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Carotid extra-media thickness in obesity and metabolic syndrome: A novel index of perivascular adipose tissue
Extra-media thickness in obesity and metabolic syndrome

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ABSTRACT

Objectives: We aimed to evaluate the association between a novel ultrasound index extra-media thickness (EMT), obesity, and metabolic syndrome (MS) using several measures of adiposity.
Methods: Four hundred patients were included in the study (age: 60.95 ± 7.3 years, F/M: 35/65%). Both common carotid arteries (CCA) indexes (EMT and intima-media thickness), anthropometric parameters, body fat percentage and ultrasound measures of different fat depots were obtained in all patients. MS was identified using three alternative definitions: International Diabetes Federation 2005 (IDF), National Cholesterol Education Program Adult Treatment Panel III 2001 (NCEP ATP III) and World Health Organization 1998 (WHO).
Results: The study group included patients with very high (80.2%) or high (19.8%) CV risk (IDF MS: 59.5%). Carotid EMT measures averaged from both sides (±SD) were as follows: mean EMT: 791 ± 126 μm, mean minimum EMT: 731 ± 115 μm and mean maximum EMT: 885 ± 210 μm. Patients with MS, irrespective of its definition and measures of obesity, displayed significantly thicker mean EMT compared to non-MS individuals: 819 ± 129 μm vs 747 ± 113 μm ($p < 0.001$; IDF), 824 ± 131 μm vs 751 ± 112 μm ($p < 0.001$; NCEP ATP III) and 825 ± 137 μm vs 773 ± 120 μm ($p < 0.001$; WHO). Moreover, EMT was related to all major parameters of general obesity, abdominal fat distribution, regional neck subcutaneous fat with weaker association between EMT and epicardial fat thickness. Finally, EMT is associated with an increasing number of CV risk factors.
Conclusions: This is the first study providing novel findings on the relationship between EMT, MS, and adiposity indexes. Our results suggest that EMT may be a new non-invasive index of perivascular adipose tissue corresponding to cardiometabolic risk.

1. Introduction

Obesity and overweight are very common disorders in clinical practice and they will become major challenges worldwide in the coming years. Obesity is the cause of several complications and comorbidities, including cardiovascular (CV) diseases and metabolic dysfunction [1]. However, the assessment of adiposity and CV risk is complex, and despite similar degrees of obesity, individuals may have different risk and clinical prognosis [2]. Precise evaluation of obesity-related risk depends on the body fat quantity, distribution, location, and bioactive function of adipocytes in the total body and in specific fat depots.

Extra-media thickness (EMT) is a novel ultrasound parameter of the common carotid arteries (CCA), which was developed primarily as an index of arterial adventitia [3]. EMT is based on various tissue components and a second major determinant is adipose tissue. However, the current knowledge regarding its association with obesity is limited and its relation to metabolic syndrome (MS) remains unknown. Available studies provided inconclusive results and used only simple measures of adiposity. Thus, we aimed to evaluate the link between EMT, obesity, and MS using several clinical and ultrasound measures of adiposity related to total body fat, type and distribution of adipose tissue, and ectopic fat depot. We also examined the relationship between EMT and estimated CV risk in a representative study group of high CV risk.

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Abbreviation list

AllC	all circumferences
AO	abdominal obesity
BAI	body adiposity index
BF%	body fat percentage
BIA	bioelectric impedance analysis
BMI	body mass index
BSA	body surface area
CAD	coronary artery disease
CCA	common carotid artery
CVD	cardiovascular disease
DM	diabetes
EFT	epicardial fat thickness
EMT	extra-media thickness
HC	hip circumference
HDL	high-density lipoprotein
IAT	intraabdominal thickness
IDF	International Diabetes Federation
IMT	intima-media thickness
MS	metabolic syndrome
NCEP ATP III	National Cholesterol Education Program Adult Treatment Panel III
PAT	perivascular adipose tissue
PrePFT	preperitoneal fat layer
PFT	pericardial fat thickness
TG	triglycerides
TTE	trans-thoracic echocardiography
WC	waist circumference
WHO	World Health Organization

2. Methods

2.1. Study group characteristics

Four hundred ninety three consecutive patients (age: 50–75 years old) admitted to the 2nd Department of Cardiology for planned cardiovascular diagnostics were screened with a consideration of exclusion criteria and four hundred patients were included in the study. All patients were sent for planned hospitalization based on typical symptoms or results of noninvasive tests suggestive of coronary artery disease (CAD). Given the purpose of the study and several potential factors affecting evaluated parameters, the predefined main exclusion criteria were as follows (total number of excluded pts: 93): congestive heart failure (Ejection Fraction < 50% or significant diastolic dysfunction and/or prior diagnosis and treatment) (42 pts), significant heart valve defects (moderate or severe) (13 pts), chronic inflammatory diseases (e.g., rheumatoid arthritis, psoriatic arthritis) (5 pts), neoplastic diseases (diagnosis and/or treatment in prior 5 years) (8 pts), secondary causes of obesity (9 pts), specific interventions aimed at obesity in prior 12 months (life style intervention or pharmacotherapy or any form of bariatric surgery) (5 pts), a 10% unintentional weight loss in prior 3 months or risk of malnutrition (Mini Nutritional Assessment score < 12 points – [4]) (7 pts), prior surgery or radiotherapy within neck (2 pts), a very poor carotid IMT or EMT image quality (1 pt) and prior diagnosis of genetic predisposition for CV diseases (1 pt).

Subjects were recruited and completed the study at the 2nd Department of Cardiology at the Medical University of Silesia. The study protocol was approved by the local Medical University of Silesia Ethic Committee.

2.2. Assessing clinical characteristics and obesity

Hypertension was determined based on blood pressure (BP) levels (systolic BP ≥140 mmHg and/or diastolic BP ≥90 mmHg) or report of a prior diagnosis of hypertension and current antihypertensive treatment. The diagnosis of hyperlipidemia was defined as abnormal plasma lipid levels (total cholesterol >190 mg/dl, LDL cholesterol >115 mg/dl, triglycerides >150 mg/dl, HDL cholesterol <40 mg/dl in men and <50 mg/dl in women) or prior diagnosis and current treatment [5]. All patients (except for individuals with prior diagnosis and current treatment) were screened for diabetes, which was determined based on fasting plasma glucose levels (≥126 mg/dl) and HbA1c (≥6.5%) and in case of discrepancies: 2-h post-load plasma glucose (≥200 mg/dl) [6,7].

All the patients had a detailed assessment of clinical and ultrasound indexes of adiposity. Overweight and obesity were classified according to body mass index (BMI = body mass (kg)/height $(m)^2$) as normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obesity (≥30.0 kg/m^2): class 1 (30.0–34.9 kg/m^2), class 2 (35.0–39.9 kg/m^2) and class 3 (≥40.0 kg/m^2).

Waist circumference (WC: midpoint between the lowest rib and the iliac crest) and Hip circumference (HC) were measured with a tape at the end of expiration. Increased WC was defined according to World Health Organization (WHO: WC in males ≥102 cm and females ≥88 cm) and International Diabetes Federation (IDF: males ≥94 cm and females ≥80 cm) criteria. Additional measures were also obtained: neck circumference just below the laryngeal prominence, midpoint thigh circumference and midpoint arm circumference and the sum of three parameters was calculated (AllC). The body adiposity index (BAI) was calculated according to the formula: $100 \times \mathrm{HC(m)}/\mathrm{height(m)} \times \sqrt{\mathrm{height(m)} - 18}$ [8]. Body surface area (BSA) was estimated using the DuBois and DuBois formula [9].

Skinfolds measured the thickness of skin and subcutaneous fat and was performed at 3 sites on the right side of the body as described by Jackson and Pollock [10,11]. All three were taken twice at each site, the values were averaged and added together (3ST).

The bioelectric impedance analysis (BIA, Bodystat 1500) was used to measure the patients' body composition with body fat percentage (BF%). All the subjects were instructed to avoid exercise or dehydratation in preceding 12 h and avoid drinking or eating in preceding 4 h, the measurements were performed according to the manufacturer's manual. The intra-observer variability of measurements in the same patient was <1%.

2.3. Obesity phenotype

Abdominal obesity (AO) was identified in subjects with increased WC according to WHO and IDF definition (above). Normal weight obesity was diagnosed in subjects with increased WC (IDF criteria) and normal BMI values. All the enrolled patients were screened for the metabolic syndrome (MS). We have identified the metabolic syndrome (MS) according to 3 alternative definitions. According to the IDF consensus (2005), subject with MS must have AO (WC: males ≥94 cm and females ≥80 cm) and two of the following: raised triglycerides (TG ≥ 150 mg/dl or treatment), reduced HDL cholesterol (HDL-C<40 mg/dl in men and <50 mg/dl in women or treatment), raised blood pressure or specific treatment, raised fasting plasma glucose or diagnosed type 2 diabetes (IDF) [12]. The WHO (1998) criteria require the presence of