

TRIGLYCERIDE TO HIGH-DENSITY LIPOPROTEIN CHOLESTEROL RATIO AND TRADITIONAL LIPID PROFILE FOR SCREENING SUBCLINICAL ATHEROSCLEROSIS

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Received: February 25, 2018; Revised: May 21, 2018; Accepted: May 22, 2018

Abstract

Background: The lipid parameters have been linked to early atherosclerosis, increased carotid intima media thickness (CIMT), and arterial stiffness. The triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) ratio may be a better predictor. Lipid ratios are underused in cardiovascular prevention. Low-density lipoprotein cholesterol (LDL-C) also predicted preclinical atherosclerosis change as measured by CIMT independently of cardiovascular risk factors, whereas the TG to HDL-C ratio independently predicted CIMT progression. **Objective:** To investigate the comparison between the TG to HDL-C ratio and traditional lipid profile with CIMT in low risk adult populations without overt cardiovascular diseases. **Materials and Methods:** A total of 302 consecutive participants were enrolled and blood samples for serum levels of lipid profiles and the lipid ratio were calculated. The CIMT was measured by ultrasound B mode. The clinical status and anthropometrics were collected. **Results:** In the low risk population; the age was 47.18 ± 10.96 years and 49% (148/302) were female. The TG to HDL-C ratio was 2.84, the total cholesterol (TC) to HDL-C ratio was 4.16, and the LDL-C to HDL-C ratio was 2.48. The TG to HDL-C ratio > 3.5 was 27.2%. The CIMT was positively correlated with the TG to HDL-C ratio ($r = 0.13, p = 0.03$), the TG to HDL-C ratio > 3.5 correlation with the CIMT ($r = 0.15, p < 0.01$), and the TG ($r = 0.13, p = 0.02$). The plasma levels of the TC, HDL-C, and LDL-C were not correlated to the CIMT. Carotid plaque was not associated with both the lipid ratios and lipid parameters. **Conclusions:** The TG to HDL-C ratio was positively more correlated with an early marker of atherosclerosis than a traditional individual plasma lipid level in the low risk population.

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Keywords: Triglyceride to high-density lipoprotein cholesterol ratio, atherosclerosis, carotid intima media thickness

Introduction

Cholesterol levels were first identified as a cardiovascular (CVP) risk factor in the Framingham Heart Study (Dawber *et al.*, 1959). Since then, lipid parameters have been linked to early atherosclerosis on autopsy (Rainwater *et al.*, 1999), increased carotid intima media thickness (Heiss *et al.*, 1991), and arterial stiffness (Brouwers *et al.*, 2009). Risk stratification may be improved by testing for apolipoprotein B (Ramjee *et al.*, 2011) or the use of lipid ratios. The triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) ratio may be a better predictor of small, dense low-density lipoprotein cholesterol (LDL-C) (Tsimihodimos *et al.*, 2007), an atherogenic lipoprotein particle that strongly predicts coronary heart disease (Onat *et al.*, 2010). In adult populations with a higher traditional lipid profile such as TG, LDL-C and lower HDL-C were found to predict coronary heart disease (Blankstein *et al.*, 2011).

Lipid ratios are underused in cardiovascular prevention, but can add to risk assessment. The lipid ratios can provide information on risk factors which are difficult to quantify by routine analyses and could be a better mirror of the metabolic and clinical interactions between lipid fractions. Carotid intima media thickness (CIMT) is an early and sensitive indicator for subclinical atherosclerotic vascular change. Small, dense LDL-C also predicted preclinical atherosclerosis change as measured by CIMT independently of cardiovascular risk factors (Cromwell *et al.*, 2007; Norata *et al.*, 2009), whereas the TG to HDL-C ratio independently predicted the CIMT progression (Maki *et al.*, 2011). The present study is not the first report of the lipid ratio and CIMT values but previous studies cannot be directly applied to the Thai population because of the differences provided by ethnic groups and environmental factors for cardio-metabolic risks and CIMT. Thus, we conducted a study to investigate the relationship between the lipid TG to HDL-C ratio and the traditional single

lipid profile (Total cholesterol (TC), TG, HDL-C, and LDL-C) with CIMT in low risk adult populations without overt cardiovascular diseases in the Thai population.

Materials and Method

Study Population

The Suranaree University of Technology Research Ethics Committee approved this study (EC-58-02). Three hundred and two consecutive subjects were randomly enrolled in 2015-2016, and all subjects underwent CIMT measurement by B-mode carotid ultrasound. Informed consent approval from the Ethics Committee of Suranaree University of Technology was taken from all the patients or their relatives before inclusion in this study. Subjects who initially were without overt cardiovascular diseases, which were defined as unstable angina, non-ST elevation myocardial infarction, previous myocardial infarction, ischemic stroke, and peripheral artery diseases, were ruled in, and those with a previous history of atherosclerotic cardiovascular diseases were ruled out.

Demographic and Clinical Characteristics Collection

Demographic and clinical characteristics such as age, gender, body mass index (BMI), smoking status, hypertension or current antihypertension therapy, dyslipidemia or use of lipid lowering medications, and diabetic mellitus were obtained by means of a computerized questionnaire.

Laboratory Examination

Fasting blood samples were drawn from each participant and transferred on ice to the central laboratory for analysis. The TC, TG, HDL-C, LDL-C, and fasting blood sugar (FBS) were also measured by the central laboratory in Suranaree University of Technology Hospital.

Carotid Intima Media Thickness Measurement

Carotid ultrasound was performed with a 5-7 MHz linear array transducer. The CIMT was defined as the distance between the leading edge of the lumen interface and the far wall of the media adventitia. The measurements were calculated for the far wall of both common carotid arteries at predefined positions (1.0 cm proximal to the bifurcation), and these 3 carotid intima media thickness readings were averaged to give the mean common CIMT. The CIMT was averaged by the left and right CIMT values. The CIMT was not measured at the site of a carotid plaque, which was defined as a focal thickening of the intima media complex ≥ 1.1 mm irrespective of echogenicity.

Statistical Analysis

All analyses were performed with a computer program. All values were expressed as mean $\pm$ standard deviation or percentage. Correlation between ratios with demographic and clinical characteristics were evaluated by the Pearson correlation. A p -value < 0.05 was considered to be a significant difference.

Results and Discussion

Demographic data of the study population, as shown in Table 1, showed that the age of the participants was 47.18 ± 10.96 years and that 49% (148/302) of the participants were female. Approximately 100% were nonsmokers, the BMI was 25.84 ± 7.07 kg/m², systolic blood pressure was 126.98 ± 14.64 mmHg, and diastolic blood pressure 71.78 ± 10.76 mmHg. Plasma levels of the TC, TG, HDL-C, and LDL-C were 216.18, 139.14, 55.05, and 129.24 mg/L, respectively. The TG to HDL-C ratio was 2.84, the TC to HDL-C ratio was 4.16, and the LDL-C to HDL-C ratio was 2.48. The TG to HDL-C ratio > 3.5 was 27.2%.

Correlation between the TG to HDL-C ratio, traditional lipid parameters, and the early atherosclerosis markers CIMT and carotid plaque were shown in Table 2. For the entire study, the CIMT was positively correlated with the TG to HDL-C ratio ($r = 0.13$, $p = 0.03$), the TG to HDL-C ratio > 3.5 correlation with the CIMT ($r = 0.15$, $p < 0.01$), and the TG ($r = 0.13$, $p = 0.02$). The plasma level of the TC, HDL-C, and LDL-C were not correlated to the CIMT. As a consequence, we found a significant

Table 1. Clinical characteristics, biochemical profile, and values of carotid intima media thickness of the study population, according to sex

Characteristics	n = 302
Age (years)	47.18 ± 10.96
Systolic blood pressure (mmHg)	126.98 ± 14.64
Diastolic blood pressure (mmHg)	71.78 ± 10.76
Weight (kg)	70.26 ± 39.83
Height (cm)	162.82 ± 8.60
Waist circumference (inch)	34.43 ± 4.31
Hip circumference (inch)	38.78 ± 4.34
Body mass index (kg/m ²)	25.84 ± 7.07
Fasting blood sugar (mg/dl)	101.82 ± 24.73
Total cholesterol; TC (mg/dl)	216.18 ± 43.84
Triglyceride; TG (mg/dl)	139.14 ± 81.93
High-density lipoprotein cholesterol; HDL-C (mg/dl)	55.05 ± 15.65
Low-density lipoprotein cholesterol; LDL-C (mg/dl)	129.24 ± 36.96
TC/HDL-C ratio	4.16 ± 1.26
TG/HDL-C ratio	2.84 ± 2.07
LDL-C/HDL-C ratio	2.48 ± 0.88
CIMT (mm)	0.71 ± 0.15

association to the CIMT only on the TG to HDL-C ratio, and no association with the TC to HDL-C ratio ($r = 0.04$, $p = 0.50$) and LDL-C to HDL-C ratio ($r = 0.01$, $p = 0.84$). Carotid plaque was not associated with both the lipid ratio and traditional lipid parameters.

In this study, we have found that there was a significant association between CIMT only on the TG to HDL-C ratio, and there was no association with the total cholesterol to HDL-C ratio and LDL-C to HDL-C ratio. A correlation between the TG to HDL-C ratio and carotid artery intima media thickness was shown in a study of a population in which the participants were children (Pacifico *et al.*, 2014). In a young age group, there was a high TG to HDL-C ratio (>2.0) independent of obesity correlation with endothelial dysfunction, impaired fasting glucose, high blood pressure, and high waist circumference compared with those with a TG to HDL-C ratio <2 (Bonito *et al.*, 2012; de Giorgis *et al.*, 2014). Our present study shows that in adult participants without overt atherosclerotic cardiovascular diseases, there was a TG to HDL-C ratio of 2.84 and a correlation with early atherosclerosis CIMT. There was a significant association between CIMT only in the TG to HDL-C ratio, and no association with the TC to HDL-C ratio. The risk stratification target levels were: the TC to HDL-C ratio >5 in male and >4.5 in female,

the LDL-C to HDL-C ratio >3.5 in male and >3 in female, total cholesterol to HDL-C <4.5 in male and <4 in female, and the LDL-C to HDL-C <3 in male and <2.5 in female in primary prevention (Gotto *et al.*, 2000; Genest *et al.*, 2003; Holme *et al.*, 2008). In our study the lipid ratios were estimated in the low risk group in which the TG to HDL-C ratio was 2.84, the TC to HDL-C ratio was 4.16, and the LDL-C to HDL-C ratio was 2.48 lower than the risk categories and target for primary prevention. Only 27.2% of the participants had a TG to HDL-C ratio >3.5 in our study. Previous study found that intima media thickening is more marked from the age of 40-50 years and is strongly dependent on age especially in subjects without traditional cardiovascular risk factors (Jarauta *et al.*, 2010). In our study, the mean age was 47.18 ± 10.96 years and it was a low risk population (diabetes mellitus 6%, hypertension 25%, and nonsmokers), and there was a correlation between age and CIMT. The systolic blood pressure of 127 mmHg correlation with the TG to HDL-C ratio was the same result as a previous study in subjects without traditional risk where association is stronger for systolic blood pressure above 120 mmHg and weaker with CIMT progression.

During recent years, several studies have clearly demonstrated the role of atherogenic dyslipidemia in the pathogenesis of

Table 2. Lipid parameters and early atherosclerosis marker carotid intima media thickness and carotid plaque

Lipid parameters		CIMT		Carotid plaque	
		Pearson Correlation	p-value	Pearson Correlation	p-value
Traditional lipid	Total cholesterol; TC	0.02	0.76	0.09	0.14
	Triglyceride; TG	0.13	0.02*	0.09	0.13
	High-density lipoprotein cholesterol; HDL-C	0.04	0.44	0.10	0.07
	Low-density lipoprotein cholesterol; LDL-C	0.04	0.49	0.02	0.71
Lipid ratio	TC/HDL-C ratio	0.04	0.50	0.03	0.56
	TG/HDL-C ratio	0.13	0.03*	0.06	0.28
	TG/HDL-C ratio > 3.5	0.15	$< 0.01^*$	0.04	0.47
	LDL-C/HDL-C ratio	0.01	0.84	0.04	0.54

* Significant difference at $p < 0.05$.

atherosclerosis. The hallmarks of atherogenic dyslipidemia are increased TG and normal or minimally elevated levels of LDL-C and decreased HDL-C (Kavey and Mietus-Snyder, 2012). However, in adults with an increased cardiometabolic risk, the combination of TG and HDL-C in a single ratio seems to have a better predictive power for cardiovascular disease than individual values of lipid parameter total cholesterol, TG, HDL-C, and LDL-C (Kim-Dorner *et al.*, 2010). Our results are of interest mainly in the CIMT, the carotid plaque of recent findings suggesting a role of the TG to HDL-C ratio for the identification of early atherosclerotic vascular change. Further investigation is needed for ascertaining if a high TG to HDL-C ratio has any causative effect on cardiac abnormalities as well as on their progression in CIMT.

Strength and Weakness of the Study

The strength of our study was the comprehensive analysis of all lipid ratios and the weakness of the study was that there was no study between the lipid ratio correlation with the cardiovascular outcome in the Thai population.

Limitation of Study

The sample size is 1 year and it does not cover all regions of Thailand and so may not reflect the situation for the whole country.

Future Recommendations

However, it is important to observe a correlation between lipid ratios and the CIMT risk of developing subclinical atherosclerosis in non-overt cardiovascular diseases, which is of great significance in reducing the incidence of cardiovascular disease among the Thai and Asian populations.

Conclusions

This study provides evidence that in a low risk adult population, the TG to HDL-C ratio is a useful marker related to cardiovascular risk factors and early signs of vascular damage and reiterates the concept that early signs of

cardiovascular disease are already detectable in a population without overt cardiovascular diseases.

Disclosures

No conflicts of interest, financial or otherwise, are declared by the authors.

Acknowledgements

We thank all who participated in the study, and the staff at the cardiovascular clinic and reproductive clinic of Suranaree University of Technology Hospital who assisted the study.

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