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

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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 sphygmomanometer (HEM-7300, Omron®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: $eGFR = 186 \times \text{serum creatinine}^{-1.154} \times \text{Age}^{-0.203} \times$

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) ≥ 90 cm in men and ≥ 85 cm in women) , fasting TG ≥ 150 mg/dL (1.7 mmol/L), fasting HDL-C < 40 mg/dL (1.0 mmol/L), FPG ≥ 110 mg/dL (6.10 mmol/L) or 2 hour blood glucose after glycemic load ≥ 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 (≥ 90 cm for Chinese men and ≥ 80 cm for women) and fulfills two items of the following: TG ≥ 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 ≥ 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 requecies are presented as percentages. Statistical comparison of continuous variables between groups was conducted using ANOVA or Kruskal-Wallis test, whereas χ^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, hyperurecemia 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, hyperurecemia 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, hypertriglyceridaemia and hypo-high density lipoproteinemia play an important role in the pathogenesis in MetS. A previous study has reported that hypertriglyceridaemia 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 hypertriglyceridemia 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 hypercholesterolemia (35.8%) is notably higher than that of hypertriglyceridemia (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, hypercholesterolemia and hypertriglyceridemia 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: confidence 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.

References

1. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. 2005;365(9468):1415-1428.
2. Saklayen MG. The Global Epidemic of the Metabolic Syndrome. *Curr Hypertens Rep.* 2018;20(2):12.
3. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 2002; 288: 2709-2716.
4. Pal K, Mukadam N, Petersen I, Cooper C. Mild cognitive impairment and progression to dementia in people with diabetes, prediabetes and metabolic syndrome: A systematic review and meta-analysis. *Soc Psychiatry Psychiatr Epidemiol.* 2018;53(11):1149-1160.
5. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care* 2005;28(7):1769-1778 .
6. Barkas F, Elisaf M, Liberopoulos E, Liontos A, Rizos EC. High triglyceride levels alter the correlation of apolipoprotein B with low- and non-high-density lipoprotein cholesterol mostly in individuals with diabetes or metabolic syndrome. 2016 Apr;247:58-63.
7. Adiels M, Olofsson SO, Taskinen MR, Borén J. Overproduction of very low-density lipoproteins is the hallmark of the dyslipidemia in the metabolic syndrome. *Arterioscler Thromb Vasc Biol.* 2008;28(7):1225-36.
8. Lu J, Wang L, Li M, Xu Y, Jiang Y, Wang W, et al. Metabolic Syndrome Among Adults in China: The 2010 China Noncommunicable Disease Surveillance. *J Clin Endocrinol Metab.* 2017;102(2):507-515.
9. Shin D, Kongpakpaisarn K, Bohra C. Trends in the prevalence of metabolic syndrome and its components in the United States 2007-2014. *Int J Cardiol.* 2018;259:216-219.
10. Gao M, Zheng Y, Zhang W, Cheng Y, Wang L, Qin L. Non-high-density lipoprotein cholesterol predicts nonfatal recurrent myocardial infarction in patients with ST segment elevation myocardial infarction. *Lipids Health Dis.* 2017;23;16(1):20,
11. Dobiášová M, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)). *Clin Biochem.* 2001;34(7):583-588.
12. Fernández-Macías JC, Ochoa-Martínez AC, Varela-Silva JA, Pérez-Maldonado IN. Atherogenic Index of Plasma: Novel Predictive Biomarker for Cardiovascular Illnesses. *Arch Med Res.* 2019 ;50(5):285-294.
13. Huang G, Xu JB, Zhang TJ, Nie XL, Li Q, Liu Y, et al. Hyperuricemia is associated with cardiovascular diseases clustering among very elderly women - a community based study in Chengdu, China. *Sci*

Rep. 2017;7(1):996.

14. Liu, L.S. & Writing Group of 2010 Chinese Guidelines for the Management of Hypertension. 2010 Chinese guidelines for the management of hypertension [in Chinese]. *Xin. Xue. Guan. Bing. Za. Zhi.* 2011; **39**, 579-615.
15. Joint committee for guideline revision. 2016 Chinese guidelines for the management of dyslipidemia in adults. *J Geriatr Cardiol.* 2018; **15**, 1-29.
16. International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome. <https://www.idf.org/e-library/consensus-statements/60-idfconsensus-worldwide-definitionof-the-metabolic-syndrome.html>.(2006)(Date of access: 08/01/2020).
17. Nilsson PM, Tuomilehto J, Rydén L.The metabolic syndrome - What is it and how should it be managed.*Eur J Prev Cardiol.* 2019 Dec;26(2_suppl):33-46.
18. Raal FJ.Pathogenesis and management of the dyslipidemia of the metabolic syndrome.*Metab Syndr Relat Disord.* 2009 Apr;7(2):83-8.
19. Yin X, Willinger CM, Keefe J, Liu J, Fernández-Ortiz A, Ibáñez B, et al. Lipidomic profiling identifies signatures of metabolic risk. 2019;51:102520.
20. Wang ZH, Wang LH, Li YC, Zhang M, Hu N, Wang LM.Current status of diabetes, hypertension and dyslipidemia among older Chinese adults in 2010.*Zhonghua Yu Fang Yi Xue Za Zhi.* 2012 Oct;46(10):922-926.
21. Zhang X, Zhang X, Li X, Feng J, Chen X. Association of metabolic syndrome with atherogenic index of plasma in an urban Chinese population A 15-year prospective study.*Nutr Metab Cardiovasc Dis.* 2019;29(11):1214-1219.
22. Li Zhu , Zhan Lu , Liren Zhu , Xiaoxiao Ouyang , Yang Yang , et al .Lipoprotein ratios are better than conventional lipid parameters in predicting coronary heart disease in Chinese Han people. *Kardiol Pol.* 2015;73(10):931-938.

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•1.73m ²)	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 (Chinsese 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.