

The association between 24-hour ambulatory blood pressure measurement and selected biochemical and anthropometric parameters in women with polycystic ovary syndrome

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Abstract. – **OBJECTIVE:** Polycystic ovary syndrome (PCOS) is a complex endocrine and metabolic disorders, which may contribute to the development of cardiovascular diseases. The aim of our study was to evaluate the association between of 24-hour ambulatory blood pressure measurement (ABPM) and selected biochemical and anthropometric parameters in women with PCOS.

PATIENTS AND METHODS: The study involved 153 Polish, Caucasian women with PCOS hospitalized in the Department of Endocrinology Gynecology from January 2018 to March 2020. All women had stable body mass during the 3-month period. ABPM was performed using a portable lightweight device with oscillometric technology accepted by International Protocol of European Society of Hypertension (ABPM, HoICARD CR-07, Poland).

RESULTS: The first factor taken into consideration was the variability phenotypic subgroups of PCOS on the values of 24-hour ABPM. We revealed that the daytime and night-time systolic and diastolic blood pressure values were significantly higher in phenotype A subgroup than in other subgroups. Moreover, daytime and night-time systolic and diastolic blood pressure value as well as day-time heart rate value were significantly higher in subgroup with than without hyperandrogenemia. The obese women with PCOS were characterized of the highest value of all night-time measurements among women with PCOS and normal weight, overweight or obesity. In addition, insulin resistance in the PCOS subgroup was associated with lower value of sys-

tolic, diastolic blood pressure and both at day-time and night-time heart rate value than in insulin sensitive PCOS subgroup.

CONCLUSIONS: Hyperandrogenemia and obesity were the crucial influencing factors on 24-hour ABPM in the group of women with PCOS. In addition, hypertension, apart from visceral obesity, hyperinsulinemia and insulin resistance, could be considered as component of metabolic syndrome in women with PCOS.

Key Words:

Polycystic ovary syndrome, PCOS, 24-hour ambulatory blood pressure measurement, ABPM, Hypertension, Insulin resistance, Blood pressure, Obesity, Metabolic syndrome.

Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine and metabolic disorders, which may contribute to the development of cardiovascular diseases (CVD)^{1,2}. The cardiovascular risk factors occur frequently in PCOS women including hyperandrogenism, obesity, insulin resistance (IR) and dyslipidemia^{3,4}. The main complication of obesity is hypertension, an important cardiovascular risk factor⁵⁻⁷. Approximately 38%-88% of women with PCOS are also diagnosed with overweight or obesity⁸. Even in young women with PCOS hyperandrogenemia is associa-

ted with an elevated systolic blood pressure (SBP) and diastolic blood pressure (DBP) independently from obesity, IR, and dyslipidemia. Hyperinsulinemia is the compensatory mechanism of IR participated in pathogenesis of the hypertension³. Furthermore, insulin stimulates the release of insulin-like growth factor type 1 (IGF-1) and inhibits IGF-binding protein that causes vascular smooth muscle hypertrophy⁹.

Sleep disturbances¹⁰ and obstructive sleep apnea (OSA)² can be also added to the list of risk factors of hypertension development in PCOS.

One of the best and non-invasive procedure in the management of hypertension is 24-hour ambulatory blood pressure measurement (ABPM)¹¹. This measurement better predicts cardiovascular mortality and morbidity than isolated blood pressure (BP) measurements done in clinics¹². ABPM provides a unique opportunity to measure BP at pre-determined intervals during sleep and to assess dipping status. Usually, the systemic pressure should drop by approximately 5-10 mmHg in the early hours of the night. The absence of this nocturnal blood pressure drop is often the first symptom of hypertension development. Little is known about 24-hour ABPM in the group of women with PCOS^{13,14}. The aim of this study was to evaluate the 24-hour ABPM outcome in the group of Polish women with PCOS and correlate obtained results with selected anthropometric and biochemical parameters characteristic in this disease.

Patients and Methods

The study involved 153 Polish, Caucasian women with PCOS hospitalized in the Department of Endocrinology Gynecology from January 2018 to March 2020. All women had stable body mass during last 3-month period. PCOS, including phenotypes, was diagnosed based on Rotterdam ESHRE/ASRM criteria from 2003 (Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group, 2004). The ultrasound examination was performed using GE Healthcare Voluson 730 Expert. Hypothyroidism, and hyperprolactinemia may all cause secondary amenorrhea, therefore we also assayed the concentration of TSH, fT3, fT4 and prolactin, respectively. To exclude Cushing's syndrome the concentration of cortisol at 7:00 am, 10:00 pm and after 1 mg oral dose of dexamethasone was measured. In addition, the concentration of 17 α -hydroxyprogesterone (17 α -OHP) and dehydroepiandrosterone sulfate

(DHEA-S) was investigated to exclude late-onset congenital adrenal hyperplasia and adrenal tumor, respectively. Acne was graded according to the Global Acne Severity Scale. Hirsutism was defined using the modified Ferriman-Gallwey method (mFG). Hirsutism was considered with mFG score of ≥ 8 ^{15,16}. Body composition was assessed by bioimpedance method using Bodystat 1500 (Douglas, Isle of Man). Any pharmacological therapy, smoking and alcohol abuse were among the exclusion criteria. We excluded women with earlier diagnosed hypertension. Study protocol was approved by the Ethical Committee of Medical University of Silesia.

Fifteen mL venous blood were withdrawn during the follicular phase (within 3 and 5 days of the menstrual cycle) in the morning between 8.00 and 9.00 am, after an overnight fast (≥ 8 h). The blood samples were collected according to the standard procedures. Serum and plasma samples were stored frozen at -80°C.

Biochemical Measurements

Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), androstenedione and DHEA-S were determined by ELISA (DRG Instruments GmbH, Marburg, Germany) with a lower limit of sensitivity 0.86 mIU/mL, 1.27 mIU/mL, 0.019 μ g/L, 0.044 mg/L. The respective intra- and inter-assay coefficients of variations were 5.5% and 6.1% for FSH, 5.6% and 6.2% for LH, 6.5% and 10.2% for androstenedione, 4.8% and 7.5% for DHEA-S.

Serum total and free testosterone, as well as sex hormone-binding globulin (SHBG), were determined by the ECLIA method using Cobas E411 analyzer (Roche Diagnostics GmbH, Mannheim, Germany) with LOQs: 0.083 μ g/L, 0.002 ng/L and 0.2 nmol/L, respectively; the respective intra- and inter-assay coefficients of variations were 3.6% and 7.1% for total testosterone, 6.4% and 8.0% for free testosterone, 5.3% and 9.0% for SHBG.

17 α -OHP was assayed by RIA (Diagnostic Products) with lower detectable concentrations of 0.2 nmol/L. The respective inter- and intraassay coefficients of variation were 5.6% and 8.0%.

Plasma glucose and lipids were estimated by colorimetric methods using the commercially available test kits (Roche, Switzerland). Serum insulin concentration was determined by ELISA (DRG Instruments GmbH, Marburg, Germany) with a lower limit of sensitivity of 1.76 mIU/mL and inter-assay coefficients of variations of 2.2% and 4.4%, respectively.

Ambulatory Blood Pressure Monitoring

Before 24-hour ABPM all women with PCOS reported not having been diagnosed as hypertensive. ABPM was performed using a portable lightweight device with oscillometric technology accepted by the International Protocol of European Society of Hypertension (ABPM, HolCARD CR-07, Poland). It was applied to the non-dominant arm and initiated between 7 am and 10 am and ended after 24 hours. The day-time BP measurements were made at an interval of 15 minutes (7:00-23:00) and the night-time BP measurements at an interval of 30 minutes (23:00-7:00). All types of daily activities, including sleep, was normally carried out while wearing this device. A portable lightweight device will be attached in the laboratory at the Department of Endocrinological Gynecology.

The mean value of SBP and DBP at day- and night-time were calculated. According to Health Quality Ontario¹¹ the suggested values for day-time, night-time, and 24-hour average ABP levels are as follows:

Daytime: optimal, < 130/80 mm Hg; normal, < 135/85 mm Hg; abnormal, > 140/90 mm Hg

Night-time: optimal, < 115/65 mm Hg; normal, < 120/70 mm Hg; abnormal, > 125/75 mm Hg

24-hour: optimal, < 125/75 mm Hg; normal, < 130/80 mm Hg; abnormal, > 135/85 mm Hg¹¹.

Calculated Parameters

The free androgen index (FAI) was calculated according to the standard formula¹⁷:

$$FAI = 100 \times \frac{\text{Total testosterone}}{SHBG}$$

The value of HOMA-IR was calculated according to:

$$HOMA-IR = \frac{\text{fasting concentration of insulin } (\mu U/ml) \times \text{fasting concentration of glucose } (mmol/L)}{22.5}$$

Insulin resistance was defined by HOMA-IR ≥ 2.0 ¹⁷.

The percentage (%) of blood pressure drop was calculated according to:

$$\% \text{ of night drop in BP} = \left(\frac{\text{mean day BP} - \text{mean night bBP}}{\text{mean day BP}} \right) \times 100$$

Data Analysis

The women with PCOS were divided according to four phenotypes of PCOS, BMI value (normal weight, overweight and obesity) and HOMA-IR

value (<2.0 and ≥ 2.0) as well as higher concentration of androgens.

Statistical Analysis

The obtained data was analyzed with the use of the Statistica Software Package, version 13.3 (Polish version; StatSoft, Kraków, Poland). The nominal α value for hypothesis testing was 0.05. Shapiro-Wilk W-test was used to check for normality of distribution. Levene test was used to check for equality of variance between the compared groups. Parametric tests were preferred. In the case of normality distribution and equality of variance, the Student t-test was used. In the case of lack of normality distribution, the non-parametric Mann-Whitney (U) test was used. Differences between four phenotype groups and between three groups divided according to BMI value were analyzed using Kruskal-Wallis one-way analysis of variance by ranks. In addition, linear regression analysis was conducted to examine the association between selected anthropometric, hormonal, and biochemical parameters and blood pressure measurements. The results were considered as statistically significant with a p -value of less than 0.05.

Results

Characteristics of the women with PCOS are listed in Table I. After 24-hour ABPM outcome, 21.4% women with PCOS had higher mean value of BP at day ($\geq 140/90$) and/or at night ($\geq 125/75$).

The mean value of 24-hour ABPM is summarized in Table II.

We observed significantly higher the daytime and night-time mean heart rate (HR) values in phenotype A subgroup than in other phenotype subgroups (Table III).

In addition, the obese women with PCOS were characterized of higher value of all night-time measurements among women with PCOS and normal weight, overweight or obesity (Table IV).

The values of SBP, DBP and HR both at daytime and night-time were significantly lower in the insulin resistant than in the insulin sensitive PCOS subgroup (Table V).

Moreover, daytime and night-time SBP and DBP value as well as day-time HR value was significantly higher in subgroup with than without hyperandrogenemia (Table VI).

There were positive correlations between daytime SBP value and BMI value ($r=0.21$; $p=0.01$) or

Table I. Characteristics of the group of women with PCOS.

Variable	PCOS; n = 153
Age [years]	28.1 ± 5.7
BMI [kg/m ²]	33.3 ± 8.4
Normal weight/ overweight/obesity [n]	29/18/106
Ferriman-Gallwey score	8.9 ± 6.3
Acne [five-category scale]	0.8 ± 0.9
Hypertension [N%]	21.4
Glucose [mg/dL]	95.0 ± 10.8
Insulin [uIU/mL]	14.5 ± 11.2
HOMA-IR	3.4 ± 3.1
Insulin resistance [N%]	66.0
Cholesterol [mg/dL]	4.96 ± 0.89
LDL- cholesterol [mg/dL]	116.2 ± 31.3
HDL- cholesterol [mg/dL]	48.3 ± 13.2
Triglycerides [mg/dL]	136.7 ± 70.4
LH [IU/L]	6.8 ± 4.1
FSH [IU/L]	5.5 ± 1.5
LH/FSH	1.3 ± 0.8
SHBG [nmol/L]	39.7 ± 26.9
Total testosterone [ng/mL]	0.5 ± 0.2
Free testosterone [pg/mL]	2.5 ± 1.5
FAI	5.5 ± 4.2
Androstenedione [ng/mL]	3.4 ± 1.8
DHEA-S [μg/mL]	342.8 ± 144.0
17-OHP [nmol/L]	1.7 ± 0.6

PCOS – polycystic ovary syndrome; BMI – body mass index; HOMA-IR – homeostatic model assessment for insulin resistance; LH – luteinizing hormone; FSH – follicle-stimulating hormone; SHBG – sex hormone-binding globulin; FAI – free androgen index; DHEA-S – dehydroepiandrosterone sulfate; 17 OH P – 17- α hydroxyprogesterone.

FAI value ($r=0.21$; $p=0.03$). While the daytime DBP value correlated positively with age ($r=0.17$; $p=0.03$) or BMI value ($r=0.47$; $p=0.001$). We observed also positive correlation between night-time SBP value and BMI value ($r=0.29$; $p=0.001$),

Table II. Ambulatory blood pressure measurement in the group of women with PCOS.

24-hour ABPM outcome	PCOS; n = 153
dSBP [mmHg]	126.0 ± 11.9
dDBP [mmHg]	78.8 ± 8.4
nSBP [mmHg]	115.1 ± 14.9
nDBP [mmHg]	67.1 ± 11.0
dHR [BPM]	76.3 ± 8.0
nHR [BPM]	67.0 ± 8.9
% night drop	12.1 ± 8.3

PCOS – polycystic ovary syndrome; dSBP – day-time systolic blood pressure; dDBP – day-time diastolic blood pressure; nSBP – night-time systolic blood pressure; nDBP – night-time diastolic blood pressure; dHR – day-time heart rate; nHR – night-time heart rate; BPM – beat per minute; NS – non-significant.

HOMA-IR value ($r=0.17$; $p=0.04$) or FAI values ($r=0.21$; $p=0.04$). While the night-time DBP value correlated positively only with age ($r=0.20$; $p=0.01$). Higher value of HR at day- and night-time was associated with higher FAI value ($r=0.24$; $p=0.01$ at day and $r=0.33$; $p=0.001$ at night) and younger age ($r=-0.27$; $p=0.001$ at day and $r=-0.19$; $p=0.02$ at night). In addition, night-time HR value was positively correlated with BMI value ($r=0.24$; $p=0.01$) and HOMA-IR value ($r=0.20$; $p=0.01$). The percentage of night BP drop correlated negatively with BMI value ($r=-0.21$; $p=0.04$).

Discussion

The aim of this study was to evaluate the 24-hour ABPM outcome in the group of women with PCOS and correlate obtained results with selected anthropometric and biochemical parameters characteristic in this disease. Only two studies investigated 24-hour ABPM in the group of women with PCOS, one performed in Spanish women¹³ albeit subtle abnormalities in the regulation of BP observed in these women might suggest a mild masculinization of their cardiovascular system. To study the influence of obesity and androgen excess on BP and echocardiographic profiles of women with the syndrome, we conducted a cross-sectional case-control study comparing office and ambulatory BP monitoring, as well as echocardiographic assessments, in 63 premenopausal women with the classic phenotype, 33 nonhyperandrogenic women with regular menses, and 25 young men. Forty-nine subjects were lean and 72 had weight excess (body mass index ≥ 25 kg/m² (2 and second in Turkish women¹⁴).

The first factor taken into consideration was the evaluation of obesity-related hypertension in the group of women with PCOS. Overweight or obesity is generally a main behavioral risk factors for hypertension. In addition, women having a higher prevalence of obesity than men¹⁸. The incidence of obesity in women with PCOS is 50-70%¹⁹. In the present study, 69% of PCOS women were obese (BMI ≥ 30.0). Furthermore, obesity exacerbates hormonal and clinical features of PCOS²⁰. Obesity is associated with activation of both the sympathetic nervous system and the renin-angiotensin system contributing to the emergence of hypertension²¹. The evaluation of influence of BMI value on 24-hour ABPM revealed significant changes in all night-time measurements (SBP, DBP, HR) among women with PCOS and normal

Table III. The effect of phenotype on ambulatory blood pressure measurement.

	Phenotype of PCOS				
	A (n = 88)	B (n = 35)	C (n = 17)	D (n = 13)	p
dSBP [mmHg]	126.7 ± 12.2	126.6 ± 10.5	121.2 ± 11.2	121.1 ± 8.1	NS
dDBP [mmHg]	78.3 ± 8.6	79.7 ± 7.3	78.0 ± 9.3	76.7 ± 5.9	NS
nSBP [mmHg]	114.8 ± 15.1	118.0 ± 15.7	109.9 ± 11.4	111.0 ± 9.1	NS
nDBP [mmHg]	66.9 ± 10.1	67.0 ± 14.1	66.8 ± 10.8	65.8 ± 5.6	NS
dHR [BPM]	77.8 ± 7.8	73.7 ± 6.1	76.7 ± 10.3	71.7 ± 7.6	0.01
nHR [BPM]	68.5 ± 9.0	65.9 ± 8.8	64.8 ± 8.9	62.4 ± 5.0	< 0.04
% night drop	12.3 ± 8.0	12.1 ± 10.8	12.3 ± 5.5	11.4 ± 7.4	NS

PCOS – polycystic ovary syndrome; dSBP – day-time systolic blood pressure; dDBP – day-time diastolic blood pressure; nSBP – night-time systolic blood pressure; nDBP – night-time diastolic blood pressure; dHR – day-time heart rate; nHR – night-time heart rate; BPM – beat per minute; NS – non-significant.

Table IV. The effect of BMI value on ambulatory blood pressure measurement in the group of PCOS women.

	PCOS group			p
	Normal weight (n = 30)	Overweight (n = 17)	Obese (n = 106)	
dSBP [mmHg]	111.5 ± 9.6	122.7 ± 10.4	128.9 ± 11.4	NS
dDBP [mmHg]	76.8 ± 7.8	77.1 ± 8.8	78.9 ± 8.4	NS
nSBP [mmHg]	104.6 ± 9.2	112.9 ± 15.0	118.4 ± 14.7	0.0001
nDBP [mmHg]	62.1 ± 13.3	64.7 ± 8.1	68.9 ± 10.2	0.01
dHR [BPM]	76.6 ± 7.3	76.6 ± 7.3	76.5 ± 7.1	NS
nHR [BPM]	63.3 ± 11.2	64.2 ± 6.2	68.5 ± 8.1	0.0001
% night drop	15.6 ± 9.2	12.4 ± 6.1	11.0 ± 8.1	NS

PCOS – polycystic ovary syndrome; dSBP – day-time systolic blood pressure; dDBP – day-time diastolic blood pressure; nSBP – night-time systolic blood pressure; nDBP – night-time diastolic blood pressure; dHR – day-time heart rate; nHR – night-time heart rate; BPM – beat per minute; NS – non-significant.

weight, overweight or obesity. The highest value of 24-hour ABPM was detected in the obese women with PCOS. This observation also confirmed a positive correlation between higher BMI value and increased value of daytime and night-time of SBP, DBP and HR. Further, BMI value was the main factor effects on insufficient nocturnal drop BP. The lowest value in nocturnal drop BP (% ni-

ght drop) was found in the PCOS women with the highest BMI value.

In addition, the negative correlation between BMI value and the value of nocturnal drop BP also confirmed the adverse relationship between those parameters. Similar to the results obtained earlier^{1,22,23}, we observed a significant and progressive impact of BMI on 24-hour ABPM re-

Table V. The effect of the insulin resistance on ambulatory blood pressure measurement in the group of PCOS women.

	HOMA-IR ≤ 2.0 (n = 64)	HOMA-IR > 2.0 (n = 89)	p
dSBP [mmHg]	130.0 ± 10.6	122.9 ± 12.0	0.0001
dDBP [mmHg]	81.7 ± 8.1	76.7 ± 8.1	0.0001
nSBP [mmHg]	117.8 ± 14.4	113.1 ± 15.2	0.01
nDBP [mmHg]	69.0 ± 8.8	66.5 ± 10.5	0.01
dHR [BPM]	78.3 ± 6.5	74.8 ± 8.8	0.01
nHR [BPM]	68.9 ± 8.4	65.7 ± 8.9	< 0.05
% night drop	11.2 ± 7.0	13.1 ± 8.8	NS

PCOS – polycystic ovary syndrome; HOMA-IR - homeostatic model assessment for insulin resistance; dSBP – day-time systolic blood pressure; dDBP – day-time diastolic blood pressure; nSBP – night-time systolic blood pressure; nDBP – night-time diastolic blood pressure; dHR – day-time heart rate; nHR – night-time heart rate; BPM – beat per minute; NS – non-significant.

Table VI. The effect of high androgens level on ambulatory blood pressure measurement in the group of the PCOS women.

	High androgen concentration (n = 99)	Normal androgens levels (n = 54)	p
dSBP [mmHg]	133.1 ± 10.0	125.4 ± 11.7	<0.05
dDBP [mmHg]	82.8 ± 6.8	78.5 ± 8.3	< 0.05
nSBP [mmHg]	125.4 ± 17.6	113.8 ± 14.2	< 0.05
nDBP [mmHg]	71.2 ± 8.3	66.6 ± 11.2	< 0.05
dHR [BPM]	80.4 ± 6.9	76.3 ± 7.9	< 0.05
nHR [BPM]	70.3 ± 11.2	66.9 ± 8.6	NS
% night drop	10.3 ± 7.0	12.9 ± 7.8	NS

PCOS – polycystic ovary syndrome; dSBP – day-time systolic blood pressure; dDBP – day-time diastolic blood pressure; nSBP – night-time systolic blood pressure; nDBP – night-time diastolic blood pressure; dHR – day-time heart rate; nHR – night-time heart rate; BPM – beat per minute; NS – non-significant.

sults. Our results confirmed earlier investigation that obesity predisposes to hypertension^{24,25}. Moreover, similar to results have been obtained by Kargili et al²⁶, who showed that the overweight/obesity and the lower value of nocturnal drop BP probably are an independent predictors of future cardiovascular events in women with PCOS.

We also analyzed the effect of phenotype of PCOS on 24-hour ABPM. The more severe PCOS phenotypes are associated with a greater magnitude of CVD risk, and this has been found in obese and non-obese women²⁷. We did not find any significant differences in SBP or DBP value between those subgroups. However, the highest mean in daytime and night-time value of HR was revealed in phenotype A subgroup. Heart rate is an important factor that is widely used in determining the cardiovascular health. In patients with CVD, high resting HR serves as an indicator of total and CVD mortality, irrespective of other major coronary heart disease risks factors²⁸. In addition, it was well documented²⁹ that elevated HR is associated with development of hypertension. Higher value of daytime and night-time HR in phenotype A could indicate higher risk of hypertension and CVD in the future. It was also shown that hyperandrogenic PCOS patients have a higher incidence of hypertension compared to non-androgenic PCOS patients³⁰. Androgen excess in PCOS may directly influence the vascular properties of arterial walls and induce the atherogenic process³¹. In addition, hyperandrogenemia itself may activate renin-angiotensin system¹³. Moreover, elevated androgens concentration were reported to be associated with IR, obesity, and changes in lipid metabolism³, which can induce hypertension. In our study, in the women with PCOS and higher androgen concentration higher value of SBP and DBP both at daytime and night-time as well as higher day-time HR

were found. In addition, higher FAI value was correlated with increased value of both daytime and night-time SBP and HR, which confirmed close and adverse effects of those parameters.

Presumably, the increased CVD risk noted in younger women with PCOS may plateau in women with PCOS as they age³². A small increase in SBP after oral estrogen administration was observed in postmenopausal women. On the other hand, menopause is accompanied by a significant rise in the prevalence of hypertension in women, suggesting a protective role of endogenous estradiol on BP³³. In the present study we found that age was positively correlated with night-time DBP, whereas negatively with HR value both at daytime and night-time.

The last factor taken into consideration was the effect of IR on 24-hour ABPM. In the group of women with PCOS and coexisting IR, lower value of 24-hour ABPM including SBP, DBP and HR were detected. Already in 1992, Zimmerman et al³⁴, proposed as a working hypothesis, that since PCOS women are highly insulin resistant, they would have significantly higher blood pressure. Nevertheless, their hypothesis was not supported by the results. The lack of higher BP in PCOS women with IR was explained by the mechanism in which hyperinsulinemia from IR may have a stimulatory effect at sites involved in BP regulation. An experimental study showed that chronic insulin infusions fail to raise plasma catecholamine concentrations or blood pressure, although a modest sodium retention was observed³⁵. High insulin concentration may have also a vasodilatory effect, which could also explain lower BP measurements in PCOS women with IR. However, it was also revealed that high IR can promote vasoconstriction^{25,36}, therefore, this part of the study should be continued.

It is important to mention, that all investigated parameters influenced on the night-time HR value. The correlation coefficients were weak, but statistically significant. We confirmed earlier results¹³ albeit subtle abnormalities in the regulation of BP observed in these women might suggest a mild masculinization of their cardiovascular system. To study the influence of obesity and androgen excess on BP and echocardiographic profiles of women with the syndrome, we conducted a cross-sectional case-control study comparing office and ambulatory BP monitoring, as well as echocardiographic assessments, in 63 premenopausal women with the classic phenotype, 33 nonhyperandrogenic women with regular menses, and 25 young men. Forty-nine subjects were lean and 72 had weight excess (body mass index ≥ 25 kg/m²) that higher average value of HR in the group of women with PCOS could be associated with androgen excess, obesity, hypertension and cardiovascular diseases development in the future.

Conclusions

It is important to perform 24-hour ABPM in group of women with PCOS to evaluate the BP outcome. Many factors including body mass, phenotypes, IR, and elevated concentration of androgens are associated with disorders in 24-hour ABPM in women with PCOS. Presumably, hypertension, apart from visceral obesity, hyperinsulinemia and insulin resistance, could be considered as component of metabolic syndrome in the women with PCOS.

Conflict of Interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Consent for Publication

All researchers give their permission for the publication of this study.

References

- Bentley-Lewis R, Seely E, Dunaif A. Ovarian hypertension: polycystic ovary syndrome. *Endocrinol Metab Clin North Am* 2011; 40: 433-449.
- Fernandez RC, Moore VM, Van Ryswyk ME, Varcoe TV, Rodgers RJ, March WA, Moran LJ, Avery CJ, McEvoy RD, Davies MJ. Sleep disturbances in women with polycystic ovary syndrome: prevalence, pathophysiology, impact and management strategies. *Nat Sci Sleep* 2018; 10: 45-64.
- Chen MJ, Yang WS, Yang JH, Chen CL, Ho HN, Yang YS. Relationship between androgen levels and blood pressure in young women with polycystic ovary syndrome. *Hypertension* 2007; 49: 1442-1447.
- Amiri M, Tehrani FR, Behboudi-Gandevani S, Bidhendi-Yarandi R, Carmina E. Risk of hypertension in women with polycystic ovary syndrome: a systematic review, meta-analysis and meta-regression. *Reprod Biol Endocrinol* 2020; 18: 23.
- Luque-Ramírez M, Escobar-Morreale HF. Polycystic ovary syndrome as a paradigm for prehypertension, prediabetes, and preobesity. *Curr Hypertens Rep* 2014; 16: 500.
- Mačut D, Bačević M, Božić-Antić I, Bjekić-Macut J, Čivčić M, Erceg S, Milutinović DV, Stanojlović O, Andrić Z, Kastratović-Kotlica B, Šukilović T. Predictors of subclinical cardiovascular disease in women with polycystic ovary syndrome: interrelationship of dyslipidemia and arterial blood pressure. *Int J Endocrinol* 2015; 2015: 812610.
- Joham AE, Boyle JA, Zoungas S, Teede HJ. Hypertension in reproductive-aged women with polycystic ovary syndrome and association with obesity. *Am J Hypertens* 2015; 28: 847-851.
- Barber TM, Hanson P, Weickert MO, Franks S. Obesity and polycystic ovary syndrome: implications for pathogenesis and novel management strategies. *Clin Med Insights Reprod Health* 2019; 13: 1179558119874042.
- Cho LW, Randeve HS, Atkin SL. Cardiometabolic aspects of polycystic ovarian syndrome. *Vasc Health Risk Manag* 2007; 3: 55-63.
- Franik G, Krysta K, Madej P, Gimlewicz-Pięta B, Oślizło B, Trukawka J, Olszanecka-Glinianowicz M. Sleep disturbances in women with polycystic ovary syndrome. *Gynecol Endocrinol* 2016; 32: 1014-1017.
- Health Quality Ontario. Twenty-four-hour ambulatory blood pressure monitoring in hypertension: an evidence-based analysis. *Ont Health Technol Assess Ser* 2012; 12: 1-65.
- Madin K, Iqbal P. Twenty four hour ambulatory blood pressure monitoring: a new tool for determining cardiovascular prognosis. *Postgrad Med J* 2006; 82: 548-551.
- Luque-Ramírez M, Martí D, Fernández-Durán E, Alpañés M, Álvarez-Blasco F, Escobar-Morreale HF. Office blood pressure, ambulatory blood pressure monitoring, and echocardiographic abnormalities in women with polycystic ovary syndrome: role of obesity and androgen excess. *Hypertension* 2014; 63: 624-629.
- Özkan S, Yılmaz ÖÇ, Yavuz B. Increased masked hypertension prevalence in patients with polycystic ovary syndrome (PCOS). *Clin Exp Hypertens* 2020; 42: 681-684.
- Espinós JJ, Calaf J, Estadella J, Checa MA. Hirsutism scoring in polycystic ovary syndrome:

- concordance between clinicians' and patients' self-scoring. *Fertil Steril* 2010; 94: 2815-2816.
- 16) Hatch R, Rosenfield RL, Kim MH, Tredway D. Hirsutism: implications, etiology, and management. *Am J Obstet Gynecol* 1981; 140: 815-830.
- 17) Ożga K, Krzyczkowska-Sendrakowska M, Hubalowska-Dydejczyk A, Gilis-Januszewska A, Ratajczak M, Ratajczak M, Chaykivska Z, Jach R. The value of the free androgen index depends on the phenotype of polycystic ovary syndrome - a single-centre experience. *Endokrynol Pol* 2019; 70: 330-335.
- 18) Everett B, Zajacova A. Gender differences in hypertension and hypertension awareness among young adults. *Biodemography Soc Biol* 2015; 61: 1-17.
- 19) Moulana M, Lima R, Reckelhoff JF. Metabolic syndrome, androgens, and hypertension. *Curr Hypertens Rep* 2011; 13: 158-162.
- 20) Naderpoor N, Shorakae S, Joham A, Boyle J, De Courten B, Teede HJ. Obesity and polycystic ovary syndrome. *Minerva Endocrinol* 2015; 40: 37-51.
- 21) Leggio M, Lombardi M, Caldarone E, Severi P, D'Emidio S, Armeni M, Bravi V, Bendini MG, Mazza A. The relationship between obesity and hypertension: an updated comprehensive overview on vicious twins. *Hypertens Res* 2017; 40: 947-963.
- 22) Barcellos CRG, Rocha MP, Hayashida SAY, Mion Junior D, Lage SG, Marcondes JAM. Impact of body mass index on blood pressure levels in patients with polycystic ovary syndrome. *Arq Bras Endocrinol Metabol* 2007; 51: 1104-1109.
- 23) Tamimi W, Siddiqui IA, Tamim H, AlEisa N, Adham M. Effect of body mass index on clinical manifestations in patients with polycystic ovary syndrome. *Int J Gynaecol Obstet* 2009; 107: 54-57.
- 24) Re RN. Obesity-related hypertension. *Ochsner J* 2009; 9: 133-136.
- 25) Shariq OA, McKenzie TJ. Obesity-related hypertension: a review of pathophysiology, management, and the role of metabolic surgery. *Gland Surg* 2020; 9: 80-93.
- 26) Kargili A, Karakurt F, Kasapoglu B, Derbent A, Koca C, Selcoki Y. Association of polycystic ovary syndrome and a non-dipping blood pressure pattern in young women. *Clin Sao Paulo Braz* 2010; 65: 475-479.
- 27) Fauser BCJM, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, Carmina E, Chang J, Yildiz BO, Laven JSE, Boivin J, Petraglia F, Wijeyeratne CN, Norman RJ, Dunaif A, Franks S, Wild RA, Dumesic D, Barnhart K. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertil Steril* 2012; 97: 28-38.e25.
- 28) Saxena A, Minton D, Lee DC, Sui X, Fayad R, Lavie CJ, Blair SN. Protective role of resting heart rate on all-cause and cardiovascular disease mortality. *Mayo Clin Proc* 2013; 88: 1420-1426.
- 29) Reule S, Drawz PE. Heart rate and blood pressure: any possible implications for management of hypertension? *Curr Hypertens Rep* 2012; 14: 478-484.
- 30) Hoang V, Bi J, Mohankumar SM, Vyas AK. Liraglutide improves hypertension and metabolic perturbation in a rat model of polycystic ovarian syndrome. *PLoS One* 2015; 10: e0126119.
- 31) Christakou CD, Diamanti-Kandarakis E. Role of androgen excess on metabolic aberrations and cardiovascular risk in women with polycystic ovary syndrome. *Womens Health (Lond)* 2008; 4: 583-594.
- 32) Dumesic DA, Oberfield SE, Stener-Victorin E, Marshall JC, Laven JS, Legro RS. Scientific statement on the diagnostic criteria, epidemiology, pathophysiology, and molecular genetics of polycystic ovary syndrome. *Endocr Rev* 2015; 36: 487-525.
- 33) Ashraf MS, Vongpatanasin W. Estrogen and hypertension. *Curr Hypertens Rep* 2006; 8: 368-376.
- 34) Zimmermann S, Phillips RA, Dunaif A, Finegood DT, Wilkenfeld C, Ardeljan M, Gorlin R, Krakoff LR. Polycystic ovary syndrome: lack of hypertension despite profound insulin resistance. *J Clin Endocrinol Metab* 1992; 75: 508-513.
- 35) Hall JE, Brands MW, Kivlighn SD, Mizelle HL, Hildebrandt DA, Gaillard CA. Chronic hyperinsulinemia and blood pressure. Interaction with catecholamines? *Hypertension* 1990; 15: 519-527.
- 36) Manrique C, Lastra G, Sowers JR. New insights into insulin action and resistance in the vasculature. *Ann N Y Acad Sci* 2014; 1311: 138-150.