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Association of cardio-ankle vascular index with cardiovascular risk factors and cardiovascular events in metabolic syndrome patients

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ABSTRACT

Objectives: We aimed to investigate the association between arterial stiffness assessed as cardio-ankle vascular index (CAVI) and cardiovascular (CV) risk factors and CV events in the middle-aged metabolic syndrome (MS) patients.

Materials and methods: A follow-up study was carried out in 2106 middle-aged (53.83 ± 6.17 years old, 62% women) MS subjects without overt atherosclerotic disease. Patients were initially recruited in 2009–2011 as participants of the Lithuanian High Cardiovascular Risk (LitHiR) primary prevention program and followed up for 3.8 ± 1.7 years for CV events. Thorough cardiometabolic risk assessment was carried out at inclusion.

Results: Subjects with higher CAVI had worse lipid and glucose metabolism profile: elevated total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C), decreased high-density lipoprotein cholesterol (HDL-C), higher fasting and oral glucose tolerance test (OGTT) glucose levels (all $P < 0.001$), and lower fasting insulin ($P = 0.021$). Greater age ($P < 0.001$), heart rate ($P = 0.016$), and mean arterial pressure ($P < 0.001$) were also associated with higher CAVI. Over the follow-up period, 93 (4.4%) patients developed a cardiovascular event: 55 (2.6%) patients had myocardial infarction and 38 (1.8%) suffered a cerebrovascular event. Fatal CV events comprised 6.5% ($n = 6$) of all CV events. CAVI was statistically significantly associated with occurrence of myocardial infarction ($P = 0.027$) and total cardiovascular events ($P = 0.045$), but not cerebrovascular events ($P = 0.65$). However, this association was dependent on age and gender.

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Conclusions: In the middle-aged MS patients, higher CAVI was associated with altered lipid and glucose metabolism, older age, greater heart rate and mean arterial pressure, and worse cardiovascular outcome.

1. Introduction

Metabolic syndrome (MS) is a complex of cardiovascular (CV) risk factors such as impaired glucose tolerance, high blood pressure, dyslipidemia and abdominal obesity [1,2]. Patients with MS also frequently manifest a prothrombotic and proinflammatory state [3], therefore MS is considered to be a chronic inflammatory condition [4]. Almost one-quarter of the world's adult population already have MS [5], which accounts for a 2-fold increase in the risk of developing cardiovascular disease [6]. Moreover, MS is associated with impaired arterial stiffness [7], which has an independent predictive value for all-cause and CV mortality [8]. Therefore, it is believed that early evaluation of arterial stiffness might prevent future cardiovascular events in patients with MS. However, data on the predictive value of blood pressure-independent arterial stiffness index CAVI for cardiovascular events in MS patients are not available.

Aortic pulse wave velocity (PWV) is considered to be the ''gold standard'' for measuring arterial stiffness [9]. Furthermore, recent meta-analysis of 17 longitudinal studies has shown that PWV is a predictor of cardiovascular events and all-cause mortality in various populations [10]. In pre-diabetic and diabetic patients, the value of PWV as an integrated index of vascular function predicting mortality was first shown by Cruickshank et al. [11]. However, the major limitation to clinical usage of the PWV is its dependence on blood pressure during measurement [12].

Recently, another arterial stiffness parameter, the cardio-ankle vascular index (CAVI), has been developed. CAVI reflects the stiffness of the aorta, femoral and tibial artery, and it can be assessed simultaneously with ankle-brachial index by a non-invasive VaSera device (Fukuda Denshi Co., Tokyo, Japan) [13]. Contrary to PWV, CAVI is essentially independent of blood pressure at measuring time [14–16] because it is calculated by Bramwell–Hill equation, which corrects for blood pressure parameters [12]. Consequently, CAVI represents both 'functional' and 'organic' arterial stiffness [17] and reflects both the state of smooth muscle contraction and mechanical properties of the arterial wall [18]. Moreover, CAVI enables evaluation of the real effect of blood pressure control on arteries during antihypertensive therapy [12,19]. These theoretical presuppositions and first findings of the clinical studies [20,21] support the assertion that CAVI might be equal or superior to PWV as a long-term CV risk predictor.

Several studies have investigated the association between the new index of arterial stiffness CAVI and MS. Satoh et al. [22] reported that CAVI values were significantly higher in MS than in non-MS patients. Liu et al. [23] demonstrated that CAVI increased with the number of MS components. However, there have been no large population-based studies on the association of various CV risk factors and CAVI in MS patients, and, to our best knowledge, there is no follow-up study reporting the association of CAVI and CV outcome in MS patients. In addition, most of the aforementioned studies were done on Asian populations.

Hence, the objective of this study was to evaluate the association of CAVI with traditional CV risk factors and with CV events in middle-aged MS patients.

2. Materials and methods

2.1. Subjects and study design

A follow-up study was carried out among 2106 MS subjects without overt atherosclerotic disease. All patients were recruited between 2009 and 2011 as participants of the Lithuanian High Cardiovascular Risk (LitHiR) primary prevention program, which enrolled employable age women (aged 50–65 years) and men (aged 40–55 years) without prior history of CV disease as described previously [24]. Our study cohort was comprised of the LithHir patients admitted to the Vilnius University Hospital Santariškių Klinikos (VUHSK) with diagnoses of MS according to the revised National Cholesterol Education Program Adult Treatment Panel III (NCEP ATPIII) criteria [25].

Data on the fatal and non-fatal cardiovascular events (myocardial infarction, stroke or transient ischemic attack, and sudden cardiac death) were obtained after a follow-up period greater than 3 years. The outcome follow-up was carried-out by submitting an inquiry about CV events to the National Death Registry and National Healthcare Fund Disease and Services Database. The outcome data were retrieved in June 2014.

The study was approved by the Regional Ethics Committee (Permission No. 158200-13-641-205).

2.2. Baseline measurements

All patients underwent detailed assessment of the physical status, anthropometry, and CV risk profile, including height, weight, waist circumference, and body mass index (BMI) measurements and evaluation of the CV risk factors (smoking, positive family history of CV disease). BMI was calculated as weight in kilograms divided by height in meters squared. Smoking was recorded if the subject smoked at least one cigarette a day. Positive CVD family history was defined as