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Adiponectin, leptin, resistin and insulin blood concentrations in patients with ischaemic cerebral stroke

Stężenie adiponektyny, leptyny, rezystyny i insuliny we krwi chorych z niedokrwiennym udarem mózgu

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Abstract

Introduction: Stroke, due to its worldwide prevalence, is not only a medical challenge, but also a serious social problem. Recently, ongoing research has examined whether there are associations between adipose tissue hormones and the risk, mechanisms and course of stroke. The aim of our study was to determine whether there are significant differences in blood concentrations of insulin, adiponectin, leptin, resistin and in insulin resistance among patients in the acute phase of ischaemic stroke, compared to healthy subjects. In addition, we wanted to investigate if those biochemical values show a correlation with the neurological condition of our patients.

Material and methods: Adiponectin, leptin, resistin and insulin were measured in patients (n = 69) with first-ever ischaemic stroke (confirmed by CT), using specific electrochemoluminescence, radioimmunoassay and ELISA methods. Neurological evaluation was performed using Barthel ADL index on the day of admission and on the ninth day of hospitalisation. Insulin resistance value was obtained via the HOMA-IR calculator. Data was compared to that of healthy individuals (n = 26).

Results: Insulin concentration (51.08 *v.* 17.02 uU/mL) and HOMA-IR value (6.3 *v.* 2.2) were significantly higher in the study group. Leptin (14.98 *v.* 10.47 ng/mL) and resistin (28.92 *v.* 12.25 ng/mL) levels were elevated among the stroke survivors compared to controls, but no significant difference was noted in adiponectin. Negative correlations of adiponectin level and Barthel score were observed.

Conclusions: Hyperinsulinaemia and insulin resistance are involved in the pathogenesis of ischaemic stroke. Hyperleptinaemia and hyperresistinaemia play a role in the mechanism of stroke. The severity of stroke is associated with adiponectin blood concentration. **(Endokrynol Pol 2012; 63 (5): 338–345)**

Key words: *ischaemic stroke, adiponectin, leptin, resistin, insulin, HOMA*

Streszczenie

Wstęp: Udar mózgu stanowi częstą przyczynę zgonów oraz najczęstszą przyczynę trwałej niesprawności u osób powyżej 40. roku życia. Od kilku lat badana jest rola adipocytokin w patogenezie chorób OUN. Celem pracy jest próba odpowiedzi na pytanie, czy istnieją różnice w stężeniach adiponektyny, leptyny, rezystyny i insuliny we krwi między chorymi w ostrej fazie niedokrwiennego udaru mózgu a osobami zdrowymi oraz czy istnieje związek między stężeniami wyżej wymienionych hormonów we krwi a stanem neurologicznym chorych, ocenianym za pomocą skali Bartel w momencie rozpoczęcia leczenia oraz dalszej obserwacji.

Materiał i metody: Badanie przeprowadzono u 69 chorych (37 kobiet, śr. wieku 72 lata, 32 mężczyzn, śr. wieku 68 lat) z objawami udaru niedokrwiennego mózgu. U wszystkich chorych wykonano TK mózgu, dokonano oceny stanu neurologicznego przy przyjęciu oraz w 9. dobie leczenia za pomocą skali „ciężkości udaru" według Bartela oraz oznaczono we krwi stężenia adiponektyny, leptyny, rezystyny i insuliny.

Wyniki: Nie stwierdzono różnicy w stężeniu adiponektyny we krwi między grupą z niedokrwiennym udarem mózgu a grupą kontrolną (15.49 *v.* 14.32 ug/mL). Stężenia leptyny (14.98 *v.* 10.47 ng/mL), rezystyny (28.92 *v.* 12.25 ng/mL), insuliny (51.08 *v.* 17.02 uU/mL) oraz wskaźnik insulinooporności HOMA (6.3 *v.* 2.2) u chorych z niedokrwiennym udarem mózgu były większe niż u osób zdrowych. Stwierdzono ujemną korelację pomiędzy wartością skali Bartel a stężeniem adiponektyny u chorych z udarem niedokrwiennym zarówno w dniu przyjęcia ($R = -0.266$, $p < 0.05$), jak i w 9 dobie leczenia ($R = -0.302$, $p < 0.05$).

Wnioski: Wydaje się, że zarówno hiperinsulinemia i insulinooporność, jak i hiperleptynemia oraz hiperezystynemia odgrywają rolę w patogenezie niedokrwiennego udaru mózgu. Stopień ciężkości udaru w momencie wystąpienia oraz jego przebieg jest z kolei związany ze stężeniem adiponektyny we krwi. **(Endokrynol Pol 2012; 63 (5): 338–345)**

Słowa kluczowe: *udar niedokrwienny, adiponektyna, leptyna, rezystyna, insulina, HOMA*

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Introduction

Stroke is the third commonest cause of death in Western countries, after heart diseases and neoplastic diseases. It is also a leading cause of chronic disability among people over 40 years of age. In Poland, stroke incidence reaches 177.3/100,000 among men and 125/100,000 among women [1]. These numbers are similar to those occurring in other European countries. The two main types of stroke are ischaemic stroke, which accounts for about 80% of all cases, and hemorrhagic stroke, representing about 20% [2].

Progress in stroke treatment methods has been reflected in long-term studies, which show a decrease in mortality occurring in Western countries [3, 4]. Unfortunately, in Poland, the stroke mortality rate still remains much worse, being 106.4/100,000 in men and 78.7/100,000 in women [1]. It is estimated that about 400,000 people in Poland live with the permanent consequences of a stroke. These values mean that the prevention, diagnosis and therapy of stroke is not only a medical challenge, but also a significant social problem.

Adipocytokines are signalling proteins, secreted by adipose tissue, which act in paracrine and endocrine ways [5–10]. Recently, they have aroused the interest of scientists due to their multiple features. Many publications dealing with vascular diseases have claimed a link between the substances produced by fat tissue and coronary artery disease, hypertension, metabolic syndrome and venous thrombosis [5, 11–21]. Some of them also present results showing relationships between adipokines and stroke [22–28]. That is why we decided to investigate the behaviour of the discussed cytokines in a group of acute ischaemic stroke survivors.

In recent years, many studies have shown that fatty tissue is not only an energy storage organ, but also a complex and highly metabolically active endocrine organ. This tissue, apart from adipocytes, also contains connective tissue matrix, nerve tissue, stromo-vascular cells and immune system cells [8]. In physiologic conditions, fat constitutes 10–25% of total body mass, 85% of which is subcutaneous adipose tissue and 15% visceral adipose tissue. These values clearly indicate the crucial role of adipose tissue as the largest endocrine gland. From many substances secreted from this tissue, the most important are adiponectin, leptin, resistin, plasminogen activator inhibitor 1 (PAI-1), tumour necrosis factor α (TNF-α), complement system proteins and RAA (renin-angiotensin-aldosterone) axis proteins [11, 29].

The biological activity of adipokines has not been accurately determined. Nevertheless, previous studies concerning adiponectin have indicated a wide range of actions including regulation of energy metabolism, modulation of immune system and vascular system. Adiponectin is said to have an influence on glucose and the free fatty acids (FFA) metabolism, not in a direct way, but rather through sensitisation of tissues to insulin [14, 15, 22, 23, 30]. Moreover, adiponectin reduces the formation of atherosclerosis, suppresses the expression of cell adhesion molecules and proinflammatory factors like TNF-α, and also restricts macrophages transforming into foam cells. In addition, it constrains the release of growth factors, reducing the proliferation of vascular smooth muscle [14, 15]. Adiponectin also plays a role in the central nervous system, causes body temperature elevation and stimulates the sympathetic nervous system [15, 24, 31]. Taken together, these facilities place adiponectin as an anti-inflammatory and antiatherosclerotic protein.

Leptin demonstrates a relationship with body mass — it is increased in obesity and decreases as a result of weight reduction [7, 32–35]. The central actions of the discussed cytokine manifest through its impact on hunger and satiety centres; it also boosts energy expenditure, working as an anorexogenic factor. In addition, leptin affects the pituitary hormonal axes, indirectly influencing secretion of glucocorticoids, thyroid hormones, androgens and catecholamines [36–38]. Moreover, leptin is involved in the activation of the inflammatory process [7, 39, 40].

Resistin is a protein that belongs to the found in inflammatory zone (FIZZ) family. It is postulated that it affects glucose and FFA levels in blood and lowers cell insulin sensitivity [41]. All these actions should generate insulin resistance [42], but results in this matter remain contradictory. It is said that resistin plays a role in the formation of early atherosclerotic lesions [11, 39, 43–45].

The main function of insulin is to prevent hyperglycaemia and provide energy storage, which it does by encouraging cell glucose absorption, glycogenesis and lipogenesis. According to the vascular system, insulin activates transcription factors such as NFκB (nuclear factor kappa B), which promote the synthesis of proinflammatory factors involved in atherogenesis [46]. These properties contribute to insulin's role in vascular diseases including stroke [47–50].

Material and methods

Subjects

Sixty nine patients with symptoms of their first-ever ischaemic stroke, admitted to the stroke subunit of the neurology department, were included in this study. The study group consisted of 32 men and 37 women between the ages of 34 and 95 years (mean 70.2). The inclusion criterion was the first-ever ischaemic stroke, as confirmed by computer tomography imaging.

All participants underwent a full clinical evaluation including measurement of body mass index (BMI) and

Table I. *Characteristics of patients with ischaemic cerebral stroke and control group*
Tabela I. *Charakterystyka kliniczna chorych z niedokrwiennym udarem mózgu i osób grupy kontrolnej*

	Ischaemic stroke (N = 69)	Controls (N = 26)	p value
Age (years)	70.217 (SD ± 13.01)	65.077 (SD ± 13.83)	> 0.05
BMI [kg/m^2]	27.35 (SD ± 4.38)	26.01 (SD ± 3.18)	> 0.05
Glucose [mmol/L]	5.46 (SD ± 0.815)	5.02 (SD ± 0.75)	> 0.05
Total cholesterol [mmol/L]	4.99 (SD ± 1.26)	5.01 (SD ± 1.06)	> 0.05
LDL [mmol/L]	3.016 (SD ± 1.07)	3.11 (SD ± 0.99)	> 0.05
HDL [mmol/L]	1.31 (SD ± 0.47)	1.20 (SD ± 0.88)	> 0.05
TSH [μIU/mL]	2.25 (SD ± 2.45)	2.01 (SD ± 2.3)	> 0.05
ESR [mm/h]	24.779 (SD ± 2.38)	11.0 (SD ± 9.0)	≤ 0.05
CRP [mg/L]	27.70 (SD ± 56.21)	10.0 (SD ± 6.02)	≤ 0.05

BMI — body mass index; LDL — low density lipoprotein; HDL — high density lipoprotein; TSH — thyroid stimulating hormone; ESR — erythrocyte sedimentation rate after 1 h; CRP — C-reactive protein

Table II. *Glucose, insulin and HOMA-IR parameters in patients with ischaemic cerebral stroke and in control group*
Tabela II. *Ocena stężeń insuliny, wskaźnika insulinooporności oraz glikemii u chorych z niedokrwiennym udarem mózgu i u osób grupy kontrolnej*

	Ischaemic stroke	Controls	p value
Glucose [mmol/L]	5.46 (SD ± 0.815)	5.02 (SD ± 0.75)	> 0.05
Insulin [μU/mL]	51.089 (SD ± 29.13)	17.02 (SD ± 8.1)	≤ 0.05
HOMA-IR	6.3 (SD ± 0.8)	2.2 (SD ± 0.2)	≤ 0.05

HOMA-IR — homeostatic model assessment of insulin resistance

Table III. *Adiponectin, leptin and resistin blood concentrations in patients with ischaemic cerebral stroke and in control group*
Tabela III. *Stężenie adiponektyny, leptyny i rezystyny we krwi chorych z niedokrwiennym udarem mózgu i u osób grupy kontrolnej*

	Ischaemic stroke	Controls	p value
Adiponectin [μg/mL]	15.498 (SD ± 9.604)	14.325 (SD ± 8,868)	> 0.05
Leptin [ng/mL]	14.98 (SD ± 11.325)	10.471 (SD ± 7,245)	≤ 0.05
Resistin [ng/mL]	28.92 (SD ± 23.62)	12.257 (SD ± 4,21)	≤ 0.001

routine biochemical blood tests. In the study group, neurological evaluation was performed using the Barthel ADL index, either on the day of admission or on the ninth day of hospitalisation.

Stroke group candidates were excluded if they had suffered a hemorrhagic stroke, brain tumour, a stroke other than a first-ever stroke, diabetes, hypothyroidism, hyperthyroidism, moderate or severe anaemia, renal insufficiency, or dyslipidaemia treated with hypolypemic medications. Patients with stroke who died during hospital treatment were also excluded.

The control group consisted of 26 individuals admitted to hospital in order to undergo endoscopic diagnostic procedures. This group included 12 men and 14 women between the ages of 27 and 82 years (mean 65 years), who did not meet the exclusion criteria.

Blood sample analyses

Venous blood samples were collected on the admission day from the antecubital vein. The blood samples were centrifugated to obtain serum, which was rapidly frozen at -80°C for subsequent analysis. Serum insulin concentration was measured by the electrochemiluminescence method. Adiponectin and leptin serum levels were determined by the radioimmunoassay method (Merck Millipore, Billerica, MA, USA). Resistin serum

concentration was measured by the ELISA method (LINCO Research Inc., St. Charles, MO, USA)

Insulin sensitivity

Insulin sensitivity was determined by homeostatic model assessment, with a use of a HOMA-IR calculator acquired from the Diabetes Trials Unit of the Oxford Centre for Diabetes, Endocrinology and Metabolism (http://www.dtu.ox.ac.uk).

Statistical analyses

All acquired data was analysed using Statistica v. 7.1 (StatSoft Inc., Tulsa, OK, USA) and MedCalc v. 9.02 (MedCalc Software, Mariakerke, Belgium). For each quantitative parameter, basic statistical characteristics were made – mean, standard deviation, SEM (standard error of the mean), minimal and maximal value, median, quartiles 25% and 75%, 95% confidence interval.

Shapiro-Wilk test was performed for evaluation of normal distribution of parameters. For intergroup statistical dependence determination, Student's t-test was used to compare unpaired groups of parameters that follow normal distribution. Mann-Whitney U-test was used to compare independent groups of parameters that did not follow normal distribution. For assessment of intergroup correlations, a Spearman Rank Correlation test was used for univariate correlation determination, and Pearson's correlation coefficient was used for multivariate data correlation investigation.

Results

The general characteristics of the stroke survivors' group did not show statistically significant differences in basic clinical and biochemical parameters compared to the control group. We found differences in the ESR (erythrocyte sedimentation rate, 22.779 mm/h *v.* 11 mm/h, $p \leq 0.05$) and CRP values (27.7 mg/L *v.* 10 mg/L, $p \leq 0.05$), which were elevated in the study group compared to controls.

We did not observe significant differences in the blood glucose concentration between participants and the control group. By contrast, we noticed significantly higher values of insulin level (51.089 µU/mL *v.* 17.02 µU/mL, $p \leq 0.05$) and insulin resistance index HOMA-IR (6.3 *v.* 2.2, $p \leq 0.05$) in the stroke group.

We did not observe significant differences in levels of blood adiponectin between the groups. On the contrary, we found higher concentrations of leptin (14.98 ng/mL *v.* 10.471 ng/mL, $p \leq 0.05$) and resistin (28.92 ng/mL *v.* 12.257 ng/mL, $p \leq 0.05$) in stroke survivors.

Our results show a positive correlation between serum insulin and BMI, leptin and LDL cholesterol levels. We also noted a positive link between insulin resistance index and either leptin or BMI. Our study did not confirm the existence of a relationship between serum resistin and insulin resistance measured by HOMA-IR. We found that there was a negative affiliation between adiponectin and insulin or HOMA-IR.

We observed a positive correlation between adiponectin and either age or HDL cholesterol. We also noted a negative association for adiponectin and the severity of stroke assessed by the Barthel scale both on admission and on the ninth day of hospitalisation. We also revealed a positive bond connecting resistin values with CRP level and WBC count. Additionally, we found a negative relationship between resistin and total cholesterol concentration.

After dividing the study group by sex, we observed certain relationships. In the subgroup of men, we found a statistically significant positive correlation between leptin and insulin and HOMA-IR; a similar dependency, although less marked, occurred in women. A subset of women was characterised by the existence of a negative relation between adiponectin levels and insulin or HOMA-IR; similar compounds did not show up among men.

Discussion

Chronic hyperglycaemia is a well-known risk factor for vascular diseases [49, 51, 52]. Numerous studies have dealt with the role of this phenomenon in the acute phase of ischaemic stroke [46, 49, 53, 54]. It has been found experimentally that an elevated glucose concentration reduces cerebral blood flow during ischaemic stroke, with specific intensity in penumbra areas [46]. Our study, however, showed no difference in the glucose level between patients and controls, although this may be the effect of excluding from analysis people suffering from diabetes.

The increase in insulin concentrations observed during the acute phase of stroke has also been studied in the past [46]. The link between hyperinsulinaemia and thrombotic mechanism of stroke has been stated. Our results in this regard were consistent with those studies. It is interesting though that the difference in insulin did not associate with the difference in the glucose level among our groups. This fact can be explained by the fact of the rapid ascent of insulin demand during the acute phase of ischaemic stroke. Intriguing results were published by Lindsberg and Roine, suggesting that insulin may act as a neuroprotective agent by reducing hyperglycaemia and thereby reducing the amount of ROS and inflammatory factors [46].

In a prospective study, Wannamethee has shown that hyperinsulinaemia is an independent risk factor for stroke [54]. In addition, Japanese researchers have

Table IV. *Correlations of insulin concentration and HOMA-IR with clinical data and biochemical tests results in patients with ischaemic cerebral stroke*

Tabela IV. *Korelacje insulinemii i wskaźnika insulinooporności z danymi klinicznymi oraz parametrami biochemicznymi u chorych z niedokrwiennym udarem mózgu*

Correlate parameters		R	p value
Insulin	BMI	0.362	0.0019
Insulin	Leptin	0.472	0.0001
Insulin	LDL	0.253	0.0347
Insulin	Adiponectin	–0.272	0.0319
Insulin	Resistin	–0.105	> 0.05
Insulin	Bartel start	–0.008	> 0.05
Insulin	Bartel end	–0.009	> 0.05
HOMA-IR	BMI	0.371	0.0017
HOMA-IR	Leptin	0.433	0.0001
HOMA-IR	Adiponectin	–0.289	0.0225
HOMA-IR	Resistin	–0.079	> 0.05
HOMA-IR	CRP	0.064	> 0.05

Bartel start — Bartel scale evaluation on admission; Bartel end — Bartel scale evaluation on the ninth day following admission

Table V. *Correlations of blood adipocytokines concentrations with clinical data and biochemical tests results in patients with ischaemic cerebral stroke*

Tabela V. *Korelacje pomiędzy stężeniami adipocytokin a danymi klinicznymi oraz parametrami biochemicznymi u chorych z niedokrwiennym udarem mózgu*

	Adiponectin [μg/mL]		Leptin [ng/mL]		Resistin [ng/mL]	
	R	p value	R	p value	R	p value
Age (years)	0.363	0.0037	0.133	> 0.05	0.055	> 0.05
BMI [kg/m^2]	–0.168	> 0.05	0.435	0.0001	0.104	> 0.05
Total cholesterol [mmol/L]	0.134	> 0.05	0.039	> 0.05	–0.274	0.0293
LDL [mmol/L]	–0.039	> 0.05	–0.023	> 0.05	–0.221	> 0.05
HDL [mmol/L]	0.418	0.0007	0.222	> 0.05	0.059	> 0.05
ESR [mm/h]	–0.133	> 0.05	0.016	> 0.05	0.230	> 0.05
CRP [mg/L]	–0.08	> 0.05	0.064	> 0.05	0.475	0.0001
WBC [1000/mL]	–0.121	> 0.05	0.059	> 0.05	0.330	0.008
Bartel start	–0.2669	≤ 0.05	–0.1352	> 0.05	–0.1674	> 0.05
Bartel end	–0.302	≤ 0.05	–0.203	> 0.05	–0.161	> 0.05

BMI — body mass index; LDL — low density lipoproteins; HDL — high density lipoproteins; ESR — erythrocyte sedimentation rate after 1 h; CRP — C-reactive protein; WBC — white blood cells; Bartel start — Bartel scale evaluation on admission; Bartel end — Bartel scale evaluation on ninth day following admission

demonstrated a relationship between hyperinsulinaemia and the propagation of atherosclerotic lesions, defined as intima-media thickness in the carotid artery [55]. In a similar vein, the results of a 22-year follow-up study of Helsinki policemen indicated a role for insulin concentration in the development of atherosclerosis [56]. Swedish scientists have linked the role of insulin in stroke risk elevation with impaired coagulation and fibrinolysis systems and activation of PAI-1 by this hormone [57].

The results of our study also took into consideration the value of HOMA-IR index. This indicator informs as to the number of insulin particles needed for glucose to enter the cells. Our data demonstrated an increase of

Table VI. *Correlations of adiponectin and leptin blood concentrations with insulin level HOMA-IR and BMI in men and women with ischaemic cerebral stroke*

Tabela VI. *Korelacje pomiędzy stężeniami adiponektyny i leptyny we krwi a stężeniem insuliny, wskaźnikiem HOMA oraz BMI u mężczyzn i kobiet z niedokrwiennym udarem mózgu*

Men with ischaemic stroke				Women with ischaemic stroke			
Correlated parameters		**R**	**p value**	**Correlated parameters**		**R**	**p value**
Leptin [ng/mL]	HOMA-IR	0.705	< 0.0001	Leptin [ng/mL]	HOMA-IR	0.43	0.013
Leptin [ng/mL]	Insulin [μU/mL]	0.666	< 0.0001	Leptin [ng/mL]	Insulin [μU/mL]	0.481	0.0053
Leptin [ng/mL]	BMI [kg/m^2]	0.499	0.0042	Leptin [ng/mL]	BMI [kg/m^2]	0.45	0.0088
Adiponectin [μg/mL]	HOMA-IR	0.002	> 0.05	Adiponectin [μg/mL]	HOMA-IR	–0.539	0.0018
Adiponectin [μg/mL]	Insulin [mU/mL]	–0.07	> 0.05	Adiponectin [μg/mL]	Insulin [μU/mL]	–0.484	0.0057
Adiponectin [μg/mL]	BMI [kg/m^2]	–0.017	> 0.05	Adiponectin [μg/mL]	BMI [kg/m^2]	–0.3850	0.032

HOMA-IR — homeostatic model assessment of insulin resistance; BMI — body mass index

HOMA-IR in the stroke survivors. Moreover, we showed positive associations of HOMA-IR with BMI and leptin, and a negative association with adiponectin. That puts our findings in line with the reports of other research groups [30, 48].

We found no differences in adiponectin concentration between the studied group and controls. These results were a surprise to us, because other researchers have suggested the presence of low adiponectin levels among patients with stroke [25]. On the other hand, some authors have confirmed our observation [26]. We also noted a positive correlation between adiponectin levels and age or HDL cholesterol, and as already mentioned, a negative link with insulin and HOMA-IR, which is consistent with the data obtained by Ryan and Macko [58]. Moreover, analysis of the relationship between adiponectin concentration and the severity of stroke has shown that high levels of this protein are accompanied by a worse neurological state. Similar results were published in 2009 by Marousi and Theodorou [59]. In our case, the discussed correlation disappeared after the division of stroke group based on sex, which we believe was due to the small number of study participants.

Current publications state the role of adiponectin in the pathogenesis of cardiovascular diseases [60, 61]. It has been proven that adiponectin levels connect with myocardial infarction risk [17], exacerbation of coronary artery disease [14] and the risk of restenosis after coronary intervention [19]. Low levels of this cytokine correlate with progression of atherosclerosis, independently of other factors [14, 62]. Some scientists have interpreted this as a phenomenon secondary to the vascular repair process, in which the decrease in the amount of adiponectin is the consequence of accumulation in damaged areas, where it inhibits inflammation and atherogenesis [19, 63].

Interesting information about the activity of adiponectin in stroke was provided by Chen, who in an experimental study demonstrated that administration of exogenous adiponectin to rats with ischaemic stroke causes reduction of central nervous system damage. This phenomenon of neuroprotection is explained by the inhibition of the release of proinflammatory factors — TNF-α and IL-6, it also decreases NFκB activity [64].

The relation between adiponectinaemia and stroke risk was proposed in the PROSPER (Prospective Study of Pravastatin in the Elderly at Risk) study [65], in which hypoadiponectinaemia was indicated as a risk factor for cerebral ischaemia. These results are contrary to data published by Soderberg [66] and Matsumoto [26]. This difference may be explained by the fact that the PROSPER study included patients on statin therapy, which can elevate adiponectin levels.

Our results show higher concentrations of leptin in stroke survivors. Moreover, we found a positive correlation between leptin and BMI, insulin level or HOMA-IR. These findings suggest a role of leptin in the development of insulin resistance, which is consistent with previous reports [9, 40, 66, 67]. The physiological secretion of leptin is though dependent on insulin action on adipocytes [40]. However, the increase of body fat, plasma FFA, androgens and glucocorticoids, may cause hyperleptinaemia in an insulin independent way.

Many scientists have claimed a link between leptin and vascular diseases [40, 65, 68, 69]. Wolk et al. also demonstrated a relationship between hyperlepitnaemia and the risk of cerebral ischaemia, which was independent of other risk factors [70]. Similar results were presented by Soderberg [66, 67]. The proposed mechanism through which leptin acts is to influence the sympathetic nervous system, resulting in an elevation of blood pressure [40], as well as a direct effect on the vascular wall [66], endothelium [58, 66, 68, 71] and

thrombocytes [40, 66]. Surprisingly, Valerio and Dossena have presented data suggesting that an increase of leptin level during the acute phase of a stroke may act as a neuroprotective factor protecting the brain from ischaemic damage [72].

Our results revealed the presence of higher concentrations of resistin in the study group than in the control group. In addition, we noted a negative correlation between resistin and total cholesterol, while it was positive with CRP and WBC count. This may display the role of resistin in inflammatory response. Therefore we did not observe a link connecting resistin with insulin resistance, as has been postulated in animal studies [73], but this is consistent with other human study results [74–76]. With regard to stroke, Japanese researchers presented an association between resistin concentration and the severity of stroke [77]. This found no confirmation in our results.

After the division of studied group by sex, we revealed significant differences in adiponectin and leptin concentrations, which were both higher in women. It is interesting that the relationship between adiponectin and Barthel index score disappeared after the split. The lack of a significantly higher incidence of stroke in females, despite higher leptin concentrations, is explained in two popular theories. The first says that women are less sensitive to leptin than men [78]. The second suggests that the incidence of stroke is rather related to the leptin/adiponectin ratio, which is preferable in females, because of the antagonistic actions of both cytokines [66].

Conclusions

The role of insulin and adipocytokines in the pathogenesis and mechanism of stroke still remains not fully understood. However, we suggest a significant influence of these particles on the vascular system, including cerebral circulation.

Our study showed that hyperinsulinaemia and insulin resistance measured by HOMA-IR favour the occurrence of a stroke. Among adipocytokines, we recorded the role of leptin and resistin in the stroke phenomenon, but we found no similar dependence in relation to adiponectin. In addition, we noted a strong correlation between resistin and proinflammatory factors, which confirms the role of this protein in acute phase reactions.

Among our patients, we have also found a negative correlation of adiponectin concentration with the stroke severity measured using the Barthel index. This fact was a surprise. However, it is possible that the interpretation should take into consideration the age of our patients. Moreover, we have observed that women do not present a higher stroke incidence, despite higher leptin levels in comparison to men, which may be connected with the antagonistic actions of leptin and adiponectin, which is also elevated.

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