

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>info.bmjopen@bmj.com</u>

BMJ Open

BMJ Open

Prediction of metabolic syndrome among an elderly Chinese population: A cross-sectional study

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-041519
Article Type:	Original research
Date Submitted by the Author:	12-Jun-2020
Complete List of Authors:	Nie, Guqiao; Huazhong University of Science and Technology, Tongji Medical College Zhang, Meng; Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Peng, Wen; Huazhong University of Science and Technology Tongji Medical College, the aDepartment of Geriatrics, Union Hospital
Keywords:	GERIATRIC MEDICINE, Valvular heart disease < CARDIOLOGY, Lipid disorders < DIABETES & ENDOCRINOLOGY





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Prediction of metabolic syndrome among an elderly Chinese population: A cross-sectional study

Authors:

Guqiao Nie¹ (https://orcid.org/0000-0002-5467-6431), Meng Zhang², *Wen Peng

Author affiliations:

¹Department of Geriatrics, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

²Department of Geriatrics, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

*Corresponding author : Professor Wen Peng

Address:Department of Geriatrics, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Email: pengwen666@sina.com

Word count: 1938.

ABSTRACT

Objectives: To investigate the relationship between triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio and metabolic syndrome in the elderly population of China, and to determine the best critical value of TG/HDL-C in predicting metabolic syndrome in this population.

Design: Cross-sectional study.

Setting: Our study was conducted in a community physical examination center in Wuhan, China between January 1, 2016 and December 31, 2016.

Participants: The physical examination data from 1267 elderly people (aged over 65 years) in the community were analyzed in this study. The average age of the study participants was 71.64 ± 5.605 years.

Primary outcome measures: Correlation between the TG/HDL-C ratio and metabolic syndrome; the optimum cutoff of the TG/HDL-C ratio for the prediction of metabolic syndrome.

Results: The TG/HDL-C ratio showed a significant positive correlation with metabolic syndrome (r = 0.420, p < 0.001) in the elderly Chinese population. Binary logistic regression analysis showed that the TG/HDL-C ratio was an independent risk factor for metabolic syndrome (odds ratio = 3.07 [95% CI: 2.402, 3.924], p < 0.001) after adjusting for blood pressure, blood glucose, age, sex, and body mass index. The receiver operating characteristic curves of TG/HDL-C ratio and metabolic syndrome showed that in the elderly population a TG/HDL-C ratio of 1.49 can be used as the critical value for predicting metabolic syndrome. At this value, the specificity and sensitivity of the measure were optimal (80.8% and 72.4%, respectively).

Conclusion: In this study, we found a significant correlation between TG/HDL-C ratio and metabolic syndrome. Therefore, the TG/HDL-C ratio can be used to predict metabolic syndrome among elderly people in China.

Keywords: Metabolic syndrome; Triglyceride-to-HDL cholesterol ratio;

Cardiovascular disease.

Strengths and limitations of this study

- The study sample had a wide age range (65–93 years), and the study included information on their basic characteristics like sex, waist circumference (WC), marital status, diagnosis of hypertension, etc.
- This study is the first to explore the correlation between the TG/HDL-C ratio and metabolic syndrome among elderly Chinese people.
- Our study did not adjust for possible confounders such as exercise and lipid-regulating drugs.
- The study population came from only one community.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

INTRODUCTION

Metabolic syndrome (MetS) refers to a pathological state involving the impaired metabolism of proteins, fats, carbohydrates, and other substances in the human body. It is a complex group of metabolic disorder syndromes, including risk factors associated with cardiovascular disease (CVD) and diabetes.[1, 2] The prevalence of MetS is high and rapidly increasing among the elderly population in China.[3] Risk factors include central obesity, increased blood pressure, increased fasting blood glucose (FBG) levels, and abnormal blood lipids. The prevalence of cardiovascular events and the risk of mortality are higher among patients with MetS than among the general population.[4] Therefore, the early diagnosis of MetS and timely intervention can prevent the unnecessary complications related to its progression and help reduce the risk of CVD caused by metabolic disorders. From a clinical perspective, individuals can benefit from the establishment of appropriate diagnostic methods and criteria that can accurately distinguish patients with MetS from healthy people.

This study aimed to explore the correlation between the ratio of triglycerides to high-density lipoprotein cholesterol in the blood (TG/HDL-C) and MetS in the elderly Chinese population, calculate the cutoff value of TG/HDL-C to predict MetS in this population, and determine the optimal critical value for predicting MetS, in order to provide a theoretical basis for the early identification and management of elderly patients with MetS, as well as prevent the development of cardiovascular and cerebrovascular diseases.

PARTICIPANTS AND METHODS

Study population

This was a cross-sectional study , involving data from 1267 elderly individuals examined and interviewed at a community physical examination center, between January 1, 2016 and December 31, 2016. Participants' data were included in this study if the patient met all of the following inclusion criteria: lived in China, aged \geq 65 years, provided basic demographic information, provided accurate biochemical measurements, and consented to a full clinical examination.

Participants were excluded if they met one or more of the following exclusion criteria: incomplete data provided; presence of one of the following conditions: physical disability, acute infection, acute myocardial infarction, acute cerebral infarction, renal failure, dialysis, or active stage malignancies; or use of the following medications: hormone replacement therapy and oral or injectable glucocorticoids.

Clinical characteristics

Data for this study were obtained from the physical examination records of the elderly people in the community. General demographic and clinical data such as age, sex, marital status, height, weight, WC, and history of hypertension were obtained through oral interview. The doctor used a mercury sphygmomanometer on the upper arm to measure blood pressure–systolic blood pressure (SBP) and diastolic blood pressure (DBP). The average value of two blood pressure measurements taken at least five minutes apart was used.

Biochemical parameters

Biochemical indices including FBG, blood lipids, and uric acid (UA) were all measured using venous blood obtained from the participants on an empty stomach. Levels of serum UA, TGs, HDL-C and low-density lipoprotein cholesterol (LDL-C), and fasting blood glucose (FBG) were measured using Roche E602 and Roche C701 (both of which are automatic biochemical analyzers).

Definition of metabolic syndrome in this study

The diagnosis of MetS in this study was made according to the following definition provided by the Chinese Diabetes Society:

1. Overweight and/or obese: Body Mass Index (BMI) \ge 25 kg/m².

2. Hyperglycemia: FBG \ge 6.1 mmol/L (110 mg/dL), and/or 2h-plasma glucose (2h-PG) \ge 7.8 mmol/L (140 mg/dL), and/or people with diagnosed and treated diabetes.

3. Hypertension: SBP/DBP \geq 140/90 mm Hg and/or with diagnosed and treated hypertension.

4. Dyslipidemia: Fasting TGs ≥ 1.7 mmol/L (150 mg/dL) and/or fasting blood HDL-C <
0.9 mmol/L (35 mg/dL) (among males) and < 1.0 mmol/L (39 mg/dL) (among females).

MetS was diagnosed if at least three of the above four components were present.

Participant and public involvement

Participants were not involved in the design or conduct of the study. It is an anonymous, non-invasive examination, only oral notification, waiving the signing of written informed consent.

Ethics approval

This study was conducted in accordance with the contents of the Declaration of Helsinki. Since this study included deidentified data, participants were not required to provide informed consent.

Statistical analyses

First, the data were divided into two groups according to the diagnosis of MetS, MetS group and non-MetS group. The percentage of participants in the above two groups that were positive for each component were reported and compared using the chi-square (X^2) test. The mean value \pm standard deviation (SD) was calculated for each of the continuous variables and compared using independent-samples t-tests, and other categorical variables were compared using the X^2 test. The Kendall's tau-b and Spearman's Rank correlation coefficients were used to analyze the correlation between MetS and the TG/HDL-C ratio, UA, BMI, WC, age, sex, and education. Binary logistic regression was used to analyze risk factors, and the results for each risk factor were described in terms of the non-standardized coefficient B, odds ratio (OR), its 95% confidence interval (95% CI), and p value. A receiver operating characteristic curve of MetS vs TG/HDL-C ratio was drawn to determine the optimum cutoff point for MetS diagnosis.

RESULTS

Clinical characteristics

The characteristics of the 1267 participants included in this study are shown in Table 1. The mean age of the participants was 71.64 ± 5.605 years. Participants diagnosed with MetS (MetS group) have statistically significant differences in the TG/HDL-C ratio, age, blood pressure, WC, FBG, UA level, hypertension, TG, and HDL-C compared with participants not diagnosed with MetS (Non-MetS group).

Table 1 Clinical characteristics of the different groups				
Characteristic or	$M_{0}+C(N = 224)$	Non-MetS		
parameter	MetS (N = 234)	(N = 1033)	p-value	
	Mean ± SD	Mean ± SD		
Age, years	71.64 \pm 5.605	71.39 ± 5.409	< 0.001	
BMI, kg/m²	27.14 ± 3.19	23.98 ± 3.25	< 0.001	
DBP, mm Hg	82.97 ± 10.97	76.54 ± 11.29	< 0.001	
SBP, mm Hg	148.08 ± 13.82	131.26 ± 18.17	< 0.001	
Waist circumference, cm	68.42 ± 10.29	60.39 ± 9.94	< 0.001	
TG/HDL-C	2.07 ± 1.09	1.17 ± 0.89	< 0.001	
TC, mmol/L	4.78 ± 1.10	4.60 ± 0.89	0.024	
HDL, mmol/L	1.02 ± 0.22	2.75 ± 0.77	< 0.001	
LDL, mmol/L	2.92 ± 0.91	2.76 ± 0.76	0.005	
UA, μmol/L	381.91 ± 95.01	337.31 ± 89.48	< 0.001	
FBG, mmol/L	6.76 ± 2.03	5.33 ± 1.18	< 0.001	

	N (%)	N (%)	
Sex (% male)	107 (45.72)	449 (43.46%)	0.560
Hypertension	205 (87.61)	332 (32.14)	< 0.001
Abnormal ECG	148 (63.25)	615 (59.54)	0.302

Variables are described in terms of either mean ± SD or percentage. The p-value was calculated using the Student's t-test or the X² test. BMI: body mass index; SBP: systolic blood pressure; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; UA: uric acid; FBG: Fasting blood glucose; MetS: metabolic syndrome

Bivariate correlation analyses between the covariates and MetS

The results of the bivariate correlation analyses are shown in Table 2. The TG/HDL-C ratio, UA, BMI, WC, FBG, TG, DBP, SBP, and age were significantly correlated with MetS; however, sex, marital status, education, and ECG results were not.

Table 2 Correlations of patient characteristics with diagnosis of metabolic syndrome

Characteristic or	0	p-value
parameter		p-value
TG/HDL-C	0.420	< 0.001
UA, mmol/L	0.189	< 0.001
BMI, kg/m²	0.363	< 0.001
Waist circumference	0.308	< 0.001
FBG, mmol/L	0.364	< 0.001
LDL-C, mmol/L	0.059	0.037
HDL-C, mmol/L	-0.301	< 0.001
TC, mmol/L	0.057	0.044

TG	0.383	< 0.001
Sex	0.018	0.530
ECG	0.03	0.286
Age, years	-0.012	0.672
Education	-0.012	0.647
Hypertension	0.436	< 0.001
Marital status	-0.010	0.712
DBP, mm Hg	0.217	< 0.001
SBP, mm Hg	0.381	< 0.001

r = Kendall's tau-b correlation coefficient or Spearman's Rank correlation coefficient

Logistic regression analysis between TG/HDL-C ratio and MetS

Model 1 shows the association between the TG/HDL-C ratio and MetS without adjusting for any confounders (Table 3). The TG/HDL-C ratio is an independent risk factor for MetS. The unadjusted OR is 2.280 (95% CI: 1.947, 2.670), p < 0.001. After adjusting for potential confounders, we found that the TG/HDL-C ratio is still an independent risk factor for MetS (OR = 3.07 [95% CI: 2.402, 3.924], p < 0.001).

Table 3 Logistic regression results of the association of patient characteristics with MetS.

Model	Exposure	В	p-value	OR (95% CI)
Model 1	TG/HDL-C	0.824	<0.001	2.280 (1.947, 2.670)
	TG/HDL-C	1.136	<0.001	3.113 (2.442, 3.970)
	UA	0.003	0.022	1.003 (1.000, 1.005)
Model 2	BMI	0.305	<0.001	1.357 (1.264, 1.457)
	FBG	0.791	<0.001	2.205 (1.896, 2.564)
	Hypertensio	-4.469	<0.001	0.011 (0.005, 0.028)

	n			
	SBP	-0.009	0.351	0.991 (0.974, 1.009)
	DBP	-0.001	0.905	0.999 (0.979, 1.019)
	TG/HDL-C	1.122	<0.001	3.070 (2.402, 3.924)
	UA	0.003	0.023	1.003 (1.000, 1.005)
	BMI	0.299	<0.001	1.349 (1.225, 2.556)
	FBG	0.787	<0.001	2.198 (1.890, 2.556)
Model 3	Hypertensio n	-4.459	<0.001	0.012 (0.005, 0.029)
	SBP	-0.007	0.461	0.993 (0.975, 1.011)
	DBP	-0.004	0.733	0.996 (0.975, 1.018)
	Age	-0.024	0.254	0.976 (0.937, 1.017)
	Sex	-0.057	0.812	0.945 (0.593, 1.507)
1				

Model 1: crude model; Model 2: adjusted for UA, BMI, FBG, history of hypertension, SBP, DBP; Model 3: adjusted for age, sex, UA, BMI, FBG, history of hypertension, SBP, DBP

Receiver operating characteristic curve

By drawing receiver operating characteristic (ROC) curves, we found the best critical value is 1.49; the specificity and sensitivity were optimal (80.8% and 72.4%, respectively).

Figure1 Receiver operating characteristic curve

As shown in Figure 1, the horizontal axis represents one minus the specificity, and the vertical axis represents sensitivity. The area under the curve (AUC) for the TG vs HDL-C graph was 0.813 (95% CI: 0.784, 0.842), with a statistically significant prediction effect (p < 0.001).The Jordan index is 0.532, which also indicates that TG/HDL ratio has a good effect in predicting metabolic syndrome.

DISCUSSION

In this study, we verified the correlation between the TG/HDL-C ratio and MetS, and our results established the accuracy of the TG/HDL-C ratio as a diagnostic predictor of MetS among the elderly people in China.

In metabolic syndrome, TG and HDL are part of the diagnostic criteria, but the International Diabetes Association does not include TG/HDL-C ratio in the diagnosis of metabolic syndrome.[5] However, TG/HDL-C ratio seems to play an important role in metabolic disorders.[6] Large-scale prospective studies show that the TC/HDL-C ratio can be used as a reliable index to predict coronary heart disease and death.[7-14] A large number of studies have shown that TG/HDL-C can be used as a simple alternative indicator of insulin resistance. [15, 17] NCEP ATP III (the National Cholesterol Education Program Adult Treatment PanelIII) is the commonly used diagnostic standard of metabolic syndrome in the world. It considers insulin resistance, hypertension, atherosclerosis, and abdominal obesity as diagnostic criteria, [18] which indirectly shows that TG/HDL-C is feasible to predict metabolic syndrome. Recently, the TC/HDL-C ratio has been proposed as an alternative method to diagnose MetS. In a study of children and adolescents with obesity, the TG/HDL-C ratio had high sensitivity (80%) and specificity (75%) to MetS, with a cutoff point of 1.25.[6] In our study on an elderly population, a TG/HDL-C ratio of 1.49 was found to be the best critical value for predicting MetS. Clinical studies have shown that the TG/HDL-C ratio can be used to predict MetS and to assess the risk of cardiovascular events in older people. [19, 20] Most studies are limited to specific populations and races. For example, the TG/HDL-C ratio has been found to have a high predictive value for MetS among Korean adolescents.[21] Prior to our study, research on the link between TG/HDL-C and MetS in the Chinese elderly was rare. Additionally, many clinical trials to date have shown that lipid metabolism disorder has toxic effects on cells, which can affect the function of islet β cells and cause or aggravate insulin resistance.[22] Insulin resistance and deficiency of insulin secretion can further aggravate lipid metabolism disorders. [23,24] In the future, studies can carefully investigate the effectiveness of the TG/HDL-C ratio in the diagnosis of insulin

 BMJ Open

resistance since these measurements are usually easier to obtain than performing the insulin resistance test.

In our study, uric acid also showed a significant positive correlation with MetS. Experimental studies have shown that uric acid can penetrate smooth muscle fibers through the organic anion transport system, thereby activating various transmission pathways and increasing the expression of inflammatory mediators.[25,26] Therefore, further research into the relationship between uric acid and metabolic syndrome are needed in the future.

Our study found that with an increase in the TG/HDL-C ratio there was a gradual increase in the number of people diagnosed with MetS. The early detection of patients at a high risk for MetS through the measurement of the TG/HDL-C ratio can help to actively prevent or treat them before disease symptoms appear, thus providing patients with the greatest clinical benefit.

Limitations

The study participants all come from one community in China; therefore, the sample may not be representative of the elderly population in China. We recruited only those who had completed the comprehensive health examination, which may have biased our main findings. In addition, our analysis adjusted for age, sex, etc., but not for physical exercise and diet that are known to affect blood lipids. We expect more research to be done in the future based on this study.

CONCLUSIONS

We found a strong correlation between the TG/HDL-C ratio and MetS. Elderly Chinese people with a high TG/HDL-C ratio are at high risk of MetS. In our study sample, a TG/HDL-C ratio of 1.49 was found to be the optimal critical value for predicting MetS. This study is of great significance for the early identification and management of MetS among the elderly people in China. The measurement of the TG/HDL-C ratio can help clinicians to identify elderly people who need targeted

treatment, management, and follow-up.

ACKNOWLEDGMENTS: We would like to thank the participants for their contribution to this study.

AUTHOR CONTRIBUTIONS:

Study concept and design: Nieguqiao and Pengwen; **Data acquisition:** Nieguqiao and HouShukai; **Data analyses:** Nieguqiao, Zhangmeng and Pengwen; **Data interpretation:** Pengwen, Guqiao Nie. All authors contributed to writing, revising, and approving the final manuscript.

FUNDING: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

COMPETING INTERESTS: None declared.

PARTICIPANT CONSENT FOR PUBLICATION: Not required.

PROVENANCE AND PEER REVIEW: Not commissioned; externally peer reviewed.

DATA AVAILABILITY STATEMENT: No data are available.

REFERENCES

[1] Mohan V, Deepa M. The metabolic syndrome in developing countries. Diabetes Voice. 2006; 51: 15 - 17

[2] Fod ES,LiC,Sattar N.Metabolic sydrome and incident diabetes.Diabetes Care.2008;31(9):1989-1904

[3] Liu M, Wang J, Jiang B, Sun D, Wu L, Yang S, Wang Y, Li X, He Y. Increasing prevalence of metabolic syndrome in a Chinese elderly population: 2001-2010. PLoS One. 2013;8(6):e66233

[4] Vega GL, Barlow CE, Grundy SM, et al Triglyceride -toHigh-Density-Lipoprotein

-Cholesterol High-Density-Lipoprotein-Cholesterol Ratio Is an Index of Heart Disease Mortality and of Incidence of Type 2 Diabetes Mellitus in Men Journal of Investigative Medicine 2014;62:345-349

[5] Zimmet P, Alberti G, Kaufman F, Tajima N, Silink M, Arslanian S, et al. The metabolic syndrome in children and adolescents. Lancet 2007;369:2059 – 61

[6] Liang J, Fu J, Jiang Y, Dong G, Wang X, Wu W. TriGlycerides and high-density lipoprotein cholesterol ratio compared with homeostasis model assessment insulin resistance indexes in screening for metabolic syndrome in the chinese obese children: a cross section study. BMC Pediatr 2015;15:138

[7]Packard CJ, Shepherd J. Lipoprotein heterogenity and apolipoprotein B metabolism. Arterioscler Thromb Vasc Biol. 1999;19:2456 - 64

[8] McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. Ann Intern Med. 2003;139:802 – 9

[9]Giannini C, Santoro N, Caprio S, Kim G, Lartaud D,Shaw M, et al. The triglyceride-to-HDL cholesterol ratio:association with insulin resistance in obese youths of different ethnic backgrounds. Diabetes Care 2011;34:1869-74

[10] Grover SA, Palmer CS, Coupal L. Serum lipid screening to identify high-risk individuals for coronary death. The results of the Lipid Research Clinics prevalence cohort. Arch Intern Med 1994;154:679-84

[11] Maruyama C, Imamura K, Teramoto T. Assessment of LDL particle size by triglyceride/HDL-cholesterol ratio in non-diabetic, healthy subjects without prominent hyperlipidemia. J Atheroscler Thromb. 2003;10:186 – 91

[12] Pacifico L, Bonci E, Andreoli G, Romaggioli S, Di Miscio

R, Lombardo CV, et al. Association of serum triglyceride-to-HDL cholesterol ratio with carotid artery intima-media thickness, insulin resistance and nonalcoholic fatty liverdisease in children and adolescents. Nutr Metab Cardiovasc Dis 2014;24:737-43.

[13]Sang-Yhun Ju, MD, PhD,a,*June-Young Lee, PhD,b,and Do-Hoon Kim, MD, PhDc Association of metabolic syndrome and its components with all-cause and cardiovascular mortality in the elderly Medicine (Baltimore). 2017 Nov; 96(45): e8491

[14] Castelli WP, Garrison RJ, Wilson PW, Abbott RD, Kalousdian S, Kannel WB. Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham Study. JAMA 1986;256:2835-8

[15]Geloneze B, Vasques ACJ, Stabe CFC, Pareja JC, Rosado LEFPD, de Queiroz EC, et al. HOMA1-IR and HOMA2-IR indexes in identifying insulin resistance and metabolic syndrome - Brazilian Metabolic Syndrome Study (BRAMS). Arq Bras Endocrinol. 2009;53(2):281 – 7

[16] Galgani JE, Moro C, Ravussin E. Metabolic flexibility and insulin resistance. Am J
 Physiol Endocrinol Metab. 2008;295(5):E1009 - E1017.
 doi:10.1152/ajpendo.90558.2008

[17]Xingxing Ren 1, Zeng.ai Chen 2, Shuang Zheng 1, Tingting Han 1, Yangxue Li 1, Wei Liu 1, Yaomin Hu 1 * Association between Triglyceride to HDL-C Ratio (TG/HDL-C) and Insulin Resistance in Chinese Patients with Newly Diagnosed Type

BMJ Open

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
52	
53	
54	
55	
56	
57	
58	
59	

2PLOS ONE 2016; 11(4): e0154345

[18]Pérez-Martí nez P, Mikhailidis DP, Athyros VG, et al. Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation. Nutr Rev. 2017;75(5):307 - 326. doi:10.1093/nutrit/nux014

[19]Salazar MR, Carbajal HA, Espeche WG, Aizpurúa M, Maciel PM, Reaven GM.
 Identification of cardiometabolic risk: visceral adiposity index versus triglyceride/HDL
 cholesterol ratio. Am J Med.2014;127:152 - 7

[20] Da luz PL, Cesena FH, Favarato D, Cerqueira ES. Comparison of serum lipid values in patients with coronary artery disease at <50, 50 to 59, 60 to 69, and >70 years of age. Am J Cardiol.2005;96:1640 – 3

[21] Shou-Yu Chu, MD, Ji-Hyun Jung, MD, and Shin-Hye Kim, MD, PhD Ann

Pediatr Endocrinol Metab Risk assessment of metabolic syndrome in adolescents using the triglyceride/high-density lipoprotein cholesterol ratio and the total cholesterol/high-density lipoprotein cholesterol ratio. 2019 Mar; 24(1): 41 – 48

[22] Maruyama C, Imamura K, Teramoto T J Atheroscler Thromb. Assessment of LDL particle size by triglyceride/HDL-cholesterol ratio in non-diabetic, healthy subjects without prominent hyperlipidemia. 2003; 10(3):186-91

[23] Chen QJ Lai HM Chen BD Li XM Zhai H He CH Pan S Luo JY Gao J Liu F Ma YT Yang YN Appropriate LDL-C-to-HDL-C Ratio Cutoffs for Categorization of Cardiovascular Disease Risk Factors among Uygur Adults in Xinjiang, China. Int J Environ Res Public Health.Feb 192016 Feb 19;13(2):235

[24] Wei-Chung Yeh Yu-Chung Tsao Wen-Cheng Li I-Shiang Tzeng Liang-Sien Chen and Jau-Yuan ChenElevated Triglyceride-to-HDL cholesterol ratio is an indicator for insulin resistance in middle-aged and elderly Taiwanese population: a cross-sectional study Yeh et al. Lipids in Health and Disease 2019 Oct 11;18(1):176

[25] Soltani Z, Rasheed K, Kapusta DR, Reisin E Potential role of uric acid in metabolic

syndrome, hypertension, kidney injury, and cardiovascular diseases: is it time for reappraisal Curr Hypertens Rep. 2013 Jun; 15(3):175-81.

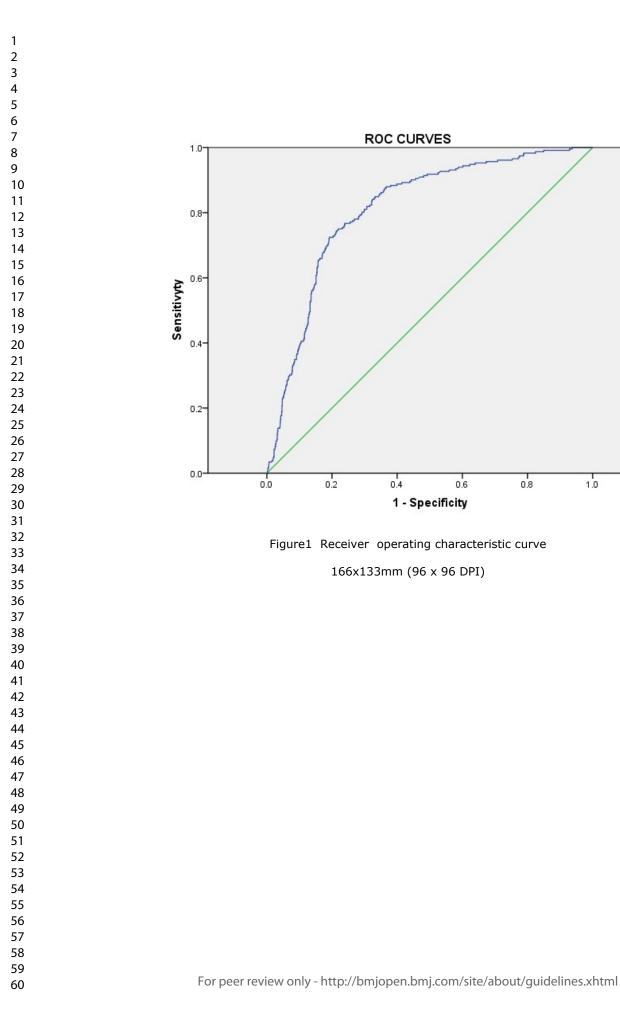
[26] Mukhopadhyay P, Ghosh S, Pandit K, Chatterjee P, Majhi B, Chowdhury S. Uric acid and its correlation with various metabolic parameters: A population-based study. Indian J Endocr Metab 2019;23:134-9.

for occurrence in the second

FIGURE LEGENDS

Figure 1. Receiver operating characteristic (ROC) curve of the TG/HDL-C ratio as a predictor of metabolic syndrome

to beet terien only



BMJ Open

BMJ Open

High TG/HDL ratio suggests a higher risk of metabolic syndrome among an elderly Chinese population: A crosssectional study

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-041519.R1
Article Type:	Original research
Date Submitted by the Author:	12-Nov-2020
Complete List of Authors:	Nie, Guqiao; Huazhong University of Science and Technology, Tongji Medical College Zhang, Meng; Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, HOU, KAI; Community health service center,Gutianstreet,Qiaokou District,Wuhan, Peng, Wen; Huazhong University of Science and Technology Tongji Medical College, the aDepartment of Geriatrics, Union Hospital
Primary Subject Heading :	Nutrition and metabolism
Secondary Subject Heading:	Cardiovascular medicine, Diabetes and endocrinology, Nutrition and metabolism
Keywords:	GERIATRIC MEDICINE, Valvular heart disease < CARDIOLOGY, Lipid disorders < DIABETES & ENDOCRINOLOGY

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

High TG/HDL ratio suggests a higher risk of metabolic syndrome among an elderly Chinese population: A cross-sectional study

Authors:

Guqiao Nie¹ (https://orcid.org/0000-0002-5467-6431) , Meng Zhang², Kaishu Hou^{3,} *Wen Peng

Author affiliations:

¹Department of Geriatrics, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

²Department of Geriatrics, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

³Community health service center, Gutian street, Qiaokou District, Wuhan 68 Gutian 2nd Road, Qiaokou District, Wuhan, China

*Corresponding author : Professor Wen Peng

Address:Department of Geriatrics, Union Hospital, Tongji Medical College,

Huazhong University of Science and Technology, Wuhan, China

Email: pengwen666@sina.com

Word count: 1938.

ABSTRACT

Objectives: To investigate the relationship between triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio and metabolic syndrome in the elderly population of China, and to determine the best critical value of TG/HDL-C in higher risk of metabolic syndrome in this population.

Design: Cross-sectional study.

Setting: Our study was conducted in a community physical examination center in Wuhan, China between January 1, 2016 and December 31, 2016.

Participants: The physical examination data from 1267 elderly people (aged over 65 years) in the community were analyzed in this study. The average age of the study participants was 71.64 ± 5.605 years.

Primary outcome measures: Correlation between the TG/HDL-C ratio and metabolic syndrome; the optimum cutoff of the TG/HDL-C ratio for the prediction of metabolic syndrome.

Results: The TG/HDL-C ratio showed a significant positive correlation with metabolic syndrome (r = 0.420, p < 0.001) in the elderly Chinese population. Binary logistic regression analysis showed that the TG/HDL-C ratio was an independent risk factor for metabolic syndrome (odds ratio = 3.07 [95% CI: 2.402, 3.924], p < 0.001) after adjusting for blood pressure, blood glucose, age, sex, and body mass index. The receiver operating characteristic curves of TG/HDL-C ratio and metabolic syndrome showed that in the elderly population a TG/HDL-C ratio of 1.49 can be used as the critical value for a higher risk of metabolic syndrome. At this value, the specificity and sensitivity of the measure were optimal (80.8% and 72.4%, respectively).

Conclusion: In this study, we found a significant correlation between TG/HDL-C ratio and metabolic syndrome. Therefore, the TG/HDL-C ratio metabolic syndrome among elderly people in China.

Keywords: Metabolic syndrome; Triglyceride-to-HDL cholesterol ratio;

Cardiovascular disease.

Strengths and limitations of this study

- The study sample had a wide age range (65–93 years), and the study included information on their basic characteristics like sex, waist circumference (WC), marital status, diagnosis of hypertension, etc.
- This study is the first to explore the correlation between the TG/HDL-C ratio and metabolic syndrome among elderly Chinese people.
- Our study is a cross-sectional study, which cannot reflect the causal relationship between TG/HDL and metabolic syndrome.
- Our study did not adjust for possible confounders such as exercise and lipid-regulating drugs.
- The study population came from only one community.



INTRODUCTION

Metabolic syndrome (MetS) refers to a pathological state involving the impaired metabolism of proteins, fats, carbohydrates, and other substances in the human body. It is a complex group of metabolic disorder syndromes, including risk factors associated with cardiovascular disease (CVD) and diabetes.[1, 2] The prevalence of MetS is high and rapidly increasing among the elderly population in China.[3] Risk factors include central obesity, increased blood pressure, increased fasting blood glucose (FBG) levels, and abnormal blood lipids. The prevalence of cardiovascular events and the risk of mortality are higher among patients with MetS than among the general population.[4] Therefore, the early diagnosis of MetS and timely intervention can prevent the unnecessary complications related to its progression and help reduce the risk of CVD caused by metabolic disorders. From a clinical perspective, individuals can benefit from the establishment of appropriate diagnostic methods and criteria that can accurately distinguish patients with MetS from healthy people.

This study aimed to explore the correlation between the ratio of triglycerides to high-density lipoprotein cholesterol in the blood (TG/HDL-C) and MetS in the elderly Chinese population, calculate the cutoff value of TG/HDL-C for higher risk of MetS in this population, and determine the optimal critical value for higher risk of MetS, in order to provide a theoretical basis for the early identification and management of elderly patients with MetS, as well as prevent the development of cardiovascular and cerebrovascular diseases.

PARTICIPANTS AND METHODS

Study population

This was a cross-sectional study , involving data from 1267 elderly individuals examined and interviewed at a community physical examination center, between January 1, 2016 and December 31, 2016. Participants' data were included in this study if the patient met all of the following inclusion criteria: lived in China, aged \geq 65 years, provided basic demographic information, provided accurate biochemical measurements, and consented to a full clinical examination.

Participants were excluded if they met one or more of the following exclusion criteria: incomplete data provided; presence of one of the following conditions: physical disability, acute infection, acute myocardial infarction, acute cerebral infarction, renal failure, dialysis, or active stage malignancies; or use of the following medications: hormone replacement therapy and oral or injectable glucocorticoids.

Clinical characteristics

Data for this study were obtained from the physical examination records of the elderly people in the community. General demographic and clinical data such as age, sex, marital status, height, weight, WC, and history of hypertension were obtained through oral interview. The doctor used a mercury sphygmomanometer on the upper arm to measure blood pressure–systolic blood pressure (SBP) and diastolic blood pressure (DBP). The average value of two blood pressure measurements taken at least five minutes apart was used.

Biochemical parameters

Biochemical indices including FBG, blood lipids, and uric acid (UA) were all measured using venous blood obtained from the participants on an empty stomach. Levels of serum UA, TGs, HDL-C and low-density lipoprotein cholesterol (LDL-C), and fasting blood glucose (FBG) were measured using Roche E602 and Roche C701 (both of which are automatic biochemical analyzers).

Definition of metabolic syndrome in this study

The diagnosis of MetS in this study was made according to the following definition provided by the Chinese Diabetes Society:

1. Overweight and/or obese: Body Mass Index (BMI) \ge 25 kg/m².

2. Hyperglycemia: FBG \ge 6.1 mmol/L (110 mg/dL), and/or 2h-plasma glucose (2h-PG) \ge 7.8 mmol/L (140 mg/dL), and/or people with diagnosed and treated diabetes.

3. Hypertension: SBP/DBP \geq 140/90 mm Hg and/or with diagnosed and treated hypertension.

4. Dyslipidemia: Fasting TGs ≥ 1.7 mmol/L (150 mg/dL) and/or fasting blood HDL-C <
0.9 mmol/L (35 mg/dL) (among males) and < 1.0 mmol/L (39 mg/dL) (among females).

MetS was diagnosed if at least three of the above four components were present.

Participant and public involvement

Participants were not involved in the design or conduct of the study. It is an anonymous, non-invasive examination, only oral notification, waiving the signing of written informed consent.

Ethics approval

This study was conducted in accordance with the contents of the Declaration of Helsinki. Since this study included identified data, participants were not required to provide informed consent. The study was approved by the Institutional Review Board of Tongji Medical College, Huazhong University of Science and Technology.(S273)

Statistical analyses

First, the data were divided into two groups according to the diagnosis of MetS, MetS group and non-MetS group. The percentage of participants in the above two groups that were positive for each component were reported and compared using the chi-square (X^2) test. The mean value \pm standard deviation (SD) was calculated for each of the continuous variables and compared using independent-samples t-tests, and other categorical variables were compared using the X^2 test. The Kendall's tau-b and Spearman's Rank correlation coefficients were used to analyze the correlation between MetS and the TG/HDL-C ratio, UA, BMI, WC, age, sex, and education. Binary logistic regression was used to analyze risk factors, and the results for each risk factor were described in terms of the non-standardized coefficient B, odds ratio (OR), its 95% confidence interval (95% CI), and p value. A receiver operating characteristic curve of MetS vs TG/HDL-C ratio was drawn to determine the optimum cutoff point for MetS diagnosis.

RESULTS

Clinical characteristics

The characteristics of the 1267 participants included in this study are shown in Table 1. The mean age of the participants was 71.64 ± 5.605 years. Participants diagnosed with MetS (MetS group) have statistically significant differences in the TG/HDL-C ratio, age, blood pressure, WC, FBG, UA level, hypertension, TG, and HDL-C compared with participants not diagnosed with MetS (Non-MetS group).

Table 1 Clinical characteristics of the different groups				
Characteristic or	MetS (N = 234)	Non-MetS	n valuo	
parameter	Wets (N – 254)	(N = 1033)	p-value	
	Mean ± SD	Mean ± SD		
Age, years	71.64 \pm 5.605	71.39 ± 5.409	< 0.001	
BMI, kg/m ²	27.14 ± 3.19	23.98 ± 3.25	< 0.001	
DBP, mm Hg	82.97 ± 10.97	76.54 ± 11.29	< 0.001	
SBP, mm Hg	148.08 ± 13.82	131.26 ± 18.17	< 0.001	
Waist circumference, cm	68.42 ± 10.29	60.39 ± 9.94	< 0.001	
TG/HDL-C	2.07 ± 1.09	1.17 ± 0.89	< 0.001	

TC, mmol/L	4.78 ± 1.10	4.60 ± 0.89	0.024
HDL, mmol/L	1.02 ± 0.22	2.75 ± 0.77	< 0.001
LDL, mmol/L	2.92 ± 0.91	2.76 ± 0.76	0.005
UA, μmol/L	381.91 ± 95.01	337.31 ± 89.48	< 0.001
FBG, mmol/L	6.76 ± 2.03	5.33 ± 1.18	< 0.001
	N (%)	N (%)	
Sex (% male)	107 (45.72)	449 (43.46%)	0.560
Hypertension	205 (87.61)	332 (32.14)	< 0.001
Abnormal ECG	148 (63.25)	615 (59.54)	0.302

Variables are described in terms of either mean ± SD or percentage. The p-value was calculated using the Student's t-test or the X² test. BMI: body mass index; SBP: systolic blood pressure; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; UA: uric acid; FBG: Fasting blood glucose; MetS: metabolic syndrome

Bivariate correlation analyses between the covariates and MetS

The results of the bivariate correlation analyses are shown in Table 2. The TG/HDL-C ratio, UA, BMI, WC, FBG, TG, DBP, SBP, and age were significantly correlated with MetS; however, sex, marital status, education, and ECG results were not.

Table 2 Correlations of patient characteristics with diagnosis of metabolic syndrome

Characteristic or	r	p-value
parameter		·
TG/HDL-C	0.420	< 0.001
UA, mmol/L	0.189	< 0.001
BMI, kg/m²	0.363	< 0.001
Waist circumference	0.308	< 0.001

, 0		
SBP, mm Hg	0.381	< 0.001
DBP, mm Hg	0.217	< 0.001
Marital status	-0.010	0.712
Hypertension	0.436	< 0.001
Education	-0.012	0.647
Age, years	-0.012	0.672
ECG	0.03	0.286
Sex	0.018	0.530
TG	0.383	< 0.001
TC, mmol/L	0.057	0.044
HDL-C, mmol/L	-0.301	< 0.001
LDL-C, mmol/L	0.059	0.037
FBG, mmol/L	0.364	< 0.001

r = Kendall's tau-b correlation coefficient or Spearman's Rank correlation coefficient

Logistic regression analysis between TG/HDL-C ratio and MetS

Model 1 shows the association between the TG/HDL-C ratio and MetS without adjusting for any confounders (Table 3). The TG/HDL-C ratio is an independent risk factor for MetS. The unadjusted OR is 2.280 (95% CI: 1.947, 2.670), p < 0.001. After adjusting for potential confounders, we found that the TG/HDL-C ratio is still an independent risk factor for MetS (OR = 3.07 [95% CI: 2.402, 3.924], p < 0.001).

Table 3 Logistic regression results of the association of patient characteristics with					
MetS.					
Model	Exposure	В	p-value	OR (95% CI)	
Model 1	TG/HDL-C	0.824	<0.001	2.280 (1.947, 2.670)	
Model 2	TG/HDL-C	1.136	<0.001	3.113 (2.442, 3.970)	

	UA	0.003	0.022	1.003 (1.000, 1.005)
	BMI	0.305	<0.001	1.357 (1.264, 1.457)
	FBG	0.791	<0.001	2.205 (1.896, 2.564)
	Hypertension	-4.469	<0.001	0.011 (0.005, 0.028)
	SBP	-0.009	0.351	0.991 (0.974, 1.009)
	DBP	-0.001	0.905	0.999 (0.979, 1.019)
Model 3	TG/HDL-C	1.122	<0.001	3.070 (2.402, 3.924)
	UA	0.003	0.023	1.003 (1.000, 1.005)
	BMI	0.299	<0.001	1.349 (1.225, 2.556)
	FBG	0.787	<0.001	2.198 (1.890, 2.556)
	Hypertension	-4.459	<0.001	0.012 (0.005, 0.029)
	SBP	-0.007	0.461	0.993 (0.975, 1.011)
	DBP	-0.004	0.733	0.996 (0.975, 1.018)
	Age	-0.024	0.254	0.976 (0.937, 1.017)
	Sex	-0.057	0.812	0.945 (0.593, 1.507)
1				

Model 1: crude model; Model 2: adjusted for UA, BMI, FBG, history of hypertension, SBP, DBP; Model 3: adjusted for age, sex, UA, BMI, FBG, history of hypertension, SBP, DBP

Receiver operating characteristic curve

By drawing receiver operating characteristic (ROC) curves, we found the best critical value is 1.49; the specificity and sensitivity were optimal (80.8% and 72.4%, respectively).

Figure1 Receiver operating characteristic curve

As shown in Figure 1, the horizontal axis represents one minus the specificity, and the vertical axis represents sensitivity. The area under the curve (AUC) for the TG vs HDL-C graph was 0.813 (95% CI: 0.784, 0.842), with a statistically significant prediction effect (p < 0.001). The Jordan index is 0.532, which also indicates that

TG/HDL ratio has a good effect in higher risk of metabolic syndrome.

DISCUSSION

In this study, we verified the correlation between the TG/HDL-C ratio and MetS, and our results established the accuracy of the TG/HDL-C ratio as a diagnostic for higher risk of MetS among the elderly people in China.

In metabolic syndrome, TG and HDL are part of the diagnostic criteria, but the International Diabetes Association does not include TG/HDL-C ratio in the diagnosis of metabolic syndrome.[5] However, TG/HDL-C ratio seems to play an important role in metabolic disorders.[6] Large-scale prospective studies show that the TC/HDL-C ratio can be used as a reliable index to predict coronary heart disease and death.[7-14] A large number of studies have shown that TG/HDL-C can be used as a simple alternative indicator of insulin resistance.[15-17] NCEP ATP III(the National Cholesterol Education Program Adult Treatment PanelIII) is the commonly used diagnostic standard of metabolic syndrome in the world. It considers insulin resistance, hypertension, atherosclerosis, and abdominal obesity as diagnostic criteria, [18] which indirectly shows that TG/HDL-C is feasible to predict metabolic syndrome. Recently, the TC/HDL-C ratio has been proposed as an alternative method to diagnose MetS. In a study of children and adolescents with obesity, the TG/HDL-C ratio had high sensitivity (80%) and specificity (75%) to MetS, with a cutoff point of 1.25.[6] In our study on an elderly population, a TG/HDL-C ratio of 1.49 was found to be the best critical value. Clinical studies have shown that the TG/HDL-C ratio can be used to predict MetS and to assess the risk of cardiovascular events in older people. [19, 20] Most studies are limited to specific populations and races. For example, the TG/HDL-C ratio has been found to have a high predictive value for MetS among Korean adolescents. [21] Prior to our study, research on the link between TG/HDL-C and MetS in the Chinese elderly was rare. Additionally, many clinical trials to date have shown that lipid metabolism disorder has toxic effects on cells, which can affect the function of islet β cells and cause or aggravate insulin

BMJ Open

resistance.[22] Insulin resistance and deficiency of insulin secretion can further aggravate lipid metabolism disorders.[23,24] In the future, studies can carefully investigate the effectiveness of the TG/HDL-C ratio in the diagnosis of insulin resistance since these measurements are usually easier to obtain than performing the insulin resistance test.

In our study, uric acid also showed a significant positive correlation with MetS. Experimental studies have shown that uric acid can penetrate smooth muscle fibers through the organic anion transport system, thereby activating various transmission pathways and increasing the expression of inflammatory mediators.[25,26] Therefore, further research into the relationship between uric acid and metabolic syndrome are needed in the future. After consulting the literature, we have studies suggesting that there is a correlation between uric acid, age, sex and metabolic syndrome, [27-29]and our research has also found this. In order to eliminate these variables known to be associated with metabolic syndrome, we performed a multiple logistic regression analysis to eliminate the interference of these confounding factors.

Our study found that with an increase in the TG/HDL-C ratio there was a gradual increase in the number of people diagnosed with MetS. When TG/HDL is greater than 1.49, it indicates that the patient is at a high risk of metabolic syndrome. At the same time, we need to attach great importance to the patient's uric acid, fasting blood sugar, and blood pressure. The early detection of patients at a high risk for MetS through the measurement of the TG/HDL-C ratio can help to actively prevent or treat them before disease symptoms appear, thus providing patients with the greatest clinical benefit.

Limitations

The study participants all come from one community in China; therefore, the sample may not be representative of the elderly population in China. We recruited only those who had completed the comprehensive health examination, which may have biased our main findings. Our study is a cross-sectional study, which cannot reflect the causal relationship between TG/HDL and metabolic syndrome. In addition, our analysis adjusted for age, sex, etc., but not for physical exercise and diet that are known to affect blood lipids. We expect more research to be done in the future based on this study.

CONCLUSIONS

We found a strong correlation between the TG/HDL-C ratio and MetS. Elderly Chinese people with a high TG/HDL-C ratio are at high risk of MetS. In our study sample, a TG/HDL-C ratio of 1.49 was found to be the optimal critical value. This study is of great significance for the early identification and management of MetS among the elderly people in China. The measurement of the TG/HDL-C ratio can help clinicians to identify elderly people who need targeted treatment, management, and follow-up.

ACKNOWLEDGMENTS: We would like to thank the participants for their contribution to this study.

AUTHOR CONTRIBUTIONS:

Study concept and design: Nieguqiao and Pengwen; **Data acquisition:** Nieguqiao and HouKaishu; **Data analyses:** Nieguqiao, Zhangmeng and Pengwen; **Data interpretation:** Pengwen, NieGuqiao. All authors contributed to writing, revising, and approving the final manuscript.

FUNDING: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

COMPETING INTERESTS: None declared.

PARTICIPANT CONSENT FOR PUBLICATION: Not required.

PROVENANCE AND PEER REVIEW: Not commissioned; externally peer reviewed.

1 2	
3	
4	DATA AVAILABILITY STATEMENT: No data are available.
5	
6 7	
7 8	
9	
10	
11	
12	
13 14	
14	
16	
17	
18	
19	
20 21	
21	
23	
24	
25	
26	
27 28	
28	
30	
31	
32	
33 34	
35	
36	
37	
38	
39 40	
40	
42	
43	
44	
45 46	
40 47	
48	
49	
50	
51 52	
52 53	
54	
55	
56	
57	
58 50	
59 60	

REFERENCES

[1] Mohan V, Deepa M. The metabolic syndrome in developing countries. Diabetes
 Voice. 2006; 51:15 - 17

[2] Fod ES,LiC,Sattar N.Metabolic sydrome and incident diabetes.Diabetes Care.2008;31(9):1989-1904

[3] Liu M, Wang J, Jiang B, Sun D, Wu L, Yang S, Wang Y, Li X, He Y. Increasing Prevalence of Metabolic Syndrome in a Chinese Elderly Population: 2001-2010. PLoS One. 2013 Jun 18;8(6):e66233.

[4] Vega GL, Barlow CE, Grundy SM, Leonard D, DeFina LF. Triglyceride-to-high-density-lipoprotein-cholesterol ratio is an index of heart disease mortality and of incidence of type 2 diabetes mellitus in men. J Investig Med. 2014 Feb;62(2):345-9.

[5] Zimmet P, Alberti G, Kaufman F, Tajima N, Silink M, Arslanian S, et al. The metabolic syndrome in children and adolescents. Lancet 2007;369:2059 – 61

[6] Liang J, Fu J, Jiang Y, Dong G, Wang X, Wu W. TriGlycerides and high-density lipoprotein cholesterol ratio compared with homeostasis model assessment insulin resistance indexes in screening for metabolic syndrome in the chinese obese children: a cross section study. BMC Pediatr 2015;15:138

[7]Packard CJ, Shepherd J. Lipoprotein heterogenity and apolipoprotein B metabolism. Arterioscler Thromb Vasc Biol. 1999;19:2456 - 64

[8] McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. Ann Intern Med. 2003;139:802 – 9

[9]Giannini C, Santoro N, Caprio S, Kim G, Lartaud D,Shaw M, et al. The triglyceride-to-HDL cholesterol ratio:association with insulin resistance in obese youths of different ethnic backgrounds. Diabetes Care 2011;34:1869-74

BMJ Open

[10] Grover SA, Palmer CS, Coupal L. Serum lipid screening to identify high-risk individuals for coronary death. The results of the Lipid Research Clinics prevalence cohort. Arch Intern Med 1994;154:679-84

[11] Maruyama C, Imamura K, Teramoto T. Assessment of LDL particle size by triglyceride/HDL-cholesterol ratio in non-diabetic, healthy subjects without prominent hyperlipidemia. J Atheroscler Thromb. 2003;10:186 – 91

[12] Pacifico L, Bonci E, Andreoli G, Romaggioli S, Di Miscio R, Lombardo CV, Chiesa C. Association of serum triglyceride-to-HDL cholesterol ratio with carotid artery intima-media thickness, insulin resistance and nonalcoholic fatty liver disease in children and adolescents. Nutr Metab Cardiovasc Dis. 2014 Jul;24(7):737-43..

[13]Sang-Yhun Ju, MD, PhD,a,*June-Young Lee, PhD,b,and Do-Hoon Kim, MD, PhDc Association of metabolic syndrome and its components with all-cause and cardiovascular mortality in the elderly Medicine (Baltimore). 2017 Nov; 96(45): e8491

[14] Castelli WP, Garrison RJ, Wilson PW, Abbott RD, Kalousdian S, Kannel WB. Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham Study. JAMA 1986;256:2835-8

[15]Geloneze B, Vasques ACJ, Stabe CFC, Pareja JC, Rosado LEFPD, de Queiroz EC, et al. HOMA1-IR and HOMA2-IR indexes in identifying insulin resistance and metabolic syndrome - Brazilian Metabolic Syndrome Study (BRAMS). Arq Bras Endocrinol. 2009;53(2):281 – 7

[16] Galgani JE, Moro C, Ravussin E. Metabolic flexibility and insulin resistance. Am JPhysiol Endocrinol Metab. 2008 Nov;295(5):E1009-17

[17] Ren X, Chen ZA, Zheng S, Han T, Li Y, Liu W, Hu Y. Association between Triglyceride to HDL-C Ratio (TG/HDL-C) and Insulin Resistance in Chinese Patients with Newly Diagnosed Type 2 Diabetes Mellitus. PLoS One. 2016 Apr 26;11(4):e0154345.

[18]Pérez-Martínez P, Mikhailidis DP, Athyros VG, et al. Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation. Nutr Rev. 2017;75(5):307 - 326.

[19]Salazar MR, Carbajal HA, Espeche WG, Aizpurúa M, Maciel PM, Reaven GM. Identification of cardiometabolic risk: visceral adiposity index versus triglyceride/HDL cholesterol ratio. Am J Med.2014;127:152 - 7

[20] Da luz PL, Cesena FH, Favarato D, Cerqueira ES. Comparison of serum lipid values in patients with coronary artery disease at <50, 50 to 59, 60 to 69, and >70 years of age. Am J Cardiol.2005;96:1640 – 3

[21] Shou-Yu Chu, MD, Ji-Hyun Jung, MD, and Shin-Hye Kim, MD, PhD Ann

Pediatr Endocrinol Metab Risk assessment of metabolic syndrome in adolescents using the triglyceride/high-density lipoprotein cholesterol ratio and the total cholesterol/high-density lipoprotein cholesterol ratio. 2019 Mar; 24(1): 41 – 48

[22] Maruyama C, Imamura K, Teramoto T. Assessment of LDL particle size by triglyceride/HDL-cholesterol ratio in non-diabetic, healthy subjects without prominent hyperlipidemia. J Atheroscler Thromb. 2003;10(3):186-91.

[23] Chen QJ Lai HM Chen BD Li XM Zhai H He CH Pan S Luo JY Gao J Liu F Ma YT Yang YN Appropriate LDL-C-to-HDL-C Ratio Cutoffs for Categorization of Cardiovascular Disease Risk Factors among Uygur Adults in Xinjiang, China. Int J Environ Res Public Health.Feb 192016 Feb 19;13(2):235

[24] Yeh WC, Tsao YC, Li WC, Tzeng IS, Chen LS, Chen JY. Elevated triglyceride-to-HDL cholesterol ratio is an indicator for insulin resistance in middle-aged and elderly Taiwanese population: a cross-sectional study. Lipids Health Dis. 2019 Oct 11;18(1):176.

[25] Soltani Z, Rasheed K, Kapusta DR, Reisin E Potential role of uric acid in metabolic syndrome, hypertension, kidney injury, and cardiovascular diseases: is it time for reappraisal Curr Hypertens Rep. 2013 Jun; 15(3):175-81.

[26] Mukhopadhyay P, Ghosh S, Pandit K, Chatterjee P, Majhi B, Chowdhury S. Uric acid and its correlation with various metabolic parameters: A population-based study. Indian J Endocr Metab 2019;23:134-9.

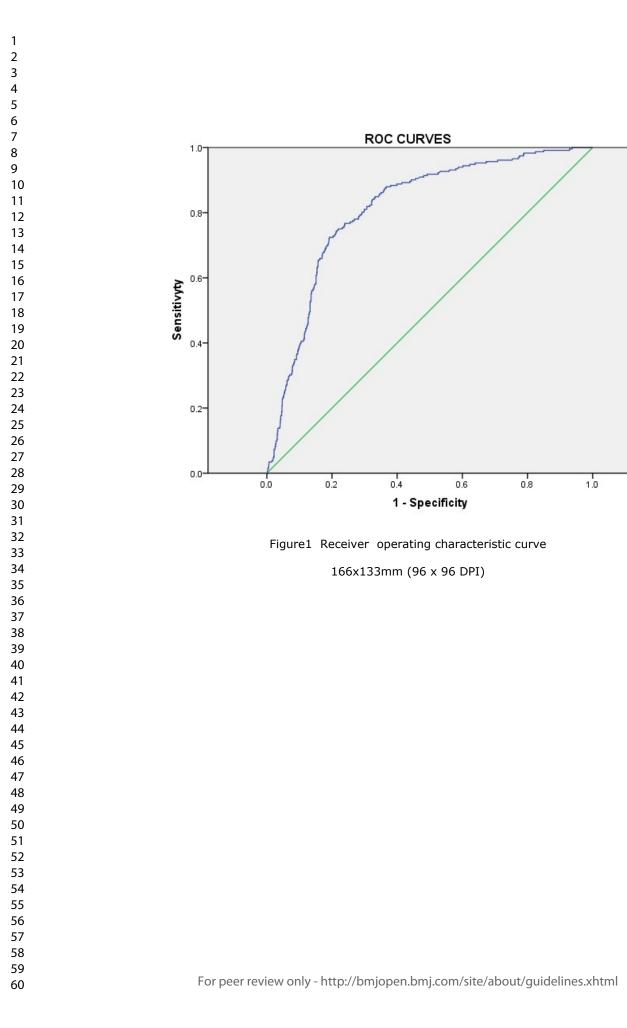
[27] King C, Lanaspa MA, Jensen T, Tolan DR, Sánchez-Lozada LG, Johnson RJ. Uric Acid as a Cause of the Metabolic Syndrome. Contrib Nephrol. 2018;192:88-102.

[28] Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Med. 2011 May 5;9:48.

[29] Kanbay M, Jensen T, Solak Y, Le M, Roncal-Jimenez C, Rivard C, Lanaspa MA, Nakagawa T, Johnson RJ. Uric acid in metabolic syndrome: From an innocent bystander to a central player. Eur J Intern Med. 2016 Apr;29:3-8.

FIGURE LEGENDS

Figure 1. Receiver operating characteristic (ROC) curve of the TG/HDL-C ratio as a high-risk indicators of metabolic syndrome



	Item No	Recommendation	Pag No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	2
		(<i>b</i>) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods		A	
Study design	4	Present key elements of study design early in the paper	5,6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5,6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	13
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how due study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	7,8
		(b) Describe any methods used to examine subgroups and interactions(c) Explain how missing data were addressed	7,8
		(<i>d</i>) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	 (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage 	
Descriptive data	14*	(c) Consider use of a flow diagram(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8,9
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(<i>a</i>) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10,11

3
4
5
6
7
8
9
10
11
12
13
13 14
14
15
16
17
18
19
20
21
22
22
23 24
25
26
27
28
29
30
31
32
32 33
34
35
36
37
38
39
40
41
43
44
45
46
47
48
49
50
51
51 52
53
54
55
56
57
58
59
29

1 2

		(<i>b</i>) Report category boundaries when continuous variables were categorized	
		(<i>c</i>) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9,10,11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential	13
		bias or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	12
-		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

BMJ Open

High TG/HDL ratio suggests a higher risk of metabolic syndrome among an elderly Chinese population: A crosssectional study

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-041519.R2
Article Type:	Original research
Date Submitted by the Author:	26-Dec-2020
Complete List of Authors:	Nie, Guqiao; Huazhong University of Science and Technology, Tongji Medical College Zhang, Meng; Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, HOU, KAI; Community health service center,Gutianstreet,Qiaokou District,Wuhan, Peng, Wen; Huazhong University of Science and Technology Tongji Medical College, the aDepartment of Geriatrics, Union Hospital
Primary Subject Heading :	Nutrition and metabolism
Secondary Subject Heading:	Cardiovascular medicine, Diabetes and endocrinology, Nutrition and metabolism
Keywords:	GERIATRIC MEDICINE, Valvular heart disease < CARDIOLOGY, Lipid disorders < DIABETES & ENDOCRINOLOGY

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

High TG/HDL ratio suggests a higher risk of metabolic syndrome among an elderly Chinese population: A cross-sectional study

Authors:

Guqiao Nie¹ (https://orcid.org/0000-0002-5467-6431) , Meng Zhang², Kaishu Hou^{3,} *Wen Peng

Author affiliations:

¹Department of Geriatrics, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

²Department of Geriatrics, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

³Community health service center, Gutian street, Qiaokou District, Wuhan 68 Gutian 2nd Road, Qiaokou District, Wuhan, China

*Corresponding author : Professor Wen Peng

Address:Department of Geriatrics, Union Hospital, Tongji Medical College,

Huazhong University of Science and Technology, Wuhan, China

Email: pengwen666@sina.com

Word count: 2026.

ABSTRACT

Objectives: To investigate the relationship between triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio and metabolic syndrome in the elderly population of China, and to determine the best critical value of TG/HDL-C in higher risk of metabolic syndrome in this population.

Design: Cross-sectional study.

Setting: Our study was conducted in a community physical examination center in Wuhan, China between January 1, 2016 and December 31, 2016.

Participants: The physical examination data from 1267 elderly people (aged over 65 years) in the community were analyzed in this study. The average age of the study participants was 71.64 ± 5.605 years.

Primary outcome measures: Correlation between the TG/HDL-C ratio and metabolic syndrome; the optimum cutoff of the TG/HDL-C ratio for the prediction of metabolic syndrome.

Results: The TG/HDL-C ratio showed a significant positive correlation with metabolic syndrome (r = 0.420, p < 0.001) in the elderly Chinese population. Binary logistic regression analysis showed that the TG/HDL-C ratio was an independent risk factor for metabolic syndrome (odds ratio = 3.07 [95% CI: 2.402, 3.924], p < 0.001) after adjusting for blood pressure, blood glucose, age, sex, and body mass index. The receiver operating characteristic curves of TG/HDL-C ratio and metabolic syndrome showed that in the elderly population a TG/HDL-C ratio of 1.49 can be used as the critical value for a higher risk of metabolic syndrome. At this value, the specificity and sensitivity of the measure were optimal (80.8% and 72.4%, respectively).

Conclusion: In this study, we found a significant correlation between TG/HDL-C ratio and metabolic syndrome. Therefore, the TG/HDL-C ratio metabolic syndrome among elderly people in China.

Keywords: Metabolic syndrome; Triglyceride-to-HDL cholesterol ratio;

Cardiovascular disease.

Strengths and limitations of this study

- The study sample had a wide age range (65–93 years), and the study included information on their basic characteristics like sex, waist circumference (WC), marital status, diagnosis of hypertension, etc.
- This study is the first to explore the correlation between the TG/HDL-C ratio and metabolic syndrome among elderly Chinese people.
- Our study is a cross-sectional study, which cannot reflect the causal relationship between TG/HDL and metabolic syndrome.
- Our study did not adjust for possible confounders such as exercise and lipidregulating drugs.
- The study population came from only one community.



INTRODUCTION

Metabolic syndrome (MetS) refers to a pathological state involving the impaired metabolism of proteins, fats, carbohydrates, and other substances in the human body. It is a complex group of metabolic disorder syndromes, including risk factors associated with cardiovascular disease (CVD) and diabetes.[1, 2] The prevalence of MetS is high and rapidly increasing among the elderly population in China.[3] Risk factors include central obesity, increased blood pressure, increased fasting blood glucose (FBG) levels, and abnormal blood lipids. The prevalence of cardiovascular events and the risk of mortality are higher among patients with MetS than among the general population.[4] Therefore, the early diagnosis of MetS and timely intervention can prevent the unnecessary complications related to its progression and help reduce the risk of CVD caused by metabolic disorders. From a clinical perspective, individuals can benefit from the establishment of appropriate diagnostic methods and criteria that can accurately distinguish patients with MetS from healthy people.

This study aimed to explore the correlation between the ratio of triglycerides to high-density lipoprotein cholesterol in the blood (TG/HDL-C) and MetS in the elderly Chinese population, calculate the cutoff value of TG/HDL-C for higher risk of MetS in this population, and determine the optimal critical value for higher risk of MetS, in order to provide a theoretical basis for the early identification and management of elderly patients with MetS, as well as prevent the development of cardiovascular and cerebrovascular diseases.

PARTICIPANTS AND METHODS

Study population

This was a cross-sectional study , involving data from 1267 elderly individuals examined and interviewed at a community physical examination center, between January 1, 2016 and December 31, 2016. Participants' data were included in this study if the patient met all of the following inclusion criteria: lived in China, aged \geq 65 years, provided basic demographic information, provided accurate biochemical measurements, and consented to a full clinical examination.

Participants were excluded if they met one or more of the following exclusion criteria: incomplete data provided; presence of one of the following conditions: physical disability, acute infection, acute myocardial infarction, acute cerebral infarction, renal failure, dialysis, or active stage malignancies; or use of the following medications: hormone replacement therapy and oral or injectable glucocorticoids.

Clinical characteristics

Data for this study were obtained from the physical examination records of the elderly people in the community. General demographic and clinical data such as age, sex, marital status, height, weight, WC, and history of hypertension were obtained through oral interview. The doctor used a mercury sphygmomanometer on the upper arm to measure blood pressure–systolic blood pressure (SBP) and diastolic blood pressure (DBP). The average value of two blood pressure measurements taken at least five minutes apart was used.

Biochemical parameters

Biochemical indices including FBG, blood lipids, and uric acid (UA) were all measured using venous blood obtained from the participants on an empty stomach. Levels of serum UA, TGs, HDL-C and low-density lipoprotein cholesterol (LDL-C), and fasting blood glucose (FBG) were measured using Roche E602 and Roche C701 (both of which are automatic biochemical analyzers).

Definition of metabolic syndrome in this study

The diagnosis of MetS in this study was made according to the following definition provided by the Chinese Diabetes Society:

1. Overweight and/or obese: Body Mass Index (BMI) \ge 25 kg/m².

2. Hyperglycemia: FBG \geq 6.1 mmol/L (110 mg/dL), and/or 2h-plasma glucose (2h-PG) \geq 7.8 mmol/L (140 mg/dL), and/or people with diagnosed and treated diabetes.

3. Hypertension: SBP/DBP \geq 140/90 mm Hg and/or with diagnosed and treated hypertension.

4. Dyslipidemia: Fasting TGs ≥ 1.7 mmol/L (150 mg/dL) and/or fasting blood HDL-C <
0.9 mmol/L (35 mg/dL) (among males) and < 1.0 mmol/L (39 mg/dL) (among females).

MetS was diagnosed if at least three of the above four components were present.

Participant and public involvement

Participants were not involved in the design or conduct of the study. It is an anonymous, non-invasive examination, only oral notification, waiving the signing of written informed consent.

Ethics approval

This study was conducted in accordance with the contents of the Declaration of Helsinki. Since this study included identified data, participants were not required to provide informed consent. The study was approved by the Institutional Review Board of Tongji Medical College, Huazhong University of Science and Technology.(S273)

Statistical analyses

First, the data were divided into two groups according to the diagnosis of MetS, MetS group and non-MetS group. The percentage of participants in the above two groups that were positive for each component were reported and compared using the chi-square (X^2) test. The mean value \pm standard deviation (SD) was calculated for each of the continuous variables and compared using independent-samples ttests, and other categorical variables were compared using the *X*² test. The Kendall's tau-b and Spearman's Rank correlation coefficients were used to analyze the correlation between MetS and the TG/HDL-C ratio, UA, BMI, WC, age, sex, and education. Binary logistic regression was used to analyze risk factors, and the results for each risk factor were described in terms of the non-standardized coefficient B, odds ratio (OR), its 95% confidence interval (95% CI), and p value. A receiver operating characteristic curve of MetS vs TG/HDL-C ratio was drawn to determine the optimum cutoff point for MetS diagnosis.

RESULTS

Clinical characteristics

The characteristics of the 1267 participants included in this study are shown in Table 1. The mean age of the participants was 71.64 ± 5.605 years. Participants diagnosed with MetS (MetS group) have statistically significant differences in the TG/HDL-C ratio, age, blood pressure, WC, FBG, UA level, hypertension, TG, and HDL-C compared with participants not diagnosed with MetS (Non-MetS group).

Table 1 Clinical characteristics of the different groups					
Characteristic or	MetS (N = 234)	Non-MetS	p-value		
parameter	Mets (N – 254)	(N = 1033)	p-value		
	Mean ± SD	Mean ± SD			
Age, years	71.64 \pm 5.605	71.39 ± 5.409	< 0.001		
BMI, kg/m ²	27.14 ± 3.19	23.98 ± 3.25	< 0.001		
DBP, mm Hg	82.97 ± 10.97	76.54 ± 11.29	< 0.001		
SBP, mm Hg	148.08 ± 13.82	131.26 ± 18.17	< 0.001		
Waist circumference, cm	68.42 ± 10.29	60.39 ± 9.94	< 0.001		
TG/HDL-C	2.07 ± 1.09	1.17 ± 0.89	< 0.001		
TC, mmol/L	4.78 ± 1.10	4.60 ± 0.89	0.024		

HDL, mmol/L	1.02 ± 0.22	2.75 ± 0.77	< 0.001
LDL, mmol/L	2.92 ± 0.91	2.76 ± 0.76	0.005
UA, μmol/L	381.91 ± 95.01	337.31 ± 89.48	< 0.001
FBG, mmol/L	6.76 ± 2.03	5.33 ± 1.18	< 0.001
	N (%)	N (%)	
Gender (% male)	107 (45.72)	449 (43.46%)	0.560
Hypertension	205 (87.61)	332 (32.14)	< 0.001
Abnormal ECG	148 (63.25)	615 (59.54)	0.302

Variables are described in terms of either mean ± SD or percentage. The p-value was calculated using the Student's t-test or the X² test. BMI: body mass index; SBP: systolic blood pressure; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; UA: uric acid; FBG: Fasting blood glucose; MetS: metabolic syndrome

Bivariate correlation analyses between the covariates and MetS

The results of the bivariate correlation analyses are shown in Table 2. The TG/HDL-C ratio, UA, BMI, WC, FBG, TG, DBP, SBP, and age were significantly correlated with MetS; however, gender, marital status, education, and ECG results were not.

Table 2 Correlations of patient characteristics with diagnosis of metabolic syndrome

Characteristic or parameter	r	p-value
TG/HDL-C	0.420	< 0.001
UA, mmol/L	0.189	< 0.001
BMI, kg/m²	0.363	< 0.001
Waist circumference	0.308	< 0.001
FBG, mmol/L	0.364	< 0.001

LDL-C, mmol/L	0.059	0.037
HDL-C, mmol/L	-0.301	< 0.001
TC, mmol/L	0.057	0.044
TG, mmol/L	0.383	< 0.001
Gender	0.018	0.530
ECG	0.03	0.286
Age, years	-0.012	0.672
Education	-0.012	0.647
Hypertension	0.436	< 0.001
Marital status	-0.010	0.712
DBP, mm Hg	0.217	< 0.001
SBP, mm Hg	0.381	< 0.001

r = Kendall's tau-b correlation coefficient or Spearman's Rank correlation coefficient

Logistic regression analysis between TG/HDL-C ratio and MetS

Model 1 shows the association between the TG/HDL-C ratio and MetS without adjusting for any confounders (Table 3). The TG/HDL-C ratio is an independent risk factor for MetS. The unadjusted OR is 2.280 (95% CI: 1.947, 2.670), p < 0.001. After adjusting for potential confounders, we found that the TG/HDL-C ratio is still an independent risk factor for MetS (OR = 2.301 [95% CI: 1.884,2.811], p < 0.001).

Table 3 Logistic regression results of the association of patient characteristics with MetS.				
Model	Exposure	В	p- value	OR (95% CI)
Model 1	TG/HDL-C	0.824	<0.001	2.280 (1.947, 2.670)
	TG/HDL	0.842	<0.001	2.321 (1.903,2.831)
Model	FBG	0.616	<0.001	1.852 (1.638,2.095)

0.250	<0.001	
0.259	<0.001	1.295 (1.218,1.377)
0.003	0.009	1.003(1.001,1.005)
0.056	<0.001	1.058(1.044,1.072)
0.023	0.019	1.023 (1.004,1.043)
0.834	<0.001	2.301(1.884,2.811)
0.616	<0.001	1.851(1.636,2.094)
0.255	<0.001	1.29(1.212,1.374)
0.003	0.009	1.003(1.001,1.005)
0.058	<0.001	1.06(1.046,1.074)
0.021	0.039	1.021(1.001,1.041)
-0.038	0.858	0.963(0.635,1.459)
-0.023	0.219	0.977(0.942,1.014)
	-0.023	-0.038 0.858 -0.023 0.219 odel; Model 2: adjusted for UA, BN

adjusted for age, gender, UA, BMI, FBG, SBP, DBP

Receiver operating characteristic curve

By drawing receiver operating characteristic (ROC) curves, we found the best critical value is 1.49; the specificity and sensitivity were optimal (80.8% and 72.4%, respectively).

Figure1 Receiver operating characteristic curve

As shown in Figure 1, the horizontal axis represents one minus the specificity, and the vertical axis represents sensitivity. The area under the curve (AUC) for the TG vs HDL-C graph was 0.813 (95% CI: 0.784, 0.842), with a statistically significant prediction effect (p < 0.001). The Jordan index is 0.532, which also indicates that TG/HDL ratio has a good effect in higher risk of metabolic syndrome. In addition, In view of the influence of gender in metabolic syndrome, we drew ROC curves for men and women. The best cutoff values are 1.437 and 1.196 respectively. The sensitivity and specificity are 74.8%, 78.4% for men and 86.4% for women. 67.4%.Finally, we

use TG and HDL to draw the ROC curve separately, and we can see that the predicted value of both is lower than the ratio of the two as the figure1 shows (the AUC of TG and HDL are 0.786, 0.276, respectively).

DISCUSSION

 In this study, we verified the correlation between the TG/HDL-C ratio and MetS, and our results established the accuracy of the TG/HDL-C ratio as a diagnostic for higher risk of MetS among the elderly people in China.

In metabolic syndrome, TG and HDL are part of the diagnostic criteria, but the International Diabetes Association does not include TG/HDL-C ratio in the diagnosis of metabolic syndrome.[5] However, TG/HDL-C ratio seems to play an important role in metabolic disorders. [6] Large-scale prospective studies show that the TC/HDL-C ratio can be used as a reliable index to predict coronary heart disease and death.[7-14] A large number of studies have shown that TG/HDL-C can be used as a simple alternative indicator of insulin resistance. [15-17] NCEP ATP III (the National Cholesterol Education Program Adult Treatment PanelIII) is the commonly used diagnostic standard of metabolic syndrome in the world. It considers insulin resistance, hypertension, atherosclerosis, and abdominal obesity as diagnostic criteria, [18] which indirectly shows that TG/HDL-C is feasible to predict metabolic syndrome. Recently, the TC/HDL-C ratio has been proposed as an alternative method to diagnose MetS. In a study of children and adolescents with obesity, the TG/HDL-C ratio had high sensitivity (80%) and specificity (75%) to MetS, with a cutoff point of 1.25.[6] In our study on an elderly population, a TG/HDL-C ratio of 1.49 was found to be the best critical value. Clinical studies have shown that the TG/HDL-C ratio can be used to predict MetS and to assess the risk of cardiovascular events in older people. [18-20]Most studies are limited to specific populations and races. For example, the TG/HDL-C ratio has been found to have a high predictive value for MetS among Korean adolescents.[21]Prior to our study, research on the link between TG/HDL-C and MetS in the Chinese elderly was rare. Additionally, many clinical trials to date

Page 13 of 18

BMJ Open

have shown that lipid metabolism disorder has toxic effects on cells, which can affect the function of islet β cells and cause or aggravate insulin resistance.[22] Insulin resistance and deficiency of insulin secretion can further aggravate lipid metabolism disorders.[21, 23, 24] In the future, studies can carefully investigate the effectiveness of the TG/HDL-C ratio in the diagnosis of insulin resistance since these measurements are usually easier to obtain than performing the insulin resistance test.

In our study, uric acid also showed a significant positive correlation with MetS. Experimental studies have shown that uric acid can penetrate smooth muscle fibers through the organic anion transport system, thereby activating various transmission pathways and increasing the expression of inflammatory mediators.[25, 26]Therefore, further research into the relationship between uric acid and metabolic syndrome are needed in the future. After consulting the literature, we have studies suggesting that there is a correlation between uric acid, age, sex and metabolic syndrome, [27-29]and our research has also found this. In order to eliminate these variables known to be associated with metabolic syndrome, we performed a multiple logistic regression analysis to eliminate the interference of these confounding factors.

Our study found that with an increase in the TG/HDL-C ratio there was a gradual increase in the number of people diagnosed with MetS. When TG/HDL is greater than 1.437 for men and 1.194 for women, it indicates that the patient is at a high risk of metabolic syndrome. At the same time, we need to attach great importance to the patient's uric acid, fasting blood sugar, and blood pressure. The early detection of patients at a high risk for MetS through the measurement of the TG/HDL-C ratio can help to actively prevent or treat them before disease symptoms appear, thus providing patients with the greatest clinical benefit.

Limitations

The study participants all come from one community in China; therefore, the

BMJ Open

sample may not be representative of the elderly population in China. We recruited only those who had completed the comprehensive health examination, which may have biased our main findings. Our study is a cross-sectional study, which cannot reflect the causal relationship between TG/HDL and metabolic syndrome. In addition, our analysis adjusted for age, sex, etc., but not for physical exercise and diet that are known to affect blood lipids. We expect more research to be done in the future based on this study.

CONCLUSIONS

We found a strong correlation between the TG/HDL-C ratio and MetS. Elderly Chinese people with a high TG/HDL-C ratio are at high risk of MetS. In our study sample, a TG/HDL-C ratio of 1.49 was found to be the optimal critical value. This study is of great significance for the early identification and management of MetS among the elderly people in China. The measurement of the TG/HDL-C ratio can help clinicians to identify elderly people who need targeted treatment, management, and follow-up.

ACKNOWLEDGMENTS: We would like to thank the participants for their contribution to this study.

AUTHOR CONTRIBUTIONS:

Study concept and design: Nieguqiao and Pengwen; Data acquisition: Nieguqiao and HouKaishu; Data analyses: Nieguqiao, Zhangmeng and Pengwen; Data interpretation: Pengwen, NieGuqiao. All authors contributed to writing, revising, and approving the final manuscript.

FUNDING: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

COMPETING INTERESTS: None declared.

PARTICIPANT CONSENT FOR PUBLICATION: Not required.

4 5 6

7 8

9

11

21

37

41

47

49

PROVENANCE AND PEER REVIEW: Not commissioned; externally peer reviewed. DATA AVAILABILITY STATEMENT: No data are available. REFERENCES 10 Eckel, R.H., S.M. Grundy, and P.Z. Zimmet, The metabolic syndrome. Lancet, 2005. 365(9468): 1. 12 p. 1415-28. 13 2. Kassi, E., et al., Metabolic syndrome: definitions and controversies. BMC Med, 2011. 9: p. 48. 14 15 3. Liu, M., et al., Increasing Prevalence of Metabolic Syndrome in a Chinese Elderly Population: 16 2001-2010. PLoS One, 2013. 8(6): p. e66233. 17 4. Vega, G.L., et al., Triglyceride-to-high-density-lipoprotein-cholesterol ratio is an index of heart 18 19 disease mortality and of incidence of type 2 diabetes mellitus in men. J Investig Med, 2014. 20 62(2): p. 345-9. 5. Wittcopp, C. and R. Conroy, Metabolic Syndrome in Children and Adolescents. Pediatr Rev, 22 23 2016. **37**(5): p. 193-202. 24 6. Liang, J., et al., TriGlycerides and high-density lipoprotein cholesterol ratio compared with 25 homeostasis model assessment insulin resistance indexes in screening for metabolic syndrome 26 in the chinese obese children: a cross section study. BMC Pediatr, 2015. 15: p. 138. 27 28 7. Packard, C.J. and J. Shepherd, Lipoprotein heterogeneity and apolipoprotein B metabolism. 29 Arterioscler Thromb Vasc Biol, 1997. 17(12): p. 3542-56. 30 8. McLaughlin, T., et al., Use of metabolic markers to identify overweight individuals who are 31 32 insulin resistant. Ann Intern Med, 2003. 139(10): p. 802-9. 33 9. Giannini, C., et al., The triglyceride-to-HDL cholesterol ratio: association with insulin resistance 34 in obese youths of different ethnic backgrounds. Diabetes Care, 2011. 34(8): p. 1869-74. 35 10. Grover, S.A., C.S. Palmer, and L. Coupal, Serum lipid screening to identify high-risk individuals 36 for coronary death. The results of the Lipid Research Clinics prevalence cohort. Arch Intern Med, 38 1994. 154(6): p. 679-84. 39 Maruyama, C., K. Imamura, and T. Teramoto, Assessment of LDL particle size by 11. 40 triglyceride/HDL-cholesterol ratio in non-diabetic, healthy subjects without prominent 42 *hyperlipidemia.* J Atheroscler Thromb, 2003. **10**(3): p. 186-91. 43 12. Pacifico, L., et al., Association of serum triglyceride-to-HDL cholesterol ratio with carotid artery 44 45 intima-media thickness, insulin resistance and nonalcoholic fatty liver disease in children and 46 adolescents. Nutr Metab Cardiovasc Dis, 2014. 24(7): p. 737-43. Ju, S.Y., J.Y. Lee, and D.H. Kim, Association of metabolic syndrome and its components with all-13. 48 cause and cardiovascular mortality in the elderly: A meta-analysis of prospective cohort studies. 50 Medicine (Baltimore), 2017. 96(45): p. e8491. 51 Castelli, W.P., et al., Incidence of coronary heart disease and lipoprotein cholesterol levels. The 14. 52 Framingham Study. JAMA, 1986. 256(20): p. 2835-8. 53 54 15. Geloneze, B., et al., HOMA1-IR and HOMA2-IR indexes in identifying insulin resistance and 55 metabolic syndrome: Brazilian Metabolic Syndrome Study (BRAMS). Arq Bras Endocrinol 56 Metabol, 2009. 53(2): p. 281-7. 57 58 16. Galgani, J.E., C. Moro, and E. Ravussin, Metabolic flexibility and insulin resistance. Am J Physiol 59 Endocrinol Metab, 2008. 295(5): p. E1009-17. 60

2	
3	
4	
5	
6	
7	
, 8	
-	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	
60	

- Ren, X., et al., Association between Triglyceride to HDL-C Ratio (TG/HDL-C) and Insulin Resistance in Chinese Patients with Newly Diagnosed Type 2 Diabetes Mellitus. PLoS One, 2016.
 11(4): p. e0154345.
- 18. Salazar, M.R., et al., *Identification of cardiometabolic risk: visceral adiposity index versus triglyceride/HDL cholesterol ratio.* Am J Med, 2014. **127**(2): p. 152-7.
- 19. da Luz, P.L., et al., *Comparison of serum lipid values in patients with coronary artery disease at* <50, 50 to 59, 60 to 69, and >70 years of age. Am J Cardiol, 2005. **96**(12): p. 1640-3.
- 20. Perez-Martinez, P., et al., *Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation.* Nutr Rev, 2017. **75**(5): p. 307-326.
- 21. Chu, S.Y., et al., *Risk assessment of metabolic syndrome in adolescents using the triglyceride/high-density lipoprotein cholesterol ratio and the total cholesterol/high-density lipoprotein cholesterol ratio.* Ann Pediatr Endocrinol Metab, 2019. **24**(1): p. 41-48.
- 22. Bjornstad, P. and R.H. Eckel, *Pathogenesis of Lipid Disorders in Insulin Resistance: a Brief Review.* Curr Diab Rep, 2018. **18**(12): p. 127.
- Chen, Q.J., et al., Appropriate LDL-C-to-HDL-C Ratio Cutoffs for Categorization of Cardiovascular Disease Risk Factors among Uygur Adults in Xinjiang, China. Int J Environ Res Public Health, 2016. 13(2): p. 235.
- 24. Yeh, W.C., et al., *Elevated triglyceride-to-HDL cholesterol ratio is an indicator for insulin resistance in middle-aged and elderly Taiwanese population: a cross-sectional study.* Lipids Health Dis, 2019. **18**(1): p. 176.
- 25. Soltani, Z., et al., *Potential role of uric acid in metabolic syndrome, hypertension, kidney injury, and cardiovascular diseases: is it time for reappraisal?* Curr Hypertens Rep, 2013. **15**(3): p. 175-81.
- 26. Mukhopadhyay, P., et al., *Uric Acid and Its Correlation with Various Metabolic Parameters: A Population-Based Study.* Indian J Endocrinol Metab, 2019. **23**(1): p. 134-139.
- 27. King, C., et al., *Uric Acid as a Cause of the Metabolic Syndrome*. Contrib Nephrol, 2018. **192**: p. 88-102.
- 28. Pucci, G., et al., *Sex- and gender-related prevalence, cardiovascular risk and therapeutic approach in metabolic syndrome: A review of the literature.* Pharmacol Res, 2017. **120**: p. 34-42.
- 29. Kanbay, M., et al., *Uric acid in metabolic syndrome: From an innocent bystander to a central player.* Eur J Intern Med, 2016. **29**: p. 3-8.

FIGURE LEGENDS

Figure 1. Receiver operating characteristic (ROC) curve of the TG/HDL-C ratio as a highrisk indicator of metabolic syndrome



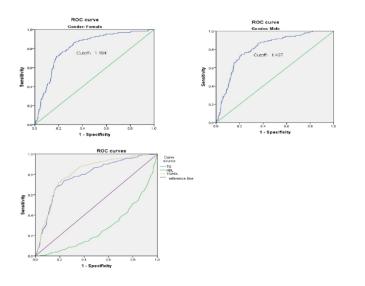


Figure 1: Receiver operating characteristic (ROC) curve of the TG/HDL-C ratio as a highrisk indicator of metabolic syndrome

75x89mm (600 x 600 DPI)

2
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24 25
25 26
20 27
27
20
30
31
32
33
34
35 36
36
37 38
38
39
40
41
42
43
44
45
46
47
48
49 50
50
51 52
52 53
55 54
54 55
56
57
58
59
60

STROBE Statement—Checklist of item	s that should be included in reports of <i>cross-sectional studies</i>

	Item No	Recommendation	Page No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3
.		was uone and what was found	
Introduction Background/rationale	2	Explain the scientific background and rationale for the investigation being	5
background/rationale	2	reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			-
Study design	4	Present key elements of study design early in the paper	5,6
Setting	5	Describe the setting, locations, and relevant dates, including periods of	5,6
Setting	Ŭ	recruitment, exposure, follow-up, and data collection	2,0
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	6
1		participants	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders,	6
		and effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods	13
measurement		of assessment (measurement). Describe comparability of assessment	
		methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If	10
		applicable, describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	7,8
		confounding	
		(b) Describe any methods used to examine subgroups and interactions	7,8
		(c) Explain how missing data were addressed	
		(d) If applicable, describe analytical methods taking account of sampling	
		strategy	
		(<u>e</u>) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers	
		potentially eligible, examined for eligibility, confirmed eligible, included	
		in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical,	8,9
		social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of	
		interest	
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted	10,11
		estimates and their precision (eg, 95% confidence interval). Make clear	
		which confounders were adjusted for and why they were included	

		(b) Report category boundaries when continuous variables were	
		categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute	9,10,1
		risk for a meaningful time period	
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions,	
		and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential	13
		bias or imprecision. Discuss both direction and magnitude of any potential	
		bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	12
		limitations, multiplicity of analyses, results from similar studies, and other	
		relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study	14
		and, if applicable, for the original study on which the present article is	
		based	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.