Atherosclerosis 233 (2014) 381–386

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Association between postprandial triglycerides and coronary artery disease detected by coronary computed tomography angiography

Henrique L. Staniak [a,b], Wilson Salgado Filho [b], Márcio H. Miname [b], Isabela M. Benseñor [a], Paulo A. Lotufo [a], Rodolfo Sharovsky [a], Carlos E. Rochitte [b], Márcio S. Bittencourt [a], Raul D. Santos [b,*]

[a] Hospital Universitário, University of São Paulo, São Paulo, Brazil
[b] Lipid Clinic Heart Institute (InCor), University of São Paulo Medical School Hospital, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 16 September 2013
Received in revised form
12 November 2013
Accepted 3 December 2013
Available online 18 January 2014

Keywords:
Triglycerides
Postprandial lipemia
Coronary computed tomography angiography
Atherosclerosis

ABSTRACT

Background: Studies have demonstrated the association of severe anatomical coronary artery disease (CAD) with postprandial triglycerides (TG) concentrations. Nevertheless the relationship between less severe atherosclerosis plaque burden and postprandial TG is less established.
Objective: to study the relationship between postprandial TG and CAD detected by coronary computed tomographic angiography (CTA).
Material and methods: 130 patients who underwent an oral fat tolerance test were enrolled (85 with CAD detected by CTA and 45 without). Postprandial lipemia was studied by measuring TG from T0h to T6h with 2-h intervals, and analyzed the TG change over time using a longitudinal multivariable linear mixed effects model with the log normal of the TG as the primary outcome.
Results: The majority of individuals with CAD had non-obstructive disease (63.3%) Patients with CAD had a slower clearance of postprandial TG change from 4 h to 6 h ($p < 0.05$) compared to patients without CAD. These results remained significant after adjustment for fasting TG and glucose, age, gender, body mass index, and waist circumference. However, those differences did not reach statistical significance after adjustment for fasting HDL-C.
Conclusion: Patients with mild (<25% lumen obstruction) and moderate CAD (25–50% lumen obstruction) detected by coronary CTA had an impaired postprandial metabolism, with a delayed TG clearance, when compared to individuals with no CAD. This difference was partially explained by the lower HDL-C. Thus, though postprandial TG may contribute to the development of CAD, this association is partially related to low HDL-C.

1. Introduction

Atherosclerotic cardiovascular disease accounts for more than 19 million deaths each year [1], mainly due to coronary artery disease (CAD). Although traditional risk factors, such as cigarette smoking, diabetes, hypertension and hypercholesterolemia can explain up to 90% of the excess risk for CAD [2], individuals with no traditional risk factors may still experience cardiovascular events. This may be explained by several factors such as prothrombotic factors [3], inflammatory biomarkers [4–6] and atherogenic lipoprotein phenotypes which comprise increased concentrations of triglyceride-rich-lipoproteins (TRLs), increased low density lipoprotein (LDL) particle number and decreased concentration of high density lipoprotein cholesterol (HDL-C) [4].

Fasting triglycerides (TG) are an indirect measure of TRLs. However, the TRLs represent a heterogeneous population of particles with different origins and composition. Their atherogenic potential is different and partially explained by their size and ability to enter into the arterial intima and induce atherosclerosis [7]. It has been demonstrated that patients with fasting TG levels >25 mmol/L (>2214 mg/dL) and familial chylomicronemia syndrome rarely develop atherosclerosis [8], whereas patients with moderate hypertriglyceridemia such as in familial hypertriglyceridemia, familial combined hyperlipidemia, remnant hyperlipidemia and metabolic syndrome often develop severe atherosclerosis [9].

Although TG is routinely measured after overnight fasting to allow more stable values, most individuals eat regular meals

* Corresponding author. Unidade Clínica de Lípides-InCor HCFMUSP, Av Dr Eneas C. Aguiar, 44 Bloco 2 Segundo Andar sala 4, Cep-05403-900 Sao Paulo, Brazil.
E-mail addresses: rdsf@uol.com.br, raul.santos@incor.usp.br (R.D. Santos).

0021-9150/$ – see front matter © 2014 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.atherosclerosis.2013.12.036

throughout the day and remain in the non-fasting state most of their lives. Thus, the fasting measures may not be representative of the true TG burden, and the role of non-fasting state in the atherosclerosis development may be underestimated in clinical practice [10]. Some large epidemiological studies [11,12] have demonstrated that non-fasting TG is associated with increased cardiovascular disease risk while others have demonstrated that lipid, lipoprotein and apolipoprotein levels measured in the non-fasting state may even be better markers of increased cardiovascular risk [13]. Despite these epidemiological studies, there is a paucity of studies relating postprandial lipemia to coronary atherosclerosis.

Coronary computed tomography angiography (CTA) is a well-validated non-invasive method to detect coronary atherosclerosis presence and stenosis [14,15], which also allows the study of plaque composition [16]. The present study sought to investigate the relationship between the postprandial lipemia and coronary atherosclerosis detected by CTA.

2. Methods

2.1. Subjects

We enrolled subjects between 40 and 75 years from both genders without prior known coronary heart disease (defined as prior myocardial infarction, unstable or stable angina, or prior coronary revascularization procedures) who underwent a coronary artery calcium score (CAC) quantification and coronary CTA to evaluate for CAD presence at the Heart Institute (InCor) Hospital das Clínicas and Hospital Universitário, both hospitals from University of São Paulo Medical School, Brazil from 2010 to 2012. Most participants ($n = 735$) were healthy volunteers from the University of São Paulo to study the prevalence of CAD and risk factors, which involved CAC score and CTA. A minority (15%) of the included participants ($n = 20$) reported an atypical chest pain.

Subjects with body mass index >40 kg/m^2, diabetes mellitus, fasting LDL-cholesterol (LDL-C)> 160 mg/dL, TG > 250 mg/dL or hypolipemic drug use, thyroid dysfunction, kidney disease, intake of more than 30 g of alcohol daily or with any contraindication for coronary CTA were excluded.

Other drugs that could affect TG metabolism such as diuretics, beta blockers and calcium channel blockers were discontinued three days before the oral fat tolerance test (OFT). The subjects were allocated to two groups. Group 1 included subjects without coronary atherosclerosis defined by zero CAC score and absence of coronary plaque in coronary CTA. Group 2 included individuals with documented atherosclerosis, defined as CAC >0 or presence of plaque defined as any tissue structures >1 mm that existed either within the coronary artery lumen or adjacent to the coronary artery lumen that could be discriminated from surrounding pericardial tissue, epicardial fat, or the vessel lumen itself [17].

2.2. Laboratory analyses and postprandial lipemia test

Measurements of plasma total cholesterol, TG, HDL-C, glucose, were performed by enzymatic methods (Roche, Manhein, Germany). C reactive protein (CRP) was measured by immune-nephelometry and LDL-C was obtained using the direct measurement (Roche, Manhein, Germany). All tests were performed after overnight fasting of at least 12 h.

Each participant received a standardized fat overload shake which provided 20% of total energy as carbohydrate, 15% as protein and 65% as fat with a polyunsaturated to saturated ratio of 0.3 [18]. Each subject received 50 g of fat per square meter of body surface. Blood samples were obtained at 0, 2, 4 and 6 h after the load test and were collected in sodium EDTA (2 mg/ml), kept on ice and centrifuged; finally plasma was stored at −80 °C. TG concentrations were measured by an enzymatic method (Roche, Manhein, Germany) at each time point. Magnitude of the postprandial lipemia was determined initially by the TG area under the curve (AUC) over the 6 h. The trapezoidal rule [19] was used to calculate total area under the curve (AUC) and AUC above baseline (incremental AUC). For the incremental AUC, it was used the difference between fasting and postprandial TG values.

2.3. Computed coronary angiographic tomography

Study subjects underwent an ECG-gated prospective coronary CTA and CAC quantification. All coronary CTAs were performed to evaluate suspected CAD. All patients with a heart rate above 60 bpm received oral beta-blockers prior to the image acquisition. The coronary CTA scans were performed in a 64 row multi-slice scanner (Brilliance 64, Philips Healthcare, Best, Netherlands and Toshiba Aquilion 64, Toshiba Medical Systems, Otawara, Japan). Patients with heart rate above 60 bpm despite beta-blockers underwent multiphase scan. After the scout images, all patients underwent ECG gated prospective calcium score scan with a tube potential of 120 kV and a tube current of 55 mA for the Brilliance 64 and tube potential of 120 KV with tube current of 300 mA for the Toshiba device. The contrast enhanced prospective coronary CTA was performed with a collimation of 64 × 0.625 mm, gantry rotation time 400 ms with tube current of 150 mA and tube potential of 120 kV for the Brilliance 64 and using 120 KV with 400 mA for the Toshiba device. The slice thickness was selected as 0.8 mm, increment of 0.4 mm, using 80–100 ml of iodine contrast (Ultravist 370, Bayer, Germany) injected with a dual head injector (Medrad Inc., U.S.A.) at a rate of 6 ml/s followed by 60 ml of saline at the same rate. Automated bolus tracking was used by placing a circular region of interest in the descending aorta and acquisition was triggered when the average attenuation value in the region of interest reached 150 Hounsfield Unit. The 75% R–R interval image was used for image reconstruction and coronary analysis. Images were reconstructed using standard filtered back projection kernels. The CAC was expressed as Agatston units and percentiles. The coronary tree was segmented in 17 segments model [20] and all arteries of at least 1.5 mm were analyzed. The degree of stenosis in all coronary segments was visually evaluated by experienced cardiologists with level III training in coronary CTA according to the Society of Cardiovascular Computed Tomography guidelines and was reported as no obstruction, luminal obstruction <25% (mild CAD), luminal obstruction 25–50% (moderate), luminal obstruction 50–70% (moderately severe) and luminal obstruction >70% (severe) for each segment. Plaque characteristics were described as calcified plaque (>130 HU), non-calcified plaque (<130 HU) and mixed plaque for each segment. A detailed analysis of the extent and severity of the CAD were performed using previously validated scores. We used the segment involvement score (SIS), which is calculated with the sum of the number of segments with CAD, ranging from 0 to 17 [21] and the segment severity score (SSS). In this score, each segment receives a value according the amount of disease present in the vessel (0: no CAD, 1: non-obstructive CAD, 2: 50–70% stenosis, 3: >70% stenosis) and the final score is the sum of each individual score, ranging from 0 to 51 [22].

2.4. Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) or median and interquartile range, as appropriate. Categorical variables are presented as frequencies. Differences between groups were tested using chi-square or Fisher's exact tests for discrete variables and student's *t* test for continuous variables.