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ORIGINAL ARTICLE

The TyG Index as a Marker of Subclinical Atherosclerosis and Arterial Stiffness in Lean and Overweight Postmenopausal Women

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Background The present study aims to examine the association of the metabolic syndrome (MS) as well as of the triglyceride-glucose index (TyG-Index), a novel marker of insulin resistance, with subclinical atherosclerosis in a cohort of postmenopausal women, stratified according to their body mass index.

Methods A total of 473 informed-consenting, non-diabetic postmenopausal women, without overt cardiovascular disease, were included in this study. We aimed to compare the association between structural and functional indices of subclinical atherosclerosis (i.e. carotid artery intima-media thickness (IMT), flow-mediated dilation of the brachial artery, pulse wave velocity (PWV)) with the TyG-index or MS, separately for lean and overweight/obese women.

Results The TyG-Index correlated significantly with carotid IMT ($r = 0.155$, $p = 0.012$) and PWV ($r = 0.157$, $p = 0.013$) only in the group of lean women. Multivariate analysis showed that subclinical atherosclerosis was predicted by MS, in the overweight/obese group (OR = 2.517, 95% CI: 1.078–5.878, $p = 0.033$), and by the TyG-Index the lean group (OR = 3.119, 95% CI: 1.187–8.194, $p < 0.001$). Using a TyG-Index cut-off value of 8.0 in the lean subpopulation, women above the cut-off had 44.1% prevalence of subclinical atherosclerosis compared to 29.4% in women below the cut-off ($p = 0.043$).

Conclusions The TyG-Index is associated with carotid atherosclerosis and arterial stiffness mainly in lean postmenopausal women, while the MS serves as a better predictor of subclinical atherosclerosis in overweight/obese

Abbreviations: MS, metabolic syndrome; TyG-index, triglyceride–glucose index; CVD, cardiovascular disease; BMI, body mass index; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-cholesterol, high density lipoprotein cholesterol; LDL-cholesterol, low density lipoprotein cholesterol; CCA, common carotid artery; CB, carotid bulb; ICA, internal carotid artery; IMT, intima-media thickness; FMD, flow mediated dilation; PWV, pulse wave velocity; HOMA-IR, homeostasis model assessment of insulin resistance

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women. The TyG-Index may prove a useful marker for identifying high-risk women in the normal-weight postmenopausal population.

Keywords Triglyceride–glucose index • Insulin resistance • Subclinical atherosclerosis • Arterial stiffness • Carotid intima-media thickness • Postmenopausal women

Introduction

The menopause transition has been related to pro-atherogenic changes in cardiovascular risk factors such as lipids and lipoproteins, body mass index (BMI), central adiposity, carbohydrate metabolism and blood pressure [1]. Additionally, BMI has been positively associated with arterial stiffness in the ageing female population [2]. Women tend to gain weight during the menopausal transition, mainly in the trunk region, resulting in increased central adiposity and increased prevalence of the metabolic syndrome [3,4]. While overweight and obese postmenopausal women tend to have a clustering of co-existing cardiovascular risk factors, mainly constituents of the metabolic syndrome, and are thus more easily risk-stratified, it is more difficult to risk-stratify lean postmenopausal women [5].

Insulin resistance (IR) is implicated as an important mechanism promoting atherosclerosis, through its association with other metabolic abnormalities prevalent in postmenopausal women, such as hyperglycaemia, dyslipidaemia, hyperinsulinaemia and hypertension [6,7]. The triglyceride-glucose index (TyG-Index), the product of fasting plasma glucose and triglycerides, is a simple marker that strongly correlates with the degree of insulin resistance [8–10]. A higher TyG-Index has been significantly associated with fat distribution and fat depots, metabolic parameters, markers of subclinical atherosclerosis related to IR and an increased risk of developing cardiovascular disease (CVD) [10–12].

The purpose of this study was to examine the association of the TyG-Index, an easily assessed on a routine clinical basis cardiovascular risk marker, with the presence of subclinical atherosclerosis and arterial stiffness in a sample of non-diabetic postmenopausal women with no diagnosed cardiovascular disease. Furthermore, we sought to test the performance of this marker, in comparison to the presence of the metabolic syndrome, separately in lean and in overweight/obese women.

Material and Methods

Subjects

This cross-sectional study included 473 informed-consenting, postmenopausal women, retrieved from the Menopause Clinic of the Aretaieio Hospital, University of Athens, between 2012 and 2015. Before recruitment, all participants were subjected to a routine evaluation program which included breast mammography, transvaginal sonography, gynaecological evaluation and Papanicolaou smear, as well as measurement of plasma glucose and assessment of thyroid, liver and renal function. Inclusion criteria were a sonographically assessed endometrial thickness of 5 mm or less, absence of premature menopause or gynaecological malignancy, familial hypercholesterolaemia, inflammatory disease, clinically overt or treated coronary artery disease, peripheral artery disease and thromboembolism. The menopausal status was defined as absence of menses for at least 12 consecutive months. Postmenopausal women with fasting blood glucose levels above 6.9 mmol/L, or those under treatment with hypoglycaemic medications as well as women with adherence and retention concerns (e.g. alcoholism) were not included in the study.

Protocol Study Procedures

A detailed medical history was recorded for every subject. We recorded demographic and lifestyle parameters, presence of cardiovascular risk factors as well as gynaecological and obstetrical history. Moreover, we evaluated levels of blood pressure (SBP and DBP: systolic and diastolic), as well as measures of waist and hip circumference, weight and height in the morning and in light clothing. The BMI and waist-to-hip ratio (WHR) were calculated using traditional equations. Patients were instructed to fast and not to smoke for 12 hours and subsequently, fasting venous blood samples were drawn between 8:30 and 9:30 a.m., centrifuged and the serum was stored at −80 °C until assessment. Ultrasound evaluations were performed immediately thereafter in one session. Metabolic syndrome (MS) was defined according to the Joint Definition [13], as the presence of at least three of the following factors: 1) hypertriglyceridaemia, defined as levels of triglycerides ≥1.69 mmol/L or intake of specific treatment; 2) low levels of high density lipoprotein (HDL) cholesterol, defined as HDL-cholesterol < 50 mg/dL or intake of specific treatment; 3) hypertension, defined as SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg or intake of antihypertensive medications; 4) hyperglycaemia, defined as fasting blood glucose (FBG) ≥5.6 mmol/L. Institutional Review Board approval was obtained by the Ethics Committee of Aretaieio Hospital.

Biochemical and Hormone Assays

The cholesterol assay (Abbott) was used to measure total cholesterol with a total CV ≤ 3% and sensitivity 5.0 mg/dL. Triglycerides were assessed using the triglyceride assay (Abbott) with a total CV ≤ 5% and sensitivity 0.06 mmol/L. The Ultra HDL assay (Abbott) was used to measure the HDL-cholesterol with a total CV ≤ 4% and sensitivity 2.5 mg/dL. The low-density lipoprotein (LDL) cholesterol was estimated using the Friedewald equation (LDL cholesterol = total cholesterol−triglycerides/5−HDL cholesterol).

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