Is there any association between mild hypertension and hot flash experience among women?

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Summary

Objective: To determine the association between ambulatory blood pressure (ABP), heart rate, and hot flash (HF) experience among women. *Materials and Methods:* The authors recruited 110 women aged 22 to 65 years with mild essential hypertension or normotension confirmed by 24-hour ABP monitoring. None of the women had organ damage, inflammatory diseases, on estrogen replacement therapy or any other risk factors. Participants wore an ABP monitor that both records heart rate during 24 hours and noted their awake and sleep times. HF were assessed using an everyday complaint questionnaire that included symptoms associated with menopause. Each participant was asked whether or not she had experienced each symptom during the two weeks before the interview. *Results:* Fifty-five of the participants (45%) reported having had HF during the two weeks before they completed the questionnaire. The results show that the prevalence of essential hypertension (EH) in the group of women who had HF was significantly higher than the group of women that did not have HF ($p = 0.035$). The authors also found that hypertensive women had HF more often than normotensive women ($p = 0.035$), but other parameters including mean awake and sleep systolic BP values, mean awake and sleep diastolic BP values, heart rates, and nocturnal dipping of BP did not differ statistically among the group of women who had HF and the group of women who did not have HF ($p > 0.05$). *Conclusions:* These data suggest that the prevalence of EH in the group of women who have HF is significantly higher than the group of women that does not have HF.

Key words: Hot flashes; Hypertension; Ambulatory blood pressure; Heart rate variability; Menopause.

Introduction

During menopausal years, approximately 70% to 80% of women have symptoms and clinical findings due to an estrogen deficiency and symptoms appear after the beginning of the changes in ovarian function. However, cardiovascular diseases, which are associated with a high morbidity and mortality, manifest in the later period of women's life. [1, 2]. Increased blood pressure is a risk factor for cardiovascular diseases. [3, 4] Furthermore, several studies showed that menopause was associated with increased blood pressure (BP). [5,6] Changes in the sex steroids, endothelin, renin-angiotensin system (RAS), gaining weight, and activation of the sympathetic system have all found to be responsible for this blood pressure changes [7].

Most postmenopausal women experience vasomotor symptoms up to a some degree [8]. Currently, the mechanism of hot flashes (HF) thought to be the result of activation of the sympathetic nervous system, may also be responsible for postmenopausal hypertension (HT) [7, 9].

If there was any association between HF and HT, HF would probably trigger or disclose this association. The authors aimed to investigate whether there is any relationship between HF and HT.

Materials and Methods

A total of 110 women were invited for this study from Zekai Tahir Burak Education and Research Hospital, Gynecology Clinic and Yüksek Ihtisas Heart-Education and Research Hospital, Cardiology Clinic between 2008 and 2009. Patient's mean age was 49.06 ± 9.5 (range 22-65). Exclusion criteria were defined as any systemic disease or cardiovascular disease except mild essential HT which was defined as BP less than 160/100 mmHg and patients who were prescribed hormone replacement or oral contraceptive therapy in the last six months. This project was approved by Local Ethical Review Board and informed consent was taken from all participants.

All personal and medical information including age, education level, illicit drug and alcohol use, cigarette smoking, average coffee and tea consumption per day, past medical history, oral contraceptive use in the last six months, and family history of HT were obtained by a questionnaire. During the same visit, anthropomorphic measurements (weight, height) were recorded. Body mass index (BMI) was calculated as follows: weight (kilograms)/height (meters) [2]. Menopause was defined as the absence of menstrual periods in the last twelve months. Patients who did not have any periods less than twelve months were considered as premenopausal or peri-menopausal. Greene climacteric scale [10] was used for the assessment of vasomotor symptoms occurring in the prior two weeks. Patients' HFs or night sweats were scored between 0 - 3 according to severity of their symptoms. (absent, mild, moderate, and severe).

All women's BP were assessed by measuring 24-hour ambulatory BP (ABP). Left arm was used for BP measuring if they were not left-handed and recording machine was wrapped around the patient's waist. Patients were instructed not to use left arms during BP measurement and all BP data were delivered to computer after 24-

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Table 1. — *The socio-demographic data of women according to hot flashes.*

Variables	Hot flash (-) (n=49)	Hot flash (+) (n=61)	*p*
Age	47.2 ± 11.9	50.5 ± 7.0	0.092
Age Groups			0.019*
<45 years old (n:31, 28.2%)	19 (38,8%)	12 (19.7%)	
45-54 years old (n:39, 35.5%)	11 (22.4%)	28 (45.9%)	
>54 years old (n:40, 36.4%)	19 (38.8%)	21 (34.4)	
Menopausal state			0.430
Pre- or peri-menopausal	27 (55.1%)	29 (47.5%)	
Post-menopausal	22 (44.9%)	32 (52.5%)	
BMI	28.2 ± 5.8	29.3 ± 4.4	0.234
Occupational State			0.876
Works	29 (59.2%)	37 (60.7%)	
Do not work	20 (40.8%)	24 (39.3%)	
Education level			0.215
Uneducated	6 (12.2%)	4 (6.6%)	
Primary	13 (26.5%)	27 (44.3%)	
Secondary	4 (8.2%)	8 (13.1%)	
High school	12 (24.5%)	11 (18.0%)	
University	14 (28.6%)	11 (18.0%)	
Gravity	3 (0 - 9)	4 (0 - 12)	0.010*
Parity	2 (0 - 5)	2 (0 - 8)	0.077
Smoking	10 (20.4%)	17 (27.9%)	0.366
Hypertension	19 (38.8%)	36 (59.0%)	0.035*
Family history of HT	34 (69.4%)	46 (75.4%)	0.481
Night sweats	3 (6.1%)	36 (59.0%)	< 0.001*
Tea consumption	3 (0-15)	4 (0-12)	0.452
Coffee consumption	0 (0-3)	0 (0-3)	0.444

hour period. During the day, BP recordings were performed every 15 minutes and during night, BP measurements were performed every 30 minutes and mean BP were calculated as all BP measurements divided by total number of recordings. Sleeping and non-sleeping periods were assigned by patients. At least five BP measurements during night and daytime were required in order to be included in the study. Mean BP measurement count was 68.7 ± 11.66. Hypertension was defined as any patient who have been under treatment of HT or whose 24-hour ambulatory mean systolic and diastolic BP were above 130 mmHg and/or 80 mmHg, respectively, or women who had daytime mean BP above 135/85 mmHg or overnight mean BP above 120/70 mmHg (European Society of Hypertension - European Society of Cardiology: ESH-ESC 2007).[11] Patients who were under HT drug therapy stopped treatment before two weeks of this study. Patients who had BP above 160/100 mmHg before or after treatment were also excluded from the study. Absolute dipping was calculated as subtraction of mean overnight systolic BP from mean daytime systolic blood pressure. Relative dipping was calculated as 1 was subtracted from the ratio between the mean overnight systolic BP and mean daytime BP. Patients who had less than 15% decrease of overnight mean BP from mean daytime BP were considered as non-dipper which is also found to be associated with cardiovascular diseases.[12]

Statistical analysis of the study was performed using the SPSS version 11.5. Shapiro Wilk test was used whether continuous variables distributed normally. Descriptive statistics for the continuous variables were expressed as mean ± standard deviation or median (minimum-maximum), for the categorical variables, they were expressed as case count or percentage (%). To determine whether or not differences existed between the groups in age and BMI, student's t test was employed. For the other parameters including gravity, parity, tea and coffee consumption, and 24-hour BP, Mann-Whitney U test was employed. All p values below 0.05 were considered statistically significant. Pearson's chi-square test was used for categorical variables.

Results

The socio-demographic data of women are shown on Table 1. Study patients' age range were between 22 and 65 with a mean of 49 years. Fifty-five of the patients were hypertensive and remaining 55 patients were normotensive. Fifty-four of the patients (49%) were post-menopausal and remaining 56 patients (51%) were pre- or peri-menopausal (55%).

HF were seen in 55.4% of the patients and there was no difference in the mean age who had HF and who did not them ($p = 0.092$). However, distribution of the age were different between the groups since women who did not have HF were mostly under 45 years and women who had HF were mostly between 45-54 years ($p = 0.019$).

When severity of the HF were assessed, 45.9% of the women had mild, 34.4% women had moderate, 19.7% of the women had severe HF, and 35.5% of the study participants had night sweats.

There was not any statistical difference between the HF and non-HF group in terms of menopausal state, BMI, education level, occupational state, tea and coffee consumption ($p > 0.05$).

Table 2. — *Comparison of the hot flashes with some of the 24-hour BP, pulse, and pulse pressure measurements*

Variables	Hot flash (-) (n=49)	Hot flash (+) (n=61)	*p*
Mean systolic BP mmHg	122.3 ± 16.4	126.8 ± 16.5	0.097
Mean diastolic BP mmHg	77.5 ± 10.6	78.8 ± 11.8	0.630
Daytime systoliC BP mmHg	124.7 ± 15.7	129.9 ± 16.3	0.067
Daytime diastolic BP mmHg	79.7 ± 10.8	81.8 ± 11.6	0.529
Overnight systolic BP mmHg	116.2 ± 19.2	118.6 ± 18.6	0.400
Overnight diastolic BP mmHg	71.4 ± 12.5	71.2 ± 12.2	0.945
Mean measurement count	70.3 ± 11.8	67.4 ± 11.5	0.108
Daytime measurement count	53.2 ± 12.7	51.2 ± 11.2	0.164
Overnight measurement count	16.7 ± 4.7	16.2 ± 4.0	0.779
Dipping absolute mmHg	9.2 ± 9.4	11.2 ± 10.1	0.204
Dipping relative %	7.6 ± 7.8	8.9 ± 7.7	0.295
Mean pulse/min	74.6 ± 9.2	74.7 ± 8.0	0.789
Daytime pulse/min	77.7 ± 9.9	77.8 ± 8.1	0.754
Overnight pulse/min	65.4 ± 8.7	66.3 ± 7.8	0.411
Mean pulse pressure mmHg	44.9 ± 9.5	47.9 ± 11.0	0.127
Daytime pulse pressure mmHg	45.0 ± 9.6	48.3 ± 11.5	0.133
Overnight pulse pressure mmHg	44.8 ± 9.8	47.2 ± 11.5	0.254
Dipper	9 (18.4%)	11 (18.0%)	0.964

Table 3. — *Demographic features according to blood pressure status.*

Variables	HT (-) (n=55)	HT (+) (n=55)	p
Age	45.4 ± 9.8	52.7 ± 7.9	< 0.001*
Age groups			< 0.001*
<45 years	22 (40.0%)	9 (16.4%)	
45-54 years	22 (40.0%)	17 (30.9%)	
>54 years	11 (20.0%)	29 (52.7%)	
Menopausal state			0.008*
Pre- or peri-menopausal	35 (63.6%)	21 (38.2%)	
Post-menopausal	20 (36.4%)	34 (61.8%)	
BMI	27.3 ± 4.4	30.3 ± 5.2	0.002*
Occupational state			0.119
Works	29 (52.7%)	37 (67.3%)	
Does not work	26 (47.3%)	18 (32.7%)	
Education level			0.622
Uneducated	5 (9.1%)	5 (9.1%)	
Primary	17 (30.9%)	23 (%41,8%)	
Secondary	5 (9.1%)	7 (%12,7%)	
High school	13 (23.6%)	10 (%18,2%)	
University	15 (27.3%)	10 (%18,2%)	
Gravity	3 (0 - 10)	3 (0 - 12)	0.010*
Parity	2 (0 - 8)	3 (0 - 7)	0.077
Smoking	16 (29.1%)	11 (20.0%)	0.268
HF 25 (45.5%)	36 (65.5%)	0.035*	
Night Sweat	13 (23.6%)	26 (47.3%)	0.010*
Family history of HT	35 (63.6%)	45 (81.8%)	0.032*
Tea consumption	4 (0 - 12)	3 (0 - 2)	0.452
Coffee consumption	0 (0 - 3)	0 (0 - 2)	0.444

The prevalence of the HT and night sweats were significantly higher in HF group compared to the non-hot-HF ($p = 0.035$ vs $p < 0.001$).

Twenty-four hour BP, pulse, and pulse pressure measurements were compared between the HF and non-HF-group and none of the parameters compared were statistically different ($p > 0.05$, Table 2).

Table 3 shows the demographic features of the patients who were grouped according to their HT status. Mean age of the hypertensive patients were significantly higher than the normotensive women ($p < 0.001$). Post-menopausal state prevalence and BMI of the hypertensive group were significantly higher than normotensive group *(p* = 0008 and $p = 0.002$, respectively).

Table IV. — *24-hour BP measurements according to history of hypertension*

Variables	HT (-) (n=55)	HT(+) (n=55)	*p*
Mean systolic BP mmHg	113.6 ± 9.2	136.0 ± 14.4	< 0.001*
Mean diastolic BP mmHg	70.6 ± 6.4	85.9 ± 9.8	< 0.001*
Daytime systolic BP mmHg	117.1 ± 9.5	138.1 ± 14.5	< 0.001*
Daytime diastolic BP mmHg	73.5 ± 7.3	88.2 ± 9.7	< 0.001*
Overnight systolic BP mmHg	104.7 ± 9.6	130.3 ± 17.1	< 0.001*
Overnight systolic BP mmHg	63.1 ± 6.8	79.5 ± 11.0	< 0.001*
Mean measurement count	65.7 ± 12.7	71.7 ± 9.8	0.015*
Daytime measurement count	49.5 ± 13.1	54.7 ± 10.0	0.026*
Overnight measurement count	16.2 ± 4.6	16.7 ± 4.1	0.375
Dipping absolute mmHg	13.1 ± 7.9	7.6 ± 10.8	0.003*
Dipping relative %	11.0 ± 6.6	5.7 ± 8.0	< 0.001*
Mean pulse/min	73.5 ± 8.8	75.8 ± 8.2	0.122
Daytime pulse/min	76.8 ± 9.3	78.7 ± 8.5	0.194
Overnight pulse /min	64.6 ± 8.0	67.2 ± 8.2	0.091
Mean pulse pressure mmHg	42.9 ± 7.0	50.1 ± 12.0	< 0.001*
Daytime pulse pressure mmHg	43.5 ± 7.5	50.1 ± 12.5	0.004*
Daytime pulse pressure mmHg	41.7 ± 6.7	50.5 ± 12.3	< 0.001*
Dipper	14 (25.5%)	6 (10.9%)	0.048*

In the hypertensive group, 24-hour mean BP was 136/85 mmHg, mean, daytime mean BP was 138/88 mmHg, and overnight BP was 130/79 mmHg. In the normotensive group, 24-hour mean BP was 113/70 mmHg, daytime mean BP was 117/ 73 mmHg, and overnight BP was 104/ 63 mmHg. Absolute and relative dipping values were significantly lower in the hypertensive group ($p = 0.003$ and $p < 0.001$, respectively). Mean daytime and overnight pulse did not differ ($p > 0.05$). Mean daytime and overnight pulse pressures were significantly higher in the hypertensive group ($p < 0.01$). In the mean time, dipper frequency was significantly higher in the normotensive group ($p = 0.048$, Table 4).

The women in the hypertensive women was found to be suffering from HF and night sweats were 65.5 and 47.3, respectively. In the normotensive group, 45.5% of the women were determined to have HF and 23.6% of them were determined to have night sweats.

Night sweats and HF frequency were significantly higher in the hypertensive group than normotensive group ($p < 0.05$).

Discussion

The present data suggest that the prevalence of essential HT in the group of women who have HF is significantly higher than the group of women that does not have them

HF prevalence was found to be 55.45% in the present study participants. This ratio was higher from many studies [13-16].

Gerber *et al.* showed that women who had HF were postmenopausal and older which is consistent with previous studies [13, 15-17]. In the present study, there was no statistical difference in the menopausal state between HF and non-HF group.

There has been some controversy with the association between HF and BMI. Some investigators found that more HF were seen when BMI increased and this was linked to the isolation effect in the thermo-neutral zone by the adipose tissue [18-20]. Conversely, some studies showed that decreased BMI was associated with HF which was thought to be caused by less conversion of androgens to estrogen [21]. The present authors did not show any difference in the BMI of the HF and non-HF groups and their result was in agreement with the study done by Gerber *et al.* [13] and Zhang *et al.*[22].

There were some studies performed in order to explain the mechanism of the HF. Activation of the sympathetic nervous system might have a role in this mechanism [23]. Several studies showed increased level of 3-methoxy-4 hydroxyphenylglycole, which is a central metabolite of the norepinephrine in women who had HF compared to the women who did not have them [9, 23, 24]. In other studies trying to elucidate the association between HF and HT, Gerber *et al.* did not show any difference in hypertensive and normotensive women considering the HF. [13] In the present study, hypertensive women had significantly higher rate of HF.

James *et al.* [25] showed that symptomatic HF group (HF during study) had higher BP at work than the asymptomatic (HF in the past) and non-HF group (no history of HF). Gerber *et al.* [13] found increased daytime and overnight systolic BP in HF group. Gast *et al.* [26] showed that women with complaints of flushing or night sweats have an unfavorable cardiovascular risk profile with increased cholesterol levels, systolic and diastolic BPs, and BMI compared with women without vasomotor complaints. The present authors did not find any statistical difference between HF and non-HF group regarding the 24-hour, daytime and overnight mean systolic and diastolic BP measurements.

Many studies showed that essential hypertensive and nondipper patients were at risk of target organ damage. Verdeccia *et al.* found that left ventricular (LV) mass was greater in hypertensive subjects with nondipping [27]. Increased activation of the sympathetic nervous system and decreased activation of the parasympathetic system might have a role in nondipping BP mechanism [28, 29]. They found that the night time fall in both norepinephrine (NE) and epinephrine (EPI) excretion rates was reduced in nondippers compared with dippers [28]. This result might make us think that women have HF experience can have nondipper pattern and as a result HF women can have more cardiovascular morbidity.

However in the study of Gerber *et al.,* decreasing HP overnight (dipping) was no different between hypertensive group and normotensive group, HF, and non-HF group [13]. Conversely, the present authors found that hypertensive group had decreased absolute dipping and relative dipping values, but they did not show any difference in the dipping pattern of HF and non-HF groups and this result was in agreement with the study of Gerber *et al.* [13].

Conclusion

The prevalence of essential HT in the group of women who have HF is significantly higher than the group of women that does not have them. Vasomotor symptoms may be the preliminary manifestations of HT that is one of the major risk factor for cardiovascular diseases. So until further studies will be performed and the association between HF and HT clearly explained, women who complain of HF should be evaluated for HT in the office and appropriate treatment should be commenced promptly.

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References

[1] Speroff L.: "Menopause and postmenapausal hormone therapy". In: Glass R.H., Kasa N.G., Speroff L. (eds). *Clinical gynecologic endocrinology and infertility*, 5th ed. Baltimore, Williams and Wilkins, 1996, 583.
[2] Hammond C.B.: "Climacteric". In: Scott J.R., Disoio P.J., Hammond C.B., Spellacy W.N. (eds). *Danforths obstetrics and gynecology.* 7th ed. Philadelphia, J.B. Lippincott Co., 1994,771.
[3] MacMahon S., Peto R., Cutler J., Collins R., Sorlie P., Neaton J., *et al.*: "Blood pressure, stroke, and coronary heart disease. Part 1: prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias". *Lancet*, 1990, *335*, 765.
[4] World Health Organization. "World Health Report 2002. Reducing risks, promoting healthy life". Available at: www.who.int/whr/2002. Accessed February 2,2010.
[5] Owens J.F., Stoney C.M., Matthews K.A.: "Menopause status influences ambulatory blood pressure levels and blood pressure changes during mental stress". *Circulation*, 1993, *88*, 2794.
[6] Staessen J.A., Ginocchio G., Thijs L., Fagard R.: "Conventional and ambulatory blood pressure and menopause in a prospective population study". *J. Hum. Hypertens.*, 1997, *11*, 507.
[7] Reckelhoff J.F., Fortepiani L.A.: "Novel mechanisms responsible for postmenopausal hypertension". *Hypertension*, 2004, *43*, 918. Epub 2004 Mar 15.
[8] Kronnenberg F., Barnard R.M.: "Modulation of menopausal hot flashes by ambient temperature". *J. Therm. Biol.*, 1992, *17*, 43
[9] Freedman R.R.: "Physiology of hot flashes". *Am. J. Hum. Biol.*, 2001, *13*, 453
[10] Greene J.G.: "Constructing a standard climacteric scale". *Maturitas,* 1998, *29*, 25.
[11] European Society of Hypertension - European Society of Cardiology: "ESH-ESC 2007". Available at: www.medspace.com/viewarticle1560317-2. Accessed April 2, 2010.
[12] Chobanian A.V., Bakris G.L., Black H.R., Cushman W.C., Green L.A., Izzo J.L. Jr., *et al.*: "The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report". *JAMA*, 2003, *289*, 2560.
[13] Gerber L.M., Sievert L.L., Warren K, Pickering T.G., Schwartz J.E.: "Hot flashes are associated with increased ambulatory systolic blood pressure". *Menopause*, 2007, *14*, 308.
[14] Lock M.: "Menopause: lessons from anthropology". *Psychosom. Med.*, 1998, *60*, 410.
[15] Avis N.E., Stellato R., Crawford S., Bromberger J., Ganz P., Cain V., Kagawa-Singer M.: "Is there a menopausal syndrome? Menopausal status and symptoms across racial/ethnic groups". *Soc. Sci. Med.*, 2001, *52*, 345.
[16] Rizk D., Bener A., Ezimokhai M., Hassan M., Micallef R.: "The age and symptomatology of natural menopause among United Arab Emirates women". *Maturitas*, 1998, *29*, 197.
[17] Guthrie J.R., Dennerstein L., Hopper J.L., Burger H.G.: "Hot flashes, menstrual status, and hormone levels in a population-based sample of midlife women". *Obstet. Gynecol.*, 1996, *88*, 437.
[18] World Health Organization: "Research on the Menopause in the 1990s". Geneva, Switzerland: World Health Organization, 1996. WHO Technical Report Series, No. 866". Available at: http://whqlibdoc.who.int/trs/WHO_TRS_866.pdf
[19] Obermeyer C.M., Ghorayeb F., Reynolds R.: "Symptom reporting around the menopause in Beirut, Lebanon". *Maturitas*, 1999, *33*, 249.
[20] Thurston R.C., Sowers M.F.R., Sternfeld B., Gold E.B., Bromberger J., Chang Y.: "Gains in body fat and vasomotor symptom reporting over the menopausal transition". *Am. J. Epidemiol.*, 2009, *170*, 766.
[21] den Tonkelaar I., Seidell J.C., van Noord P.A.H.: "Obesity and fat distribution in relation to hot flashes in Dutch women from the DOM-project". *Maturitas*. 1996, *23*, 301.
[22] Zhang Q., Li F., Yu Y., Yu X., Sheng Q., Zhang X.: "Differential factors associated with hot flashes in Chinese perimenopausal and postmenopausal women". *Maturitas*, 2009, *63*, 94. doi: 10.1016/j.maturitas.2009.02.007. Epub 2009 Mar 25.
[23] Freedman R.R., Woodward S., Sabharwal S.C.: "α2-Adrenergic mechanism in menopausal hot flashes". *Obstet. Gynecol.*, 1990, *76*, 573.
[24] Freedman R.R., Dinsay R.: "Clonidine raises the sweating threshold in symptomatic but not in asymptomatic postmenopausal women". *Fertil. Steril.*, 2000, *74*, 20.
[25] James G.D., Sievert L.L., Flanagan E.: "Ambulatory blood pressure and heart rate in relation to hot flash experience among women of menopausal age". *Ann. Hum. Biol.*, 2004, *31*, 49.

[26] Gast G.C., Grobbee D.E., Pop V.J., Keyzer J.J., Wijnands-van Gent C.J., Samsioe G.N.,et al.: "Menopausal complaints are associated with cardiovascular risk factors". *Hypertension*, 2008, *51*, 1492. doi: 10.1161/HYPERTENSIONAHA.107.106526. Epub 2008 Apr 7.
[27] Verdeccia P., Schillaci G., Borgioni C., Ciucci A., Sacchi N., Battistelli M., *et al.*: "Gender, day–night blood pressure changes and left ventricular mass in essential hypertension: dippers and peakers". *Am. J. Hypertens.*, 1995, *8*, 193.
[28] Sherwood A., Steffen P.R., Blumenthal J.A., Kuhn C., Hinderliter A.L.: "Nighttime blood pressure dipping: the role of the sympathetic nervous system". *Am. J. Hypertens.*, 2002, *15*, 111.
[29] Nakano Y., Oshima T., Ozono R., Higashi Y., Sasaki S., Matsumoto T., *et al.*: "Non-dipper phenomenon in essential hypertension is related to blunted nocturnal rise and fall of sympatho-vagal nervous activity and progress in retinopathy". *Auton. Neurosci.*, 2001, *88*, 181.

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