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

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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 are 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/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 Point 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 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) based on the presence of 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 employed to analyze the odds ratio (OR) and 95% confidence interval (CI) between lipid ratios and

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

Results Comparisons between the MS and non-MS groups showed statistically significant differences in age, gender, 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). In males, the AUC of TG/HDL-C was greater than in females (Z=4.299, P<0.001), while the AUC of LDL-C/HDL-C was lower than in females (Z=2.061, P=0.039). Multivariate Logistic regression analysis results demonstrated 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 <60 years, $ 60 years, male, female, BMI < 24.0 kg/m2, BMI $24.0 kg/m2, smoking, non-smoking, alcohol consumption, and non-alcohol consumption, with stronger correlations between TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, non-HDL-C and MS observed 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 paid 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

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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 waves. Baseline data were collected, and participants were divided into MS group (n=4,981) and non-MS group (n=16,746) according to MS status. 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 men and women separately. The Delong test was used to compare differences in area under the ROC curve (AUC) values of lipid ratios for predicting MS. Multivariate logistic regression models were used to analyze odds ratios (OR) and 95% confidence intervals (CI) between lipid ratios and MS, and to evaluate influencing factors for MS in subgroups 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 was higher in males than in females (Z=4.299, P<0.001), while the AUC of LDL-C/HDL-C was lower in males than 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 in populations stratified by age (<60 years, $ 60*years*), *sex*(*male*, *female*), *BMI*(< 24.0*kg*/*m*^{2}$, $ 24.0*kg*/*m*^{2}), *smokingstatus*(*smokers*, *non* − *smokers*), *andalcoholconsumption*(*drinkers*, *non* − *drinkers*).*Theassociationsweres* 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 females, 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 not only a risk factor 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]. However, waist circumference measurement 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 power 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 for cardiovascular event assessment [16-19] but also show associations with MS occurrence [14,20]. Therefore, lipid ratios can serve as both clinical markers for MS diagnosis and simple screening indicators that replace complex measurement standards. 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 Southwest 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 were involved in four national surveillance waves: 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. Using multistage cluster random sampling, permanent residents aged 18 years and older who had lived in the surveillance areas for more than 6 months were selected from various monitoring sites in Guizhou Province. Specific 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, initially including 23,902 participants. After excluding outliers in waist circumference, blood glucose, blood pressure, and lipid measurements, as well as those with missing important covariates, a total of 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 Survey: Face-to-face interviews were conducted to collect demographic information (age, sex, ethnicity, marital status, education level), medical history (hypertension, type 2 diabetes), and lifestyle factors (smoking, alcohol consumption).

Physical Examination: Height was measured using a stadiometer, body weight using an electronic scale, waist circumference using a measuring tape, and blood pressure using an Omron electronic sphygmomanometer. Body mass index (BMI) was calculated from height and weight measurements.

Laboratory Testing: Fasting venous blood samples were collected, and 2-hour blood samples were obtained from participants without self-reported diabetes after oral administration of 75 g anhydrous glucose. Fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), HDL-C, LDL-C, and 2-hour plasma glucose were measured.

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; **alcohol consumption** was defined as self-reported drinking within the past 12 months.
3. **Metabolic syndrome** was diagnosed using the National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria [10], defined by the presence of three or more of the following: (1) waist circumference $ $90 cm in men and $ $80 cm in women; (2) elevated TG: TG $ $1.7 mmol/L or receiving treatment; (3) reduced HDL-C: <1.03 mmol/L in men and <1.29 mmol/L in women or receiving treatment; (4) blood pressure $ $130/85 mmHg (1 mmHg=0.133 kPa) or previously diagnosed hypertension receiving treatment; (5) FPG $ $5.6 mmol/L or previously diagnosed type 2 diabetes receiving treatment.
4. **Hypertension** was diagnosed if any of the following were present [26]: (1) self-reported hypertension or use of antihypertensive medication; (2) systolic blood pressure $ $140 mmHg and/or diastolic blood pressure $ $90 mmHg.
5. **Type 2 diabetes** was diagnosed if any of the following were present [12]: (1) self-reported diabetes or previous diagnosis by a health professional;

(2) FPG $ $7.0 mmol/L; (3) 2-hour plasma glucose $ $11.1 mmol/L.

1.4 Grouping Participants were divided into MS group (n=4,981) and non-MS group (n=16,746) based on the presence of MS.

1.5 Statistical Analysis Data analysis was performed using SPSS 25.0 and R version 3.6.3. Normally distributed continuous variables were expressed as mean ± standard deviation ($\bar{x}\pm s$) and compared between groups using independent samples t-tests. Non-normally distributed continuous variables were expressed as median (interquartile range) [M(P25, P75)] and compared using Mann-Whitney U tests. Categorical variables were expressed as percentages and compared using ^{2} tests. 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 men and women separately. The Delong test was used to compare differences in AUC values of lipid ratios for predicting MS. Multivariate logistic regression models were used to analyze the association between lipid ratios and MS, expressed as odds ratios (OR) with 95% confidence intervals (CI), and to evaluate influencing factors for MS in subgroups stratified by survey time, age, sex, BMI, smoking, and alcohol consumption. Statistical significance was set at $P<0.05$.

Results

2.1 Baseline Characteristics of Study Participants The mean age of all participants was $(49.1\$\pm15.7)years.Theprevalenceof MSacrossthefoursurveyperiodswas14.9\pm15.9), (50.7\pm1$ years, respectively. Significant differences between the 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 TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C for MS ROC curves were plotted to evaluate the predictive value of TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C for MS. Separate ROC curves were generated for men and women. The AUC of TG/HDL-C was significantly 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 was higher in men than in women ($Z=4.299$, $P<0.001$), while the AUC of LDL-C/HDL-C was lower in men than in women ($Z=2.061$, $P=0.039$) [TABLE:2-4]. The 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 [Figure 1: see original paper]. Sex-specific ROC curves are presented in Figure 2 [Figure 2: see original paper] for men and Figure 3 [Figure 3: see original paper] for women.

2.3 Multivariate Logistic Regression Analysis of Factors Associated with MS 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). The results showed that TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C were significantly associated with MS prevalence (P<0.05) .

Stratified analysis by survey period (December 2010-December 2012, January 2013-May 2014, November 2015-March 2016, and October 2018-May 2019) using Model 3 showed that TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C were influencing factors for MS across all time periods (P<0.05) .

2.4 Stratified Multivariate Logistic Regression 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 cutoffs. Stratified analysis by age, sex, BMI, alcohol consumption, and smoking status using Model 3 revealed that TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and non-HDL-C were associated with MS in all subgroups: age <60 years and $ 60years, menandwomen, BMI < 24.0kg/m^{2}$ and $ 24.0kg/m^{2}, smokersandnon - smokers, anddrinkersandnon - drinkers.Notably, theassociationswerestrongeramongfemales, in 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 waves of a multistage cross-sectional study in Guizhou Province. The prevalence of MS was higher in women than in men, consistent with findings from different ethnic populations where female MS prevalence exceeds that of males [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 results. 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 performance 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 markers for HOMA-IR in MS screening, a conclusion consistent with studies from Korean, Japanese, Ghanaian, and Maltese populations [14-15,29-30]. Our results confirm that TG/HDL-C is a good diagnostic factor for MS, consistent

with previous research [13,31]. The optimal cut-off values of TG/HDL-C for MS diagnosis in our Guizhou population were 1.25 for men and 1.08 for women, which differ significantly from those reported in Iranian (3.00/2.61) and Korean (3.3/3.8) populations [32]. These discrepancies may be attributed to racial differences and varying MS definition 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 possesses antioxidant and anti-inflammatory properties [33]. The TC/HDL-C and LDL-C/HDL-C ratios can serve as indicators for lipid evaluation and MS screening. Our findings indicate that TC/HDL-C and LDL-C/HDL-C are associated with MS risk but have lower diagnostic value compared to TG/HDL-C. CHU et al. [32] reported strong correlations between TC/HDL-C and both 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 MS diagnosis was lower in men than in women in our Guizhou population, consistent with findings from GASEVIC et al. [13] and KAWAMOTO et al. [15]. Non-HDL-C is often used as a therapeutic target for dyslipidemia [23]. KHAN et al. [35] and WANG et al. [20] found higher non-HDL-C levels in MS populations compared to non-MS populations. Our study also identified an association between non-HDL-C and MS occurrence, suggesting its potential reference value for MS diagnosis.

To further explore the association between lipid ratios and MS in different subpopulations and identify high-risk groups, we conducted stratified analyses by age, sex, BMI, smoking, and alcohol consumption. The associations were stronger among individuals with BMI<24 kg/m^2, non-smokers, non-drinkers, and females. 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 to other populations, Chinese individuals have higher rates of metabolic abnormalities at the same BMI [36]. While overweight individuals are prone to metabolic diseases, overweight status does not equate to metabolic disease, and measuring lipid concentrations or ratios along with BMI is a practical method for MS screening [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 suppress 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 questionnaire did not quantify smoking intensity 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 among women than men in Guizhou Province, with women comprising 62.7% of the MS group compared to 37.3% for men, and all four lipid ratios were higher in the MS group

than in the non-MS group. Therefore, individuals with BMI<24 kg/m^2, females, non-smokers, and non-drinkers who show metabolic abnormalities should receive increased attention.

This study analyzed the association between lipid ratios and MS in a multistage cross-sectional population in Guizhou Province and explored their diagnostic value. However, several limitations should be noted. 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 derived from the natural population of Guizhou Province; future research could expand to a national prospective cohort study.

In summary, this study found that elevated levels of 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, representing economical and straightforward screening indicators for MS in Chinese populations.

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