Informative value of metabolic risk hormonal markers in individuals with various body mass

K.V. Misiura

State Institution «V. Danilevskiy Institute for Endocrine Pathology Problems of National Academy of Medical Sciences of Ukraine»

Abstract. The objective of the work is to perform comprehensive evaluation of correlations between fractalkine, clusterin, vaspin and omentin levels in the residents of Kharkiv, as representatives of Ukrainian population, related to their body mass index, adipose tissue contents, fat accumulation degree and topography, blood insulin level, HOMA insulin resistance index. **Materials and Methods.** 250 residents of Kharkiv were examined (mean age 65.48±11.86 year). Body mass index was calculated, waist and hip circumferences were measured in the observed patients; bioimpedance technique was used to determine adipose, relative adipose and active body cell masses; fractalkine, clusterin, vaspin, omentin and insulin circulatory levels were determined with immunoassay technique; HOMA insulin resistance index was calculated. **Results.** Obese patients demonstrated reliably ($p<0.001$) higher levels of blood fractalkine, clusterin, vaspin, and lower contents of omentin compared to those with normal and excess body mass. Statistically significant ($p<0.001$) correlations of the examined peptides, anthropometric features, parameters of body composition, insulin and HOMA index were obtained. It was revealed that insulin resistant Ukrainian population representatives showed average fractalkine blood contents at the level of (937.20±87.08) ng/mL; clusterin — (126.16±16.59) ng/mL; vaspin — (671.39±135.54) ng/mL, and omentin (385.47±70.08) ng/mL. Clusterin, fractalkine, vaspin and omentin blood levels regression equations related to anthropometric parameters and HOMA index were calculated. **Conclusions.** Correlation between the increasing body mass (first of all due to adipose mass) and insulin and peptides blood contents which are markers of adipose tissue local inflammation, systemic low-intense in flammation in the body and development of cardial pathology was proved for the representatives of Ukrainian population.

Keywords: excess body mass, obesity, adipose mass, fractalkine, clusterin, omentin, vaspin, insulin.

Progressive spread of obesity (OB) and severe comorbidity which cause life quality impairment, early working capacity loss and untimely mortality in the population determines the urgent need to optimize diagnosis and treatment approaches to the patients with excess body weight. It is grounded scientifically by the necessity to determine diagnostic criteria for OB progressing and its complications related to the hormonal and metabolic features of the body [1-3].

* Адреса для листування (Correspondence): ДУ «Інститут проблем ендокринної патології ім. В.Я. Данилевського НАМН України», вул. Алчевських, 10, м. Харків, 61002, Україна. E-mail: nauka@ipep.com.ua

© *K.V. Misiura*

The last mentioned characteristics depend mostly on endocrine function of adipose tissue which determines special features of hemodynamics, hemostasis, endothelial function, lipid and glucose metabolism, degree of tissue insulin sensitivity, plays and important role in atherosclerotic plaque formation, its stability [4-8].

Adipose tissue excessive accumulation in obesity causes inflammation which changes significantly its secretory function [3], that favors development and progressing of methabolic disorders [9].

Local inflammation in adipose tissue provokes the development of low-intensity systemic inflammation in the body which is one of the important constituents of atherogenesis [5].

The above mentioned processes taken into consideration will favor optimizing the present diagnostic medical approaches to rendering aid to the patients with excess weight. The latter dictates necessity to determine markers of methabolic risk, which may allow to make it possible to provide comprehensive description of the degree of adipose tissue inflammation, systemic body inflammation, insulin resistance and risk of cardiovascular morbidity development.

According to the up-to-date scientific research findings, chemokines which characterize intensity of adipose tissue infiltration by lymphocytes and macrophages, are considered to be the markers of adipose tissue inflammation activity [5]. Fractalkine may be referred to such markers. Fractalkine has an important capacity to express as a transmembrane protein, that allows, in contrast to the other chemokines, to determine its level in blood circulation [10-13]. The results of the research concerning fractalkine are ambiguous [14-21]. Determination of fractalkine level in representatives of Ukrainian population with various body mass in respect to its correlations with the markers of systemic inflammation, adipose tissue deposition degree and increased risk of comorbidity development has not been done at all, that determines topicality of the research aiming at it.

Glycoprotein clusterin (apoliprotein J) which is secreted by human hepatocytes is considered to be one of the markers of systemic inflammation. It is supposed that any inflammation, including that of adipose tissue in OB, may cause clusterin increased secretion [22, 23].

Several research concerning correlations between the clusterin serum level and metabolic syndrome components (including body mass index (BMI), visceral OB degree, blood glucose degree) have been performed in the world [24]. But their results are contradictory [25], that may be explained by considerable differences in cohorts of patients, who were examined [26]. In Ukraine such works have not been performed up to date.

Chronic endocrine and cardiovascular comorbidity is the main negative consequence of the metabolic disorders developed in OB patients. Vaspin is one of adipokines which play an important role in cardiovascular disease and diabetes mellitus formation and progressing in the patients with excess weight [27-30]. It was revealed that vaspin level is a predictive marker of the development of cardiac failure in the patients with type 2 diabetes mellitus [8], OB at post-infarction cardiosclerosis [31], metabolic syndrome in males, coronary atherosclerosis in females [32]. Vaspin mRNA increased expression is registered in the patients with OB, insulin resistance and type 2 diabetes mellitus [33].

Omentin, which is a secretory protein expressed by visceral fatty tissue, is one more of up-to-date prospective candidates for the part of markers of adipose tissue function and increased risk of cardiovascular comorbidity development in the patients with excess weight [6, 34]. Omentin expression changes under conditions of inflammation including those at OB which are accompanied by low-grade systemic inflammation [35].

Modulation of insulin peripheral effects is considered to be the physiological meaning of this adipokine [36]. But the value of omentin in OB pathogenesis has not been definitely determined yet. Some authors mention increase of its level in OB and insulin resistance [37]. The others associate growth of OB grade and insulin resistance with decreased omentin level due to negative impact of hyperglycemia and hyperinsulinemia on omentin mRNA expression [38-40]. According to the findings given by [6], the patients with type 2 diabetes mellitus and present excess body mass (excBM) or OB, with different degree of vascular complications, demonstrate no significant alterations in omentin blood serum concentration.

Role of omentin in the development of OB comorbidity, first of all, in cardiovascular sys-

VERTE

tem and type 2 diabetes mellitus, is a topical issue. Nowadays, single researches have proved compensatory character of omentin influence on vascular complications in type 2 diabetes mellitus [41]. The role of omentin in chronic cardiac failure development and progressing in the patients with post-infarction cardiosclerosis and accompanying type 2 diabetes mellitus is proven: it is considered a new predictor for risk stratification of heart failure development in the patients of such cohort [8].

At the same time, correlations of circulatory omentin and vaspin levels related to the markers of adipose tissue inflammation and systemic body inflammation, parameters of metabolic syndrome in representatives of Ukarinian population were not studied at all.

The objective of this work is to perform comprehensive evaluation of fractalkine, clusterin, vaspin and omentin levels correlation in Kharkiv City inhabitants, as representatives of Ukrainian population, related to the body mass index, adipose tissue contents, degree and topography of its deposition, blood insulin level, HOMA insulin resistance index.

Material and Methods

250 patients (mean age 65.48±11.86 year) were examined. All the observed individuals were measured for their body mass, and their body mass index (BMI) was calculated; waist (WC) and hip circumferences (HC) (cm) were measured.

According to the BMI value, 4 groups of the examined patients were formed:

group 1 — patients with excess body mass (exc BM) — (n=62 patients; m/f=46/16);

group 2 — patients with OB, grade 1 — (n=59 patients; m/f=39/20);

group 3 — patients with OB, grade 2 — (n=45 patients; m/f=23/22);

group 4 — patients with OB, grade 3 — (n = 40 patients; m/f=17/23).

Control group included 44 practically healthy individuals with normal body mass (nBM) (m/f=18/26).

The following body composition parameters as adipose tissue mass (AM) and active body cell mass (ACM) (mass of all cells with subtracted fatty mass, where metabolic processes are in progress) were determined by bioimpedance method with software-hardware complex «Diamant-AIST-IRGT» (Diamant, CJSC) [42]. Relative adipose mass (% AM) was calculated by the formula: (adipose mass / body mass (AM/BM)* 100%).

Fractalkine, clusterin, vaspin and omentin circulatory levels were determined by immunoassay technique with Human Fractalkine ELISA Kit; Human / Mouse / Rat Vaspin Enzyme Immunoassay Kit («RayBio®», Georgia) and commercial test-systems Human Clusterin ELISA, Human Omentin-1 ELISA («BioVendor», Check Republic), respectively. Insulin concentration was determined by immunoassay technique with commercial test-system INSULIN ELISA KIT produced by «Monobind» (USA). The research was performed at the Biochemistry department of Central scientific research laboratory of Kharkiv National Medical University, Ministry of Health of Ukraine, using immunoassay analyzer «Lab Line-90» (Austria).

Insulin resistance index (HOMA-IR), determined in the patients, was calculated in accordance with the formula:

HOMA-IR=(glycemia on an empty stomach (mmol/L)* insulin on an empty stomach (mcUnit/L)) / 22.5.

The normal value for this parameter was considered to be equal up to 2.7. In case when HOMA-IP values were equal to 2.7-4.0, we diagnosed moderate, and over 4.00 — significantly reduced tissue insulin sensitivity.

To confirm correlation between the levels of clusterin, fractalkine, vaspin, omentin and insulin resistance, all the examined individuals were distributed additionally into 2 groups:

а) individuals with HOMA index ranged in normal values (n=110 patients; m/f=73/37);

б) individuals with HOMA index more than 2.77 (n=140 patients; m/f=70/70).

We used methods of descriptive statistical analysis to prosess clinical functional results. Disperse intergroup analysis was used according to the Kruskal–Wallis test by ranks. Formulas for determination of clusterin, fractalkine, vaspin and omentin values were developed considering anthropometric parameters (BMI, WC, HC, % AM, ACM, ACM/MA and HOMA-IR index) by multiple correlation statistical processing «Multiple regression» method based on the analysis

of correlation between independent (anthropometric) variables and non-independent variable (fractalkine, clusterin, vaspin, omentin).

Results and their discussion

The research established that excBM patients demonstrate no distinctions in fractalkine, clusterin, omentin, vaspin and insulin blood serum levels compared to the figures obtained in the examined nBM subjects, in contrast to the OB (grades 1, 2, 3) patients. The last mentioned patients demonstrated statistically significant ($p<0.001$, $p<0.001$, $p<0.001$) differences of the values obtained for these parameters compared to the excBM patients ($p<0.001$) (**Table 1**).

Statistically significant ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$) positive correlations at $r=0.488$; $r=0.539$, $r=0.526$ and $r=0.426$ levels, respectively, were registered between BMI and fractalkine, clusterin, vaspin and insulin levels. Inverse correlation — ($r = -0.578$, $p<0.001$) was registered between circulatory omentin level and BMI.

Evidence of statistically significant correlations between the studied peptides and parameters which characterize topography of adipose tissue deposition — WC and HC was proved (**Table 2**).

It was determined that levels of all studied peptides correlate with the degree of adipose tissue deposition within anterior abdominal wall and gluteofemoral adipose depot. The latter does not exclude the role of gluteofemoral fatty tissue in the development of insulin resistance and comorbid pathology.

The research evaluated as well presence and degree of interrelations between the levels of fractalkine, clusterin, vaspin and insulin (**Table 3**). It was proved that all of them are correlated at $p<0.001$ statistical significance level.

It was determined that vaspin blood level showed positive correlations with insulin, fractalkine and clusterin blood contents.

According to the obtained research evidence, negative correlation between the contents of

Table 2. Correlation matrix of fractalkine, clusterin, omentin, vaspin and waist circumference, hip circumference*

Parameter	Fractalkine	Clusterin	Vaspin	Omentin
Waist circumference	0.451	0.434	0.440	– 0.393
Hip circumference	0.497	0.487	0.512	– 0.527

*Note: * — P — correlation significance at p<0.001.*

Table 3. Correlation matrix of fractalkine, clusterin, omentin, vaspin, insulin*

	Fractalkine	Clusterin	Vaspin	Omentin	Insulin
Fractalkine	1.000	0.779	0.938	– 0.863	0.780
Clusterin	0.779	1.000	0.871	– 0.852	0.744
Vaspin	0.938	0.871	1.000	– 0.941	0.796
Omentin	– 0.863	– 0.852	– 0.941	1.000	– 0.797
Insulin	0.780	0.744	0.796	– 0.797	1.000

*Note: * — P — correlation significance at p<0.001 level.*

Table 1. Results of examination of the patients with various body mass*

Parameter	Statistical parameter	Study group					P
		nMT (n=44)	excBM (n=62)	OB, grade 1 (n=59)	OB, grade 2 (n=45)	OB, grade 3 (n=40)	
Fractalkine, ng/mL	Mean (SD)	738.78 (183.72)	776.18 (153.91)	906.55 (85.88)	926.06 (96.33)	956.02 (106.42)	P*<0.001
	Median	729.86	738.16	878.52	854.32	985.09	
	[Q1-Q3]	[680.23-934.33]	[709.86-937.17]	[820.51-987.34]	[839.16-1007.41]	[857.31-1028.28]	
Clusterin, ng/mL	Mean (SD)	109.56 (11.57)	112.99 (6.17)	120.31 (12.53)	128.01 (18.31)	137.25 (21.67)	P*=0.031
	Median	110.38	111.56	116.34	114.93	145.99	P**< 0.001
	[Q1-Q3]	[107.96-114.68]	[109.34-117.51]	[109.62-126.93]	[111.97-140.29]	[115.02-156.30]	
Omentin, ng/mL	Mean (SD)	488.37 (57.74)	485.14 (53.07)	387.77 (71.31)	374.36 (76.15)	359.37 (81.64)	P*=0.712
	Median	515.90	511.26	445.37	440.00	302.16	P** < 0.001
	[Q1-Q3]	[428.16-530.37]	[421.16-528.19]	[317.13-453.38]	[297.24-448.26]	[281.52-443.34]	
Vaspin, ng/mL	Mean (SD)	444.95 (171.97)	479.28 (129.46)	659.82 (151.58)	672.62 (151.83)	710.17 (160.66)	P*=0.712
	Median	433.72	447.42	539.74	546.29	829.90	P**< 0.001
	[Q1-Q3]	[378.89-611.37]	[401.54-611.54]	[511.51-810.16]	[530.83-829.52]	[545.54-849.84]	
Insulin, mcIU/mL	Mean (SD)	12.82 (6.64)	12.55 (6.38)	16.80 (6.47)	20.31 (7.55)	21.75 (9.43)	P*=0.788
	Median	8.99	9.17	14.69	17.93	18.64	P**<0.001
	[Q1-Q3]	[7.92-19.82]	[8.16-18.67]	[11.04-23.68]	[15.38-27.34]	[39.34-43.32]	

*Note: * — P — mean differences in patients with excess body mass compared to the patients with normal body mass; ** — P — mean differences in patients with excess body mass compared to the patients with OB, grades 1, 2, 3; *** — P — all mean differences compared to the individuals with normal body mass.*

VERTE

vaspin and omentin was registered that proves the increased risk of cardiovascular morbidity development in the patients with omentin reduced level which can modulate peripheral effects of insulin. All this proves once again that cardiovascular comorbidity development is associated with the degree of adipose tissue local inflammation, systemic low-intensity body inflammation, insulin blood level and tissue insulin sensitivity.

It was revealed that parameters of body composition — adipose mass (AM), relative adipose mass (% AM) and ACM correlate with metabolic characteristics of the organism [42].

The carried research established that the patients with excBM, OB (grades 1, 2, 3) demonstrate the 1.3, 2.1, 2.7 and 3.5-fold, respectively, bigger AM values compared to the patients with nBM ($p<0.001$) (**Table 4**). In these groups, % AM showed 1, 1.4, 1.8 and 1.9–fold differences, respectively; at the same time, 1.2, 1.2, 1.3 and 1.4–fold increased ACM absolute values were registered. But, while BMI increase, the ACM/AM ratio was revealed to be decreased from 2.4 to 2.0, 1.4, 1.1 and 0.9 (1.2, 1.7, 2.1 and 2.7 — fold differences, respectively).

Along with increasing AM, % AM and ACM, an increase of fractalkine, clusterin and vaspin blood levels were registered as well: between them and AM and ACM we revealed positive statistically significant ($p<0.001$) correlation, but the correlation degrees were in some way different (**Table 5**).

It was revealed that AM and% AM corresponded more closely with these paremetres rather than with ACM, that indicates the principal role exactly of adipose tissue accumulation in the development of cardiovascular OB comorbidities.

Table 5. Correlation matrix of fractalkine, clusterin, omentin, vaspin and parameters of the body composition*

	Fractalkine	Clusterin	Omentin	Vaspin
AM	0.524	0.559	– 0.613	0.553
% AM	0.556	0.520	– 0.645	0.572
ACM	0.317	0.394	– 0.332	0.358
ACM/AM	– 0.502	– 0.355	0.516	– 0.456

*Note: * — P — correlation significance at p<0.001 level.*

The research proved that between% AM, ACM and omentin blood level there is an inverse statistically significant ($p<0.001$) correlation at the level of $r= –0.645$ and $r= –0.332$, respectively, and positive correlation with ACM/AM ratio ($r=0.516$, $p<0.001$). It proves correlation of metabolic disorders in OB, related to the changes in tissue insulin sensitivity, primarily, with% AM.

Consequently, this research analyzed in details association of insulin blood level and HOMA insulin resistance index not only with body mass index, but body composition parameters as well (**Figure 1**).

The work determined regression equations according to which insulin level (mclU/mL) correlates closely with:

1) AM — [8.2773 +0.2848*AM], r=0.4651, p=0.0001;
2) %AM — [2.1133 +0.4663*%AM], r=0.5173, p=0.0001;
3) ACM — [6.26 +0.2414*ACM], r=0.2105, p=0.001.

So, the performed research of the Ukrainian population representatives confirmed the correlation between the increased body mass (firstly, due to adipose tissue) and insulin and peptides blood contents which are markers of local inflammation of adipose tissue, systemic low-intensity inflammation in the body, insulin resistance and cardiac morbidity development.

Table 4. Body composition parameters in the examined patients with different body mass*

Parameter	Statistical parameter	Study group				
		nBM (n=44)	excBM (n=62)	OB grade 1 (n=44)	OB grade 2 (n=44)	OB grade 3 (n=44)
Adipose mass, kg*	Mean (SD)	14.61 (2.87)	19.27 (3.31)	30.18 (3.48)	38.83 (3.75)	49.77 (5.96)
	Median	14.84	19.49	29.59	38.57	48.66
	[Q1-Q3]	[12.63-16.55]	[17.10-21.30]	[27.36-32.69]	[37.14-40.77]	[45.65-52.08]
% Adipose mass, %**	Mean (SD)	22.50 (6.34)	24.14 (4.66)	31.95 (4.92)	36.69 (4.74)	42.14 (4.94)
	Median	24.15	24.06	31.62	37.47	41.97
	[Q1-Q3]	[17.36-27.33]	[21.31-26.50]	[27.65-35.87]	[32.77-39.65]	[39.69-45.13]
Active body cell mass, kg*	Mean (SD)	33.89 (5.20)	39.13 (4.92)	41.90 (5.43)	42.68 (5.66)	45.84 (5.61)
	Median	30.57	41.35	44.35	44.75	45.21
	[Q1-Q3]	[29.57-39.42]	[33.09-42.78]	[35.42-45.59]	[37.56-47.64]	[40.91-51.30]

*Note: * — P — reliably significant all mean differences; ** — P — mean differences in the normal and excess body mass patients compared to those in grades 1, 2, 3 obesity patients.*

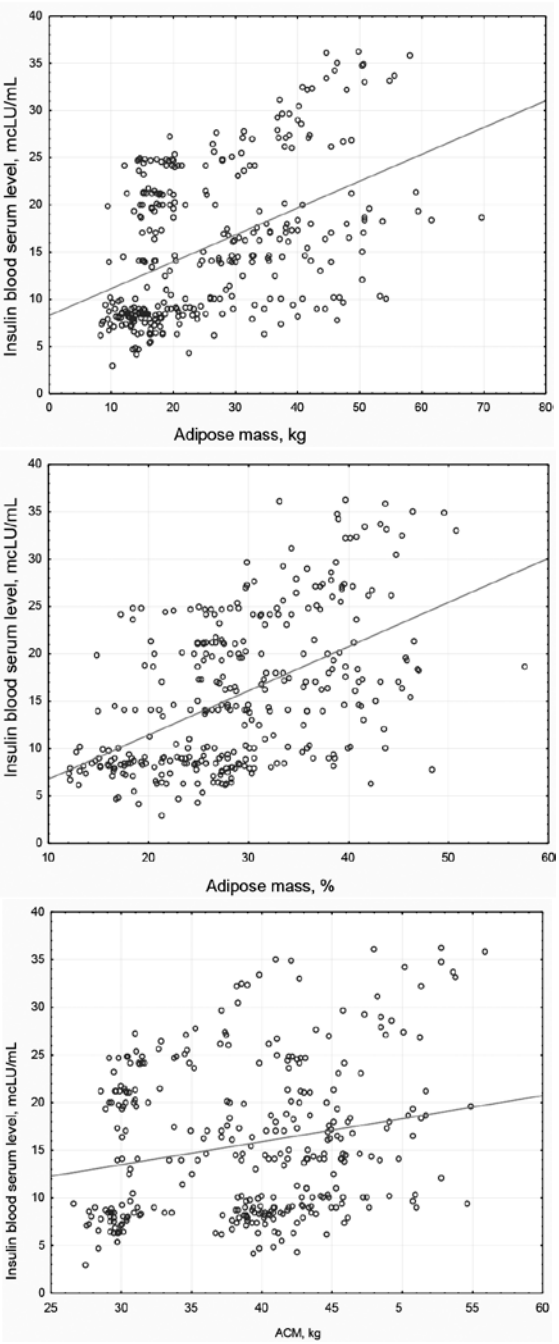

Fig. 1. Correlation of insulin blood level with adipose, relative adipose and active body cell mass of the examined patients.

Presence of correlation between insulin resistance and levels of fractalkine, clusterin, vaspin and omentin is confirmed with statistical difference at p<0.001 level of value of these parameters in the groups of insulin resistant patients and those with normal tissue insulin sensitivity **(Table 6)**.

It was determined that in insulin resistant patients fractalkine level is registered in average at the level of (937.20±87.08) ng/mL; clusterin — at the level of (126.16±16.59) ng/mL; vaspin — at the level of (671.39±135.54) ng/mL and omentin — at the level of (385.47±70.08) ng/mL, that is, respectively, 1.2, 1.4 and 1.7 — fold higher and 1.3 — fold less than those in non-insulin resistant patients.

As a result of multiple move regression, the regression equations for blood contents of clusterin, fractalkine, vaspin and omentin, related to anthropometric parameters and HOMA-IR index were determined **(Table 7)**.

Table 6. Blood serum levels of the studied peptides of the examined insulin resistant and non-insulin resistant patients*

Parameter	Statistic parameter	Non-insulin resistant individuals (n = 110)	Insulin resistant patients (n =140)	Spearman's coef. with HOMA	Independent insulin resistance U-test	U-test p-level
Clusterin, ng/mL	Mean (SD)	107.69 (9.21)	126.16 (16.59)	0.78	2750.5	0.001
	Median	109.42	120.17			
	[Q1-Q3]	[108.00-111.44]	[113.01-139.20]			
Fractalkine, ng/mL	Mean (SD)	692.42 (143.28)	937.20 (87.08)	0.84	1606.1	0.001
	Median	719.16	948.34			
	[Q1-Q3]	[648.24-759.61]	[854.34-1000.20]			
Vaspin, ng/mL	Mean (SD)	404.79 (140.11)	671.39 (135.54)	0.83	1701.2	0.001
	Median	421.55	631.42			
	[Q1-Q3]	[379.53-464.23]	[543.43-819.32]			
Omentin, ng/mL	Mean (SD)	505.05 (47.54)	385.47 (70.08)	– 0.82	1807.1	0.001
	Median	519.38	412.90			
	[Q1-Q3]	[503.57-530.51]	[308.16-443.48]			

Table 7. Regression equation for the studied peptides related to anthropometric parameters and HOMA insulin resistance index*

Parameter	Regression equation	R2	F-test, p	Standard error
Fractalkine, ng/mL	407.478 +57.1702*HOMA-IR +2.2580*WC	0.626	F=273.85 p<0.0000	103.85
Clusterin, ng/mL	78.491 +5.4932*HOMA-IR+0.2071*WC	0.6011	F=245.69 p<0.0000	10.458
Omentin, ng/mL	618.3103-25.6928*HOMA-IR– 2.9962*%AM	0.676	F=339.89 p<0.0000	48.81
Vaspin, ng/mL	81.6022+61.9746*HOMA-IR+1.8584*WC+ 2.4729*%AM	0.651	F=202.27 p<0.0000	113.53

*Notes: * — significance at p<0.001 level; HOMA-IR — HOMA index;% AM — related adipose mass of the body (%); WC — waist circumference (cm); R2 — determination coefficient; F-test — Fisher's test.*

VERTE

Analysis of the evidence obtained in the research allowed to perform comprehensive evaluation of interrelation between dynamics of fractalkine, clusterin, vaspin and omentin blood levels, HOMA index (HOMA-IR) and relative contents of adipose tissue (AM, %) (**Figure 2**).

It was determined that for the inhabitants of Kharkiv in average deposited fatty mass over 25% of total body mass is an ascertained increase in blood levels of fractalkine from 750 ng/mL and higher, clusterin — from 100 ng/mL and higher, vaspin from 460 ng/mL and higher; decrease of circulatory omentin contents to 500 ng/mL and under, and worsening of tissue insulin sensitivity (HOMA index >2.77). More than 34% of total body mass accumulation of adipose tissue determines the development of marked insulin resistance (HOMA index >4.00), which is accompanied with fractalkine blood level elevation almost to 900 ng/mL and higher, clusterin — from 120 ng/mL and over, vaspin from 650 ng/mL and over; decreased omentin circulatory level of 400 ng/mL and under. It may cause deepening of morbid alterations in modulation of insulin peripheral effects that increases considerably risk of comorbidity development.

As a conclusion to the results of the research, we should emphathize that individuals with OB demonstrate higher levels of fractalkin, clusterin, vaspin, insulin and lower level of omentin compared to those with nBM and excBM, that proves presence of the more marked inflammation in adipose tissue, systemic low-intensity inflammation in the body, growth of insulin resistance and increased risk of cardiovascular morbidity development.

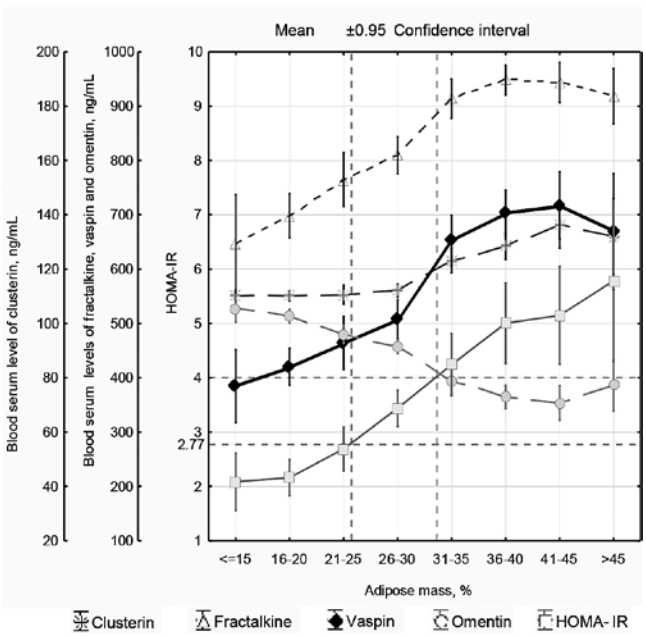

Fig. 2. Levels of HOMA index and circulatory clusterin, fractalkine, vaspin and omentin depending on the relative adipose tissue contents.

Note: Kruskal-Wallis test index for clusterin, at p<0.001; fractalkine, p<0.001; vaspin, p<0.001; omentin, p<0.001; HOMA-IR, p<0.001.

Markers of these all mentioned morbid conditions correlate significantly between each other and depend on the level of accumulated adipose tissue and body mass index.

Understanding of these processes may construct the basis for optimization of the available diagnostic medical approaches concerning rendering medical aid to the patients with excess weight, development of effective prevention programs for population.

Conclusions

1. Significant changes of fractalkine, clusterin, vaspin and omentin blood serum levels were revealed in obese patients compared to those with normal and excess body mass that proves their developed elevated level of adipose tissue inflammation, low-intensity systemic body inflammation, insulin resistance and cardiovascular comorbidity.
2. 'Relative adipose body mass' parameter is of informational value in respect to the changes in fractalkine, clusterin, vaspin and omentin blood serum levels, as well as 'body mass index' parameter.
3. Visceral adipose tissue and adipose tissue accumulation in gluteofemoral fatty depot influences significantly on the level of inflammation, insulin resistance and cardiovascular comorbidity development in overweight patients.
4. Inhabitants of Kharkiv show significant reduction of tissue insulin sensitivity accompanied with fractalkinemia at level from 900 ng/mL and higher; clusterinemia — from 120 ng/mL and over; vaspinemia — from 650 ng/mL and over, omentinmia — from 400 ng/mL and under.
5. Regression equations concerning contents of clusterin, fractalkine, vaspin and omentin in blood depending on anthropometric parameters and HOMA index are presented.

References

1. Асташкин ЕИ, Глезер МГ. Ожирение и артериальная гипертония. Consilium Medicum. 2014;16(40):75. (Astashkin EI, Glezer MG. Obesity and arterial hypertension. Consilium Medicum. 2014;16(4):75).
2. Окороков ПЛ, Васюкова ОВ, Воронцов АВ, Ильин АВ, Владимирова ВП, Аверкиева ЕВ. Уровни адипоцитарного белка-переносчика жирных кислот и адипонектина у подростков с ожирением и их связь с распределением жировой ткани. Проблемы эндокринологии. 2014;60(2):13-9. (Okorokov PL, Vasjukova OV, Vorontsov AV, Il'in AV, Vladimirova V., Averkieva EV. Levels of adipocyte protein-carrier of fatty acids and adiponectin in adolescents with obesity and their relationship to the distribution of adipose tissue. Problemy Endokrinologii. 2014;60(2):13-9).
3. Солнцева АВ, Загребаева ОЮ, Кончиц ЕС. Ранние детерминанты развития ожирения у детей в пубертатне. Современная педиатрия. 2013; 6:36-42. (Solntseva AV, Zagrebaeva OYu., Konchits ES. Early determinants of obesity in children in puberty. Sovremennaya pediatriya. 2013;6:36-42).
4. Вербовой АФ, Соломонова ЕС, Пашенцева АВ. Лептин, резистин и оментин у пациентов с нарушенной толерантностью к глюкозе и сахарным диабетом 2-го типа. Известия высших учебных заведений. Поволжский регион. Медицинские науки. 2012;3(23): 52-9. (Verbovoy AF, Solomonova ES, Pashentseva AV. Leptin, resistin and omentin in patients with impaired glucose tolerance and type 2 diabetes mellitus. Izvestiya vysshih uchebnykh zavedeniy. Povolzhskiy region. Meditsinskie nauki. 2012;3(23):52-9).
5. Шварц В. Жировая ткань как эндокринный орган. Проблемы эндокринологии. 2009;55(1):38-44. (Shvarts V. Adipose tissue as an endocrine organ. Problemy Endokrinologii. 2009;55(1):38-44).
6. Горшунська МЮ. Оментин-1 у хворих на цукровий діабет 2 типу: зв'язок з атерогенезом. Пробл ендокрин патології. 2015;2:15-21. (Gorshuns'ka MYu. Omentin-1 in patients with type 2 diabetes: association with atherogenesis. Probl endokryn patologii. 2015;2:15-21).
7. Rabe K, Lehrke M, Parhofer KG, Broedl UC. Adipokines and insulin resistance. Mol Med. 2008;14:741-51.
8. Кравчун ПГ, Кравчун ППП. Значение адипоцитокинов в развитии и прогрессировании хронической сердечной недостаточности у больных с постинфарктным кардиосклерозом и сахарным диабетом 2 типа. Медицина [Казахстан]. 2015;1(151):5-9. (Kravchun PG, Kravchun PP. The importance of adipocytokines in the development and progression of chronic heart failure in patients with postinfarction cardiosclerosis and type 2 diabetes mellitus. Meditsina [Kazakhstan]. 2015;1(151):5-9).
9. Журавлева АК. Инсулинорезистентность и абдоминальное ожирение у пациентов с сочетанным течением неалкогольной жировой болезни печени и сахарного диабета 2 типа. 2013; repo.knmu.edu.ua. (Zhuravljova AK. Insulin resistance and abdominal obesity in patients with a combined course of non-alcoholic fatty liver disease and type 2 diabetes mellitus. 2013; repo.knmu.edu.ua).
10. Зыков КА, Масенко ВП, Наконечников СН, Чазова ИЕ. Фракталкин — новый маркер сердечно-сосудистой патологи. Кардиологический вестник (архив 2006-2013 гг.). 2008;2:34-7. (Zykov KA, Masenko VP, Nakonechnikov SN, Chazova IE. Fraktalin — a new marker of cardiovascular pathology. Kardiologicheskij vestnik (arhiv 2006-2013). 2008;2:34-7).
11. Garton KJ, Gough PJ, Blobel CP, Murphy G, Greaves DR, Dempsey PJ, et al. Tumor necrosis factor-alpha-converting enzyme (ADAM17) mediates the cleavage and shedding of fractalkine (CX3CL1). J Biol Chem. 2001;276(41):7993-8001.
12. Hundhausen C, Misztela D, Berkhout TA, Broadway N, Saftig P, Reiss K, et al. The disintegrin-like metalloproteinase ADAM10 is involved in constitutive cleavage of CX3CL1 (fractalkine) and regulates CX3CL1-mediated cell-cell adhesion. Blood. 2003;102:1186-95.
13. Кухтина НБ, Арефьева ТИ, Рулева НЮ, Сидорова МВ, Азьмуко АА, Беспалова ЖД и др. Пептидные фрагменты хемокинового домена фракталкина: влияние на миграцию моноцитов человека. Биоорганическая химия. 2012;38(6):660-666. (Kukhtina NB, Aref'eva TI, Ruleva NYu, Sidorova MV, Az'muko AA, Bespalova ZhD, et al. Peptide fragments of the chemokine domain of fractalkin: effect on the migration of human monocytes. Bioorganicheskaya khimiya. 2012;38(6):660-6).
14. Спирина ММ. Клинико-диагностическое значение исследования плазменного фракталкина при бронхиальной астме: автореф. дис. ... канд. мед. наук. Астрахань, 2011:14 с. (Spirina MM. Clinical and diagnostic significance of plasma fractalkine in bronchial asthma: avtoref. dis. ... kand. med. nauk. — Astrakhan', 2011;14 p.).
15. Hyakudomi M, Matsubara T, Hyakudomi R, Yamamoto T, Kinugasa S, Yamanoi A., et al. Increased expression of fractalkine is correlated with a better prognosis and an increased number of both CD8+ T cells and natural killer cells in gastric adenocarcinoma. Ann Surg Oncol. 2008;15(6):1775-82.
16. Murphy G, Caplice N, Molloy M. Fractalkine in rheumatoid arthritis: a review to date. Rheumatology (Oxford). 2008;47(10):1446-51.
17. Ikejima H, Imanishi T, Tsujioka H, Kashiwagi M, Kuroi A, Tanimoto T, et al. Upregulation of fractalkine and its receptor, CX3CR1, is associated with coronary plaque rupture in patients with unstable angina pectoris. Circulation J. 2010;74:337-45.
18. Журавлева ЛВ, Лопина НА. Уровень фракталкина и его значение в прогнозировании наличия и выраженности атеросклеротического поражения венечных сосудов. Укр. кардіол. журн. 2016;4:62-7. (Zhuravlyova LV, Lopina NA. The level of fractalkan and its significance in predicting the presence and severity of atherosclerotic lesions of coronary vessels. Ukr kardiol zhurn. 2016;4:62-7).
19. Liu H, Jiang D, Zhang S, Ou B. Aspirin inhibits fractalkine expression in atherosclerotic plaques and reduces atherosclerosis in ApoE gene knockout mice. Cardiovascular Drugs and Therapy. 2010;24:17-24.
20. White GE, Tan TC, John AE, Whatling C, McPheat WL, Greaves DR. Fractalkine has antiapoptotic and proliferative effects on human vascular smooth muscle cells via epidermal growth factor receptor signaling. Cardiovascular Res. 2010;85:825-35.
21. Журавлева ЛВ, Лопина НА. Уровни фракталкина и ассиметричного диметиларгинина у больных ишемической болезнью сердца в зависимости от наличия сахарного диабета 2 типа и характера поражения коронарних артерий сосудов. Научный результат. Медицина и фармация. 2016;2(3):11-7. (Zhuravliova LV, Lopina NA. Levels of fractalkine and asymmetric dimethylarginine in patients with ischemic heart disease, depending on the presence of type 2 diabetes and the nature of the lesion of coronary arteries of blood vessels. Nauchnyy rezul'tat. Meditsina i farmaciya. 2016;2(3):11-7).
22. Choi-Miura NH, Takahashi Y, Nakano Y, Tobe T, Tomita M. Identification of the disulfide bonds in human plasma protein SP-40,40 (apolipoprotein-J). J Biochem. 1992 Oct;112(4):557-61.
23. Rosenberg ME, Silkensen J. Clusterin: physiologic and pathophysiologic considerations. Int J Biochem Cell Biol. 1995; 27:633-45.
24. Kujiraoka T, Hattori H, Miwa Y, Ishihara M, Ueno T, Ishii J, et al. Serum apolipoprotein j in health, coronary heart disease and type 2 diabetes mellitus. J Atheroscler Thromb. 2006;13:314-22.
25. Arnold T, Brandlhofer S, Vrtikapa K, Stangl H, Hermann M, Zwiauer K, et al. Effect of obesity on plasma clusterin, [corrected] a proposed modulator of leptin action. Pediatr Res. 2011;69:237-42.
26. Won JC, Park CY, Oh SW, Lee ES, Youn BS, Kim MS. Plasma clusterin (ApoJ) levels are associated with adiposity and systemic inflammation. PLoS One. 2014;9(7):e103351.
27. Wang XH, Dou LZ, Gu C. Plasma levels of omentin-1 and visfatin in senile patients with coronary heart disease and heart failure. Trop Med. 2014; 7(1):55-62.
28. Mm WQ, Fan J, Khor S, Song M, Hong W, Dai X. Serum vaspin levels and vaspin mRNA expression in subcutaneous adipose tissue in women with gestational diabetes mellitus. Eur J Obstet Gynecol Reprod Biol. 2014;182:98-101.
29. Feng R, Li Y, Wang C, Luo C, Liu L, Chuo F, et al. Higher vaspin levels in subjects with obesity and type 2 diabetes mellitus: a meta-analysis. Diabetes Res Clin Pract. 2014;106(1):88-94.
30. Yan M, Su B, Peng W, Li L, Li H, Zhuang J, et al. Association of serum vaspin and adiponectin levels with renal function in patients with or without type 2 diabetes mellitus. J Diabetes Res. 2014;2014:868732.
31. Кравчун ППП. Роль гормонів жирової тканини в патогенезі ожиріння у хворих з постінфарктним кардіосклерозом. Сімейна медицина. 2015;4 (60):66-8. (Kravchun PP. The role of adipose tissue hormones in the pathogenesis of obesity in patients with postinfarction cardiosclerosis. Simeina meditsina. 2015;4(60):66-8).
32. Choi SH, Kwak SH, Lee Y, Moon MK, Lim S, Park YJ, et al. Plasma vaspin concentrations are elevated in metabolic syndrome in men and are correlated with coronary atherosclerosis in women. Clin Endocrinol (Oxf). 2011;75:628-35.

VERTE ▶

33. Blüher M. Vaspin in obesity and diabetes: pathophysiological and clinical significance. Endocrine. 2012;41(2):176-82.
34. Вербовой АФ, Соломонова ЕС, Пашенцева АВ. Лептин, резистин и оментин у пациентов с нарушенной толерантностью к глюкозе и сахарным диабетом 2-го типа. Известия высших учебных заведений. Поволжский регион. Медицинские науки. 2012;3(23):52-9. (Verbovoy AF, Solomonova ES, Pashentseva AV. Leptin, resistin and omentin in patients with impaired glucose tolerance and type 2 diabetes mellitus. Izvestiya vysshih uchebnykh zavedeniy. Povolzhskiy region. Meditsinskie nauki. 2012;3(23):52-9).
35. Halabis M, Dziedzic M, Warchulinska J, Kaznowska-Bystryk I, Solski J. Omentin — a new adipokine with many roles to play. Cur Is Pharm Med Sci. 2015; doi: https://doi.org/10.1515/cipms-2015-0067.
36. Shibata R, Ouchi N, Takahashi R, Terakura Y, Ohashi K, Ikeda N, et al. Omentin as a novel biomarker of metabolic risk factors. Diabetol Metab Syndr. 2012;4:37.
37. Jan RZ, Lee MJ, Hu X, Pray J, Wu HB, Hansen BC, et al. Identification of omentin as a new depot-specific adipokine in human adipose tissue: a possible role in modulating the action of insulin. Am J Physiol Endocrinol Metab. 2006;290:E1253-61.
38. Mirzayi K, Hossein-Nejad A, Shamari M, Shahbazi S. Evidence of the role of ANGPTL6 in resting metabolic rate and its possible application in the treatment of obesity. Minerva Endocrinol. 2011;36:13-21.
39. Moreno-Navarrete JM, Catalan V, Ortega F, Gómez-Ambrosi J, Ricart W, Frühbeck G, et al. Circulatory omentin concentration increase after weight loss // Nutr Metab (Lond). 2010;7:27.
40. Tan BK, Adya R, Farhatullah S, Lewandowski KC, O'Hare P, Lehnert H, et al. Omentin-1, a Novel adipokine, is decreased in overweight insulin-resistant women with polycystic ovary syndrome. Diabetes. 2008; 57(4):801-8.
41. Hossein-nezhad A, Khadijeh M, Alatab S, Ahmadivand Z, Najmafshar A. Circulatory omentin-1 in obesity and metabolic syndrome status compared to control subjects. https://www.omicsonline.org/circulatory-omentin-1-in-obesity-and-metabolic-syndrome-status-compared-to-control-subjects-2161-1017.S1-008.php?aid=3888.
42. Руднев СГ, Соболева НП, Стерликов СА, Николаев ДВ, Старунова ОА, Черных СП и др. Биоимпедансное исследование состава тела населения России. Москва: РИО ЦНИИОИЗ, 2014:493. (Rudnev SG, Soboleva NP, Sterlikov SA, Nikolaev DV, Starunova OA, Chernych SP, et al. Bioimpedance study of the body composition of the population in Russia. Moskva: RIO CNIIOIZ, 2014:493).

(Надійшла до редакції 01.08.2017 р.)

Информативность гормональных маркеров риска метаболических нарушений у лиц с различной массой тела

Е.В. Мисюра

ГУ «Институт проблем эндокринной патологии им. В.Я. Данилевского НАМН Украины»

Резюме. С **целью** комплексной оценки взаимосвязей уровней фракталкина, кластерина, васпина и оментина у представителей украинской популяции в зависимости от индекса массы тела, содержания жировой ткани, степени и топографии ее отложения, уровня инсулина в крови, индекса инсулинорезистентности HOMA обследованы 250 жителей г. Харькова (средний возраст 65,48±11,86 года), сформировавших в зависимости от индекса массы тела 4 группы: 1) лица с избыточной массой тела (n=62); 2) лица с ожирением 1-й степени (n=59); 3) лица с ожирением 2-й степени (n=45); 4) лица с ожирением 3-й степени (n=40). Контрольная группа — здоровые лица с нормальной массой тела (n=44). **Результаты.** У пациентов с ожирением регистрируются достоверно более высокие уровни в крови фракталкина, кластерина, васпина, более низкие — оментина по сравнению с показателями лиц с нормальной и избыточной массой тела. Установлено наличие статистически значимых (p<0,001) корреляционных связей между исследуемыми пептидами, антропометрическими характеристиками, параметрами состава тела, инсулином и индексом HOMA. Определены средние значения содержания фракталкина, кластерина, васпина и оментина у пациентов с инсулинорезистентностью. Получены уравнения регрессии содержания кластерина, фракталкина, васпина и оментина в крови представителей украинской популяции в зависимости от антропометрических параметров и индекса HOMA. **Выводы.** У представителей украинской популяции доказано наличие связи между увеличением массы тела (в первую очередь за счет жировой массы) и содержанием в крови инсулина и пептидов — маркеров локального воспаления жировой ткани, системного низкоинтенсивного воспаления в организме, инсулинорезистентности и развития кардиальной патологии. Доказана их связь с индексом HOMA и уровнем инсулина в крови.

Ключевые слова: избыточная масса тела, ожирение, жировая масса, фракталкин, кластерин, оментин, васпин, инсулин.

Інформативність гормональних маркерів ризику метаболічних порушень в осіб із різною масою тіла

К.В. Місюра

ДУ «Інститут проблем ендокринної патології ім. В.Я. Данилевського НАМН України»

Резюме. З **метою** комплексної оцінки взаємозв'язків рівнів фракталкіну, кластерину, васпіну й оментину в представників української популяції залежно від індексу маси тіла, вмісту жирової тканини, ступеня та топографії її відкладення, рівня інсуліну в крові, індексу інсулінорезистентності HOMA обстежено 250 жителів м. Харкова (середній вік 65,48±11,86 року), які залежно від індексу маси тіла сформували 4 групи: 1) особи з надмірною масою тіла (n=62); 2) особи з ОЖ 1-го ступеня (n=59); 3) особи з ОЖ 2-го ступеня (n=45); 4) особи з ОЖ 3-го ступеня (n=40). Контрольна група — здорові особи з нормальною масою тіла (n=44). **Результати.** У пацієнтів з ожирінням реєструються вірогідно вищі рівні в крові фракталкіну, кластерину, васпіну, нижчі — оментину порівняно з показниками осіб із нормальною і надмірною масою тіла. Встановлено наявність статистично значущих (p<0,001) кореляційних зв'язків між досліджуваними пептидами, антропометричними характеристиками, параметрами складу тіла, інсуліном та індексом HOMA. Визначено середні значення вмісту фракталкіну, кластерину, васпіну та оментину в пацієнтів з інсулінорезистентністю. Отримано рівняння регресії вмісту фракталкіну, кластерину, васпіну та оментину в крові представників української популяції залежно від антропометричних параметрів та індексу HOMA. **Висновки.** У представників української популяції доведено наявність зв'язку між збільшенням маси тіла (насамперед за рахунок жирової маси) та вмістом у крові інсуліну та пептидів — маркерів локального запалення жирової тканини, системного низькоінтенсивного запалення в організмі, інсулінорезистентності та розвитку кардіальної патології. Доведено їх зв'язок з індексом HOMA та рівнем інсуліну в крові.

Ключові слова: надмірна маса тіла, ожиріння, жирова маса, фракталкін, кластерин, оментин, васпін, інсулін.