Clinical Nutrition 37 (2018) 1423–1429

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Associations of lipid parameters with insulin resistance and diabetes: A population-based study

Diaozhu Lin [1], Yiqin Qi [1], Chulin Huang, Muchao Wu, Chuan Wang, Feng Li, Chuan Yang, Li Yan, Meng Ren **, Kan Sun *

Department of Endocrinology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, 107 Yanjiang West Road, Guangzhou 510120, People's Republic of China

ARTICLE INFO

Article history:
Received 13 June 2016
Accepted 15 June 2017

Keywords:
Diabetes
Insulin resistance
Dyslipidemia
TG to HDL-C ratio

SUMMARY

Objective: A dramatic gap exists between the clinical practice and guidelines for the dyslipidemia control in patients with diabetes. It is still uncertain which routinely available lipid measure is more applicable in estimation of insulin sensitivity and blood glucose control. The present study aims to investigate associations of routine lipid profiles with insulin resistance and diabetes, respectively.

Methods: We conducted a population-based study in 9764 Chinese participants. The homeostasis model assessment of insulin resistance was calculated to estimate insulin sensitivity. Diabetes was diagnosed according to the 1999 World Health Organization diagnostic criteria.

Results: Participants with insulin resistance or diabetes presented with significantly higher triglycerides (TG), Non-high-density lipoprotein cholesterol (Non-HDL-C), Non-HDL-C/HDL-C, TG/HDL-C and lower HDL-C when compared with control subjects (all $P < 0.0001$). Such lipid measures were significantly correlated with fasting insulin, fasting plasma glucose (FPG), oral glucose tolerance test (OGTT) 2 h glucose and Hemoglobin A1c (HbA1c) in Pearson's correlation analysis and multivariate linear regression analysis (all $P < 0.0001$). In logistic regression analysis, subjects were more likely to have prevalent insulin resistance and diabetes with the elevated quartiles of TG, Non-HDL-C, Non-HDL-C/HDL-C and TG/HDL-C (all $P < 0.05$). TG/HDL-C ratio, compare with other lipid parameters, have shown the strongest correlation with increased odds of insulin resistance and diabetes.

Conclusion: Our study suggests a discordant association of lipid parameters with blood glucose level and TG/HDL-C is a better marker for evaluating insulin resistance and diabetes in Chinese population when compared with other routine lipid measures.

1. Introduction

Diabetes is one of the major public health problems worldwide. Prevalence of diabetes and the mortality from diabetes related cardiovascular disease has increased significantly in recent decades [1–3]. As a major modifiable risk factor for the development of atherosclerosis, dyslipidemia contributes significantly to the excess risk of cardiovascular events in patients with insulin resistance and diabetes. However, by investigating the prevalence, awareness, treatment, and control of dyslipidemia in patients with type 2 diabetes, our previous survey found a dramatic gap between the clinical practice and guidelines for the treatment of dyslipidemia in China [4]. Even in top-ranked hospitals in China, a phenomenon of high prevalence, low awareness, low treatment, and low-qualified control still exists in diabetes patients with dyslipidemia.

Based on recent lipid management recommendations, LDL cholesterol (LDL-C) is the main target in the treatment of diabetic dyslipidemia [5]. However, it has been shown that serum lipid levels and prevalence of dyslipidemia in patients with diabetes vary greatly depending on region, nationality, economic level, and

Abbreviations: BMI, body-mass index; WC, waist circumference; FPG, fasting plasma glucose; HbA1c, Hemoglobin A1c; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; OGTT, oral glucose tolerance test; SBP, systolic blood pressure; DBP, diastolic blood pressure; MET-h/week, metabolic equivalent hours per week; eGFR, estimated glomerular filtration rate; SD, standard deviation; OR, odds ratios; CI, confidence intervals.

* Corresponding author. Fax: +86 20 81332042.
** Corresponding author. Fax: +86 20 81332042.
E-mail addresses: lizyhenu@163.com (K. Sun), renmeng80@139.com (M. Ren).

[1] Diaozhu Lin and Yiqin Qi contributed equally to this work.

http://dx.doi.org/10.1016/j.clnu.2017.06.018
0261-5614/

health care level [6]. In addition to LDL-C, other abnormal composition of lipid constituents also can augment the risk of cardiovascular diseases and affect the prognosis of diabetes [7]. Other lipid metabolism markers, such as combined lipid ratio, may better reflect the overall interaction between lipid/lipoprotein fractions. But for now at least, it is unclear whether lipoprotein parameters other than LDL-C could provide additional clinical information regarding diabetes related insulin resistance, or indicate more appropriate treatment targets for glycemic control.

The inconclusive association of lipid parameters with insulin resistance and diabetes, to some extent, might have negative effect on developing control and treatment strategies of diabetic dyslipidemia in China. To date, previously existing literature and primary analyses have not been implemented to make a systematic comparison on the association of different lipid parameters with insulin resistance or diabetes. Therefore, we assessed the associations of routine lipid measures with insulin resistance and diabetes in a community-based population to determine the better parameter for dyslipidemia control in diabetes.

2. Subjects and methods

2.1. Study population and design

We performed a cross-sectional study in a community in Guangzhou, China from June to November, 2011. The study population was from the Risk Evaluation of cAncers in Chinese diabeTic Individuals: A lONgitudinal (REACTION) study, which was been set up as a multicenter prospective observational study with the aim of evaluating chronic diseases in the Chinese population [8,9]. During the recruiting phase, a total of 10,104 residents aged 40 years or older were invited to participate by examination notices or home visits. In total, 9916 subjects signed the consent form and agreed to participate in the survey, and the participation rate was 98.1%. The subjects who failed to provided information about lipid parameters (high-density lipoprotein cholesterol [HDL-C]: n = 20; low-density lipoprotein cholesterol [LDL-C]: n = 1; triglycerides [TG]: n = 8) or glucose parameters (fasting plasma glucose [FPG]: n = 17; oral glucose tolerance test [OGTT] 2 h glucose: n = 62; Hemoglobin A1c [HbA1c]: n = 44) were excluded from the analyses. A total of 9764 eligible individuals were included in the final data analyses. The study protocol was approved by the Institutional Review Board of the Sun Yat-sen Memorial Hospital affiliated with Sun Yat-sen University and was in accordance with the principles of the Helsinki Declaration II. Written informed consent was obtained from each participant prior to data collection.

2.2. Clinical and biochemical measurements

We collected information about lifestyle factors, medical histories, sociodemographic characteristics and family histories by using a standard questionnaire. Smoking or drinking habits were classified as ‘never’, ‘current’ (smoking or drinking regularly in the past 6 months) or ‘ever’ (cessation of smoking or drinking of more than 6 months) [10]. A short form of the International Physical Activity Questionnaire (IPAQ) was used to estimate physical activity during leisure time by adding the results for questions about the frequency and duration of moderate or vigorous activities and walking [11]. Metabolic equivalent hours per week (MET-h/week) were calculated separately to evaluate total physical activity.

All participants completed the anthropometrical measurements with the assistance of trained staff using standard protocols [8]. Blood pressure was measured three times consecutively by the same observer with 5 min intervals using an automated electronic device (OMRON, Omron Company, China). The average of the three measurements of blood pressure was used for the analysis. Body height and body weight were recorded to the nearest 0.1 cm and 0.1 kg, respectively, while participants were wearing light indoor clothing without shoes. Body mass indices (BMI) were calculated as the weight in kilograms divided by the height in meters squared (kg/m^2). Obesity was defined by BMI equal to or greater than 28, and overweight was defined by BMI equal to or greater than 24 and less than 28 [12]. Waist circumference (WC) was measured at the umbilical level with participant in the standing position at the end of a gentle expiration.

Venous blood samples were collected for laboratory tests after an overnight fasting of at least 10 h. Measurements of fasting serum insulin, FPG, OGTT 2 h glucose, TG, total cholesterol (TC), HDL-C, LDL-C and creatinine were performed with an autoanalyzer (Beckman CX-7 Biochemical Autoanalyser, Brea, CA, USA). HbA1c was assessed by high-performance liquid chromatography (Bio-Rad, Hercules, CA). Triglyceride glucose index (TyG index) was calculated as log [fasting triglycerides (mg/dL) $\times$ fasting glucose (mg/dL)/2] [13,14]. The abbreviated Modification of Diet in Renal Disease (MDRD) formula recalibrated for Chinese population was used to calculate estimated glomerular filtration rate (eGFR) expressed in mL/min per 1.73 m^2 using a formula of $eGFR = 186 \times [\text{serum creatinine} \times 0.011]^{-1.154} \times [\text{age}]^{-0.203} \times [0.742 \text{ if female}] \times 1.233$, where serum creatinine was expressed as μmol/L and 1.233 was the adjusting coefficient for Chinese population [15].

2.3. Definition of glucose and lipid metabolism status

Diabetes was diagnosed according to the 1999 World Health Organization (WHO) criteria (FPG $\geq$ 7.0 mmol/L and/or OGTT 2 h glucose $\geq$ 11.1 mmol/L, or previously diagnosed diabetes). The insulin resistance index (homeostasis model assessment of insulin resistance, HOMA-IR) was calculated as fasting insulin (μIU/ml) $\times$ fasting glucose (mmol/L)/22.5 [16]. Insulin resistance was defined by a HOMA-IR index within the top quartile (greater than 2.54 in the present study) [17]. Non-HDL-C levels were calculated from the difference between serum TC and HDL-C.

2.4. Statistical analyses

The statistical analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). We analyzed the effects of lipid parameters (TG, TC, HDL-C, LDL-C, Non-HDL-C, Non-HDL/HDL-C and TG/HDL-C ratio) on clinical factors correlated with glycometabolism, prevalent insulin resistance and diabetes, respectively. Continuous variables are presented as the means $\pm$ the standard deviation (SD) with the exception of skewed variables, which were presented as medians (interquartile ranges). Categorical variables are expressed as numbers (proportions). FPG, TG, HbA1c, HOMA-IR, and MET-h/week were logarithmically transformed prior to analysis due to non-normal distributions. Linear regression analyses were used to test for trends across groups. Differences between groups were tested with one-way ANOVAs. Comparisons between categorical variables were performed with the χ^2 test.

Unadjusted and multivariate adjusted logistic regression analyses were used to assess the prevalence of insulin resistance and diabetes according to quartiles of lipid parameters. The odds ratios (OR) and the corresponding 95% confidence intervals (95% CI) were calculated. Model 1 was unadjusted. Model 2 was adjusted for age. Model 3 was further adjusted for sex, BMI, current smoking and drinking status, physical activity level and systolic blood pressure (SBP). Model 4 was further adjusted for diabetes treatment, presence of dyslipidemia, presence of cardiovascular diseases. Smoking and drinking statuses (i.e., never, former or