Nutrition, Metabolism & Cardiovascular Diseases (2013) 23, 366–374

Available online at www.sciencedirect.com

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Nutrition, Metabolism & Cardiovascular Diseases

Association of fatty acid composition in serum phospholipids with metabolic syndrome and arterial stiffness

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Received 27 October 2010; received in revised form 19 April 2011; accepted 17 June 2011
Available online 15 September 2011

KEYWORDS
Fatty acids in serum phospholipids;
Linoleic acid;
Dihomo-γ-linolenic acid;
Metabolic syndrome;
Brachial-ankle pulse wave velocity

Abstract *Background and aim:* We examined the association of fatty acid (FA) composition in serum phospholipids with the features of metabolic syndrome (MetS) and arterial stiffness.
Methods: Korean men ($n = 593$, 30–79yrs) were categorized based on the number of MetS risk factors (RFs) and measured for the markers of MetS, serum phospholipid FA composition and brachial-ankle pulse wave velocity (baPWV), an index for the severity of arterial stiffness.
Results: Insulin resistance (HOMA-IR), baPWV, LDL size, and adiponectin were significantly altered corresponding to the number of MetS RFs. The proportions of total monounsaturated FA, palmitoleic acid (16:1), oleic acid (18:1ω-9) and dihomo-γ-linolenic acid (DGLA, 20:3ω-6) in serum phospholipids, and DGLA/linoleic acid (LA) (20:3ω-6/18:2ω-6), deta9-desaturase activity (D9D-16: 16:1/16:0 and D9D-18: 18:1ω-9/18:0) significantly increased corresponding to the number of MetS RFs, but D5D (20:4ω-6/20:3ω-6) decreased. baPWV positively correlated with HOMA-IR, palmitic acid (16:0), oleic acid, D6D (18:3ω-6/18:2ω-6), DGLA/LA and D9D-18, and negatively with adiponectin, LDL size, LA, docosahexaenoic acid (DHA, 22:6ω-3) and D5D. Multiple stepwise regression models revealed that baPWV was significantly influenced by systolic blood pressure, age, body weight, triglyceride and LA in serum phospholipids ($R^2 = 0.378$). Interestingly, baPWV (1419 ± 1 cm/s) and MetS (22%) were highest in individuals with lower proportion of LA (<12.361%) and higher proportion of DGLA (≥1.412%) in serum phospholipid FAs.
Conclusion: The features of MetS significantly related to serum phosopholipid FA composition. Particularly, arterial stiffness was associated with LA additively together with DLGA. It may suggest a potential benefit of sufficient amounts of LA in serum or in diet can reduce cardiovascular risk.

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http://dx.doi.org/10.1016/j.numecd.2011.06.006

Introduction

Numerous studies reported the relationship among dietary fat intake, serum fatty acid (FA) composition, and the features of metabolic syndrome (MetS) or cardiovascular disease (CVD) [1—3]. FA composition in serum lipid esters reflects dietary FA composition during the 6—8 weeks [4,5]: particularly, 18:2ω-6 (linoleic acid, LA) and 18:3ω-3 (α-linolenic acid, ALNA) in serum phospholipids are known as biomarkers of long-term essential FA intake. Serum FA composition and a high fat intake may influence the progression of obesity and insulin sensitivity [1,6,7]. High concentrations of 16:0 (palmitic acid) and low concentrations of LA in serum phospholipids were also observed in individuals with insulin resistance (IR) and MetS [8,9]. Desaturating enzymes, Δ9-desaturase activities (D9D) and D6D increased and D5D decreased in obese or MetS individuals [7,8]. Serum total FAs were moderately associated with serum triglyceride (TG) concentrations in patients with MetS [1]; saturated FA (SFA) was positively associated, but long-chain polyunsaturated FA (PUFA) was negatively associated with TG concentrations. Leeson et al. reported that higher proportions of 22:6ω-3 (docosahexaenoic acid, DHA) in erythrocyte lipids are associated with improved endothelial function especially in young men who had some of the features of IR [9].

Long-chain PUFA intakes were suggested to be associated with a decreased risk of CVD [10,11]. Mori et al. show that DHA lower blood pressure (BP) by influencing endothelial-dependent or -independent relaxation of forearm blood vessels [12]. However, the results are still controversial; a moderate increase in daily intake of DHA (~0.7 g) in the short term might lower diastolic BP, but does not influence endothelial function [13]. Recent studies showed that persistent MetS exacerbated the severity of arterial stiffness, a predictor for cardiovascular morbidity/mortality and a composite risk factor for early atherosclerosis [14—16] and the improvement of MetS could attenuate the progression of vascular damage [17].

Therefore, we aimed to clarify the relationship between FA composition in serum phospholipids and arterial stiffness expressed by brachial-ankle pulse wave velocity (baPWV), a simple and non-invasive index [14,16,18] as well as the features of MetS in Korean men.

Methods

Study population

Study participants (healthy/MetS) were recruited from the Health Service Center (HSC) in the course of a routine checkup visit or by a newspaper announcement for health examinations and enrolled to the study (January 2009—March 2010). Were excluded those who had orthopedic limitations, weight loss/gain over the previous 6 months, or any diagnosis of vascular disease, diabetes mellitus (DM), cancer, renal disease, liver disease, thyroid disease, and acute or chronic inflammatory diseases. MetS was defined using a combination and modification of the NCEP-ATPIII guideline, Asian-Pacific guideline and American Diabetes Association guideline [19—21]. This definition requires at least three of the following components: waist circumference>90 cm (men); TG ≥ 150 mg/dl; high density lipoprotein cholesterol (HDL-C) <40 mg/dl (men); BP ≥130/≥85 mmHg; and fasting glucose ≥100 mg/dl (but fasting glucoses ≥126 mg/ml were considered diagnostic of DM). Non-MetS Healthy individuals were defined as those without history or diagnosis of MetS, impaired glucose tolerance, DM, or the diseases mentioned above. None of the participants were taking any medications (antihypertensive, antidyslipidemic, antithrombotic, and antidiabetic drugs). From the data screened from HSC, those who satisfied the study criteria (about 80% of the visitors) were recommended to participate in the dietary intervention program. Finally, 95% of those who got recommendation consented to participated in the study. Thus, 593 men (30—79 yrs) were finally enrolled in the study. Among them, 159 were categorized into Group 1 (healthy individuals without MetS risk factors: Mets RFS = 0), 331 were into Group 2 (individuals with one or two of MetS RFs) and 103 were into Group 3 (MetS individuals: MetS RFs 3—5). Written informed consent was obtained from the participants, and the protocol was approved by the Institute of Review Board of Yonsei University.

Anthropometric parameters and blood collection

Body mass index (BMI) was calculated as body weight (kg)/height (m^2). BP was obtained from the left arm of seated individuals with an automatic BP monitor (TM-2654, A&D, Tokyo, Japan) after 20 min of rest. Study participants were interviewed regarding their smoking and drinking behavior. After an overnight fast, venous blood specimens were collected in EDTA-treated and plain tubes. The tubes were immediately placed on ice until they arrived at the analytical laboratory (1—3 h). Then, the blood specimens were separated into plasma or serum, and stored at −70 °C until analysis.

Serum lipid profile, apolipoprotein A1 and B

Serum total cholesterol and TG were measured using commercially available kits on a Hitachi 7150 Autoanalyzer (Hitachi Ltd., Tokyo, Japan). After precipitation of serum chylomicron, LDL, and VLDL with dextran sulfate-magnesium, HDL cholesterol (HDL-C) left in the supernatant was measured by an enzymatic method. LDL-C was calculated indirectly using the Friedewald formula for individuals with serum TG <400 mg/dL (4.52 mol/L). Serum apolipoprotein (Apo) A1 and B were determined by turbidometry at 340 nm using a specific anti-serum antibody (Roche, Basel, Switzerland).

Glucose, insulin and HOMA-IR

Fasting glucose was measured by a glucose oxidase method (Glucose Analyzer Beckman Instruments, Irvine, CA, USA). Insulin was measured by radioimmuno-assays with commercial kits (Immuno Nucleo Corporation, Stillwater, MN, USA). IR was calculated with the homeostasis model