Association between Lipid Ratios and Metabolic Syndrome and Evaluation of Their Diagnostic Value: A Multistage Cross-Sectional Study in Guizhou Province Postprint

Authors: Zhou Shiyu, Shaolin Shen, Deng Renli, rice substitute, Liu Tao, Tian Kunming, Tian Kunming

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Abstract

Background With the rising incidence of metabolic diseases, the prevention and control of metabolic syndrome (MS) have garnered widespread attention. Lipid ratios are important screening indicators, and their relationship with MS has emerged as a topic of intense research.

Objective To analyze the association and diagnostic value of triglyceride/high-density lipoprotein cholesterol (TG/HDL-C), total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C), low-density lipoprotein cholesterol/high-density lipoprotein cholesterol (LDL-C/HDL-C), and non-high-density lipoprotein cholesterol (non-HDL-C) with the risk of MS based on a multi-stage cross-sectional study population in Guizhou Province.

Methods A total of 21,727 natural population participants from Guizhou Province who participated in the 2010 National Disease Surveillance System survey of chronic diseases and risk factors, the 2013 China Chronic Disease and Risk Factor Surveillance, the 2015 China Adult Chronic Disease and Nutrition Surveillance, and the 2018 China Adult Chronic Disease and Nutrition Surveillance were retrospectively selected as the study subjects. Baseline data were collected, and participants were divided into an MS group (n=4,981) and a non-MS group (n=16,746) according to whether they had MS. Receiver operating characteristic (ROC) curves were plotted to evaluate the diagnostic value of TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C for MS in males and females, respectively. The Delong test was used to compare differences in the area under the ROC curve (AUC) of lipid ratios for predicting MS. A multivariate Logistic regression analysis model was used to analyze the odds ratio (OR) and 95% confidence interval (CI) between lipid ratios and MS,

and to evaluate the influencing factors for MS occurrence in study subjects stratified by survey time, age, sex, body mass index (BMI), smoking, and alcohol consumption.

Results There were statistically significant differences between the MS and non-MS groups in age, sex, ethnicity, education level, marital status, smoking, alcohol consumption, BMI, TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C (P<0.05). The AUC of TG/HDL-C was greater than that of TC/HDL-C (Z=17.822, P<0.001), LDL-C/HDL-C (Z=23.813, P<0.001), and non-HDL-C (Z=27.608, P<0.001). The AUC of TG/HDL-C in males was greater than that in females (Z=4.299, P<0.001), while the AUC of LDL-C/HDL-C was lower than that in females (Z=2.061, P=0.039). Multivariate Logistic regression analysis showed that TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C were influencing factors for MS occurrence in populations stratified by age <60 years, $ 60$years, male, female, BMI < 24.0kg/m2, BMI $24.0 kg/m2, smoking, non-smoking, drinking, and non-drinking, with stronger correlations between TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, non-HDL-C and MS in females, individuals with BMI<24 kg/m2, non-smokers, and non-drinkers (P<0.05).

Conclusion TG/HDL-C demonstrates good diagnostic efficacy for MS. TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C are influencing factors for MS occurrence. In clinical practice, greater attention should be devoted to lipid ratios in females, individuals with BMI<24 kg/m2, non-smokers, and non-drinkers.

Full Text

The Association and Diagnostic Value of Lipid Ratios to Metabolic Syndrome: A Multistage Cross-sectional Study in Guizhou Province

ZHOU Shiyu[12], CHEN Shaolin[1], DENG Renli[1], DAI Mi[1], LIU Tao[3], TIAN Kunming[14]*

[1]School of Nursing, Zunyi Medical University, Zunyi 563000, China
[2]People's Hospital of Bozhou District, Zunyi City, Zunyi 563000, China
[3]Guizhou Provincial Center for Disease Control and Prevention, Guiyang 550004, China
[4]School of Public Health, Zunyi Medical University, Zunyi 563000, China

Corresponding author: TIAN Kunming, Associate Professor; E-mail: nonstandstill@163.com

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Abstract

Background: With the rising incidence of metabolic diseases, the prevention and control of metabolic syndrome (MS) have attracted widespread attention. Lipid ratios serve as important screening indicators, and their relationship with MS has become a hot research topic.

Objective: To analyze the association and diagnostic value of triglyceride/high-density lipoprotein cholesterol (TG/HDL-C), total cholesterol/HDL-C (TC/HDL-C), low-density lipoprotein cholesterol/HDL-C (LDL-C/HDL-C), and non-HDL-C with MS risk based on a multistage cross-sectional study population in Guizhou Province.

Methods: This study retrospectively selected 21,727 natural population participants from Guizhou who participated in the 2010 National Survey of Chronic Diseases and Risk Factors in Surveillance Regions, the 2013 China Chronic Disease and Risk Factor Surveillance, and the 2015 and 2018 China Adult Chronic Disease and Nutrition Surveillance. Baseline data were collected, and participants were divided into an MS group (n=4,981) and a non-MS group (n=16,746) based on MS diagnosis. Receiver operating characteristic (ROC) curves were constructed to evaluate the diagnostic value of TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C for MS in men and women separately. The Delong test was used to compare differences in area under the ROC curve (AUC) values for lipid ratios in predicting MS. Multivariate logistic regression models were used to analyze odds ratios (OR) and 95% confidence intervals (CI) for the association between lipid ratios and MS, and to evaluate influencing factors for MS stratified by survey time, age, sex, body mass index (BMI), smoking, and alcohol consumption.

Results: There were statistically significant differences between the MS and non-MS groups in age, sex, ethnicity, education level, marital status, smoking, alcohol consumption, BMI, TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C (P<0.05). The AUC for TG/HDL-C was greater than that for TC/HDL-C (Z=17.822, P<0.001), LDL-C/HDL-C (Z=23.813, P<0.001), and non-HDL-C (Z=27.608, P<0.001). The AUC for TG/HDL-C was higher in men than in women (Z=4.299, P<0.001), while the AUC for LDL-C/HDL-C was lower in men than in women (Z=2.061, P=0.039). Multivariate logistic regression analysis showed that TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C were influencing factors for MS in populations stratified by age (<60 years, $ 60*years*), *sex*(*male*, *female*), *BMI*(< 24.0*kg*/*m*^{2}$, $ 24.0*kg*/*m*^{2}), *smokingstatus*, *andalcoholconsumptionstatus*.*Theassociationswerestrongeramongwomen*, *individualswithBMI* < non-smokers, and non-drinkers (P<0.05).

Conclusion: TG/HDL-C demonstrates good diagnostic performance for MS. TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C are influencing factors for MS occurrence. In clinical practice, greater attention should be paid to lipid ratios among women, individuals with BMI<24 kg/m^2, non-smokers, and non-drinkers.

Keywords: Metabolic syndrome; Insulin resistance; Dyslipidemias; Triacylglycerol; Low density lipoprotein cholesterol; High density lipoprotein cholesterol; Cross-sectional studies; Correlation analysis

Introduction

Metabolic syndrome (MS), also known as Syndrome X, is a pathological condition characterized by abdominal obesity, insulin resistance, hypertension, and hyperlipidemia [1]. Approximately 20-25% of adults worldwide are affected by MS [2], and obesity-related MS incidence is increasing annually among children and adolescents [3,4]. MS causes metabolic disorders and represents a risk factor not only for cardiovascular disease, diabetes, and kidney disease [5,6], but also increases the risk of cancer and all-cause mortality [7,8]. Identifying clinical risk factors facilitates early screening of high-risk populations for MS and enables early intervention to prevent serious complications.

Currently, diagnostic criteria for MS vary internationally, with all requiring waist circumference measurement [9-12], which is not routinely performed in clinical examinations [13], leading to underdiagnosis of MS. Previous studies have shown that single lipid indicators such as triglycerides (TG) or high-density lipoprotein cholesterol (HDL-C) have weaker discriminatory ability for MS than combined lipid ratios [14,15]. Research has demonstrated that lipid ratios including TG/HDL-C, total cholesterol (TC)/HDL-C, low-density lipoprotein cholesterol (LDL-C)/HDL-C, and non-HDL-C can be used not only to assess cardiovascular events [16-19] but are also associated with MS occurrence [14,20]. Therefore, lipid ratios can serve as clinical markers for MS diagnosis and as simple screening indicators to replace complex measurement criteria. However, these four lipid ratios may differ across sex, age, and ethnic groups. This study aims to analyze the association and diagnostic performance of TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C with MS occurrence and progression in a southwestern Chinese population through a multistage cross-sectional study in Guizhou Province, providing theoretical basis and clinically valuable biomarkers for early identification and prevention of MS.

Methods

1.1 Study Population This study retrospectively selected natural population participants from Guizhou who participated in four national surveillance surveys: the 2010 National Survey of Chronic Diseases and Risk Factors in Surveillance Regions, the 2013 China Chronic Disease and Risk Factor Surveillance, the 2015 China Adult Chronic Disease and Nutrition Surveillance, and the 2018 China Adult Chronic Disease and Nutrition Surveillance. Using multistage cluster random sampling, permanent residents aged 18 years and older who had lived in the surveillance areas for more than six months were selected. Detailed sampling methods are described in references [21-22]. The survey periods

were December 2010 to December 2012, January 2013 to May 2014, November 2015 to March 2016, and October 2018 to May 2019, with a total of 23,902 participants. After excluding individuals with missing values for waist circumference, blood glucose, blood pressure, lipids, and important covariates, 21,727 participants were included in the final analysis (8,353 from December 2010 to December 2012; 4,616 from January 2013 to May 2014; 4,301 from November 2015 to March 2016; and 4,457 from October 2018 to May 2019). All participants provided informed consent.

1.2 Baseline Data Collection Questionnaire surveys were conducted through face-to-face interviews to collect demographic information (age, sex, ethnicity, marital status, education level), medical history (hypertension, type 2 diabetes), and lifestyle factors (smoking, alcohol consumption). Physical examinations included height measured with a stadiometer, weight with an electronic scale, waist circumference with a measuring tape, and blood pressure with an Omron electronic sphygmomanometer. Body mass index (BMI) was calculated. Laboratory tests included fasting plasma glucose (FPG), TC, TG, HDL-C, LDL-C, and 2-hour plasma glucose after oral administration of 75 g anhydrous glucose in participants without self-reported diabetes.

1.3 Diagnostic Criteria and Definitions

(1) Non-HDL-C (mmol/L) = TC (mmol/L) - HDL-C (mmol/L) [23]. (2) Smoking was defined as self-reported current smoking, and alcohol consumption as self-reported drinking within the past 12 months. (3) MS diagnosis followed the National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria [10], defined as having three or more of the following: waist circumference $ $90 cm in men and $ $80 cm in women; elevated TG: TG $ $1.7 mmol/L or receiving treatment; reduced HDL-C: <1.03 mmol/L in men and <1.29 mmol/L in women or receiving treatment; blood pressure $ $130/85 mmHg (1 mmHg=0.133 kPa) or diagnosed hypertension; FPG $ $5.6 mmol/L or diagnosed type 2 diabetes. (4) Hypertension was diagnosed if participants had self-reported hypertension, used antihypertensive medication, or had systolic blood pressure $ $140 mmHg and/or diastolic blood pressure $ $90 mmHg [26]. (5) Type 2 diabetes was diagnosed if participants had self-reported diabetes diagnosed by health professionals, FPG $ $7.0 mmol/L, or 2-hour plasma glucose $ $11.1 mmol/L [12].

1.4 Grouping Participants were divided into an MS group (n=4,981) and a non-MS group (n=16,746) based on MS diagnosis.

1.5 Statistical Analysis Data were analyzed using SPSS 25.0 and R software version 3.6.3. Normally distributed continuous variables were expressed as mean ± standard deviation and compared between groups using independent samples

t-tests. Non-normally distributed continuous variables were expressed as median (P25, P75) and compared using Mann-Whitney U tests. Categorical variables were expressed as percentages and compared using chi-square tests. ROC curves were constructed to evaluate the diagnostic value of TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C for MS in men and women separately. The Delong test was used to compare differences in AUC values for lipid ratios in predicting MS. Multivariate logistic regression models were used to analyze the association between lipid ratios and MS, expressed as OR with 95% CI, and to evaluate influencing factors for MS stratified by survey time, age, sex, BMI, smoking, and alcohol consumption. Statistical significance was set at P<0.05.

Results

2.1 Baseline Characteristics The mean age of all participants was $(49.1\$\pm15.7) years. MS prevalence rates were 14.9\pm15.9), (50.7\pm14.5), (50.4\pm15.0), and (54.9\pm\$14.6)$ years, respectively. Significant differences between MS and non-MS groups were observed in age, sex, ethnicity, education level, marital status, smoking, alcohol consumption, BMI, TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C (P<0.05) .

2.2 Predictive Value of Lipid Ratios for MS ROC curves were constructed for TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C to predict MS. Analyses were stratified by sex, with separate ROC curves for men and women. The AUC for TG/HDL-C was greater than that for TC/HDL-C (Z=17.822, P<0.001), LDL-C/HDL-C (Z=23.813, P<0.001), and non-HDL-C (Z=27.608, P<0.001). The AUC for TG/HDL-C was higher in men than in women (Z=4.299, P<0.001), while the AUC for LDL-C/HDL-C was lower in men than in women (Z=2.061, P=0.039) [TABLE:2-4]. ROC curves for TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C in predicting MS are shown in [FIGURE:1-3].

2.3 Multivariate Logistic Regression Analysis of MS Influencing Factors Multivariate logistic regression analysis was performed with MS occurrence (assignment: 0=no, 1=yes) as the dependent variable and TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C (all as continuous variables) as independent variables. Model 1 was unadjusted. Model 2 adjusted for age (continuous), sex (1=male, 2=female), ethnicity (1=Han, 2=other), education level (1=below primary school, 2=primary school, 3=middle school, 4=high school/technical secondary school, 5=college and above), and marital status (1=married, 2=other). Model 3 further adjusted for smoking (0=no, 1=yes), alcohol consumption (0=no, 1=yes), and BMI (continuous). Results showed that TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C were influencing factors for MS (P<0.05) .

Further stratification by survey period (December 2010-December 2012, January 2013-May 2014, November 2015-March 2016, October 2018-May 2019)

and inclusion in Model 3 showed that TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C were influencing factors for MS (P<0.05) .

2.4 Stratified Analysis by Age, Sex, BMI, Alcohol Consumption, and Smoking Based on previous literature [24-25], this study used age 60 years and BMI 24 kg/m^2 as stratification nodes. Multivariate logistic regression analysis stratified by age, sex, BMI, alcohol consumption, and smoking status (included in Model 3) showed that TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C were influencing factors for MS in all subgroups: age <60 years, $ 60$years, men, women, BMI < 24.0kg/m^{2}, BMI 24.0kg/m{2}, smokers, non − smokers, drinkers, andnon − drinkers.Theassociationswerestrongeramongwomen, individualswithBMI < 24kg/m^{2}$, non-smokers, and non-drinkers (P<0.05) .

Discussion

This study analyzed the association between lipid ratios and MS and evaluated their diagnostic value using data from four stages of a cross-sectional population study in Guizhou Province (December 2010-December 2012, January 2013-May 2014, November 2015-March 2016, and October 2018-May 2019). MS prevalence was higher in women than in men, consistent with findings across different ethnic populations where women show higher MS prevalence rates [6]. MS prevalence increased with age, and the mean age of MS patients was generally higher than that of non-MS individuals [27], which aligns with our findings. Both multivariate logistic regression and ROC curve analyses demonstrated associations between TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, non-HDL-C, and MS occurrence.

Previous studies have shown that TG/HDL-C has good diagnostic efficacy for insulin resistance (HOMA-IR) [28], an important factor in MS pathogenesis. However, the euglycemic insulin clamp technique for diagnosing HOMA-IR is complex and time-consuming. Lipid ratios can serve as simple surrogate indicators for MS, consistent with findings from Korean, Japanese, Ghanaian, and Maltese populations [14-15,29-30]. Our results show that TG/HDL-C is a good diagnostic factor for MS, aligning with previous research [13,31]. The optimal cut-off values for TG/HDL-C in evaluating MS in our Guizhou population were 1.25 for men and 1.08 for women, which differ significantly from Iranian (3.00/2.61) and Korean (3.3/3.8) cut-offs [32]. These differences may be due to racial variations and different MS diagnostic criteria [27,31].

Elevated TC and LDL-C are risk factors for atherosclerosis [23], while HDL-C promotes clearance of lipid deposits in atherosclerotic lesions and has antioxidant and anti-inflammatory effects [33]. The TC/HDL-C and LDL-C/HDL-C ratios can serve as indicators for evaluating blood lipids and screening for MS. Our findings indicate that TC/HDL-C and LDL-C/HDL-C are associated with MS risk but have lower diagnostic value compared with TG/HDL-C. CHU et al. [32] reported that TC/HDL-C has strong correlations with MS and HOMA-

IR index, consistent with our results. Additionally, TC/HDL-C measurement does not require fasting, which is advantageous for populations with difficulty fasting [34].

The AUC of LDL-C/HDL-C for evaluating MS was lower in men than in women in our Guizhou population, consistent with studies by GASEVIC et al. [13] and KAWAMOTO et al. [15]. Non-HDL-C is often used as an intervention target for dyslipidemia [23]. KHAN et al. [35] and WANG et al. [20] found that non-HDL-C levels were higher in MS populations than in non-MS populations. Our study also found an association between non-HDL-C and MS occurrence, suggesting its reference value for MS diagnosis.

To further explore the association between lipid ratios and MS in different populations and identify high-risk groups, we conducted stratified analyses by age, sex, BMI, smoking, and alcohol consumption. We found stronger associations between lipid ratios and MS among individuals with BMI<24 kg/m^2, non-smokers, non-drinkers, and women. Asians generally have higher body fat percentages than Caucasians of the same age, sex, and BMI, with higher proportions of risk factors for type 2 diabetes and cardiovascular disease. Compared with other populations, Chinese individuals have higher rates of metabolic abnormalities at the same BMI [36]. Although overweight individuals are prone to metabolic diseases, being overweight does not equate to having metabolic disease. Measuring blood lipid concentrations or ratios along with BMI is a practical method for screening MS [37]. Therefore, lipid ratios may be more closely associated with MS in individuals with BMI<24 kg/m^2.

Additionally, nicotine in tobacco prevents the release of inflammatory cytokines that inhibit inflammation related to HOMA-IR, potentially reducing blood glucose [38]. Evidence also suggests that light-to-moderate alcohol consumption, particularly wine, reduces diabetes risk [39]. As diabetes is a cause of MS, and our study questionnaire did not quantify smoking or alcohol consumption, this may explain why lipid ratios were more strongly associated with MS among non-smokers and non-drinkers. The prevalence of MS was higher in women than men in Guizhou Province, with women accounting for 62.7% of the MS group compared with 37.3% for men. All four lipid ratios were higher in the MS group than in the non-MS group. Therefore, individuals with BMI<24 kg/m^2, women, non-smokers, and non-drinkers with metabolic abnormalities should receive greater attention.

This study has several limitations. First, as a cross-sectional study, the relationship between lipid ratios and MS requires further validation through cohort studies. Second, other potential confounding factors may not have been adjusted for. Finally, our study population was from Guizhou Province; future research should expand to national prospective cohort studies.

In conclusion, elevated levels of the four lipid ratios are positively associated with MS risk. In clinical practice, these ratios can serve as simple tools for rapid identification of patients at risk for MS and for early intervention, repre-

senting economical and straightforward screening indicators for MS in Chinese populations.

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Tables and Figures

Comparison of baseline characteristics between subjects without and with metabolic syndrome

Predictive values of TG/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio and non-HDL-C for metabolic syndrome in all subjects

Predictive values of TG/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio and non-HDL-C for metabolic syndrome in males

Predictive values of TG/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio and non-HDL-C for metabolic syndrome in females

Multivariate Logistic regression analysis of associated factors of metabolic syndrome

Multivariate Logistic regression analysis of associated factors of metabolic syndrome in subjects stratified by survey time

Multivariate Logistic regression analysis of factors associated with metabolic syndrome in subjects stratified by age, sex, BMI, drinking and smoking

[Figure 1: see original paper] ROC curves of TG/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio and non-HDL-C in predicting metabolic syndrome

[Figure 2: see original paper] ROC curves of TG/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio and non-HDL-C in predicting metabolic syndrome in males

[Figure 3: see original paper] ROC curves of TG/HDL-C ratio, TC/HDL-C ratio, LDL-C/HDL-C ratio and non-HDL-C in predicting metabolic syndrome in females

Note: Figure translations are in progress. See original paper for figures.