common used criteria: updated IDF, NCEP ATP III and Blood Institute (AHA/NHLBI) to compare which one is better in predicting CVD in rural elderly subjects.

Method And Material
Data source and study subjects
We used data from a community-based prospective cohort study, the Northeast China Rural Cardiovascular Health Study (NCRCHS). The survey was carried out in Liaoning province in China from 2012 and 2013; and follow-up during 2015 and 2017; the rationale, design and methods have described in detail previously [7, 12]. Questionnaire completion, physical examination and the assessment of risk factors of CVD were conducted and the data were collected by trained medical staff. In order to control potential sources of bias, we used standardized questionnaire. The Ethics Committee of China Medical University approved this study (Shenyang, China AF-SDP-07-1, 0–01). All participants have signed the written informed consent. In the present study, with the total follow-up rate was 86.6% and median 4.66 follow-up years, we enrolled only subjects ≥ 60 years, completed all surveys and examinations (n = 2486).

**Definition of Mets**

MetS in the present study was defined using three criteria.

| IDF definition | NCEP ATP III | the AHA/NHLBI |
|----------------|-------------|--------------|
| Central obesity plus any two of the following four additional factors | Three or more of the following five factors | Three or more of the following five factors |
| 1 | Central obesity: waist circumference ≥ 90 cm in men and ≥ 80 cm in women | Central obesity: waist circumference ≥ 102 cm in men and ≥ 88 cm in women | Same as NCEP APT III |
| 2 | Hypertriglyceridemia triglyceride level ≥ 1.7 mmol/L; | Same as IDF | Same as NCEP APT III |
| 3 | High blood pressure ≥ 130/85 mm Hg or treatment of previously diagnosed hypertension; | Same as IDF | Same as NCEP APT III |
| 4 | Reduced high-density lipoprotein (HDL)-cholesterol < 1.03 mmol/L in men and < 1.29 mmol/L in women, or specific treatment for these lipid abnormalities; | Same as IDF | Same as NCEP APT III |
| 5 | Hyperglycemia: fasting glucose level of ≥ 5.6 mmol/L or treatment of previously diagnosed type 2 diabetes | Hyperglycemia: fasting glucose level of ≥ 6.1 mmol/L or treatment of previously diagnosed type 2 diabetes | Hyperglycemia: fasting glucose level of ≥ 5.6 mmol/L or previously diagnosed type 2 diabetes. |

**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 [13, 14], 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 [15].

Covariates
Data on sociodemographic characteristics (age, gender, education and marital status), lifestyle (current smoking and drinking), history of chronic diseases and physical activity were collected through fact-to-fact interviews by trained researches and had been described in detail previously [7, 12]. Intensity of physical activity was define as light, moderate and severe. 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. Family history of chronic diseases diagnosed by a physician was self-reported, including hypertension, CHD and stroke.

Data analysis
Descriptive statistics were calculated for all the variables, including continuous variables (reported as mean values and standard deviations) and categorical variables (reported as numbers and percentages). Differences among categories were evaluated using t-test, ANOVA, non-parameter test or the χ2-test as appropriate. Cox proportional hazards models were used to identify the associations of MetS and its components with the risk of CHD, stroke and total CVD incidence with hazard ratios (HRs) and 95% confidence intervals (CIs) calculated. All the statistical analyses were performed using SPSS version 17.0 software, and P values less than 0.05 were considered to be statistically significant.

Results
The present study used data from 2434 subjects (aged ≥ 60 years) who received clinical examinations at baseline and follow-up. Table 1. Shows the characteristics of the 2486 elderly (1245 female and 1241 male). Except for annual income, family history of stroke, antidyslipidemic medication in 2
weeks, SBP, WC, and HDL-C, statistically significant difference were found between male and female in other demographic, anthropometric and clinical characteristics. As age increased from 60–70 years to > 80 years, prevalence of MetS defined by NCEP ATP III and hypertriglyceridemia significantly decreased. Elevated blood pressure increased in relatively older aged group compared to 60-70 years.
Table 1
Demographic, anthropometric and plasma biochemical characteristics of subjects at baseline.

| Characteristics                              | Female (n = 1245) | Male (n = 1241) | P value |
|----------------------------------------------|-------------------|-----------------|---------|
| Age (years)                                 | 66.49 ± 5.50      | 67.12 ± 5.89    | 0.006   |
| Age                                          |                   |                 | 0.016   |
| 60–70                                        | 957(76.9)         | 892(71.9)       |         |
| 70–80                                        | 255(20.5)         | 306(24.7)       |         |
| ≥80                                          | 33(2.7)           | 43(3.5)         |         |
| Ethnicity                                    |                   |                 | 0.049   |
| Han                                          | 1182(94.9)        | 1196(96.4)      |         |
| Others a                                     | 63(5.1)           | 45(3.6)         |         |
| Education status                            |                   |                 | < 0.001 |
| Primary school or below                     | 1066(85.6)        | 801(64.5)       |         |
| Middle school                                | 152(12.2)         | 359(28.9)       |         |
| High school or above                        | 27(2.2)           | 81(6.5)         |         |
| Marriage status                             |                   |                 | < 0.001 |
| Married                                      | 974(78.3)         | 1060(85.5)      |         |
| Single or divorced                          | 2(0.2)            | 26(2.1)         |         |
| Widowed                                      | 268(21.5)         | 154(12.4)       |         |
| Physical activity                           |                   |                 | < 0.001 |
| Light                                        | 794(64.6)         | 617(50.2)       |         |
| Moderate                                     | 202(16.4)         | 359(28.9)       |         |
| Severe                                       | 233(19.0)         | 410(33.3)       |         |
| Annual income (CNY/year)                    |                   |                 | 0.380   |
| ≤ 5000                                      | 296(23.8)         | 282(22.7)       |         |
| 5000–20000                                   | 703(56.6)         | 687(55.4)       |         |
| > 20000                                     | 244(19.6)         | 271(21.9)       |         |
| Current smoking status                      | 298(23.9)         | 622(50.1)       | < 0.001 |
| Current drinking status                     | 56(4.5)           | 491(39.6)       | < 0.001 |
| Family history of stroke                    | 213(17.1)         | 195(15.7)       | 0.188   |
| Family history of coronary heart disease    | 163(13.1)         | 98(7.9)         | < 0.001 |
| Family history of hypertension              | 246(19.8)         | 200(16.1)       | 0.010   |
| Antihypertension medication in 2 weeks      | 301(35.08)        | 219(25.26)      | < 0.001 |
| Antidiabetic medication in 2 weeks          | 77(36.67)         | 33(22.45)       | < 0.001 |
| Antidyslipidemic medication in 2 weeks      | 49(4.43)          | 26(3.07)        | 0.654   |
| BMI (kg/m²)                                 | 24.53 ± 3.91      | 24.10 ± 3.39    | 0.004   |
| SBP (mmHg)                                  | 151.08 ± 24.56    | 152.08 ± 23.24  | 0.296   |
| DBP (mmHg)                                  | 80.62 ± 11.84     | 83.42 ± 11.34   | < 0.001 |
| WC (cm)                                      | 82.13 ± 10.32     | 82.91 ± 9.57    | 0.053   |
| WC (cm) (NCEP ATP III and AHA/NHLBI) †      | 353(28.7)         | 33(2.7)         | < 0.001 |
| WC (cm) (IDF) ‡                             | 726(59.0)         | 306(25.0)       | < 0.001 |
| TC (mmol/L)                                 | 5.70 ± 1.09       | 5.17 ± 1.03     | < 0.001 |
| TG (mmol/L)                                 | 1.77 ± 1.24       | 1.38 ± 1.16     | < 0.001 |
| LDL-C (mmol/L)                              | 3.27 ± 0.85       | 2.90 ± 0.81     | < 0.001 |
| HDL-C (mmol/L)                              | 1.44 ± 0.37       | 1.44 ± 0.45     | 0.898   |
| FPG (mmol/L)                                | 6.15 ± 1.97       | 5.97 ± 1.60     | 0.015   |
| FPG (mmol/L) (NCEP ATP III) §               | 382(30.9)         | 333(27.1)       | 0.021   |
| FPG (mmol/L) (AHA/NHLBI and IDF) §           | 671(54.2)         | 654(53.2)       | 0.311   |

* Including some ethnic minorities in China, such as Mongol and Manchu. † Waist circumference ≥ 102 cm in men and ≥ 88 cm in women. ‡ Waist circumference ≥ 90 cm in men and ≥ 80 cm in women. § Fasting glucose level of ≥ 6.1 mmol/L. ¶ Fasting glucose level of ≥ 5.6 mmol/L. 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. AHA, American Heart Association; IDF, International Diabetes Federation; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; NHLBI, National Heart, Lung, and Blood Institute.

Figure 1 exhibited the prevalence of MetS according to different criteria and its metabolic components.
in different gender and age. Female elderly had significantly higher rates of MetS and metabolic components except for the relative lower rate of elevated blood pressure and no significant difference in hyperglycemia (P = 0.347).

Tables 2 and 3 show the estimated association between different CVD conditions and MetS or components of MetS by different definitions. Data showed that only NCEP ATP III defined MetS can predict CVD in female [HR (95% CI): 1.45 (1.00, 2.10)] but not male [HR (95% CI): 1.25 (0.80, 1.97)]. Similarly, IDF defined MetS was able to predict newly onset Stroke in female [HR (95% CI): 1.62 (1.03, 2.55)] but not male [HR (95% CI): 1.35 (0.88, 2.06)]. As for the metabolic components separately, abdominal obesity defined by NCEP ATP III and AHA/NHLBI was proved to be associated with Stroke among female [HR (95% CI): 1.60 (1.01, 2.52)]. There was lack of predictive effect of other metabolic components on CVD in both female and male.

Table 2
| Hazard ratio and 95%CI of CVD for MetS and the number of components of MetS by the NCEP, AHA/NHLBI and IDF criteria in elderly female from rural China. |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| MetS by different criteria (ref = non-MetS)      | CHD (n = 54)    | Stroke (n = 85) | CVD (n = 119)  |
| NCEP ATP III                                    | Crude HR (95% CI) | Adjusted HR (95% CI) | Crude HR (95% CI) | Adjusted HR (95% CI) | Crude HR (95% CI) | Adjusted HR (95% CI) |
|                                                | 1.38 (0.80, 2.37) | 1.27 (0.73, 2.21) | 1.52 (0.99, 2.33) | 1.54 (0.99, 2.40) | 1.45 (1.02, 2.08) | 1.45 (1.00, 2.10) |
| AHA/NHLBI                                       | 1.41 (0.82, 2.44) | 1.33 (0.77, 2.32) | 1.42 (0.93, 2.18) | 1.44 (0.92, 2.25) | 1.35 (0.94, 1.93) | 1.36 (0.94, 1.97) |
| IDF                                             | 1.09 (0.64, 1.88) | 1.10 (0.89, 1.36) | 1.56 (1.01, 2.41) | 1.62 (1.03, 2.55) | 1.36 (0.95, 1.95) | 1.36 (0.93, 1.97) |
| Metabolic components (ref = no)                 |                |                |                |                |                |                |
| Elevated Blood pressure                        | 2.06 (0.82, 5.21) | 1.69 (0.66, 4.33) | 1.43 (0.76, 2.70) | 1.29 (0.67, 2.45) | 1.49 (0.87, 2.56) | 1.31 (0.76, 2.28) |
| Hypertriglycerides                              | 1.12 (0.65, 1.93) | 1.12 (0.65, 1.94) | 1.03 (0.67, 1.60) | 1.05 (0.67, 1.64) | 1.20 (0.84, 1.73) | 1.22 (0.84, 1.76) |
| Low HDL-C                                       | 1.38 (0.81, 2.37) | 1.38 (0.80, 2.39) | 1.21 (0.79, 1.86) | 1.30 (0.83, 2.03) | 1.31 (0.91, 1.87) | 1.42 (0.98, 2.05) |
| Abdominal obesity (NCEP ATP III and AHA/NHLBI)  | 1.04 (0.58, 1.87) | 0.95 (0.52, 1.72) | 1.55 (1.00, 2.41) | 1.60 (1.01, 2.52) | 1.20 (0.82, 1.76) | 1.18 (0.80, 1.75) |
| Abdominal obesity (IDF)                         | 1.05 (0.60, 1.84) | 0.97 (0.55, 1.71) | 1.46 (0.93, 2.31) | 1.41 (0.88, 2.25) | 1.25 (0.86, 1.82) | 1.18 (0.80, 1.73) |
| Abdominal obesity (IDF)                         | 0.76 (0.41, 1.40) | 0.75 (0.40, 1.39) | 1.34 (0.86, 2.08) | 1.32 (0.83, 2.11) | 1.19 (0.81, 1.73) | 1.18 (0.80, 1.75) |
| High FPG (NCEP ATP III)                         | 0.94 (0.55, 1.61) | 0.99 (0.57, 1.72) | 1.33 (0.85, 2.06) | 1.36 (0.86, 2.16) | 1.25 (0.86, 1.80) | 1.30 (0.89, 1.90) |

Adjusted for sex, age, marital status, education, physical activity, currently smoking (yes, no), currently drinking (yes, no), family history of CHD, family history of stroke and family history of hypertension. † Waist circumference ≥ 102 cm in men and ≥ 88 cm in women. ‡ Waist circumference ≥ 90 cm in men and ≥ 80 cm in women. § Fasting glucose level of ≥ 6.1 mmol/L. ¶ Fasting glucose level of ≥ 5.6 mmol/L.
## Table 3
Hazard ratio and 95%CI of CVD for MetS and the number of components of MetS by the NCEP, AHA/NHLBI and IDF criteria in elderly male from rural China.

| MetS by different criteria (ref = non-MetS) | CHD (n = 39) | Stroke (n = 122) | CVD (n = 149) |
|-------------------------------------------|--------------|-----------------|---------------|
| NCEP ATP III                              |              |                 |               |
| Crude HR (95%CI)                          | 1.36 (0.60, 3.08) | 1.29 (0.55, 2.99) | 1.19 (0.74, 1.92) |
| Adjusted HR (95%CI)                       | 1.28 (0.79, 2.09) | 1.28 (0.79, 2.09) | 1.16 (0.74, 1.80) |
| AHA/NHLBI                                 | 1.21 (0.57, 2.55) | 1.14 (0.53, 2.44) | 1.31 (0.87, 1.99) |
| Crude HR (95%CI)                          | 1.41 (0.92, 2.15) | 1.41 (0.92, 2.15) | 1.23 (0.84, 1.81) |
| Adjusted HR (95%CI)                       | 1.23 (0.84, 1.81) | 1.23 (0.84, 1.81) | 1.32 (0.90, 1.96) |
| IDF                                       | 1.10 (0.51, 2.41) | 0.98 (0.44, 2.18) | 1.43 (0.95, 2.16) |
| Crude HR (95%CI)                          | 1.35 (0.88, 2.06) | 1.35 (0.88, 2.06) | 1.36 (0.94, 1.98) |
| Adjusted HR (95%CI)                       | 1.25 (0.80, 1.97) | 1.25 (0.80, 1.97) | 1.28 (0.87, 1.89) |

### Metabolic components (ref = no)

| Elevated Blood Pressure                  | 0.60 (0.27, 1.30) | 0.53 (0.24, 1.19) | 0.99 (0.60, 1.63) |
|                                          | 0.98 (0.59, 1.63) | 0.88 (0.57, 1.36) | 0.86 (0.55, 1.35) |
| Hypertriglycerides                       | 1.15 (0.56, 2.38) | 1.24 (0.59, 2.58) | 1.25 (0.84, 1.87) |
|                                          | 1.33 (0.89, 2.00) | 1.13 (0.78, 1.64) | 1.24 (0.85, 1.81) |
| Low HDL-C                                 | 1.58 (0.72, 3.44) | 1.19 (0.54, 2.64) | 0.89 (0.52, 1.50) |
|                                          | 0.90 (0.52, 1.53) | 0.99 (0.62, 1.57) | 0.97 (0.61, 1.55) |
| Abdominal obesity (NCEP ATP III and AHA/NHLBI) † | 2.07 (0.50, 8.62) | 2.17 (0.52, 9.14) | 0.56 (0.14, 2.27) |
|                                          | 0.56 (0.14, 2.27) | 1.06 (0.39, 2.85) | 1.10 (0.41, 2.98) |
| Abdominal obesity (IDF) ‡               | 1.21 (0.60, 2.45) | 1.12 (0.54, 2.31) | 1.17 (0.79, 1.74) |
|                                          | 1.08 (0.71, 1.64) | 1.20 (0.84, 1.72) | 1.12 (0.77, 1.62) |
| High FPG (NCEP ATP III) ¶                | 1.70 (0.89, 3.26) | 1.72 (0.88, 3.34) | 1.10 (0.75, 1.63) |
|                                          | 1.15 (0.77, 1.70) | 1.22 (0.86, 1.72) | 1.26 (0.89, 1.79) |
| High FPG (AHA/NHLBI and IDF) §           | 1.15 (0.60, 2.19) | 1.14 (0.59, 2.19) | 1.16 (0.81, 1.67) |
|                                          | 1.18 (0.82, 1.71) | 1.19 (0.86, 1.65) | 1.22 (0.88, 1.71) |

Adjusted for sex, age, marital status, education, physical activity, currently smoking (yes, no), currently drinking (yes, no), family history of CHD, family history of stroke and family history of hypertension. † Waist circumference $\geq 102$ cm in men and $\geq 88$ cm in women. ‡ Waist circumference $\geq 90$ cm in men and $\geq 80$ cm in women. ¶ Fasting glucose level of $\geq 6.1$ mmol/L. § Fasting glucose level of $\geq 5.6$ mmol/L.

### Discussion

In the present study, NCEP ATP III defined MetS at baseline was associated with significantly higher risk of newly onset CVD. Similarly, IDF defined MetS correlated with newly onset Stroke among elderly from rural China. As for individual metabolic components, only abdominal obesity defined by NCEP ATP III was found to be correlated with newly onset Stroke. All the predictive effects of MetS or metabolic components on newly onset CHD, Stroke or CVD was statistically significant among female but not male.

During the past decades, with the rapid development of economic growth, changes in lifestyle and longer life expectancy, geriatric population increase worldwide. Together with the aging population, is that age-related metabolic disorders, like hypertension, diabetes, obesity and dyslipidemia which gradually became more prevalent. The high rates of cardiometabolic risk factors resulted in
dramatically increased cardiovascular and cerebrovascular problems with a high morbidity and mortality in elderly subjects. According to the WHO definition, the prevalence of MetS in elderly population varied from 11-43% (median 21%), and 23-55% (median 31%) while according to NCEP ATP III criteria [7, 12]. Obesity and hypertension are the most prevalent individual components among them. During the past decades, cardiometabolic disorders gradually decreased in developed countries due to the effective propagation, prevention and treatment. However, they still occurred frequently in rural or developing areas. Our previous data showed that during 2012-2013 year, the prevalence of hypertension (74.8%), diabetes (14.9%), dyslipidemia (67.4%), obesity (39.9%), stroke (18.9%) and hyperuricemia (13.1%) among elderly were significantly high in rural China [17]. In the present study, the MetS by IDF criteria was 35.5% and by NCEP ATP III criteria was 28.4% closed to the data from urban cities like Beijing [MetS by NCEP criteria was 30.5% (17.6% in men, 39.2% in women) ; IDF definition was 46.3% (34.8% in men, 54.1% in women)] [18]. Due to the high prevalence of MetS among rural elderly subjects, it is necessary to estimate the possible effect of MetS on the newly onset CHD, stork, and CVD in order to better preventing and controlling cardiovascular mortality and morbidity.

There were already many previous studies, intending to estimate the relationship between MetS and CHD or stroke, coming out with inconsistent results. One cross-sectional study enrolled 4,748 residents (aged ≥ 30 years) in rural China during 2006 to 2007, concluded that NCEP-ATP III defined MetS was more suitable than IDF and Chinses Diabetes Society criteria for screening and estimating the risk of CHD and Stroke from MetS, especially in men [19]. Similarly, elderly subjects from Beijing with MetS had significantly higher risk of CHD (NCEP ATP III criteria, OR: 1.43; IDF criteria, OR: 1.69), Stroke (NCEP ATP III criteria, OR: 1.45; IDF criteria, OR: 1.58), PAD (NCEP ATP III criteria, OR: 1.47; IDF criteria, OR: 1.42) and CVD (NCEP ATP III criteria, OR: 1.50; IDF criteria, OR: 1.73) [18]. However, in the Prospective study of Pravastatin in the Elderly at Risk (PROSPER) and British Regional Heart Study (BRHS) studies, weak or no association between MetS and vascular risk in elderly subjects were found using NCEP ATP III definition [20]. Elderly subjects usually accompany with many cardiovascular risk or established coronary artery diseases. Therefore, when we evaluated the association between
cardiovascular risk factors and CVD, we should take into account about this. Ana Teresa Timóteo and colleagues reported that among subjects (a mean age of 65 ± 9 year) with high cardiovascular risk, the presence of MS at baseline was not associated with cerebral or cardiac events in long-term follow-up [21]. As far as we knew, most of the previous studies estimated relationship between MetS and CVD were cross-sectional analysis which restricted their accuracy. As a prospective study, we found that MetS defined by NCEP ATP III and IDF at baseline was correlated with newly onset CVD and stroke respectively in women but not men which help to confirm the effect of MetS on CHD, stroke or CVD. This results were coincidence with previous study which suggested that the association between MetS and CVD were more pronounced when the NCEP ATP III and AHA/NHLBI criteria were implemented compared with IDF definition [22]. However, study held in China concluded that IDF defined MetS was more strongly associated with CHD than the NCEP or revised NCEP defined MetS, but weakly or not associated with stroke which was inconsistent with our results [23]. In our study, abdominal obesity at baseline increased the newly onset stroke in female elderly but not male. This was consistent with many previous studies. Data from the National Stroke Screening Survey in 2012 and the 2010 Chinese population from sixth National Census of Populations showed that compared to male elderly, female elder subjects with stroke were more likely to have obesity, diabetes, elevated LDL-C and atrial fibrillation [23]. It might partially due to the significantly lower rate of abdominal obesity in male compared to female (2.9% vs. 29.4%, \( P < 0.001 \)) in the present study which lead to the predictive effect of MetS on newly onset Stroke become insignificant.

One interesting finding in the present study was that the predictive effect of MetS on newly onset CHD, Stroke or CVD was significant in female elderly but not male elderly. First, it might be due to the gender discrepancy in the prevalence of MetS in elderly subjects. Trevisan et al reported that subjects aged \( \geq 50 \) years, women had significantly higher prevalence of MetS than men [25]. Similarly, study held in USA elderly aged \( \geq 70 \) years showed that MetS (NCEP ATP III) was more prevalent among women than men [26]. MetS prevalence showed gender discrepancy in elderly female than in male although general epidemiological studies with adults have found higher prevalence rates of MetS in men than in women [27]. Women had significantly higher rate of MetS at baseline which might
resulted in a significant predictive effect of MetS on newly onset CVD in future. Second, except for baseline MetS, there are many possible confounders that have been analysis in our model which might cause the association between MetS and CVD became insignificant. In the present study, after adjusted for possible confounders, MetS (OR: 1.33), female gender (OR: 1.42), increasing age (OR: 1.04), and family history of hypertension (OR: 1.54) were associated with increased risk of newly onset CVD. We further analyzed the characters of female of male participants separately and found that female elderly had significantly higher rate of family history of hypertension than male elderly (19.7% vs. 16.2%, P = 0.012). Therefore, it might make the association between MetS and CVD more pronounced in female elderly.

Limitation
There are some limitations in the present study. First, there are some participant loss contact in the follow-up which might cause bias in the predictive effect of MetS on CHD, stroke or CVD. Secondly, HDL-C, LDL-C, triglyceride, fasting plasma glucose were measured only once, which might be imprecise and resulted in random errors. Thirdly, in the presents study, we did not used the WHO definition and that of the European Group for the Study of Insulin Resistance due to lack of data about insulin resistance.

Conclusion
In summary, our findings suggested that MetS is significantly associated with CVD and Stroke in the NCEP ATP III and IDF definitions of MetS separately. Among female elderly Chineses population, abdominal obesity defined by NCEP ATP III are more prevalent than other components of MetS for HRs of stroke. NCEP ATP III criteria might be more suitable to estimate the predictive effect of MetS on CVD whereas IDF criteria was preferred to be used when predicting Stroke in rural elderly female in China.

Abbreviations
CVD:cardiovascular disease; CHD:coronary heart disease; MetS:metabolic syndrome; BMI:Body mass index; SBP:systolic blood pressure; DBP:diastolic blood pressure; FPG:Fasting plasma glucose; TC:total cholesterol; LDL-C:low-density lipoprotein cholesterol; HDL-C:high-density lipoprotein cholesterol; TG:triglyceride;
Declarations
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.
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).
Competing interests
The authors declare that they have no competing interests.
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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 data analysis. YXS contributed to the study conceptions and design. All authors read and approved the final version of the manuscript.
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**Figures**

![Figure 1](image)

Figure 1

Showed the prevalence of MetS and individual metabolic components according to gender (A) and different age groups. * means P<0.05 vs. female.
