УДК 617.55-056.257-008.6-008.9
https://doi.org/10.20538/1682-0363-2025-2-116-123

Associations of Visceral Adipose Tissue Adipokines with Metabolic Disorders in Abdominal Obesity

Tuzovskaia O.V., Polonskaya Ya.V., Garbuzova E.V., Kashtanova E.V., Ragino Yu.I.

Research Institute of Internal and Preventive Medicine, Branch of the Federal Research Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences (IIPM – Branch of IC&G SB RAS)
175/1 B. Bogatkov St., 630089 Novosibirsk, Russian Federation

ABSTRACT

Aim. To identify associations of visceral adipose tissue adipokines with metabolic disorders in abdominal obesity.

Materials and methods. The study included 101 individuals aged 25–65 years (51 men). For all patients, questionnaires were completed, anthropometric measurements and 3 measurements of blood pressure were performed, fasting blood was sampled, and biopsies of visceral adipose tissue were collected during elective surgery. The parameters of the lipid profile and glucose levels were determined in the blood by enzymatic methods. Homogenates from biopsies of visceral adipose tissue were prepared. The blood levels of adiponectin, adipsin, lipocalin-2, plasminogen activator inhibitor type 1 (PAI-1), and resistin were measured, and homogenates of adipose tissue were obtained by the multiplex analysis. Sex hormone levels in the blood of all patients (estradiol in women, testosterone in men) were determined by the enzyme-linked immunosorbent assay (ELISA) kits.

Results. We identified correlations between serum levels of adipsin and adipose tissue and between adipsin from adipose tissue and PAI-1 in the blood serum. A weak negative relationship was found between the level of adiponectin and waist circumference, body mass index, and insulin resistance indices: triglyceride glucose index (TyG), lipid accumulation product (LAP), and visceral adiposity index (VAI). The level of adiponectin in visceral adipose tissue was inversely correlated with overweight in males and in the 45–65 age group. The level of resistin in visceral adipose tissue showed an inverse correlation with diastolic blood pressure, which persisted in the age group of 25–44 years.

Conclusion. Of the studied adipokines, a relationship with cardiometabolic parameters was shown for adiponectin and resistin. At the same time, adiponectin was inversely correlated with overweight in the group of men and in the age group of 45–65 years, while resistin was inversely correlated with diastolic blood pressure in the age group of 25–44 years.

Keywords: adipokine, visceral adipose tissue, adiponectin, adipsin, lipocalin-2, PAI-1, resistin

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The study was conducted within the budgetary topic of the state assignment No. FWNR-2024-0004 and funded by the RSF grant No. 21-15-00022.

Conformity with the principles of ethics. All study participants signed an informed consent. The study was approved by the Ethics Committee at IIPM – Branch of IC&G SB RAS (Minutes No. 66 dated October 24, 2023).

For citation: Tuzovskaia O.V., Polonskaya Ya.V., Garbuzova E.V., Kashtanova E.V., Ragino Yu.I. Associations of visceral adipose tissue adipokines with metabolic disorders in abdominal obesity. *Bulletin of Siberian Medicine.* 2025;24(2):116–123. https://doi.org/10.20538/1682-0363-2025-2-116-123.

✉ *Tuzovskaia Olga V.,* o-nazarenko@list.ru

Ассоциации адипокинов висцеральной жировой ткани с метаболическими нарушениями при абдоминальном ожирении

Тузовская О.В., Полонская Я.В., Гарбузова Е.В., Каштанова Е.В., Рагино Ю.И.

Научно-исследовательский институт терапии и профилактической медицины – филиал Федерального исследовательского центра «Институт цитологии и генетики Сибирского отделения Российской академии наук» (НИИТПМ – филиал ИЦиГ СО РАН)

Россия, 630089, г. Новосибирск, ул. Б. Богаткова, 175/1

РЕЗЮМЕ

Цель: выявить ассоциации между адипокинами висцеральной жировой ткани с метаболическими нарушениями при абдоминальном ожирении.

Материалы и методы. В исследовании приняли участие 101 человек в возрасте 25–65 лет. Проводилось анкетирование, антропометрия, измерение артериального давления, а также забор крови натощак и биоптатов висцеральной жировой ткани во время плановой операции. Энзиматическими методами в крови были определены показатели липидного профиля и глюкозы. Из биоптатов висцеральной жировой ткани были приготовлены гомогенаты, в которых методом мультиплексного анализа определялся уровень адипонектина, адипсина, липокалина-2, ингибитора активатора плазминогена 1 типа (PAI-1), резистина. У всех пациентов с помощью наборов enzyme-linked immunosorbent assay (ELISA) проведено измерение в крови уровня половых гормонов (у женщин – эстрадиола, у мужчин – тестостерона).

Результаты. Были выявлены связи между уровнями адипсина в сыворотке крови и жировой ткани, адипсина в жировой ткани и PAI-1 в сыворотке крови. Обнаружена слабая отрицательная связь между уровнем адипонектина и показателями окружности талии, индекса массы тела и индексами инсулинорезистентности (индекс триглицериды-глюкоза (TyG), индекс lipid accumulation product (LAP), visceral adiposity index (VAI)). Уровень адипонектина в висцеральной жировой ткани обратно ассоциирован с избыточной массой тела среди лиц мужского пола и в возрастной группе 45–65 лет. Уровень резистина в висцеральной жировой ткани демонстрировал обратную зависимость от диастолического артериального давления, что сохранялось для возрастной группы 25–44 лет.

Заключение. Из изученных нами адипокинов связь с кардиометаболическими параметрами была показана для адипонектина и резистина. При этом адипонектин обратно ассоциирован с избыточной массой тела в группе мужчин и возрасте 45–65 лет, а резистин – с диастолическим артериальным давлением в возрастной группе 25–44 лет.

Ключевые слова: адипокин, висцеральная жировая ткань, адипонектин, адипсин, липокалин-2, PAI-1, резистин

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Исследование выполнено в рамках бюджетной темы по государственному заданию № FWNR-2024-0004 и при финансовой поддержке гранта Российского научного фонда № 21-15-00022.

Соответствие принципам этики. Все участники подписали информированное согласие на участие в исследовании. Исследование одобрено этическим комитетом НИИТПМ – филиал ИЦиГ СО РАН (протокол № 66 от 24.10.2023).

Для цитирования: Тузовская О.В., Полонская Я.В., Гарбузова Е.В., Каштанова Е.В., Рагино Ю.И. Ассоциации адипокинов висцеральной жировой ткани с метаболическими нарушениями при абдоминальном ожирении. *Бюллетень сибирской медицины.* 2025;24(2):116–123. https://doi.org/10.20538/1682-0363-2025-2-116-123.

INTRODUCTION

Obesity makes a significant contribution to the pathogenesis of cardiovascular diseases (CVD) and metabolic disorders, such as type 2 diabetes mellitus (T2DM), arterial hypertension (AH), and dyslipidemia [1]. The distribution of adipose tissue is a key factor in this process. Abdominal obesity (AO), which involves the accumulation of fat near internal organs, is associated with the highest risk of developing cardiovascular and metabolic diseases [1, 2]. Only recently it has been discovered that adipose tissue is not merely an energy storage but also an endocrine organ [3]. Despite this, the list of biomolecules synthesized by adipocytes, known as adipokines, continues to grow. Currently it includes over 700 adipokines [4]. All of them are involved in the pathogenesis of obesity and participate in the formation of other components of the metabolic syndrome. Most studies are limited to the determination of adipokines in the blood as the most accessible biomaterial for study. The study of these biomolecules in adipose tissue, in particular in the visceral depot, is associated with a number of limitations, therefore, the number of works on this topic is not large [5–8]. Meanwhile, this issue is of fundamental and clinical interest.

The aim of this study was to identify associations between adipokines of visceral adipose tissue and metabolic disorders observed in patients with AO.

MATERIALS AND METHODS

The study included 101 people aged 25–65 years who were hospitalized in the Surgical Department of the City Clinical Hospital No.2 for elective surgery (surgery for anterior abdominal wall hernia, or cholecystectomy for cholelithiasis or polyps, or diverticulosis of the colon).

The patients completed questionnaires covering their medical history and underwent anthropometric measurements (height, weight, waist circumference (WC), and hip circumference (HC)). Body mass index (BMI) was determined by the formula: BMI (kg/m²) = weight, kg/height, m². The examination included three measurements of blood pressure (BP) (with an interval of two minutes on the right arm in a sitting position after 5-minute rest using an OMRON automatic blood pressure monitor with the recording of the average value of the three measurements).

Before surgery, blood serum samples were taken from patients on an empty stomach, after a 12-hour overnight fasting period. Enzymatic methods using TermoFisher reagents on an automatic biochemical analyzer KoneLab 30i (Finland) in the blood were used to determine the parameters of the lipid profile: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and glucose. The levels of low-density lipoprotein cholesterol (LDL-C) were calculated using the Friedwald formula [9], non-high-density lipoprotein cholesterol (non-HDL-C) level was calculated using the TC–HDL-C formula. We calculated the ratio of TG/HDL-C. The TyG index was calculated according to the formula (Ln (TG in mg / dl × glucose in mg/dl))/2. The LAP (lipid accumulation product) index was calculated according to the following formulas: for men: (WC in cm – 65) × TG in mmol/l; for women: (WC in cm –58) × TG in mmol/l. VAI (visceral obesity index) for men was calculated according to the formula: WC/(39.68 + 1.88 × BMI) × (TG/1.03) × (1.31 / HDL-C); for women: WC / (36.58 + 1.89 × BMI) × (TG / 0.81) × (1.52 / HDL-C), where the values of TG and HDL-C are given in mmol/l [10]. In addition, the level of the following adipokines was determined in blood by the multiplex analysis using the MILLIPLEX MAP Human Adipokine Panel 1 kit for the determination of human adipokines: adiponectin, adipsin, lipocalin-2, plasminogen activator inhibitor type 1 (PAI-1), and resistin.

During the surgery, visceral adipose tissue biopsies (3–5 g) were collected. Homogenates were prepared from the biopsies, in which the adiponectin, adipsin, lipocalin-2, PAI-1, and resistin levels were determined by the multiplex analysis using the MILLIPLEX MAP Human Adipokine Panel 1 kit for the determination of human adipokines.

Sex hormone levels (estradiol in women and testosterone in men) were measured in all patients using enzyme-linked immunosorbent assay (ELISA) kits for subsequent standardization of this parameter in statistical analysis.

Statistical processing of the results was carried out using the SPSS software package (version 20.0). The normality of data distribution was evaluated using the Kolmogorov–Smirnov test. When comparing the groups, the nonparametric Mann–Whitney *U*-test was used for continuous data, and $\chi 2$ was applied for discrete data. The correlation analysis was carried out using the Spearman's rank correlation coefficient. To find associations with cardiometabolic disorders, the linear regression analysis was performed with the inclusion of adipokines as dependent variables. Categorical variables were presented as absolute (*n*)

and relative (%) values, continuous variables were presented as the median and the interquartile range *Me* (Q_{25}; Q_{75}). The critical significance level of the null hypothesis was calculated at $p \leq 0.05$.

RESULTS

The patients were divided into 2 groups depending on the presence of abdominal obesity (AO) according to the criteria of the All-Russian Scientific Society of Cardiology (2009): WC > 80 cm in women and WC > 94 cm in men. The main group included 74 people with AO (44 men, 30 women), the control group encompassed 27 people (7 men, 20 women) ($p = 0.033$). The groups did not differ in age: the median age was 52.50 [41.00; 61.00] years and 51.00 [41.00; 63.00] years, respectively. Significant differences in BMI were revealed: in the main group, the BMI was 31.62 [27.66; 35.51] kg/m², in the control group – 23.63 [20.31; 29.00] kg/m² ($p < 0.001$). There were no significant differences for systolic (SBP) and diastolic blood pressure (DBP), as well as in the presence of AH, coronary heart disease (CHD), ischemic stroke, T2DM, non-alcoholic fatty liver disease (NAFLD), and smoking.

Among patients from the main group, the TG level was 1.3 times higher ($p = 0.002$), and HDL-C was 1.3 times lower ($p = 0.002$) than in the control group. In the main group, TG/HDL-C was 1.6 times ($p < 0.001$), TyG – 1.04 times ($p = 0.002$), LAP – 2.6 times ($p < 0.001$), and VAI – 1.4 times ($p = 0.001$) higher than those in the control group.

Thus, among patients with AO, compared to individuals without it, the following metabolic disorders were identified: expected higher BMI, a higher TG level, a lower HDL-C level, as well as higher insulin resistance indices.

The next step was to determine the levels of the studied adipokines in visceral adipose tissue, depending on the presence of AO, overweight, and obesity.

Adiponectin, adipokine, lipocalin-2, PAI-1, and resistin did not demonstrate significant differences in protein concentration in visceral adipose tissue between patients from the main and control groups.

Table 1

Clinical Characteristics of the Patients Included in the Study, Depending on the Presence of Abdominal Obesity, *Me* (Q_{25}; Q_{75})

Parameters	Group without AO, $n = 27$	Group with AO, $n = 74$	p
Men	7 (26%)	44 (60%)	0.033
Age, years	51.00 [41.00; 63.00]	52.50 [41.00; 61.00]	0.923
BMI, kg/m²	23.63 [20.31; 29.00]	31.62 [27.66; 35.51]	0.0001
sBP, mm Hg	126.50 [113.50; 138.00]	129.75 [120.50; 143.00]	0.171
dBP, mm Hg	82.00 [75.00; 87.00]	82.25 [77.50; 91.13]	0.473
Smoking	6 (22%)	27 (36%)	0.178
History of AH	9 (33%)	41 (55%)	0.051
History of CHD	0 (0%)	6 (8%)	0.129
History of IS	0 (0%)	3 (4%)	0.291
History of T2DM	1 (4%)	10 (14%)	0.163
History of NAFLD	1 (4%)	12 (16%)	0.098
TC, mmol/l	5.35 [4.41; 5.87]	5.01 [4.04; 5.71]	0.313
TG, mmol/l	1.18 [0.90; 1.69]	1.50 [1.20; 2.01]	0.002
HDL-C, mmol/l	1.69 [1.21; 2.00]	1.30 [0.98; 1.55]	0.002
LDL-C, mmol/l	3.18 [2.10; 3.71]	2.96 [2.07; 3.56]	0.602
non-HDL-C, mmol/l	3.67 [2.72; 4.44]	3.76 [2.78; 4.51]	0.724
Glucose, mmol/l	5.60 [5.40; 6.40]	6.05 [5.50; 6.70]	0.159
TG / HDL-C index	0.78 [0.56; 0.94]	1.23 [0.89; 1.73]	0.0001
TyG index	4.20 [4.12; 4.34]	4.38 [4.23; 4.56]	0.002
LAP index	24.32 [13.84; 45.90]	64.40 [37.00; 96.06]	0.0001
VAI index	1.32 [0.72; 1.71]	1.80 [1.25; 2.96]	0.001

Note: non-HDL-C – non-high-density lipoprotein cholesterol, VAI – visceral adiposity index, LAP – lipid accumulation product.

Table 2

Adipokines of Adipose Tissue Depending on the Presence of Overweight and Obesity, *Me* (Q_{25}; Q_{75})

Adipokines	BMI < 25.0 kg / m²	BMI 25.0–29.9 kg / m²	p_1	BMI < 30.0 kg / m²	BMI ≥ 30.0 kg / m²	p_2
Adiponectin, mcg/mg of tissue	10.15 [6.24; 11.99]	6.76 [4.95; 8.56]	0.015	7.25 [5.77; 10.78]	5.84 [4.19; 8.38]	0.030
Adipsin, mcg/mg of tissue	1.22 [0.90; 2.11]	1.92 [1.21; 2.82]	0.067	1.62 [1.05; 2.26]	1.76 [1.09; 3.17]	0.273
Lipocalin-2, mcg/mg of tissue	0.12 [0.06; 0.23]	0.08 [0.05; 0.21]	0.378	0.09 [0.05; 0.21]	0.15 [0.06; 0.39]	0.041
PAI-1, ng/mg of tissue	0.89 [0.44; 1.17]	0.84 [0.51; 1.55]	0.715	0.85 [0.50; 1.18]	1.05 [0.53; 2.65]	0.144
Resistin, ng/mg of tissue	23.86 [3.74; 61.96]	13.45 [4.72; 25.13]	0.413	17.81 [4.46; 37.34]	17.85 [7.05; 65.37]	0.277

Note: p_1 – significance of differences between groups of patients with normal weight and overweight, p_2 – significance of differences between groups of patients without obesity and with obesity.

When studying these adipokines in visceral adipose tissue, depending on the presence of overweight (BMI < 25 kg/m² versus BMI 25.0–29.9 kg/m²), the level of adiponectin in patients with normal body weight was 1.5 times higher than in overweight patients ($p < 0.05$).

Obese patients (BMI ≥ 30.0 kg/m²) had lower levels of adiponectin in visceral adipose tissue compared to non-obese patients (BMI < 30.0 kg/m²). It was reduced by 1.24 times ($p < 0.05$). Lipocalin-2, on the contrary, was 1.67 times higher ($p < 0.05$) in individuals with BMI ≥ 30.0 kg/m² (Table 2).

When performing the correlation analysis to assess the relationship between the studied biomarkers in the blood serum and visceral adipose tissue, a relationship was found between the levels of adipsin ($r = 0.316$; $p = 0.007$), as well as adipsin in the adipose tissue and PAI-1 in the blood serum ($r = 0.278$; $p = 0.019$) (Table 3).

The correlation analysis of adipokines of visceral adipose tissue and clinical characteristics of patients showed a weak negative relationship between the level of adiponectin and WC ($r = –0.210$; $p = 0.044$) and BMI ($r = –0.263$; $p = 0.011$). An inverse correlation was observed for adiponectin and insulin resistance indices: for the TyG index $r = –0.268$ ($p = 0.009$), for LAP $r = –0.284$ ($p = 0.006$), for VAI $r = –0.205$ ($p = 0.049$) (Table 4).

Table 3

Correlation Analysis of Adipokines in Blood Serum and Visceral Adipose Tissue Using the Spearman's Rank Correlation Coefficient

Adipokines in VAT / Adipokines in blood	Adiponectin, mcg/mg of tissue	Adipsin, mcg/mg of tissue	Lipocalin-2, mcg/mg of tissue	PAI-1, ng /mg of tissue	Resistin, ng/mg of tissue
Adiponectin, mcg/ml	0.125 $p = 0.340$	0.160 $p = 0.211$	–0.044 $p = 0.732$	–0.220 $p = 0.091$	–0.015 $p = 0.906$
Adipsin, mcg/ml	0.123 $p = 0.326$	0.316 $p = 0.007$	–0.063 $p = 0.605$	–0.221 $p = 0.075$	–0.188 $p = 0.122$
Lipocalin-2, mcg/ml	0.192 $p = 0.122$	0.013 $p = 0.916$	–0.067 $p = 0.579$	0.056 $p = 0.655$	–0.016 $p = 0.898$
PAI-1, ng/ml	0.125 $p = 0.317$	0.278 $p = 0.019$	0.064 $p = 0.600$	0.011 $p = 0.928$	–0.017 $p = 0.892$
Resistin, ng/ml	0.035 $p = 0.784$	–0.059 $p = 0.628$	–0.080 $p = 0.518$	0.162 $p = 0.201$	0.057 $p = 0.647$

Table 4

Correlation Analysis of Visceral Adipokines and Metabolic Parameters Using the Spearman's Rank Correlation Coefficient

Adipokines in VAT / Metabolic parameters	Adiponectin, mcg/mg of tissue	Adipsin, mcg/mg of tissue	Lipocalin-2, mcg/mg of tissue	PAI-1, ng/mg of tissue	Resistin, ng/mg of tissue
WC, cm	–0.210 $p = 0.044$	0.133 $p = 0.202$	0.143 $p = 0.161$	0.166 $p = 0.139$	0.038 $p = 0.714$
BMI, kg/m²	–0.263 $p = 0.011$	0.132 $p = 0.203$	0.162 $p = 0.113$	0.167 $p = 0.137$	0.066 $p = 0.524$

End of table 3

Adipokines in VAT Metabolic parameters	Adiponectin, mcg/mg of tissue	Adipsin, mcg/mg of tissue	Lipocalin-2, mcg/mg of tissue	PAI-1, ng/mg of tissue	Resistin, ng/mg of tissue
SBP, mm Hg	–0.082 $p = 0.433$	0.116 $p = 0.265$	0.015 $p = 0.883$	–0.069 $p = 0.539$	–0.090 $p = 0.388$
DBP, mm Hg	–0.168 $p = 0.109$	0.013 $p = 0.901$	0.055 $p = 0.594$	–0.037 $p = 0.743$	–0.077 $p = 0.456$
TG / HDL-C index	–0.164 $p = 0.117$	0.065 $p = 0.532$	0.149 $p = 0.146$	**0.231** $p = 0.038$	0.110 $p = 0.290$
TyG index	–0.268 $p = 0.009$	–0.011 $p = 0.920$	0.170 $p = 0.095$	0.161 $p = 0.150$	0.194 $p = 0.060$
LAP index	–0.284 $p = 0.006$	0.058 $p = 0.576$	0.169 $p = 0.098$	0.198 $p = 0.077$	0.124 $p = 0.233$
VAI index	–0.205 $p = 0.049$	0.023 $p = 0.823$	0.169 $p = 0.098$	0.215 $p = 0.054$	0.118 $p = 0.254$

The next stage of the study was to include the studied adipokines of visceral adipose tissue in the linear regression analysis. The independent variables included cardiometabolic parameters (WC, BMI, SBP, DBP, as well as the presence of obesity, overweight, AO, BP, blood glucose ≥ 6.1 mmol/l, HDL-C < 1 for men, 1.2 mmol/l for women, LDL-C ≥ 3 mmol/l, TG ≥ 1.7 mmol) and insulin resistance indices (TG / HDL-C, TyG, LAP, VAI) with standardization by age, sex, and sex hormone levels. As a result of this analysis, it was found that the level of adiponectin in the visceral adipose tissue was inversely associated with overweight in the general group (–3.542 [–5.318; –1.766], $p = 0.0001$). This association was also observed in men (–4.303 [–6.842; –1.764], $p = 0.0001$) and in the 45–65 age group (–4.662 [–7.105; –2.219], $p = 0.001$).

The level of resistin in visceral adipose tissue, when age, sex, AO, DBP, glucose, and TG were included in the model, was found to be dependent on DBP in the overall group (–3.891 [–6.979; –0.803], $p = 0.014$) and in the 25–44 age group (–7.496 [–13.182; –1.810], $p = 0.012$).

No significant associations were found between the levels of adiponectin, lipocalin-2, and PAI-1 in visceral adipose tissue and the studied parameters.

DISCUSSION

Adiponectin is a protein with a complex tertiary structure, synthesized by adipocytes. The impact of adiponectin on the body is facilitated by the AdipoR1 and AdipoR2 receptors. One of the most significant effects of adiponectin is its ability to overcome insulin resistance. It enhances insulin sensitivity in target organs, such as the liver and skeletal muscles, by promoting fatty acid oxidation and stimulating glucose utilization through the activation of the AMPK signaling pathway. The level of adiponectin in the blood serum is inversely proportional to BMI, triglyceride levels, and insulin resistance [11].

Furthermore, adiponectin has the potential to inhibit inflammation and possibly atherogenesis by suppressing the migration of monocytes and macrophages, as well as their transformation into foam cells [12]. Studies on adiponectin in adipose tissue are scarce and often conflicting. The study of adiponectin was conducted in the visceral adipose tissue of different localizations – the epicardial and perivascular fat depots in patients with CHD. The study by O.V. Gruzdeva et al. revealed a decrease in adiponectin mRNA concentration in patients with CHD. Moreover, the more pronounced the atherosclerotic lesion of the coronary artery, the lower the level of adiponectin gene expression [5].

In the study by A. Sirbu et al., no association was found between the level of adiponectin mRNA in visceral adipose tissue and BMI or WC, as well as serum adiponectin. However, participants with obesity and insulin resistance, as assessed by the HOMA-IR index, exhibited lower adiponectin expression levels compared to participants without insulin resistance [13]. Studies by T. Hörbelt et al. [14] and M.I. Jonas et al. [15] demonstrated a decrease in adiponectin levels in visceral and subcutaneous adipose tissue in individuals with obesity. Our data also show an inverse relationship between adiponectin in visceral adipose tissue and overweight, with this relationship persisting in men and in the older age group.

One of the first discovered functions of resistin was the formation of insulin resistance, which is the basis of its name. Subsequently, it was demonstrated that resistin exerts a wide range of effects, including influencing lipid metabolism, promoting the synthesis and secretion of proinflammatory cytokines, and

facilitating the differentiation of monocytes into macrophages. Furthermore, it influences heart contractility, smooth muscle cell activity, angiogenesis, endothelial permeability, and renal function [16]. Resistin was first discovered in rodent adipocytes and was initially thought to be a protein exclusively synthesized in adipose tissue. However, the highest levels of its expression in humans were found in bone marrow cells [17]. Elevated levels of resistin mRNA and protein, accompanied by a simultaneous decrease in adiponectin in subcutaneous adipose tissue, were observed in individuals with obesity. However, no significant differences were observed in the visceral adipose tissue [15].

Another study concluded that there is a link between adipose tissue resistin and impaired fasting plasma glucose in South Asian women [18]. Our findings suggest a link between resistin and DBP levels, first discovered for adipose tissue. Interestingly, this relationship is inverse, meaning that as DBP levels increase, resistin concentrations decrease. However, the link between BP, high normal blood pressure, and resistin levels has already been established for its circulating form [19–21]. The underlying mechanism of resitin action in the presence of hypertension remains unknown.

A study conducted on mice suggests that the activation of the renin–angiotensin–aldosterone system (RAAS) by resistin through the TLR4/P65/Agt pathway is responsible for this effect. This activation leads to an increase in the expression of angiotensinogen, the precursor of angiotensin II, the primary effector of RAAS. This theory is further supported by the absence of an increase in blood pressure following the administration of resistin to mice, even after pre-treatment with angiotensin-converting enzyme inhibitors [22]. Another potential mechanism involves reducing the expression of endothelial nitric oxide synthase (eNOS) and decreasing the bioavailability of NO, which in turn disrupts endothelium-dependent vasorelaxation [23]. Our discoveries necessitate further clarification and explanation of the inverse relationship between resistin levels and DBP.

CONCLUSION

Research on adipokines in adipose tissue, particularly their association with cardiometabolic parameters, remains limited. In our study, we successfully established the link between adiponectin and resistin of visceral fat tissue, as well as cardiometabolic parameters. Adiponectin is inversely associated with overweight in the male group and in the 45–65 age group, while resistin is inversely associated with diastolic blood pressure in the 25–45 age group.

REFERENCES

1. Powell-Wiley T.M., Poirier P., Burke L.E., Després J.P., Gordon-Larsen P., Lavie C.J. et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2021;143(21):e984–e1010. DOI: 10.1161/CIR.0000000000000973/
2. Lee J.J., Pedley A., Hoffmann U., Massaro J.M., Levy D., Long M.T. Visceral and Intrahepatic Fat Are Associated with Cardiometabolic Risk Factors Above Other Ectopic Fat Depots: The Framingham Heart Study. *The American Journal of Medicine*. 2018;131(6):684–692.e12. DOI: 10.1016/j.amjmed.2018.02.002/
3. Ahima R.S., Flier J.S. Adipose tissue as an endocrine organ. *Trends in endocrinology and metabolism: TEM.* 2000;11(8):327–332. DOI: 10.1016/s1043-2760(00)00301-5
4. Zhang Y., Yu M., Dong J., Wu Y., Tian W. Identification of novel adipokines through proteomic profiling of small extracellular vesicles derived from adipose tissue. *J. Proteome Res*. 2020;19(8):3130–3142. DOI: 10.1021/acs.jproteome.0c00131.
5. Gruzdeva O.V., Dyleva Yu.A., Belik E.V., Akbasheva O.E., Borodkina D.A., Sinitsky M.Yu. et al. Expression of Adipocytokine in Heart Fat Depots Depending on the Degree of Coronary Artery Atherosclerosis in Patients with Coronary Artery Disease. *Annals of the Russian Academy of Medical Sciences*. 2021;76(2):159–168. (In Russ.).
6. Polyakova E.A., Kolodina D.A., Miroshnikova V.V., Razgildina N.D., Bogdanova E.O., Lyapina E.N. et al. Subcutaneous and Epicardial Adipose Tissue Leptin Gene Expression in Coronary Artery Disease. *Translational Medicine*. 2019;6(3):25–35. (In Russ.). DOI: 10.18705/2311-4495-2019-6-3-25-35.
7. Belik E.V., Gruzdeva O.V., Dyleva Yu.A., Bychkova E.E., Kuzmina A.A., Ivanov S.V. et al. Features of Plasminogen Activator Inhibitor-1 Synthesis by Local Fat Depots of Different Localization in Cardiovascular Diseases. *Russian Journal of Cardiology.* 2022;27(4):4866. (In Russ.). DOI: 10.15829/1560-4071-2022-4866.
8. Pobozheva I.A., Razgildina N.D., Polyakova E.A., Panteleeva A.A., Belyaeva O.D., Nifontov S.E. et al. Epicardial and Subcutaneous Adipose Tissue Adiponectin Gene Expression in Coronary Artery Disease Patients. *Kardiologiia.* 2020;60(4):62–69. (In Russ.). DOI: 10.18087/cardio.2020.4.n517.
9. Friedewald W.T., Levy R.I., Fredrickson D.S. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clinical Chemistry. 1972;18(6):499–502.
10. Ruyatkina L.A., Ruyatkin D.S., Iskhakova I.S. Opportunities and Options for Surrogate Assessment of Insulin Resistance. *Obesity and Metabolism.* 2019;16(1):27–32. (In Russ.). DOI: 10.14341/omet10082.
11. Taylor E.B.. The complex role of adipokines in obesity, inflammation, and autoimmunity. *Clin. Sci. (Lond.).* 2021;135(6):731–752. DOI: 10.1042/CS20200895.

12. Pittas A.G., Joseph N.A., Greenberg A.S. Adipocytokines and insulin resistance. The Journal of clinical endocrinology and metabolism. 2004;89(2):447–452. DOI:10.1210/jc.2003-031005
13. Sirbu A.E., Buburuzan L., Kevorkian S., Martin S., Barbu C., Copaescu C. et al. Adiponectin expression in visceral adiposity is an important determinant of insulin resistance in morbid obesity. *Endokrynologia Polska*. 2018;69(3):252–258. DOI: 10.5603/EP.a2018.0026.
14. Hörbelt T., Tacke C., Markova M., Herzfeld de Wiza D., Van de Velde F., Bekaert M. et al. The novel adipokine WISP1 associates with insulin resistance and impairs insulin action in human myotubes and mouse hepatocytes. *Diabetologia.* 2018;61(9):2054–2065. DOI: 10.1007/s00125-018-4636-9.
15. Jonas M.I., Kurylowicz A., Bartoszewicz Z., Lisik W., Jonas M., Domienik-Karlowicz J. et al. Adiponectin/resistin interplay in serum and in adipose tissue of obese and normal-weight individuals. *Diabetology & Metabolic Syndrome*. 2017;9:95. DOI: 10.1186/s13098-017-0293-2.
16. Acquarone E., Monacelli F., Borghi R., Nencioni A., Odetti P. Resistin: A reappraisal. *Mechanisms of Ageing and Development*. 2019;178:46–63. DOI: 10.1016/j.mad.2019.01.004.
17. Patel L., Buckels A.C., Kinghorn I.J., Murdock P.R., Holbrook J.D., Plumpton C. et al. Resistin is expressed in human macrophages and directly regulated by PPAR gamma activators. *Biochemical and Biophysical Research Communications*. 2003;300(2):472–476. DOI: 10.1016/s0006-291x(02)02841-3.
18. Wijetunge S., Ratnayake R.M.C.J., Kotakadeniya H.M.S.R.B., Rosairo S., Albracht-Schulte K., Ramalingam L. et al. Association between serum and adipose tissue resistin with dysglycemia in South Asian women. *Nutrition & Diabetes*. 2019;9(1):5. DOI: 10.1038/s41387-019-0071-3.
19. Papadopoulos D.P., Makris T.K., Krespi P.G., Poulakou M., Stavroulakis G., Hatzizacharias A.N. et al. Adiponectin and resistin plasma levels in healthy individuals with prehypertension. *Journal of Clinical Hypertension (Greenwich, Conn.)*. 2005;7(12):729–733. DOI: 10.1111/j.1524-6175.2005.04888.x.
20. Zhang L., Curhan G.C., Forman J.P. Plasma resistin levels associate with risk for hypertension among nondiabetic women. *Journal of the American Society of Nephrology: JASN*. 2010;21(7):1185–1191. DOI: 10.1681/ASN.2009101053.
21. Zhang Y., Li Y., Yu L., Zhou L. Association between serum resistin concentration and hypertension: A systematic review and meta-analysis. *Oncotarget.* 2017;8(25):41529–41537. DOI: 10.18632/oncotarget.17561.
22. Jiang Y., Lu L., Hu Y., Li Q., An C., Yu X. et al. Resistin induces hypertension and insulin resistance in mice via a TLR4-dependent pathway. *Scientific Reports.* 2016;6:22193. DOI: 10.1038/srep22193.
23. Chen C., Jiang J., Lü J.M., Chai H., Wang X., Lin P.H. et al. Resistin decreases expression of endothelial nitric oxide synthase through oxidative stress in human coronary artery endothelial cells. *American Journal of Physiology. Heart and Circulatory Physiology.* 2010;299(1):H193–H201. DOI: 10.1152/ajpheart.00431.2009.

Author contribution

Tuzovskaia O.V. – creation of a database, processing of statistical data, drafting of the article. Polonskaya Ya.V. – carrying out of clinical and biochemical research, creation of a database. Garbuzova E.V. – processing of statistical data, editing of the manuscript to enhance the scientific value of the article. Kashtanova E.V. – carrying out of clinical and biochemical studies. Ragino Yu.I. – conception and design, significant editing of the manuscript to enhance the scientific value of the article.

Author information

Tuzovskaia Olga V. – Junior Researcher, Laboratory for Genetic and Environmental Determinants of the Human Life Cycle, IIPM – Branch of IC&G SB RAS, Novosibirsk, o-nazarenko@list.ru, https://orcid.org/0000-0002-4936-8362

Polonskaya Yana V. – Dr. Sc.. (Biology), Senior Researcher, Laboratory for Clinical Biochemical and Hormonal Studies on Internal Diseases, IIPM – Branch of IC&G SB RAS, Novosibirsk, yana-polonskaya@yandex.ru, https://orcid.org/0000-0002-3538-0280

Garbuzova Evgenia V. – Cand. Sc. (Medicine), Researcher, Laboratory for Genetic and Environmental Determinants of the Human Life Cycle, IIPM – Branch of IC&G SB RAS, Novosibirsk, stryukova.j@mail.ru, https://orcid.org/0000-0001-5316-4664

Kashtanova Elena V. – Dr. Sc. (Biology), Head of the Laboratory for Clinical Biochemical and Hormonal Studies on Internal Diseases, IIPM – Branch of IC&G SB RAS, Novosibirsk, elekastanova@yandex.ru, https://orcid.org/0000-0003-2268-4186

Ragino Yulia I. – Dr. Sc. (Biology), Corresponding Member of the Russian Academy of Sciences, Head of the IIPM – Branch of IC&G SB RAS, Novosibirsk, ragino@mail.ru, https://orcid.org/0000-0002-4936-8362

(✉) **Tuzovskaia Olga V.,** o-nazarenko@list.ru

Received 26.08.2024;
approved after peer review 03.03.2024;
accepted 11.03.2025