Total and High Density Lipoprotein Cholesterol Ratio is Associated With Metabolic Syndrome Among Very Elderly in Chengdu, China

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Research

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Abstract

Background

Metabolic syndrome (MetS) is currently a major public health challenge worldwide. This study was to investigate the potential association between total and high density lipoprotein cholesterol ratio (THR) and MetS in very elderly population in Chengdu.

Methods

totally 1056 very elderly (aged ≥ 80 years) in Chengdu community were enrolled in this cross-sectional study. Geographic characteristics of participants were collected and laboratory measurement were performed. Metabolic syndrome (MetS) was defined according to Chinese and international diabetes federation (IDF) criteria respectively. Logistic analysis was used to investigate the potential association between THR and MetS. The receiver operating characteristic curve (ROC) analysis was used to evaluate the efficiency of THR in predicting MetS.

Results

Finally 1038 participants were included in statistical analysis. The mean age was 83.6±3.4 years and 52.6% was men and 21.6% of which suffered from MetS. Participants with MetS had relatively higher waist circumference, body weight, blood pressure, fast plasma glucose, non-high density lipoprotein cholesterol and THR. The logistic analysis revealed that THR was associated with MetS according to both Chinese (odds ratio(OR): 3.053, 95% confidence interval(CI): 2.464-3.782, P<0.001) and IDF criteria (OR: 2.458, 95%CI: 2.016-2.995, P<0.001). And the ROC analysis found that the area under curve of THR was 0.800 (95%CI: 0.749-0.852, P<0.001) and 0.727 (95%CI: 0.669-0.786, P<0.001) for predicting MetS according to Chinese and IDF criteria, respectively.

Conclusions

THR is associated with MetS in this community very elderly population in Chengdu.

Introduction

Metabolic syndrome (MetS) is nowadays a big challenge worldwide, which is characterized by a cluster of several metabolic disorders, i.e. abdominal obesity, dyslipidemia, hypertension and dysregulation of glucose [1,2]. Despite unclear common pathophysiological mechanism, MetS has been recognized to increase the risk of diabetes mellitus (DM) and series arteriosclerotic cardiovascular disease(ASCVD), i.e. coronary heart disease, cardiovascular mortality [2,3], cognitive impairment [4] and all cause mortality [5]. Lifestyle modification and risk factors management are currently recommended to decrease the risk of subsequent cardiovascular diseases. Previous studies [6,7] have emphasized the importance of dyslipidemia as one component for the diagnosis of MetS and recent epidemiological study [8] has demonstrated that more than one-thirds Chinese adults in 2010 suffered from MetS, which was similar to
the epidemiological situation in USA in 2014. Furthermore, the prevalence of MetS in Americans older than 60 years was 1.6 fold higher [9], which shows that MetS components are more likely to cluster together in older population. Dyslipidemia (hypertriglyceridemia and hypo-high density lipoproteinemia) is an important component for MetS, which plays a critical role in the progression from MetS to DM and ASCVD [6,7]. Some studies [10-12] have investigated the potential ability of total to high-density lipoprotein cholesterol (THR) and triglyceride to high-density lipoprotein cholesterol ratio to predict ASCVD in young and middle aged population, while few about very elderly has been reported until now. Therefore, this study aimed to explore the potential association between THR and MetS among community very elderly population in Chengdu.

**Methods**

**Study population**

This study was designed to investigate cardiovascular and metabolic risk factors in general community very elderly (≥ 80 years old) in Chengdu, which locates in the southwest of China [13]. From 2013 to 2015, a representative sample of very elderly in community were recruited by using of a stratified three-stage cluster sampling design, which was described previously elsewhere[13]. Totally, 1056 very elderly from 20 residential communities were enrolled according to registration data from local government. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by the ethics committee of the second people’s hospital of Chengdu. And all participants have given informed consent.

**Demographic data collection and laboratory test**

Well trained physicians and nurses were responsible for demographic data collecting (such as medical history, lifestyle, cardiovascular and metabolic risk factors) by a questionnaire-based face to face interview with a standardized questionnaire. The body mass index (BMI) was defined as weight in kilograms divided by the square of the height in meters. Blood pressure (BP) were measured three times in a sitting position by using a standardized automatic electronic sphygmanomanometer (HEM-7300, Omron\(^\text{\textregistered}\) Kyoto, Japan) according to the Chinese guideline [14] and average values were calculated and included in statistical analysis.

After fasting at least for 8 hours, blood samples were collected from all participants and biochemical parameters, such as fast plasma glucose(FPG), total cholesterol(TC), triglycerides(TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), creatinine and serum uric acid were analyzed enzymatically on an auto-analyzer (AU5421 Chemistry Analyzer, Beckman, Brea, California, United States) in the central laboratory of our hospital. The estimated glomerular filtration rate (eGFR) was calculated by using the Modification of Diet in Renal Disease study equation modified for Chinese population: eGFR = 186 × serum creatinine\(^{-1.154}\) × Age\(^{-0.203}\) ×
0.742 (if women).

**Diagnostic criteria of MetS**

In this study, MetS were defined according to the Chinese guideline for dyslipidemia management [15] and the Consensus Worldwide Definition from international diabetes federation (IDF) [16] respectively as follows:

**Chinese criteria** : MetS should fulfill any three or more of the following items: abdominal obesity (waist circumference (WC) $\geq 90$ cm in men and $\geq 85$ cm in women), fasting TG $\geq 150$ mg/dL (1.7 mmol/L), fasting HDL-C $< 40$ mg/dL (1.0 mmol/L), FPG $\geq 110$ mg/dL (6.10 mmol/L) or 2 hour blood glucose after glycemic load $\geq 140$ mg/dL (7.80 mmol/L) or anti-diabetic treatment, and BP $\geq 130/85$ mmHg or anti-hypertensive treatment.

**IDF criteria** : abdominal obesity with ethnic-specific WC cut-points ($\geq 90$ cm for Chinese men and $\geq 80$ cm for women) and fulfills two items of the following: TG $\geq 150$ mg/dL (1.7 mmol/L) or treatment for hypertriglycerides, HDL-C $< 40$ mg/dL (1.03 mmol/L) in men or $< 50$ mg/dL (1.29 mmol/L) in women or treatment for low HDL-C, FPG $\geq 100$ mg/dL (5.6 mmol/L) or previously diagnosed type 2 diabetes, and BP $\geq 130/85$ mmHg or treatment for hypertension.

**Statistical analysis**

All statistical analysis were performed by using SPSS software (Version 22.0, SPSS Inc, Chicago, IL). Continuous variables are expressed as mean $\pm$ standard deviation and frequencies are presented as percentages. Statistical comparison of continuous variables between groups was conducted using ANOVA or Kruskal-Wallis test, whereas $x^2$ test was applied to compare frequencies. Multiple logistic regression models were used to evaluate the potential association between THR and MetS. The receiver operating characteristic curve (ROC) analysis was used to evaluate the efficiency of THR in predicting MetS according to different criterion. A two-sided $P$ value $< 0.05$ was considered statistically significant.

**Results**

**Baseline characteristics**

Totally, there were 1056 participants enrolled in this study and 1038 of them were included in the final statistical analysis. In this study population, more very elderly women suffered from MetS and participants with MetS were younger, more likely to smoke and drink currently. And they had relatively higher WC, body weight, BP, FPG, non-HDL-C, serum uric acid, total and high density lipoprotein cholesterol ratio (THR) and lower eGFR.

**Logistic regression analysis for MetS risk**
The logistic analysis found that THR was associated with the increased risk of MetS both according to the Chinese criteria (odds ratio (OR): 3.211, 95% confidence interval (CI): 2.349-4.388, P<0.001) and IDF criteria (OR: 2.281, 95% CI: 1.742-2.989, P<0.001) in this very elderly population. After adjustment of sex, BMI, hyperurecima and eGFR, THR was found to be also associated with the increased risk of MetS both according to Chinese criteria (OR: 3.107, 95% CI: 2.507-3.849, P<0.001) and IDF criteria (OR:2.418, 95% CI: 1.981-2.951, P<0.001). Moreover, THR was found to be still associated with the increase of MetS according to Chinese criteria (OR: 3.053, 95% CI: 2.464-3.782, P<0.001) and IDF criteria (OR:2.458, 95% CI: 2.016-2.995, P<0.001) in this very elderly population after adjustment of sex, age, BMI, hyperurecimia and eGFR, current smoking, current drinking and physical activity.

**ROC analysis of THR for MetS predicting**

ROC analysis found that the area under the ROC curve (AUC) of THR was 0.800 (95%CI: 0.749-0.852, P<0.001) and 0.727 (95%CI: 0.669-0.786, P<0.001) for predicting MetS in very elderly according to Chinese and IDF criteria, respectively. Moreover, the AUC of THR for predicting MetS (Chinese criteria) was similar to the AUC of FPG (0.800, 95%CI: 0.745-0.856, P<0.001) and lower than TC (0.843, 95%CI: 0.795-0.8961, P<0.001). The AUC of TG was the biggest for predicting MetS according to Chinese criteria (0.843, 95%CI: 0.795-0.891, P<0.001), while the AUC of FPG was the biggest according to IDF criteria (0.771, 95%CI: 0.715-0.826, P<0.001).

**Discussion**

**Dyslipidemia and MetS**

It is well known that MetS is a cluster or combination of several metabolic abnormalities without fully understood pathogenesis currently [17]. Genetic variants in MetS are associated especially with glucose metabolism or lipid metabolism. And genetic susceptibility may exist within adipose tissue, in insulin signaling pathways, and in regulation of individual components of MetS. Insulin resistance or hyperinsulinaemia may contribute to obesity- and DM related hypertension and possibly also promote dyslipidaemia in MetS. Obesity, lifestyle, chronic inflammation and circadian rhythm disturbances may also contribute to the genesis of MetS[18].

Dyslipidaemia in MetS is mainly characterized by highly atherogenic small dense low-density lipoprotein and small triglyceride-rich dense high-density lipoprotein particles [7]. One recent study has identified more than thirty new lipids contributing to key metabolic risk factors, i.e. obesity, dyslipidemia and dysglycemia in Framingham heart study [19]. Triglyceride could result in endothelial dysfunction and foam cells formation by accelerating the oxidation of LDL-C. While in contrast, HDL-C play an anti-atherosclerosis role through transporting excess cholesterol to liver. Therefore, hypertrigleicemiea and hypo-high density lipoproteinemia play an important role in the pathogenesis in MetS. A previous study has reported that hypertrigleicemiea with a prevalence of 10.8% is the main type of lipid disorders in Chinese older than 60 years [20], especially in older women, which is in accordance with the result of our previous study [13]. In the present study, all levels of LDL-C, TC and TG, WC and BMI were higher in
participated very elderly than the mean level in Chinese adults, while FBG was similar to which in general adults [8,13]. Especially, the prevalence of abdominal obesity and hypertrigleicemiea was also higher in this very elderly population than which in general Chinese adults and middle aged population in this area [13] and the prevalence of hypercholesterolaemia (35.8%) is notably higher than that of hypertrigleicemiea (21.6%). Aside from high prevalence of hypertension, these dramatic characteristics of components above contribute significantly to the relatively high prevalence of MetS in this very elderly population.

**THR and MetS**

Among very elderly participants in this study, TC level and THR were significantly higher and HDL-C level was significantly lower in participants with MetS. Previous studies [10,11,21,22] have already demonstrated that TC/HDL and TG/HDL ratio are associated with MetS in general population. This current study has also investigated that there is an association between THR and MetS either according to Chinese or IDF criteria in very elderly population. However, statistical analyses have demonstrated that THR has a higher ROC and larger ORs for MetS prediction according to Chinese criteria than IDF criteria. And interestingly, in this very elderly population, more very elderly women were found to suffer from MetS according to both criteria, which is different from the results of a previous study in young and middle aged Chinese [20]. Although the main differences of MetS definition between Chinese and IDF criteria are the criteria of WC and HDL cholesterol cut points, the prevalence of abdominal obesity, hypercholesterolaemia and hypertrigleicemiea in this very elderly women were higher than which in young and middle aged women, which may be one of the potential explanation for the difference for predicting MetS according to different criterion.

Our study has also suggested that the ability of THR for predicting of MetS is similar to which of FPG, although it is inferior to which of TG in this very elderly population. TG and FPG abnormalities are important components of MetS according to different criterion. Except for these direct measured parameters for MetS diagnosis, THR might be a reliable indirect measured parameter for MetS predicting before the absolute increase of directly measured lipid parameters become apparent.

**Conclusions**

In conclusion, The main finding of this study is that THR is associated with the increase risk of MetS and it may be a simple predictor of MetS among very elderly population in Chengdu. According to the high prevalence of abdominal obesity, dyslipidemia and glucose abnormality in this study and the oil rich local daily food style, proper lifestyle modification, especially dietary changes are still needed to be emphasized in the prevention of MetS and ASCVD in very elderly, although the life expectancy in this population is short.

Several limitations should be considered in this study. First, this cross-sectional study could not describe any causality. Second, the study population in this study is very elderly in southwest of China, whether
current findings could be generalized to younger population or other very elderly population in other area of China needs further clarification from further longitudinal prospective studies.

**Abbreviations**

ASCVD: arteriosclerotic cardiovascular disease; AUC: area under the receiver operating characteristic curve; BMI: body mass index; BP: Blood pressure; CI: conference interval; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; FBG: fast plasma glucose; HDL: high-density lipoprotein cholesterol; IDF: international diabetes federation; LDL: low-density lipoprotein cholesterol; MetS: metabolic syndrome, OR: odds ratio; ROC: receiver operating characteristic curve; SUA: serum uric acid; TC: total cholesterol; TG: triglyceride; THR: total and high density lipoprotein cholesterol ratio; WC: Waist circumference.

**Declarations**

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**Author's contributions**

GH, JBX and TJZ contributed to the study concept and design, data analysis and interpretation, drafting, reviewing and revising of manuscript. XQD, JW, JX, LC, HXL and XQY contributed to interpretation, reviewing and revising of manuscript. All authors read and approved the final manuscript.

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**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on a reasonable request.

**Ethics approval and consent to participate**

This study was approved by the ethics committee of the second people's hospital of Chengdu, and all participants provided written informed consent.

**Consent for publication**

Not applicable.
Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Baseline characteristics of very elderly according to MetS (Chinese criteria)
|                                | MetS (n=224) | No MetS (n=814) | P value |
|--------------------------------|--------------|-----------------|---------|
| Age (yrs)                      | 83.06±2.90   | 83.71±3.49      | 0.044   |
| Male, n(%)                     | 97(43.3)     | 449(55.2)       | 0.002   |
| Current smoking, n(%)          | 27(12.1)     | 88(10.8)        | 0.649   |
| Current drinking, n(%)         | 21(9.4)      | 65(8.0)         | 0.565   |
| Medical history, n(%)          |              |                 |         |
| Hypertension                   | 138(61.6)    | 408(50.1)       | 0.005   |
| DM                             | 71(31.7)     | 107(13.1)       | <0.001  |
| Abdominal obesity, n(%)        | 202(90.2)    | 272(33.4)       | <0.001  |
| Medication, n(%)               |              |                 |         |
| Antihypertensive               | 126(56.2)    | 344(42.3)       | 0.834   |
| Antidiabetic                   | 62(27.6)     | 77(9.4)         | 0.027   |
| Lipid lowering                 | 25(11.2)     | 61(7.5)         | 0.615   |
| WC (cm)                        | 95.10±7.29   | 85.09±10.30     | <0.001  |
| Height (cm)                    | 154.78±10.11 | 155.01±10.11    | 0.512   |
| Body weight (kg)               | 60.81±9.80   | 54.05±10.74     | <0.001  |
| BMI                            | 25.34±3.35   | 22.42±3.57      | <0.001  |
| SBP (mmHg)                     | 152.9±18.8   | 146.1±22.9      | <0.001  |
| DBP (mmHg)                     | 75.8±10.6    | 74.1±12.4       | 0.030   |
| FBG (mmol/L)                   | 7.21±2.85    | 5.28±1.38       | <0.001  |
| TC (mmol/L)                    | 5.05±1.02    | 4.84±0.99       | 0.008   |
| TG (mmol/L)                    | 2.10±1.09    | 1.19±0.61       | <0.001  |
| LDL-C (mmol/L)                 | 2.81±0.74    | 2.53±0.74       | <0.001  |
| HDL-C (mmol/L)                 | 1.33±0.36    | 1.67±0.43       | <0.001  |
| THR                            | 4.00±0.96    | 3.03±0.79       | <0.001  |
| SUA (µmol/L)                   | 375.21±88.84 | 350.66±96.01    | <0.001  |
| Creatinine, µmol/L             | 109.05±41.40 | 102.81±29.72    | 0.231   |
| eGFR, ml/(min•1.73m²)          | 55.14±15.08  | 56.40±18.41     | 0.044   |
Data are expressed as mean±standard deviation for continuous variables or number (percentage) for categorical variables.

**Table 2. Association between THR and MetS according to different criteria**

| MetS (Chinese criteria) | MetS (IDF criteria) |
|-------------------------|---------------------|
| OR (95% CI)             | P value             | OR (95% CI)             | P value |
| Model 1                 | 3.211 (2.349-4.388) | <0.001                  | 2.281 (1.742-2.989) | <0.001 |
| Model 2                 | 3.107 (2.507-3.849) | <0.001                  | 2.418 (1.981-2.951) | <0.001 |
| Model 3                 | 3.053 (2.464-3.782) | <0.001                  | 2.458 (2.016-2.995) | <0.001 |

Model 1: not adjusted.

Model 2: adjusted for sex, BMI, hyperurecima and eGFR.

Model 3: adjusted for sex, age, BMI, hyperurecima and eGFR, current smoking, current drinking and physical activity.

**Figures**

**Figure 1**

ROC curves of different parameters for predicting of MetS. A. ROC analysis of THR for predicting of MetS according to Chinese criteria. The AUC of THR was 0.800 (95%CI: 0.749-0.852). B. ROC analysis of THR for predicting of MetS according to IDF criteria. The AUC of THR was 0.727 (95%CI: 0.669-0.786). AUC:
area under the ROC curve; FBG: fast plasma glucose; IDF: international diabetes federation; MetS: metabolic syndrome; ROC: Receiver operating characteristic; TC: total cholesterol; TG: triglyceride; THR: total and high density lipoprotein cholesterol ratio.