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Cutoff points of waist circumference and trunk and visceral fat for identifying children with elevated inflammation markers and adipokines: The Healthy Growth Study

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A B S T R A C T

Objectives: Excessive fat storage is accompanied by several comorbidities in children and early identification of elevated abdominal fat may be extremely valuable in early prevention of cardiometabolic risk. The aim of the present study was to establish cutoff points for waist circumference trunk and visceral fat, thus identifying increased likelihood of elevated inflammatory markers and adipokines in children.

Methods: A representative sample of schoolchildren (aged 9–13 y) participated in a cross-sectional epidemiologic study conducted in Greece. Anthropometric and physical examination data, biochemical indices, and socioeconomic information (collected from parents) were assessed for all children. Central adiposity markers (trunk and visceral fat) were collected with bioelectrical impedance analysis for 999 children.

Results: Specific cutoff values of abdominal adiposity indices indicating increased likelihood of elevated levels of C-reactive protein, interleukin-6, and leptin and decreased levels of adiponectin were calculated by sex. These cutoff values were; 67.5 cm for boys and 69.5 cm for girls for waist circumference, 17.75% for boys and 22.65% for girls for trunk fat mass percentage, and 3.95 for boys and 2.55 for girls for visceral fat rating.

Conclusions: To our knowledge, this is the first study to establish simple cutoff points for abdominal adiposity indices identifying children at high risk for elevated inflammatory markers and decreased adipokine levels. Future studies are essential to confirm these findings.

Healthy Growth Study Group: Harokopio University Research Team/ Department of Nutrition and Dietetics: Yannis Manios (coordinator), George Moschonis (project manager), Katerina P. Skenderi, Evangelia Grammatikaki, Odysseas Androutsos, Sofia Tanagra, Alexandra Koumpitski, Paraskevi-Eirini Siatitsa, Anastasia Vandorou, Aikaterini-Efstathia Kyriakou, Vasiliki Dede, Maria Kantilafti, Aliki-Eleni Farmaki, Aikaterini Siopi, Sofia Micheli, Louiza Damianidi, Panagiota Margiola, Despoina Gakni, Vasiliki Iatridi, Christina Mavrogianni, Kelaidi Michailidou, Aggeliki Giannopoulou, Efstathoula Argyri, Konstantina Maragkopoulou, Maria Spyridonos, Eirini Tsikalaki, Panagiotis Kliasios, Anthi Naoumi, Konstantinos Koutsikas, Epistimi Aggelou, Zoi Krommyda, Charitini Aga, Manolis Birbilis, Ioanna Kosteria, Amalia Zlatintsi, Elpida Voutsadaki, Eleni-Zouboulia Papadopoulou, Zoi Papazi, Maria Papadogiorgakaki, Fanouria Chlouveraki, Maria Lyberi, Nora Karatsikaki-Vlami, Eva Dionysopoulou, and Efstratia Daskalou. KK was responsible for data analysis, data interpretation, and literature search. GM prepared the study design, data collection, and data interpretation. M-CP was responsible for data collection and the literature search. GPC and CL were responsible for data interpretation. YM was responsible for study design and data interpretation. All authors were involved in writing the paper and had final approval of the submitted and published versions. The authors have no conflicts of interest to declare.

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Introduction

Obesity, in both children and adults, is associated with elevated inflammatory mediators, such as C-reactive protein (CRP), interleukin (IL)-6, and tumor necrosis factor-alpha (TNF-α), along with elevated levels of leptin and reduced circulating adiponectin levels [1,2]. Additionally, adiponectin has been inversely correlated with excessive body fat [3] and leptin levels have been positively associated with body fat mass, as well as with circulating inflammatory markers [4]. Under conditions of excessive fat storage, like obesity, elevated inflammatory markers induce oxidative stress, which is a signal for hyperleptinemia and leptin resistance [5]. Furthermore, there are remarkable alterations in adipokine secretion leading to impaired regulation of appetite and satiety, fat distribution, insulin secretion and sensitivity, energy expenditure, endothelial function, inflammation, blood pressure, and hemostasis [6].

Several studies indicate that central adiposity has a positive association with leptin levels and an inverse association with adiponectin levels in adults [7,8]. These associations, although poorly investigated, seem to also apply for children and adolescents [9]. Additionally, existing studies indicate a positive association between central adiposity with CRP and IL-6 levels in adults [10–12], which is also supported by few relevant studies conducted in children [13,14]. However, considering the previously described unfavorable health effects of inflammation and of abnormal adipokine secretion and the need to elucidate comorbidities of childhood obesity, more studies are essential to investigate the associations of markers of central adiposity with inflammatory markers and adipokines in children. Moreover, it is very important to have simple and practical indices for early recognition of metabolic and other deviations from normalcy, as a consequence of elevated fat storage in children, to begin treatment or prevention strategies timely.

To the best of our knowledge, no other study has determined cutoff points of markers of central adiposity, identifying increased likelihood of elevated inflammation markers and circulating adipokines in children. Therefore, the aim of the present study was to elucidate the association of markers of central adiposity (waist circumference [WC] and abdominal and trunk fat) with circulating levels of CRP, IL-6, leptin, and adiponectin in a group of Greek children aged 9 to 13 y and most importantly to identify cutoff points of WC and abdominal and trunk fat, above which there is an increased likelihood of abnormal levels of CRP, IL-6, leptin, and adiponectin.

Materials and methods

Sampling

The Healthy Growth Study was a large-scale cross-sectional epidemiologic study initiated in May 2007. Approval to conduct the study was granted by the Greek Ministry of National Education and the Ethics Committee of Harokopio University of Athens and was conducted in accordance with the ethical standards specified in the 1964 Declaration of Helsinki. The study population comprised schoolchildren aged 9 to 13 y, attending the fifth and sixth grades of primary schools located in municipalities within the counties of Attica, Aitoloakarnania, Thessaloniki, and Iraklio. The sampling of schools was random, multistage, and stratified by parents' educational level and total population of students attending schools within municipalities of these counties. The sampling procedure yielded 77 primary schools, representative of the total number of schools in the counties under study, which responded positively when they were invited to participate in the study. An extended letter explaining the aims of the study and a consent form for taking full measurements were provided to all parents or guardians having a child in these schools. Parents who agreed to the participation of their children in the study had to sign the consent form and provide their contact details. Signed parental consent forms were collected for 2665 of 4145 children (response rate 64.1%). Assessment of central adiposity was conducted only in a large subgroup of 999 students.

Anthropometric measurements and physical examination

Children underwent a physical examination by two trained members of the research team. The protocol and equipment used were the same in all schools. Weight was measured to the nearest 10 g using a Seca digital scale (Seca Alpha, Model 770, Hamburg, Germany). Pupils were weighed barefoot, wearing the minimum clothing possible. Height was measured to the nearest 0.1 cm using a commercial stadiometer (Leicester Height Measure, Invicta Plastics, Oadby, UK) with the pupil standing barefoot, keeping shoulders in a relaxed position, arms hanging freely and head in Frankfurt horizontal plane. Weight and height were used to calculate body mass index (BMI) and participants were categorized as normal weight, overweight, or obese using the International Obesity Task Force (IOTF) cutoff points [15]. WC was measured to the nearest 0.1 cm with the use of a nonelastic tape (Hoechstmass, Germany) with the student standing, at the end of a gentle expiration. The measuring tape was placed around the trunk, at the level of umbilicus midway, between the lower rib margin and the iliac crest. Furthermore, one well-trained and experienced female pediatrician in each prefecture determined pubertal maturation (Tanner stage) after thorough visual inspection of breast development in girls and genital development in boys.

Assessment of trunk fat and visceral fat mass

Bioelectrical impedance analysis (BIA) was used for the assessment of abdominal visceral fat mass (Tanita Viscan AB-140, Kowloon, Hong Kong). In abdominal BIA, an electric current is passed between the regions near the umbilicus and spinal cord at the umbilicus level, and the voltage generated in the lateral abdomen is recorded. Because the equipotential line that passes through visceral fat appears on the lateral abdominal surface, the amount of visceral fat can be estimated by measurement of the voltage generated at this location using a regression equation determined by computed tomography. Participants were instructed not to wear any metal object during measurement. The assessments took place with the pupils lying on a nonconductive surface at ambient room temperature. Percent trunk fat mass and visceral fat rating (rating scale from 1 to 59 units, with 0.5 increment) were read directly from the instrument.

Biochemical indices

Blood samples were obtained between 0830 and 1030 after a 12-h overnight fast. Part of the blood was collected in test tubes with no added anticoagulant, where it was allowed to clot for $\sim$2 h, as this was designated for serum separation. Clotted blood was centrifuged at 3000*g* for 15 min and the collected serum was divided into aliquots and stored at -80°C.

Serum CRP levels were measured by enzyme-linked immunosorbent assay (ELISA) with CRP sandwich ELISA kit (R&D Systems, Minneapolis, MN, USA). IL-6 was measured by a high-sensitivity ELISA, and serum leptin levels by human leptin ELISA, Clinical Range kit (BioVendor Research and Diagnostic products, Karasek, Czech Republic), according to manufacturers' instructions. Adiponectin was measured by a Human Adiponectin/Acrp30 DuoSet ELISA kit (R&D Systems, Minneapolis, MN, USA). The intra-assay coefficients for IL-6 and adiponectin were $<$10%. All determinations were made according to manufacturer's instructions. All samples were measured in duplicate.

Dietary and energy intake assessment

Dietary intake data were obtained by trained dietitians and nutritionists via morning interviews with the children at the school site for 2 consecutive weekdays and 1 weekend day, using the 24-h recall technique to avoid recall bias due to memory limitations. Specifically, all study participants were asked to describe the type and amount of foods and beverages consumed, during the previous day, provided that it was a usual day according to the participant's perception. To improve the accuracy of food description, standard household measures (cups, tablespoons, etc.) and food models were used to define amounts. Parents were not involved because it was a school-based study and all measurements and data (including dietary intake) were collected at school site. Also, according to relevant literature children $>$9 y are able to accurately recall and report their dietary intake [16,17]. At the end of each interview, the interviewers, who were dieticians rigorously trained to minimize the interviewer's effect, reviewed the collected data with the respondent to clarify entries, servings, and possible forgotten foods. Food intake data were analyzed using the Nutritionist V diet analysis software (version 2.1, 1999, First Databank, San Bruno, CA, USA), which was extensively amended to include traditional Greek recipes [18]. Furthermore, the database was updated with nutritional information of processed foods provided by independent research institutes, food companies, and fast-food chains. Daily energy intake was expressed as percentage of the Estimated Energy Requirement.