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Adipocytokines and blood pressure, lipids and glucose metabolism in hypertensive perimenopausal women

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Abstract

Background: The relationship between menopause and hypertension has been a topic of investigation for several years. In the pathogenesis of hypertension after menopause, metabolic disturbances play an important role.

Aim: To assess the relationship between adipocytokines and blood pressure, lipid and glucose metabolism in middle-aged perimenopausal women with essential hypertension.

Methods: The study included 192 women aged 40 to 60 years (mean age 51.73 ± 1.82 years), 152 with mild and moderate essential hypertension and 40 normotensive age-matched controls. The diagnosis of menopause was based on the data from medical records and confirmed by serum concentrations of the FSH. The study population was stratified according to the menopausal status into four subgroups (normotensive pre- and postmenopausal, and hypertensive pre- and postmenopausal patients). In all subjects anthropometrical measurements and 24-hour ambulatory blood pressure monitoring were performed. Serum levels of leptin, adiponectin and resistin were measured using immunochemical assays. Fasting blood samples were taken for glucose, insulin and serum lipids concentration.

Results: Postmenopausal women did not differ from premenopausal in respect to mean arterial pressure (normotensive 85.2 ± ± 5.6 *vs* 84.4 ± 4.9 mm Hg; hypertensive 99.5 ± 5.9 *vs* 98.8 ± 5.3 mm Hg). Menopause had no effects on glucose metabolism. Total cholesterol and LDL cholesterol were significantly higher in postmenopausal women. In multiple regression analysis, the strongest predictors of hypertension were waist circumference and serum leptin concentration. Adiponectin and resistin levels were not associated with blood pressure values.

Conclusions: In hypertensive postmenopausal females increased leptin level may play an important role in the pathogenesis of hypertension, independent of body mass index. Menopause per se does not affect blood pressure values. The influence of menopause on serum lipids may modulate the cardiovascular risk profile in postmenopausal females.

Key words: hypertension, leptin, adiponectin, resistin, menopause, women

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INTRODUCTION

Hypertension is a major cardiovascular risk (CV) factor possibly explaining the excessive CV morbidity and mortality in postmenopausal women. The relationship between menopause and blood pressure (BP) still remains unclear [1]. Women show a steeper increase in systolic BP after the menopause, but whether this is due to the effect of age or the menopause is still debated. Interestingly, multiple cross-sectional and longitudinal studies exploring this issue showed diverging results [2–8]. During the transition from premenopause to postmenopause, many women experience weight gain [9, 10], and central fat deposition [11]. Recently published data indicate that age-related weight gain may also importantly influence CV risk profile in perimenopausal women [7, 8]. Contemporary research suggests that the adipocyte-derived hormones, such as leptin, adiponectin and resistin may be an

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important factor linking obesity, metabolic syndrome and CV disorders.

Thus, we have undertaken the study to investigate the relationship between serum adipocytokines and BP, as well as the body mass and metabolic factors in middle aged hypertensive women with regard to the role of menopause status.

METHODS

Study population

We recruited 192 women aged 40–60 years: 152 women with newly diagnosed, never treated, mild or moderate hypertension (referred to the Hypertension Outpatient clinic between June 2004 and November 2008), and 40 age-matched normotensive controls. Diagnosis of hypertension was made based on at least two BP measurements on different occasions and confirmed by 24-hour ambulatory BP monitoring (ABPM). We excluded patients with surgical menopause, women using hormone replacement therapy or oral contraceptives, women with secondary hypertension, chronic kidney disease, diabetes mellitus and current smokers. Studied population was divided into two groups: postmenopausal women and women with regular menstrual cycles. The definition of menopause was based on two criteria: self reported menstrual characteristics (last menstruation > 1 year ago) confirmed by blood follicular stimulating hormone (FSH) level (> 40 IU/L). The study protocol was approved by the local ethical committee (KBET/378/B/2003 and KBET/51/B/2007).

Procedures

All subjects underwent a clinical assessment comprising detailed history and a physical examination with anthropometric measurements. Body weight and height were measured and body mass index (BMI) was calculated. Waist and hip circumference was determined and the waist to hip ratio (WHR) was calculated. Office BP measurements were performed with semiautomatic, validated, oscillometric monitors (OMRON 715-IT, Kyoto, Japan) in accordance with the ESC and ESH guidelines [12]. In all subjects 24-hour ABPM (SpaceLabs 90210, SpaceLabs Inc., Redmond, Washington, USA) was performed, with BP readings every 15 minutes during the daytime (6:00–22:00) and 20 minutes during the night (22:00–6:00). All blood samples were taken during the follicular phase of the menstrual cycle in premenopausal women and arbitrarily in postmenopausal women. The levels of FSH and oestradiol were measured using MEIA kits, Abbott (sensitivity 1 ng/mL for oestradiol and 0.5 mIU/mL for FSH). The concentration of leptin was determined using Quantikine® Human Leptin Immunoassay (R&D Systems). Adiponectin level was measured using the Quantikine® Human Adiponectin assay (R&D Systems). Quantitative measurement of resistin was performed with the use of biotin labelled antibody based "sandwich" enzyme immunoassay (Human Resistine ELISA, BioVendor). Routine laboratory methods were applied for measurement of basic biochemical parameters. All measurements were performed using Modular P, Roche device and appropriate Roche kits. Serum insulin concentrations were determined by radioimmunoassay (RIA-kit OriPI Swierk, Otwock, Poland) using a scintillation meter (LKB, Turku, Finland). The homeostasis model assessment HOMA index was calculated as the product of the fasting plasma insulin level [μU/mL] and the fasting plasma glucose level [mmol/L], divided by 22.5 [13, 14]. Recently developed index of the insulin sensitivity, extensively validated against the reference standard glucose clamp method, is a quantitative insulin sensitivity check index (QUICKI) [15]. The QUICKI in our study was used as the surrogate of insulin sensitivity. It was calculated according to the formula: 1/(log glucose [mg/dL] + log insulin [μU/mL]).

Statistical analysis

The results obtained were compared between the analysed groups of patients. The data are expressed as mean values and standard deviations. Statistica 7.0 software was used for the data management and statistical analyses. Analysis of variance was used to compare means and the Pearson χ^2 test to compare proportions. Age and BMI adjusting in multivariate linear regression analysis was applied when necessary to correct the between-group differences for the effects of confounding variables. As the distribution of fasting plasma leptin and adiponectin concentrations were extremely skewed, these values were log-transformed in order to improve normality for statistical testing. A p value < 0.05 was considered significant.

RESULTS

Clinical characteristics of the hypertensive and normotensive groups, including anthropometric parameters, are presented in Table 1. Hypertensive women had significantly higher BMI and waist circumference, as well as serum triglyceride level. Postmenopausal women, both in normotensive and hypertensive group, were significantly older, thus later analyses were adjusted to age (Table 2).

The relationship between adipocytokines and blood pressure

In the whole examined population a positive linear correlation between leptin level and systolic BP from 24 hours ($r = 0.32$, $p = 0.004$), day-time ($r = 0.29$, $p = 0.01$) and night-time ($r = 0.37$, $p = 0.001$) was found. Analysing the crude data of serum adipocytokines, we observed significantly higher leptin levels in the hypertensive women compared to the normotensive group (both pre- and postmenopausal) (Table 3). The highest leptin level was found in postmenopausal hypertensive women. After adjustment for BMI and age in multivariate analysis, the difference in leptin level between postmenopausal and premenopausal hypertensive women remained significant. In the whole group, a positive correlation between the level of leptin and weight

Table 1. Clinical characteristics of the studied groups

	Hypertensive women (n = 152)	Normotensive controls (n = 40)	P
Age [years]	51.1 ± 5.5	51.0 ± 2.8	0.98
Body mass index [g/m^2]	27.1 ± 3.2	25.2 ± 4.1	0.006
Waist circumference [cm]	89.7 ± 8.8	81.7 ± 9.2	< 0.001
Office SBP [mm Hg]	158.2 ± 17.2	128.7 ± 14.0	< 0.001
Office DBP [mm Hg]	91.6 ± 11.5	77.8 ± 8.4	< 0.001
24-h SBP [mm Hg]	134.4 ± 10.1	112.6 ± 6.2	< 0.001
24-h DBP [mmHg)	81.3 ± 8.7	70.8 ± 5.0	< 0.001
24-h pulse rate [beats/min]	76.1 ± 10.9	73.4 ± 7.8	0.36
Fasting blood glucose [mmol/L]	5.15 ± 0.46	5.13 ± 0.80	0.96
Serum total cholesterol [mmol/L]	5.95 ± 1.1	5.94 ± 1.2	0.99
Serum LDL-cholesterol [mmol/L]	3.74 ± 1.0	3.54 ± 0.9	0.65
Serum HDL-cholesterol [mmol/L]	1.54 ± 0.4	1.66 ± 0.4	0.46
Serum triglycerides [mmol/L]	1.91 ± 0.84	1.22 ± 0.52	0.04
Fasting glucose [mmol/L]	5.03 ± 0.45	4.95 ± 0.46	0.49
Insulin log [log μIU/mL]	1.15 ± 0.23	0.95 ± 0.22	0.02
HOMA index	3.93 ± 2.73	2.45 ± 1.53	0.01
QUICK index	1.61 ± 0.10	1.80 ± 0.32	0.03
FSH [IU/L]	42.2 ± 35.1	45.2 ± 36.1	0.71

SBP — systolic blood pressure; DBP — diastolic blood pressure; LDL — low density lipoprotein; HDL — high density lipoprotein; FSH — follicular stimulating hormone; HOMA — homeostasis model assessment index; QUICK — quantitative insulin sensitivity check index

Table 2. Blood pressure, carbohydrate and lipid metabolism indices according to the menopause status

	Normotensive controls		P	Hypertensive women		P
	Premenopausal (n = 21)	Postmenopausal (n = 19)		Premenopausal (n = 78)	Postmenopausal (n = 74)	
Age [years]	46.3 ± 2.7	55.6 ± 3.2	< 0.001	50.1 ± 2.8*	51.9 ± 2.5^	< 0.001
Body mass index [kg/m^2]	24.6 ± 4.7	25.7 ± 3.5	0.46	27.0 ± 3.1*	27.1 ± 3.3	0.81
Waist circumference [cm]	81.1 ± 7.7	82.4 ± 10.2	0.67	84.6 ± 8.3*	87.8 ± 8.3^	0.02
24-h SBP [mm Hg]	113.8 ± 5.0	111.9 ± 7.3	0.42	133.4 ± 8.1*	132.8 ± 6.3^	0.82
24-h DBP [mm Hg]	71.0 ± 4.3	70.7 ± 5.2	0.84	82.5 ± 6.7*	81.8 ± 8.7^	0.68
24-h pulse rate [beats/min]	78.2 ± 8.4	78.7 ± 8.5	0.87	80.7 ± 9.6	82.0 ± 8.7	0.67
Fasting blood glucose [mmol/L]	4.82 ± 0.33	5.10 ± 0.61	0.15	5.05 ± 0.35	5.01 ± 0.55	0.39
Serum total cholesterol [mmol/L]	5.11 ± 0.71	6.00 ± 0.97	0.02	5.36 ± 0.84	5.66 ± 1.01	0.05
Serum LDL-cholesterol [mmol/L]	3.03 ± 0.72	3.83 ± 0.86	0.003	3.07 ± 0.77	3.36 ± 0.84	0.03
Serum HDL-cholesterol [mmol/L]	1.50 ± 0.36	1.60 ± 0.30	0.37	1.52 ± 0.32	1.57 ± 0.39	0.48
Serum triglycerides [mmol/L]	1.26 ± 0.63	1.26 ± 0.61	0.99	1.74 ± 1.42*	1.63 ± 0.78^	0.55
Insulin log [log μIU/mL]	0.97 ± 0.22	0.94 ± 0.23	0.91	1.14 ± 0.19*	1.16 ± 0.26^	0.91
QUICK index	1.77 ± 0.30	1.83 ± 0.33	0.76	1.60 ± 0.12*	1.62 ± 0.09^	0.93
HOMA index	2.46 ± 1.92	2.44 ± 1.34	0.98	3.73 ± 2.73*	4.16 ± 2.73^	0.62
FSH [IU/L]	11.08 ± 9.0	75.6 ± 20.8	< 0.001	11.20 ± 9.9	71.4 ± 27.2	< 0.001

*p < 0.05 *vs* normotensive premenopausal, ^p < 0.05 *vs* normotensive postmenopausal; abbreviations as in Table 1

(correlation coefficient: r = 0.60, p < 0.0001), BMI (r = 0.65, p < 0.0001), and waist circumference (r = 0.53, p = 0.001) was observed. Moreover, a significant correlation between leptin concentration and triglycerides (r = 0.21, p = 0.003)

Table 3. Adipocytokines in hypertensive subjects and normotensive controls according to the menopause status

	Normotensive controls		P	Hypertensive women		P
	Premenopausal (n = 21)	Postmenopausal (n = 19)		Premenopausal (n = 78)	Postmenopausal (n = 74)	
Leptin [log pg/mL]	4.12 ± 0.27	4.00 ± 0.44	0.30	4.28 ± 0.28*	4.37 ± 0.25^	0.03
Leptin [log pg/mL] age/BMI adjusted	4.03 ± 0.29	4.08 ± 0.46	0.79	4.26 ± 0.29	4.35 ± 0.26^	0.01
Adiponectin [log ng/mL]	3.82 ± 0.20	3.99 ± 0.20	0.01	3.90 ± 0.26	3.91 ± 0.18	0.97
Adiponectin [log ng/mL] age/ /BMI adjusted	3.84 ± 0.29	3.97 ± 0.23	0.21	3.91 ± 0.27	3.89 ± 0.20	0.74
Resistin [ng/mL]	6.53± 1.69	6.38 ± 1.16	0.79	5.66 ± 1.60	5.90 ± 1.16	0.65
Resistin [ng/mL] age/BMI adjusted	6.51± 0.62	6.41 ± 0.43	0.44	5.86 ± 0.59	5.88 ± 0.48	0.81

*p < 0.05 *vs* normotensive premenopausal, ^p < 0.05 *vs* normotensive postmenopausal; BMI — body mass index

Table 4. Multiple regression coefficients (standard errors) for systolic blood pressure in the examined group of middle-aged women by menopause status

	Premenopausal women (n = 99)			Postmenopausal women (n = 93)		
	Regression coefficient (SE)	95% confidence interval	P	Regression coefficient (SE)	95% confidence interval	P
Age	0.03 (0.23)	–0.42–0.48	0.87	–0.13 (0.15)	–0.42–0.16	0.38
Waist	–0.39 (0.48)	–1.33–0.55	0.42	0.51 (0.22)	0.08–0.93	0.02
Body mass index	0.56 (0.49)	–0.40–1.52	0.08	–0.43 (0.27)	–0.93–0.10	0.11
Serum FSH	0.17 (0.19)	–0.20–0.54	0.38	–0.15 (0.16)	–0.46–0.16	0.32
QUICK index	–0.04 (0.22)	–0.47–0.39	0.84	–0.15 (0.18)	–0.50–0.20	0.41
Serum leptin	0.09 (0.28)	–0.46–0.64	0.74	0.47 (0.22)	0.04–0.90	0.03
Serum adiponectin	0.23 (0.19)	–0.14–0.60	0.24	0.28 (0.19)	–0.09–0.65	0.16
Serum resistin	0.04 (0.19)	–0.33–0.41	0.79	0.06 (0.11)	–0.16–0.28	0.68
R^2	19.7			42.6		

and HDL cholesterol (r = –0.30, p < 0.0001), as well as glucose (r = 0.16, p = 0.023), insulin level (r = 0.38, p = = 0.001) and HOMA index (r = 0.36, p = 0.003) was found. In multiple regression analysis 62% of leptin variability was explained by age, BMI, menopausal status, BP and indices of insulin sensitivity.

Adiponectin levels did not differ significantly between hypertensive and normotensive subjects. However, significant association between menopause and crude adiponectin level in normotensive women could be observed. In normotensive subjects adiponectin was significantly higher in postmenopausal than in premenopausal women. After the adjustment for age and BMI this difference lost its significance (Table 3). In hypertensive patients adiponectin concentration was similar in postmenopausal and premenopausal females (Table 3). Serum adiponectin significantly and negatively correlated with BMI (r = –0.20, p = 0.006), waist circumference (r = –0.27, p = 0.001), triglycerides (r = –0.22, p = 0.002), glucose (r = –0.20, p = 0.006), insulin level (r = –0.30, p = 0.008) and HOMA index (r = –0.32, p = 0.004). Adiponectin did not correlate with systolic BP (r = –0.02, p = 0.81) or diastolic BP (r = –0.06, p = 0.38).

Resistin levels were similar in normotensive and hypertensive women, irrespectively of the menopause status (Table 3). Like adiponectin, also resistin did not correlate with BP (SBP: r = 0.04, p = 0.79; DBP: r = –0.06, p = 0.68). However, a significant correlation was found with BMI (r = 0.33, p = 0.04), negative correlation with HDL cholesterol (r = –0.32, p = 0.05), positive correlation with insulin (r = 0.29, p = 0.04) and parameters of insulin resistance (HOMA index r = 0.35, p = 0.02).

The relationship between menopause and blood pressure

There were no differences in BP from 24-hour ABPM between pre- and postmenopausal women in the groups of hypertensive subjects and normotensive controls (Table 2). In postmenopausal women waist circumference and serum leptin concentration were the strongest predictors of BP (Table 4).

The relationship between menopause and lipid and carbohydrate metabolism

Postmenopausal women had significantly higher serum levels of total cholesterol and LDL cholesterol compared to premenopausal women in both hypertensive and normotensive subgroups. There were no differences in glucose concentration, parameters of insulin sensitivity (QUICKI) and resistance (HOMA index) between pre- and postmenopausal women (Table 2). Menopause had no effect on the parameters of carbohydrate metabolism in the examined group of patients.

DISCUSSION

The main finding of our study is that there is an association of serum leptin and BP in postmenopausal women, which is independent of BMI. Leptin is a protein secreted by white adipose tissue that is primarily involved in the regulation of food intake and energy expenditure. Plasma leptin concentration is proportional to the amount of adipose tissue and is markedly increased in obese individuals. Leptin is considered a homeostatic hormone regulating food intake and body weight, however strong correlation between leptin and body fat mass suggests the existence of an endogenous leptin-resistant mechanism in obesity. Chronic hyperleptinaemia may increase BP and possible mechanisms include abnormal renal sodium retention and vasoconstriction associated with sympathetic activation. The 'selective leptin resistance' theory is feasible to explain why hyperleptinaemia contributes to increased sympathetic activity and arterial pressure in obesity, whereas at the same time there is resistance to the metabolic (weight-reducing) actions of leptin. The correlation between leptin concentration and noradrenaline as well as with low frequency oscillation of heart rate variability was shown in postmenopausal women compared with regularly menstruating females [16].

A number of studies have found leptin to be positively correlated with systolic and diastolic BP in both obese [17–21] and non-obese individuals [22–24]. As in our study, other investigators [17, 18, 25] also reported higher leptin levels in hypertensives compared with normotensive individuals, even after controlling for confounders such as age and BMI. In a longitudinal study of middle aged women, Wildman et al. [26] found that greater increase in leptin over the menopause transition was associated with greater increase in diastolic BP, glucose, insulin and insulin resistance. Our study suggests that in postmenopausal women, increased leptin level may, independently of an increase in body fat, further modulate CV risk, superimposing on age-related changes and menopause influenced lipid changes. One of the possible mechanisms explaining the relationship between leptin and CV risk, in the light of previous studies, can be increase in sympathetic nervous system activity [17]. However, our study being the cross-sectional can not provide information about cause-and-effect relationships between menopause and BP.

As expected, we observed a strong, positive correlation between serum leptin and BMI, waist circumference, serum HDL-cholesterol, triglycerides and parameters of insulin resistance. The relationship between serum adiponectin and these parameters was also strong, and showed opposite direction. The inverse association was found between adiponectin and body weight, lipids, glucose and insulin concentration. However, this relationship was not followed by the correlation between adiponectin and BP.

Adiponectin has been shown to play an important role in the development of metabolic syndrome, new-onset diabetes and atherosclerotic CV events [27–29]. The role of adiponectin in the pathogenesis of hypertension remains unclear. In the recently published study, baseline serum adiponectin was a significant independent predictor of incident hypertension in the 5-year follow-up [30]. In contrast, in the population of 400 nondiabetic patients undergoing coronary angiography, adiponectin negatively correlated with the severity of coronary atherosclerosis but, similarly like in our study, not with BP [31]. In our population we did not find the relationship between menopause and BMI as well as age-adjusted adiponectin level. This observation is in agreement with recently reported data of Muscelli et al. [32]. Other studies reported discrepant results [21, 26, 33].

Resistin is a novel protein of potential importance in metabolic and vascular diseases. Growing body of evidence demonstrates that a circulating resistin level and resistin gene single nucleotide polymorphisms are associated with insulin resistance, development of diabetes, and risk of coronary heart disease [34, 35]. Although insulin resistance is strongly associated with increase in BP and development of hypertension, the direct role of resistin in the pathogenesis of hypertension is not clarified. Consistent with our results, Furuhashi et al. [36] have reported that circulating resistin was not correlated with BP among normal control subjects and subjects with nondiabetic essential hypertension. Our data indicate that although resistin significantly correlates with parameters of insulin resistance, this correlation is not related with increase in BP at the moment.

The next important finding of our study is the lack of the effects of menopause on BP. The main factor influencing BP in middle aged women is body weight and waist circumference. Consequently, in hypertensive women we observed significantly lower parameters of insulin sensitivity, without influence of menopause on indices of glucose metabolism. Cross-sectional and longitudinal studies that investigated the relationship of menopause and hypertension brought conflicting results [2, 4, 37–41]. The relationship between menopause and BP is difficult to clarify because arterial stiffness and BP, as well as serum lipids and glucose tolerance, tend to worsen with increasing age [42]. This could actually be the simplest explanation for the supposed CV adverse effects of

menopause and for the contrasting results of some studies. Several studies describing a BP increase at menopause have found it to be explained by age [4, 8] or by BMI [43, 44] or by a combination of both [5]. In our study, body mass and waist circumference seemed to be the most important factors in the pathogenesis of hypertension in middle-aged women. The effects of age are also to be taken into account as postmenopausal women in our population were significantly older than in other studies. The effects of age were found to be insignificant in a prospective study of British cohort of women, which investigated the relationship between menopause stage and CV risk factors [41]. These authors found no differences in BP between groups defined on the basis of menopause stage. Another prospective study, examining the effects of menopause on lipid profile, showed similar results, with relative odds of LDL cholesterol (> 130 mg/dL) for postmenopausal, compared with premenopausal women, being 2.1 (95% confidence interval: 1.5, 2.9) [44].

In the other population based, longitudinal study of 9364 subjects, menopause (after the adjustment for age) was not shown to influence BP [8]. The only parameter differentiating premenopausal from postmenopausal women was LDL cholesterol [8]. Our results are in agreement with the cited above prospective data, confirming that although menopause is not influencing per se BP, it may affect CV risk profile via its effect on cholesterol levels.

CONCLUSIONS

In conclusion, in hypertensive postmenopausal females increased leptin level may play a role in the pathogenesis of hypertension, independently of BMI. Menopause per se did not influence BP in the examined population. The main factor associated with BP values in middle aged women was body weight and waist circumference. The effects of menopause on serum lipid may modulate CV risk profile in postmenopausal females. These findings reflect the complex relationship between menopause, body fat distribution, aging and BP in middle-aged women.

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References

1. Pośnik-Urbańska A, Kawecka-Jaszcz K. Hypertension in post-menopausal women — selected pathomechanisms. Przegl Lek, 2006; 63: 1313–1307.
2. Staessen JA, Ginocchio G, Thijs L et al. Conventional and ambulatory blood pressure and menopause in a prospective population study. J Hum Hypertens, 1997; 11: 507–514.
3. Zanchetti A, Facchetti R, Cesana GC et al. SIMONA participants. Menopause-related blood pressure increase and its relationship to age and body mass index: the SIMONA epidemiological study. J Hypertens, 2005; 23: 2269–2276.
4. Casiglia E, d'Este D, Ginocchio G et al. Lack of influence of menopause on blood pressure and cardiovascular risk profile: a 16 years longitudinal study concerning a cohort of 568 women. J Hypertens, 1996; 14: 729–736.
5. Portaluppi F, Pansini F, Manfredini R et al. Relative influence of menopausal status, age, and body mass index on blood pressure. Hypertension, 1997; 29: 976–979.
6. Poehlman ET, Toth MJ, Ades PA et al. Menopause-associated changes in plasma lipids, insulin-like growth factor 1 and blood pressure: a longitudinal study. Eur J Clin Invest, 1997; 27: 322–326.
7. Cifkova R, Pitha J, Lejskova M et al. Blood pressure around the menopause: a population study. J Hypertens, 2008; 26: 1976–1982.
8. Casiglia E, Tikhonoff V, Caffi S et al. Menopause does not affect blood pressure and risk profile, and menopausal women do not become similar to men. J Hypertens, 2008; 26: 1983–1992.
9. Wing RR, Matthews KA, Kuller L et al. Weight gain at the time of menopause. Arch Intern Med, 1991; 151: 97–102.
10. Macdonald HM, New SA, Campbell MK et al. Longitudinal changes in weight in perimenopausal and early postmenopausal women: effects of dietary energy intake, energy expenditure, dietary calcium intake and hormone replacement therapy. Int J Obes Relat Metab Disord, 2003; 27: 669–676.
11. Zamboni M, Armellini F, Harris T et al. Effects of age on body fat distribution and cardiovascular risk factors in women. Am J Clin Nutr, 1997; 66: 111–115.
12. The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC) presents the 2007 Guidelines for the Management of Arterial Hypertension. J Hypertens, 2007; 25: 1105–1187.
13. Matthews DR, Hosker JP, Rudenski AS et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia, 1985; 28: 412–419.
14. Bonora E, Targher G, Alberichie M et al. Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity. Diabetes Care, 2000; 23: 57–63
15. Chen H, Sullivan G, Yue LQ et al. QUICKI is a useful index of insulin sensitivity in subjects with hypertension. Am J Physiol Endocrinol Metab, 2003; 284: E804–E812.
16. Czarnecka D, Posnik-Urbanska A, Kawecka-Jaszcz K et al. Indices of autonimic nervous system activity in women with mild hypertension in perimenopausal period. Kardiol Pol, 2009; 67: 243–251
17. Kunz I, Schorr U, Klaus S et al. Resting metabolic rate and substrate use in obesity hypertension. Hypertension, 2000; 36: 26–32.
18. Golan E, Tal B, Dror Y et al. Reduction in resting metabolic rate and ratio of plasma leptin to urinary nitric oxide: influence on obesity-related hypertension. Isr Med Assoc J, 2002; 4: 426–430.
19. Itoh K, Imai K, Masuda T et al. Relationship between changes in serum leptin levels and blood pressure after weight loss. Hypertens Res, 2002; 25: 881–886.
20. Al-Hazimi AM, Syiamic AY. Relationship between plasma angiotensin II, leptin and arterial blood pressure. Saudi Med J, 2004; 25: 1193–1198.
21. Hong SC, Yoo SW, Cho GJ et al. Correlation between estrogens and serum adipocytokines in premenopausal and postmenopausal women. Menopause, 2007; 14: 835–840.
22. Adamczak M, Kokot F, Wiecek AW. Relationship between plasma renin profile and leptinaemia in patients with essential hypertension. J Hum Hypertens, 2000; 14: 503–509.

23. Takizawa H, Ura N, Saitoh S et al. Gender difference in the relationships among hyperleptinemia, hyperinsulinemia, and hypertension. Clin Exp Hypertens, 2001; 23: 357–368.
24. Barba G, Russo O, Siani A et al. Plasma leptin and blood pressure in men: graded association independent of body mass and fat pattern. Obes Res, 2003; 11:160–166.
25. Canatan H, Bakan I, Akbulut M et al. Comparative analysis of plasma leptin levels in both genders of patients with essential hypertension and healthy subjects. Endocr Res, 2004; 30: 95–105.
26. Wildman RP, Mancuso P, Wang C et al. Adipocytokine and ghrelin levels in relation to cardiovascular disease risk factors in women at midlife: longitudinal associations. Int J Obes (Lond), 2008; 32: 740–748.
27. Hopkins TA, Ouchi N, Shibata R et al. Adiponectin actions in the cardiovascular system. Cardiovasc Res, 2007; 74: 11–18.
28. Duncan BB, Schmidt MI, Pankow JS et al. Adiponectin and the development of type 2 diabetes: the atherosclerosis risk in communities study. Diabetes, 2004; 53: 2473–2478.
29. Pischon T, Girman CJ, Hotamisligil GS et al. Plasma adiponectin levels and risk of myocardial infarction in men. JAMA, 2004; 291: 1730–1737.
30. Chow WS, Cheung BM, Tso AW et al. Hypoadiponectinemia as a predictor for the development of hypertension: a 5-year prospective study. Hypertension, 2007; 49: 1455–1461.
31. Cesari M, Pessina AC, Zanchetta M et al. Low plasma adiponectin is associated with coronary artery disease but not with hypertension in high-risk nondiabetic patients. J Intern Med, 2006; 260: 474–483.
32. Muscelli E, Kozàkovà M, Flyvbjerg A et al. RISC investigators. The effect of menopause on carotid artery remodeling, insulin sensitivity, and plasma adiponectin in healthy women. Am J Hypertens, 2009; 22: 364–370.
33. Tamakoshi K, Yatsuya H, Wada K et al. The transition to menopause reinforces adiponectin production and its contribution to improvement of insulin-resistant state. Clin Endocrinol (Oxf), 2007; 66: 65–71.
34. Reilly MP, Lehrke M, Wolfe ML et al. Resistin is an inflammatory marker of atherosclerosis in humans. Circulation, 2005; 111: 932–939.
35. Pischon T, Bamberger CM, Kratzsch J et al. Association of plasma resistin levels with coronary heart disease in women. Obes Res, 2005; 13: 1764–1771.
36. Furuhashi M, Ura N, Higashiura K et al. Circulating resistin levels in essential hypertension. Clin Endocrinol (Oxf), 2003; 59: 507–510.
37. Staessen J, Bulpitt CJ, Fagard R et al. The influence of menopause on blood pressure. J Hum Hypertens, 1989; 3: 427––433.
38. Akahoshi M, Soda M, Nakashima E et al. Effects of menopause on trend of serum cholesterol, blood pressure and body mass index. Circulation, 1996; 94: 61–66.
39. Izumi Y, Matsumoto K, Ozawa Y et al. Effect of age at menopause on blood pressure in postmenopausal women. Am J Hypertens, 2007; 20: 1045–1050.
40. Armellini F, Micciolo R, Ferrari P et al. Blood pressure, metabolic variables and adipose tissue distribution in pre and post-menopausal women. Acta Obstet Gynecol Scand, 1990; 69: 627–633.
41. Kuh D, Langenberg C, Hardy R et al. Cardiovascular risk at age 53 years in relation to the menopause transition and use of hormone replacement therapy: a prospective British birth cohort study. BJOG, 2005; 112: 476–485.
42. Kawecka-Jaszcz K, Czarnecka D, Dembińska-Kieć A et al. Insulin resistance and lipids in hypertensive women on hormone replacement therapy. Blood Press, 2002; 11: 28–34.
43. Grobbee DE, Van Hemert AM, Vanderbroucke JP et al. Importance of body weight in determining risk and level of blood pressure in postmenopausal women. J Hypertens, 1988; 6 (suppl. 4): S614–S616.
44. Derby CA, Crawford SL, Pasternak RC et al. Lipid changes during the menopause transition in relation to age and weight: the Study of Women's Health Across the Nation. Am J Epidemiol, 2009; 169: 1352–1361.

Stężenie adipocytokin a ciśnienie tętnicze, metabolizm lipidów i glukozy u kobiet z nadciśnieniem tętniczym w okresie okołomenopauzalnym

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Streszczenie

Wstęp: W patogenezie nadciśnienia tętniczego (NT) u kobiet po menopauzie istotną rolę mogą odrywać przyrost masy ciała i zaburzenia metaboliczne. Tkanka tłuszczowa jest obecnie postrzegana jako źródło wielu substancji aktywnych biologicznie nazywanych adipocytokinami.

Cel: Celem pracy była ocena wpływu adipocytokin na ciśnienie tętnicze krwi, parametry gospodarki lipidowej i węglowodanowej u kobiet z pierwotnym NT w okresie okołomenopauzalnym.

Metody: Do badania włączono 192 kobiety w wieku 40–60 lat (średni wiek 51,73 ± 1,82 roku), 152 z łagodnym lub umiarkowanym NT oraz 40 kobiet z prawidłowym ciśnieniem tętniczym. Rozpoznanie menopauzy ustalono na podstawie danych z wywiadu i zweryfikowano oznaczeniem stężenia FSH. Badaną grupę podzielono na cztery podgrupy — kobiety bez NT regularnie miesiączkujące, kobiety bez NT po menopauzie, pacjentki z NT przed menopauzą, pacjentki z NT po menopauzie. U wszystkich badanych wykonano pomiary antropometryczne oraz 24-godzinną automatyczną rejestrację ciśnienia tętniczego. Pomiar stężeń adiponektyny, leptyny i rezystyny wykonano metodami immunochemicznymi. Oznaczenie stężeń glukozy, insuliny i lipidów wykonano w próbkach krwi pobranych na czczo.

Wyniki: Nie stwierdzono wpływu menopauzy na wartości średniego ciśnienia tętniczego (w grupie osób z prawidłowym ciśnieniem: 85,2 ± 5,6 *v.* 84,4 ± 4,9 mm Hg; w grupie pacjentek z NT: 99,5 ± 5,9 *v.* 98,8 ± 5,3 mm Hg). Nie zanotowano różnic w parametrach metabolizmu glukozy w zależności od statusu hormonalnego. W badanej grupie zaobserwowano istotnie wyższe stężenie cholesterolu całkowitego i cholesterolu frakcji LDL u kobiet w okresie pomenopauzalnym. W analizie wieloczynnikowej najsilniejszym czynnikiem predykcyjnym ciśnienia tętniczego w badanej grupie były obwód talii i stężenie leptyny. Nie stwierdzono natomiast wpływu adiponektyny i rezystyny na wartości ciśnienia tętniczego.

Wnioski: U kobiet z pierwotnym NT w okresie pomenopauzalnym, niezależnie od wskaźnika masy ciała i obwodu talii, stężenie leptyny może ogrywać istotną rolę w patogenezie nadciśnienia tętniczego. Menopauza *per se* nie wpływa na wartości ciśnienia tętniczego, może natomiast modyfikować profil ryzyka sercowo-naczyniowego poprzez wpływ na stężenie lipidów.

Słowa kluczowe: nadciśnienie tętnicze, leptyna, adiponektyna, rezystyna, menopauza

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