



## Association between ultrasonographically measured visceral fat tissue thickness and proinflammatory adipokines in obesity

### Odnos ultrazvučne debljine visceralnog masnog tkiva i proinflamatornih adipokina u gojaznosti

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#### Abstract

**Background/Aim.** Obesity status can be assessed with numerous anthropometric, morphological and functional indices and this study was designed to assess relationship among them. The aim of this study was to investigate associations between anthropometric indices, ultrasonography measurement of visceral and subcutaneous fat tissue thickness and certain proinflammatory adipokines level. **Methods.** This cross-sectional study comprised a consecutive sample of 60 obese respondents without obesity-related comorbidities, and 20 age-matched healthy normal-weight controls. Anthropometric [body mass index (BMI), waist circumference (WC), neck circumference (NC), body fat, a body shape index (ABSI)], and ultrasonographic indices [thickness of intraabdominal fatt tissue (IAFT), visceral fat (VF), maximum subcutaneous fat (Max SFT), minimal subcutaneous fat (Min SFT)], and serum levels of chemerin and resistin were assessed in all subjects. **Results.** All anthropometric indices showed statistically significant differences between study groups. The mean IAFT, Max SFT, Min SFT and VF were significantly higher in the obese

group compared to controls ( $p < 0.01$ , for all). Serum levels of chemerin and resistin correlated positively with BMI, percentage of fat adipose tissue (FAT, %), total FAT (kg), and VF ( $p < 0.05$ , for all). Also, we observed significant correlation between resistin and NC ( $r = 0.23$ ,  $p = 0.03$ ) and ABSI ( $r = 0.22$ ,  $p = 0.04$ ). In multivariable linear regression analysis, chemerin ( $\beta = 0.23$ ;  $p = 0.008$ ) and resistin ( $\beta = 0.43$ ;  $p = 0.002$ ) were independently and significantly associated only with VF. **Conclusion.** Obesity indices, both classical and newer ones, are in positive, statistically significant correlation with the level of proinflammatory cytokines. Ultrasonographically measured VF thickness, independently associated with adipokine levels, may improve assessment of proinflammatory fat tissue characteristics. Further studies are needed to precisely define the use of ultrasonographic fat tissue measurements into clinical practice.

#### Key words:

adipokines; adipose tissue; anthropometry; metabolic diseases; obesity; resistin; severity of illness index; ultrasonography.

#### Apstrakt

**Uvod/Cilj.** Stepen gojaznosti može se proceniti brojnim antropometrijskim, morfološkim i funkcionalnim indeksima, te je ova studija dizajnirana da ispita međusobni odnos ovih parametara. Cilj studije bio je da ispita povezanost antropometrijskih indeksa, ultrasonografskih merenja debljine potkožnog i visceralnog masnog tkiva i nivoa pojedinih proinflamatornih adipokina. **Metode.** Ispitivanjem je obuhvaćeno 60 gojaznih osoba, bez prisustva komorbiditeta vezanih za gojaznost i 20 normalno uhranjenih ispitanika usklađenih po polu i godinama.

Antropometrijski pokazatelji [indeks telesne mase (BMI), obim struka (WC), obim vrata (NC), masa i procenat masnog tkiva [FAT (kg, %)], indeks oblika tela (ABSI)], ultrazvučna merenja [intra-abdominalno masno tkivo (IAFT), visceralno masno tkivo (VF), maksimalno potkožno masno tkivo (Max SFT), minimalno potkožno masno tkivo (Min SFT)], kao i serumski nivoi hemerina i rezistina određivani su kod svih ispitanika. **Rezultati.** Kod svih antropometrijskih pokazatelja uočena je statistički značajna razlika među ispitivanim grupama. Ultrazvučni pokazatelji masnog tkiva (IAFT, VF, Max SFT, Min SFT) bili su statistički značajno viši u grupi gojaznih osoba u poređenju

sa kontrolnom grupom ( $p < 0,01$  za sve). Serumski nivoi hemerina i rezistina pozitivno su korelisali sa BMI, FAT(%), FAT (kg) i VF ( $p < 0,05$  za sve). Takođe, uočena je značajna korelacija između rezistina, sa jedne i NC sa druge strane ( $r = 0,23$ ;  $p = 0,03$ ), kao i ABSI ( $r = 0,22$ ;  $p = 0,04$ ). Multivarijabilna regresiona analiza pokazala je nezavisnu i značajnu povezanost hemerina ( $\beta = 0.23$ ;  $p = 0.008$ ) i rezistina ( $\beta = 0.43$ ;  $p = 0.002$ ) samo sa VF. **Zaključak.** Pokazatelji gojavnosti, kako klasični, tako i noviji, pozitivno i statistički značajno korelišu sa nivoom proinflammatory adipokina. Debljina visceralnog masnog tkiva, merena

ultrazvukom, nezavisno povezana sa nivoima adipokina, može poboljšati procenu karakteristika proinflammatory masnog tkiva. Dalje studije su potrebne kako bi se precizno definisala upotreba ultrazvučnih mera masnog tkiva u kliničkoj praksi.

**Ključne reči:**  
**adipokini; masno tkivo; antropometrija; metaboličke bolesti; gojaznost; rezistin; bolest, indeks težine; ultrasonografija.**

## Introduction

Obesity is a disease characterized by increased fatty body mass in a degree that leads to health deterioration and development of numerous complications<sup>1</sup>. Obesity is very complex, with characteristics of global epidemic and if this trend continues, by 2030 almost about 85% of adult population will be obese and preobese<sup>2</sup>. Heterogeneous predisposing factors have significant impact on obesity occurrence, comprising genetic factors, childhood obesity – “fat cell theory”, as well as extrinsic factors including sedentary lifestyle, unhealthy diet and low physical activity<sup>3</sup>.

Numerous anthropometric measurements [body mass index (BMI), waist circumference (WC), hip circumference (HC), and their ratio – waist/hip ratio (WHR)] are being used for both obesity assessment and monitoring the effects of obesity therapy<sup>4</sup>. Emerging anthropometric parameter is a body shape index (ABSI), which proved to be superior to BMI in prediction of cardiometabolic diseases<sup>5,6</sup>.

Aside from anthropometric parameters, imaging techniques have a significant role in visualization and measurement of fat tissue compartments. Computed tomography (CT) and magnetic resonance imaging (MRI) are golden standard in fat tissue evaluation, however they present numerous limitations (machines, radiation exposure, length of examination, price). Ultrasonographic measurement of visceral and subcutaneous fat tissue compartments, as well as hepatic fat content, proved to be simple and reliable method in cardiometabolic risk evaluation, more precise and reproducible compared to WC, HC and WHR<sup>7-9</sup>.

Increased secretion of proinflammatory adipokines is one of the most important characteristics of dysfunctional fat tissue. They are related to numerous pathophysiological processes which are baseline of some chronic disorders (low degree chronic inflammation, insulin resistance, arterial hypertension, dyslipidemia) as well as cardiometabolic, malignant and other diseases. It is known that resistin originates from adipocytes, immune cells and endothelial cells, and has significant role in processes of promotion of proinflammatory adhesive molecules and intracellular adhesive molecules expression and decreasing antiinflammatory effects of adiponectin on endothelial vascular cell<sup>10</sup>. The role of chemerin is also significant,

although not sufficiently researched up to now. Chemerin is a growth factor, chemokine and adipokine, and is predominantly secreted in fatty tissue, and its expression is present in other tissues, such as liver, placenta, thrombocytes and kidneys<sup>11,12</sup>. Contemporary researches emphasize the role of chemerin and its receptors in inflammation, adipogenesis, angiogenesis and osteoclastogenesis<sup>13,14</sup>. Although experimental studies confirmed visceral fat origin of chemerin, clinical studies have not confirmed which obesity indicators, anthropometric or quantitative measurements can show increased secretion of this adipokine. Therefore, the aim of this study was to investigate association between anthropometric indices, ultrasonographic measurement of visceral and subcutaneous fat tissue thickness and levels of certain proinflammatory adipokines (chemerin and resistin).

## Methods

### *Study design and inclusion criteria*

In this cross-sectional study, we used laboratory data, anthropometric measurements, as well as ultrasonographic measurements of subcutaneous and visceral fat tissue thickness. The research was conducted at the Clinic for Endocrinology, Diabetes and Metabolic Diseases, in collaboration with the Center for Laboratory Medicine and Center for Radiology, Clinical Center of Vojvodina, Novi Sad, Serbia. The study comprised a consecutive sample of 60 obese patients (BMI  $\geq 30$  kg/m<sup>2</sup>), without diabetes mellitus [fasting glucose level  $\leq 7.0$  mmol/L and glycolized hemoglobin A1c (HgbA1c)  $\leq 42$  mmol/L]. Exclusion criteria were: presence of autoimmune, infectious, malignant and psychiatric diseases, along with previously confirmed cardiovascular diseases. Another exclusion factor was changes of body weight within the past three months. The control group comprised 20 respondents with normal body mass (BMI  $< 25$  kg/m<sup>2</sup>), clinically healthy, and sex and age matched with obese patients. The study was conducted in accordance with the Helsinki declaration, and approved by Ethics Committee of the Clinical Center of Vojvodina (No 00-15/134). Each examinee signed informed consent. Patients' privacy was guaranteed by coding laboratory samples (each sample was assigned with a unique number).

### Study protocol

All respondents were outpatients administered to the Clinic for Endocrinology, Diabetes and Metabolic Diseases in order to analyze specific anthropometric parameters, clinical examination, laboratory analysis and ultrasonographic examination. Before obtaining blood samples, patients were asked to restrain from physical activity and alcohol intake for 24 h. Fasting for 12 h was mandatory before taking blood samples from cubital vein. Standard analyses were performed immediately afterwards, except for serum levels of chemerin and resistin analysis, for which, after centrifugation, samples were frozen at temperature of  $-20^{\circ}\text{C}$  no longer than 4 weeks.

### Anthropometric measurements

Body height (BH) was measured using a Martin anthropometer with accuracy of 0.1 cm, body mass (BM) was measured with medical decimal scale with accuracy of 0.1 kg. BMI was calculated using formula  $\text{BM}/\text{BH}^2$  ( $\text{kg}/\text{m}^2$ ). Neck circumference (NC), WC and HC were measured by measuring tape, with precision of 0.1 cm. ABSI was calculated using formula:  $\text{WC} \times \text{BM}^{-2/3} \times \text{body weight}^{5/6}$ . WHR was calculated using formula  $\text{WC}/\text{HC}$ . Total fat BM (FAT mass, kg) and percentage of fat BM (FAT mass, %) were estimated by bioelectrical impedance analysis (TANITA TFB-310 Body Composition Analyzer; Tanita, Tokyo, Japan).

### Laboratory measurements

Plasma glucose level was analyzed using standard method (enzyme UV test), insulin level was analyzed using standard method [Chemiluminescent Microparticle Immuno Assay (CMIA), using device ADVIA Centaur XP, Siemens, USA]. Insulin resistance index [homeostasis model assessment of insulin resistance (HOMA-IR)] was defined by basal concentration of glucose (G) and insulin values, using formula:  $\text{HOMA-IR} = \text{G} \times \text{I}_0/22.5$ <sup>15</sup>. Concentrations of total cholesterol (C), triglycerides, HDL-C and LDL-C were analyzed by direct enzyme method (Architect ci 4,100 Abbott, USA). Magnesium ( $\text{Mg}^{2+}$ , mmol/L) level was determined spectrophotometrically on the Mindray biochemical analyzer by applying commercial sets. Serum concentrations of chemerin and resistin were determined using the Human Chemerin Quantikine ELISA set and the Human Duo Set ELISA set, respectively (R&D Systems, Minneapolis, USA), according to user manual.

Ultrasonographic measurement of visceral and subcutaneous fat tissue thickness was performed on the GE Logiq 7 ultrasonography machine, with high frequency linear probe (12 Hz for subcutaneous fat thickness) and low frequency convex probe (5 MHz for visceral fat thickness)<sup>16</sup>.

The parameters of the visceral and subcutaneous fat tissue thickness were obtained by a standard examination; the patients were examined during the expiratory phase of a quiet respiration, and the transducer was applied on the body surface without undue pressure. Minimal subcutaneous fat (Min SFT) was defined as thickness of the fat tissue layer measured as the distance from the skin surface to the *linea alba*, under the

xiphoid process. The maximum thickness of subcutaneous fat tissue-a (Max SFTa) was defined as distance from the skin surface to the *linea alba*, measured 2 cm above the umbilical cord. The maximum thickness of subcutaneous fat tissue-b (Max SFTb) was defined as the distance from the skin surface to the *linea alba*, measured 2 cm below the umbilical cord. Thickness of intraabdominal fat tissue (IAFT) was defined as the distance between the posterior aspect of the *rectus abdominis* muscle and the anterior aortic wall, measured 2 cm above the umbilical cord. Visceral fat (VF) was defined as the distance between posterior aspect of the *rectus abdominis* muscle and anterior aspect of the paravertebral muscles measured at the umbilical level<sup>16</sup>.

Two radiologists, with 15 and 7 years of experience in abdominal ultrasonography, performed double-blinded independent measurements (IAFT, Max SFTa, Max SFTb and VF). Interobserver agreement of the measurements was analyzed in the group of 20 obese patients. The coefficient of variation (intraobserver and interobserver technical error) for IAFT was 3.6% and 4.2%; Max SFTa was 2.7% and 3.6%; Max SFTb was 4.1% and 3.3%; and VF was 4.3% and 6.2%, respectively.

### Statistical methods

The Shapiro-Wilk test was used in testing for normality. Data were presented as mean  $\pm$  standard deviation for normally distributed continuous variables and median (interquartile range) for nonparametric continuous variables, while categorical data were presented as the number of the observations divided with the total number of respondents within the group. Parametric (*t*-test) and nonparametric (Mann-Whitney) statistical tests were used. The  $\chi^2$  test was used for categorical variable (gender). Correlations between serum profile of adipokines and tested parameters were evaluated by the Pearson's or Spearman's coefficients. A multivariable regression analysis was used to assess the associations between serum chemerin and resistin levels, and anthropometric characteristic, ultrasonographic measurements of visceral and subcutaneous fat tissue thickness and metabolic biochemical characteristics. Statistical analysis of obtained data was performed using IBM Statistics SPSS 23 package (Chicago, Illinois, USA).

### Results

Table 1 shows the results of anthropometric measurements in the study groups. Obese respondents had significantly higher anthropometric indices (BMI, Fat, Fat Mass, ABSI, NC, WC, HC, WHR) compared to the control group of normally nourished respondents ( $p < 0.05$  and  $p < 0.01$ , respectively).

Descriptive characteristics of visceral and subcutaneous fat tissue thickness measurements by ultrasonography for all respondents are presented in Table 2. A subcutaneous fat tissue thickness measurements (Min SFT, Max SFTa and Max SFTb) were significantly higher in the obese group

Table 1

Anthropometric characteristics of study groups			
Variable	Obese group (n = 60)	Control group (n = 20)	<i>p</i>
Age (years), mean ± SD	38.7 ± 8.3	37.1 ± 4.7	0.04
Male, n (%)	21 (35.0)	10 (50.0)	0.35
BMI (kg/m <sup>2</sup> ), median (IQR)	35 (32.00–40.00)	23 (21.00–25.00)	< 0.01
Fat (%), mean ± SD	48.3 ± 10.1	22.6 ± 4.9	< 0.01
Fat Mass (kg), mean ± SD	51.9 ± 14.9	15.8 ± 3.3	< 0.01
ABSI, median (IQR)	0.078 (0.063–0.087)	0.075 (0.083–0.068)	0.02
NC (cm), median (IQR)	39.5 (37–44)	35 (32–37)	< 0.01
WC (cm), mean ± SD	111.8 ± 14.6	80 ± 8.85	< 0.01
HC (cm), median (IQR)	117.5 (110.5–122)	86 (84–94)	< 0.01
WHR, median (IQR)	0.95 (0.9–1.0)	1.1 (0.9–1.1)	0.04

**BMI – body mass index; ABSI – A Body Shape Index; NC – neck circumference; WC – waist circumference; HC – hip circumference; WHR – waist to hip ratio; SD – standard deviation; IQR – interquartile range.**

Table 2

#### Measurement of visceral and subcutaneous fat tissue thickness by ultrasonography

Variable	Obese group (n = 60) mean ± SD	Control group (n = 20) mean ± SD	<i>p</i>
IAFT (mm)	46.7 ± 28.9	24.2 ± 9.1	< 0.01
Max SFTa (mm)	33.6 ± 17.9	16.9 ± 5.3	< 0.01
Max SFTb (mm)	37.3 ± 19.6	20.2 ± 7.6	< 0.01
Min SFT (mm)	26.7 ± 15.2	17 ± 5.8	< 0.01
VF (mm)	51.1 ± 17.8	13.5 ± 37.2	< 0.01

**IAFT – intraabdominal fat tissue thickness; Max SFTa – maximum thickness of the subcutaneous fatty tissue-a; Max SFTb – maximum thickness of the subcutaneous fatty tissue-b; Min SFT – minimal subcutaneous fat tissue thickness; VF – visceral fat tissue thickness; SD – standard deviation.**

Table 3

#### Biochemical characteristics of study groups

Variable	Obese group (n = 60)	Control group (n = 20)	<i>p</i>
FPG (mmol/L), median (IQR)	5.2 (4.8–5.6)	4.9 (4.6–5.2)	< 0.01
HDL-C (mmol/L), mean ± SD	1.2 ± 0.3	1.5 ± 0.3	< 0.01
Triglycerides (mmol/L), median (IQR)	1.4 (1.1–2)	0.9 (0.5–1.2)	< 0.01
LDL-C (mmol/L), median (IQR)	3.2 (2.6–3.9)	2.6 (2.2–3.6)	= 0.04
FPI (mU/mL), median (IQR)	13.4 (10.4–18.6)	4.9 (4–6.1)	< 0.01
HOMA-IR, median (IQR)	2.4 (1.9–3.9)	0.7 (0.6–0.8)	< 0.01
Chemerin (ng/mL), median (IQR)	41.6 (26.2–61.1)	18.3 (14.5–26.7)	< 0.01
Resistin (ng/mL), median (IQR)	4.72 (4.27–5)	4.0 (2.9–4.7)	< 0.01
Mg <sup>2+</sup> (mmol/L), mean ± SD	0.83 ± 0.07	0.82 ± 0.06	= 0.46

**FPG – fasting plasma glucose; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; FPI – fasting plasma insulin; HOMA-IR – homeostasis model assessment of insulin resistance; SD – standard deviation; IQR – interquartile range.**

compared to the control one ( $p < 0.01$ , for all). Also, the obese respondents had significantly higher VF compared to the control ones ( $p < 0.01$ ).

All metabolic biochemical parameters (Table 3) were significantly higher in the obese compared to the control group ( $p < 0.05$  and  $p < 0.01$ , respectively).

Results of correlation analysis between serum profile of adipokines and tested parameters are shown in Table 4. The serum levels of chemerin and resistin correlated positively with BMI, FAT (%), FAT (kg), VF and HOMA-IR ( $p < 0.05$ , for all). Also, we observed significant correlation between resistin and NC ( $r = 0.23$ ,  $p = 0.03$ ) and ABSI ( $r = 0.22$ ,  $p = 0.04$ ).

Chemerin levels correlated positively with FPI ( $r = 0.45$ ,  $p = 0.01$ ) and triglycerides ( $r = 0.36$ ,  $p = 0.01$ ). Negative correlation was observed between resistin and HDL-C ( $r = -0.31$ ,  $p = 0.03$ ).

In multivariable linear regression analysis, chemerin ( $\beta = 0.23$ ;  $p = 0.008$ ) and resistin ( $\beta = 0.43$ ;  $p = 0.002$ ) levels were independently and significantly associated only with VF.

#### Discussion

Obesity is a disease in which individuals with the same or similar BMI can develop different metabolic, cardiovascular diseases, and even tumors. However, BMI

**Table 4****Correlation between adipokines and anthropometric and biochemical characteristics and ultrasonographic measurements in all respondents**

Parameter	Chemerin (ng/mL)		Resistin (ng/mL)	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
BMI (kg/m <sup>2</sup> )	0.42	0.00	0.26	0.017
WC (cm)	0.31	0.07	0.29	0.07
HC (cm)	0.29	0.01	0.25	0.23
NC (cm)	0.15	0.19	0.23	0.03
ABSI	0.13	0.26	0.22	0.04
FAT (%)	0.36	0.01	0.26	0.019
FAT mass (kg)	0.3	0.01	0.25	0.02
VF (mm)	0.49	0.00	0.48	0.00
Min SFT (mm)	0.112	0.322	-0.045	0.677
Max SFTa (mm)	0.103	0.364	-0.023	0.829
Max SFTb (mm)	0.165	0.143	-0.089	0.413
IAFT (mm)	0.108	0.342	-0.033	0.763
Max PFT (mm)	0.173	0.125	-0.092	0.399
FPG (mmol/L)	0.067	0.555	0.019	0.859
FPI (mU/mL)	0.45	0.001	0.272	0.011
HOMA-IR	0.368	0.01	0.316	0.05
Triglycerides (mmol/L)	0.365	0.01	0.195	0.07
HDL-C (mmol/L)	0.212	0.058	-0.317	0.03
LDL-C (mmol/L)	0.139	0.219	0.163	0.132

**BMI – body mass index; ABSI – a body shape index; NC – neck circumference; WC – waist circumference; HC – hip circumference; WHR – waist to hip ratio; IAFT – intraabdominal fat tissue thickness; Max PFT – maximum preoperational fatty tissue thickness; Max SFTa – maximum thickness of the subcutaneous fatty tissue-a; Max SFTb – maximum thickness of the subcutaneous fatty tissue-b; Min SFT – minimal subcutaneous fat tissue thickness; VF – visceral fat tissue thickness; FPG – fasting plasma glucose; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; FPI – fasting plasma insulin HOMA-IR – homeostasis model assessment of insulin resistance; *r* – coefficient of correlation.**

does not take into account fat tissue compartments<sup>16</sup>. Indices as WC, HC and WHR are relatively simple, reproducible method which can show fat tissue distribution, but their limitation is inability to precisely assess the amount of fat tissue. Bioelectrical impedance analysis is a method which can assess precise distribution, percentage and amount of fat BM in a total BM, and differ fat from non-fat BM<sup>17</sup>. NC and ABSI are new parameters, whose practical value has not been sufficiently examined yet. Ultrasonographic measurement of fat tissue thickness is available, cheap and reproducible<sup>18</sup>, with capability of analyzing subcutaneous and visceral fat depot, and has advantage in assessment of complications related to obesity. To assess functional characteristics of the fat tissue, serum concentrations of proinflammatory adipokines, chemerin and resistin are measured.

In our study, obese patients had significantly higher values of BMI, FAT mass (kg), percentage of fat adipose tissue (FAT, %) and WC. Also, we proved statistically significantly higher values of NC in the group of obese patients compared to the group with normal nutritional status. NC correlates with metabolic disorders, such as hypertriglyceridemia, insulin resistance, type 2 diabetes mellitus etc. Moreover, it has been proven that NC above 37 cm in men and 34 cm in women are reliable indicators for presence of abdominal obesity<sup>19</sup>. This study showed statistically positive correlation between NC and resistin level in the group of obese respondents, which has been

confirmed in only one study<sup>20</sup>. Resistin is proinflammatory adipokine, and correlation between resistin and NC can point out high risk obesity in examined group, with impact on different organ systems.

Along with NC, ABSI also had statistically higher values in the obese group in comparison to the control one. ABSI is a good anthropometric parameter for defining comorbidities related to obesity, chronic diseases and lethal outcome<sup>21-23</sup>. In our study, ABSI also had statistically significant correlation with resistin levels. This finding is even more significant considering that resistin is proinflammatory adipokine, and that its elevated concentrations in obese patients can indicate increased risk for numerous diseases related to obesity. To our knowledge, review of the literature showed no information on relation between resistin and ABSI.

In our research, obese patients had statistically significantly higher values of the subcutaneous and VF tissue compartment thickness compared to those in the control group. Also, the VF tissue thickness had statistically significant correlation with serum concentrations of chemerin and resistin. From pathophysiological aspect, this finding is very important considering that chemerin is adipokine with numerous different roles in human body, and that chemerin expression is higher in the visceral than in subcutaneous fat tissue<sup>24</sup>. These findings indicate that intrinsic factors of the VF tissue can play a crucial role in understanding main pathophysiological mechanisms which

lead to development of cardiovascular diseases, metabolic syndrome and inflammation in visceral adiposopathy<sup>25</sup>. Study of Schlecht et al.<sup>26</sup> did not prove statistically significant correlation between resistin values and the VF tissue measured by ultrasound, while research of McTernan et al.<sup>27</sup>, Azuma et al.<sup>28</sup> and Jain et al.<sup>29</sup> showed positive correlation of the VF tissue amount and serum values of proinflammatory resistin. Such controversial results imply the necessity of additional researches to further explain the connection of resistin and adipose tissue.

Beside anthropometric parameters and fat tissue thickness measurements, metabolic characteristics of the obese respondents showed significantly higher values of glycemia, insulinemia, HOMA-IR and proatherogenic cholesterol (LDL-C) and triglycerides, together with statistically significantly lower values of HDL-C compared to respondents with normal nutritional status. Moreover, there was statistically positive correlation between chemerin and insulin, HOMA-IR and triglycerides levels, as well as statistically positive correlation of resistin and HOMA-IR, and negative correlation of resistin and HDL-C. Multicentric study of American authors<sup>30</sup> also showed positive correlation of chemerin and values of insulin, HOMA-IR and triglycerides in patients with newly discovered metabolic syndrome. The same study proved positive correlation of chemerin and the subcutaneous fat tissue, which was not confirmed in our study. Research of German authors<sup>31</sup> showed that chemerin is a good biomarker of insulin resistance in healthy adult men. However, data regarding dyslipidemia and inflammation are yet debatable<sup>32,33</sup>. Due to this, further research of chemerin role in metabolic disorders is highly desirable.

It is known that resistin is secreted from adipocytes and macrophages, and is also a trigger for development of insulin resistance. In most of the published studies, increased resistin values were detected in obesity, metabolic syndrome, and type 2 diabetes mellitus<sup>34-36</sup>. Our study did not confirm statistically positive correlation between resistin and triglycerides levels as parameter of metabolic syndrome. Studies of de Luis et al.<sup>37</sup>, and Uslu et al.<sup>38</sup> showed positive correlation of resistin with LDL-C, and negative correlation with HDL-C fraction, which is in compliance with results of our study. Hypothesis of inverse correlation of resistin with cholesterol serum levels can be explained by resistin dependent cholesterol sequestration in macrophages. Another

possible explanation of inverse correlation between resistin and HDL-C can be explained by the fact that cholesterol concentration depends on resistin concentration<sup>39-41</sup>. Our study proved statistically positive correlation between resistin and HOMA-IR, which was confirmed in previous studies<sup>42</sup>.

Advantage of our study was direct comparison of two actual adipocytokines with precisely defined amount of the fat tissue in specific compartments and with anthropometric parameters, as well as correlation of proinflammatory adipokines with metabolic markers. The main limitations of the current study were small sample size and cross-sectional study design. Also, as the measurement of serum concentration of chemerin and resistin is not current practice, there is a limited implementation of this study in general practice.

Therefore, further prospective studies could have far more significant role in defining and monitoring comorbidities related to obesity. Early identification of pathogenetic factors in development of obesity related comorbidities (insulin resistance, chronic inflammation, fat tissue dysfunction etc.) could result in personalized prevention and/or personalized treatment of obese, high-risk patients.

### Conclusion

There is positive, statistically significant correlation between obesity indices, both classical and newer ones, and the level of proinflammatory cytokines (chemerin and resistin). Ultrasonographically measured VF thickness may improve assessment of proinflammatory fat tissue characteristics. Further studies are needed to precisely define the use of ultrasonographic fat tissue measurements in clinical practice.

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