ISSN 1607-419X
ISSN 2411-8524 (Online)
УДК 616.12-008.331.1

Inter-arm difference and orthostatic changes of brachial blood pressure in the very elderly patients under antihypertensive treatment

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Received 24 January 2016; accepted 12 February 2016.

Abstract

Background. Inter-arm difference in blood pressure (BP) and orthostatic BP response are significant prognostic factors in hypertensive patients, especially in the elderly ones. However, data on their prevalence, predictors and clinical associations remain contradictory. **The aim of our study** was to investigate inter-arm difference and orthostatic response and to establish their clinical associations in the very elderly hypertensive patients. **Design and methods.** We enrolled 67 hypertensive subjects older than 80 years (mean age 84.1 ± 3.1 years, 25,5 % male, mean clinic brachial systolic BP (SBP) 134.8 ± 23.2 mm Hg) in a cross-sectional study. Simultaneous bilateral brachial BP measurements were performed using oscillometric validated cuff-based device in sitting position and then 2 minutes after standing up. Central pulse waveform characteristics and arterial stiffness parameters were estimated by BPLab Vasotens system (Petr Telegin, Russia). **Results.** The median of inter-arm difference in SBP (IADSBP) was 4,00 (2.50, 9.00) mm Hg. IADSBP was ≥ 10 mm Hg in 25.4 % participants. Compared to others, those with IADSBP ≥ 10 mmHg had significantly higher body mass index (31.39 ± 5.73 vs 28.48 ± 4.1 kg/m^2, $p < 0.05$), waist circumference (116.3 ± 13.6 vs 107.7 ± 11.2 cm, $p < 0.05$) and pulse wave velocity in aorta (11.65 ± 1.46 vs 10.75 ± 1.71 m/s, $p < 0.05$). A positive correlation between IADSBP and augmentation index was revealed ($r = 0.277$, $p < 0.05$). Patients with asymptomatic orthostatic hypotension (22,4 % participants) had higher levels of brachial SBP and pulse pressure while central BP and markers of arterial stiffness did not differ from those without orthostatic hypotension. **Conclusions.** Significant IADSBP is associated with increased arterial stiffness and abdominal obesity in the very elderly hypertensive patients, whereas there is no evidence of interrelation between orthostatic response and arterial stiffness in these patients.

Key words: arterial hypertension, inter-arm difference, orthostatic hypotension, very elderly patients

For citation: Kobalava ZhD, Kotovskaya YuV, Ashraful Alam, Ezhova NE. Inter-arm difference and orthostatic changes of brachial blood pressure in the very elderly patients under antihypertensive treatment. Arterial’naya Gipertenziya = Arterial Hypertension. 2016;22(1):52–60. ***doi: 10.18705/1607-419X-2016-22-1-52-60.***

Различия между руками и ортостатические изменения артериального давления в плечевой артерии у очень пожилых пациентов с артериальной гипертензией на фоне медикаментозной терапии

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Статья поступила в редакцию 24.01.16 и принята к печати 12.02.16.

Резюме

Актуальность. Различия артериального давления (АД) между руками и ортостатическая реакция АД существенно влияют на прогноз пациентов с артериальной гипертензией (АГ) и потенциально имеют важное клиническое значение у людей пожилого возраста, однако данные о распространенности, предикторах и клинических ассоциациях этих феноменов противоречивы. **Цель исследования** — изучение различий АД между руками, ортостатической реакции и их предикторов у больных АГ очень пожилого возраста. **Материалы и методы.** В поперечное исследование были включены 67 пациентов с леченой АГ в возрасте 80 лет и старше (средний возраст — 84,1 ± 3,1 года, 25,5 % мужчин, средний уровень клинического систолического АД (САД) — 134,8 ± 23,2 мм рт. ст.). АД было измерено осциллометрическим методом, одновременно на обеих руках, в положении сидя, с последующим определением АД через 2 минуты после перехода в вертикальное положение. Для оценки параметров центральной пульсовой волны и артериальной ригидности использовалась система «BPLab Vasotens» (ООО «Петр Телегин», Россия) в режиме офисного измерения. **Результаты.** Медиана различий (Δ) САД между руками составила 4,00 (2,50; 9,00) мм рт. ст. Доля пациентов с Δ САД ≥ 10 мм рт. ст. составила 25,4 %. Последние характеризовались существенно бóльшими индексами массы тела (31,39 ± 5,73 против 28,48 ± 4,1 кг/м^2, $p < 0,05$) и окружностью талии (116,3 ± 13,6 против 107,7 ± 11,2 см, $p < 0,05$) в сравнении с пациентами с меньшей асимметрией САД. Скорость распространения пульсовой волны была значимо выше у пациентов с большей Δ САД: 11,65 ± 1,46 против 10,75 ± 1,71 м/с ($p < 0,05$). Была выявлена положительная корреляция величины Δ САД с индексом прироста в аорте ($r = 0,277$, $p < 0,05$). У пациентов с бессимптомной ортостатической гипотензией (ОГ) (22,4 % всех больных) отмечены более высокие уровни САД и пульсового давления в плечевой артерии; при этом уровни САД в аорте и параметры артериальной ригидности значимо не отличались от таковых у пациентов без ОГ. **Заключение.** Увеличение различий САД между руками у очень пожилых пациентов ассоциировано с наличием абдоминального ожирения и более выраженной артериальной ригидностью. Значимые клинические предикторы ортостатической реакции АД установить не удалось. По всей видимости, в данной группе пациентов феномены ортостатической гипо- и гипертензии не ассоциированы с параметрами артериальной ригидности.

Ключевые слова: артериальная гипертензия, ортостатическая гипотензия, различия артериального давления между руками, очень пожилые лица

Для цитирования: Кобалава Ж.Д., Котовская Ю.В., Ашрафул А., Ежова Н.Е. Различия между руками и ортостатические изменения артериального давления в плечевой артерии у очень пожилых пациентов с артериальной гипертензией на фоне медикаментозной терапии. Артериальная гипертензия. 2016;22(1):52–60. ***doi: 10.18705/1607-419X-2016-22-1-52-60.***

Introduction

Differences in blood pressure (BP) between the right and the left arm and orthostatic response of BP are the factors that have a significant impact on the prognosis of patients with arterial hypertension (HTN), and it was also stated in 2013 ESH/ESC Guidelines for the management of arterial hypertension [1]. Clinical measurement of BP is recommended to be conducted on both arms simultaneously in order to exclude the possible impact of short-term BP variability. Further readings of the arm with higher BP should be used. Differences of systolic BP (SBP) exceeding 10 mm Hg are considered relevant; there is evidence that such differences increase the risk of adverse cardiovascular outcomes [2]. Data on the prevalence of such differences and predictors (aorta and great vessel diseases were exclusion criteria) is inconsistent.

Elderly age is considered to be a factor associated with higher prevalence of orthostatic hypotension (OH) [3]. For instance, TILDA study showed that OH prevalence in the general population is 6.9 %, whereas among persons over 80 years old it is almost three times higher (18.5 %) [4]. Due to this fact it is recommended to measure BP in elderly persons after 1 and 3 minutes of staying in upright position. OH is determined as SBP decrease by more than 20 mm Hg or diastolic BP (DBP) decrease by more than 10 mm Hg after 3 minutes of standing [1]. OH was shown to be associated with higher mortality and higher prevalence of cardiovascular events [5–7]. The phenomenon of orthostatic hypertension has received less attention than OH, although recent evidence has showed it can also be associated with unfavourable prognosis and the increase of ischemic stroke risk, increase of silent stroke and left ventricular hypertrophy prevalence [8].

It is assumed that both phenomena are associated with arterial stiffness.

Thus, measurement of clinical BP in both arms and during the tilt-test in elderly persons can provide very important and clinically valuable i nformation. For this reason clinical relationships of phenomena associated with BP differences between the arms and orthostatic BP response are of special interest.

Therefore, the **objective of this study** is the investigation of arm-to-arm BP differences, orthostatic response and their predictors in elderly patients with HTN.

Design and methods

Patients aged 80 years and older were enrolled in this cross-sectional study. Excluded were patients with left ventricular ejection fraction < 40 %, aortic stenosis, clinical and sonographic signs of aorta or brachiocephalic vessels atherosclerotic lesions that could lead to the differences in BP between the arms, persistent atrial fibrillation, decompensated diabetes mellitus, chronic heart failure higher than NYHA functional class II with stages IIb or III according to Strazhesko-Vasilenko, glomerular filtration rate under 30 ml/min/1.73m2, severe chronic diseases, amputations of extremities.

BP was measured with a validated oscillometric device with two cuffs, that enabled simultaneous BP measurement in both arms. The measurement was carried out twice with 1-minute interval in sitting position according to the common rules of BP measurement [1]. An average of two measurements was taken. The SBP difference between the arms was calculated as an absolute difference between SBP in the right and left arms. In the arm with higher

BP, an additional BP measurement was carried out 2 minutes after the tilt-test.

For the assessment of central pulse wave and arterial stiffness parameters, an office BP measurement was conducted using the BPLab Vasotens system (OOO "Peotr Telegin", Russia). All arterial stiffness markers (aortic pulse wave velocity (PWV), aortic augmentation index, reflected pulse wave transmission time, arterial stiffness index) were standardized against the heart rate.

Echocardiography was carried out with the device Vivid 7 (General Electrics, USA) according to the standard protocol. Left ventricular ejection fraction was evaluated according to Simpson method, left ventricular mass index (LVMI) was calculated as left ventricular mass according to ASE formula indexed to the patient's body surface area (according to DuBois).

Statistical analysis was carried out in the GraphPad Prism program, version 5.00 for Windows. Quantitative variables are given as averages with standard deviations (M ± SD) in case of normal distribution of the parameter or as median with the interquartile range [Me (the 25th percentile, the 75th percentile)] in case of abnormal distribution. Discrete variables are given in absolute (n) and relative (%) values. For the comparison of parameters of the central and peripheral pulse wave, arterial stiffness and other signs in tertiles of the peripheral SBP, one way analysis of variance ANOVA was used combined with additional Bonferroni test if multiple comparisons were required; in case of abnormal distribution Kruskal–Wallis test with subsequent Dunn test was used. In order to find differences in two groups, unpaired t-test was used in case of normal distribution, otherwise medians were compared using Mann-Whitney test. For the correlation analysis, Pearson and Spearman coefficients were used for normal and abnormal parameter distribution, respectively. For the assessment of distribution normality D'Agostino-Pearson test was used. Differences in average values and correlations were considered statistically significant at significance level $p < 0.05$.

Results

Patient data

We enrolled 67 patients aged 80 and over (Table 1). All patients received combined antihypertensive therapy including an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, a beta-blocker, a thiazide-type diuretic. SBP in the sitting position in the arm with the maximum level ranged from 102 to 201 mm Hg,

Table 1

CLINICAL AND DEMOGRAPHICAL DATA OF EXAMINED PATIENTS AND CARDIOVASCULAR RISK FACTORS (n = 67)

Category	Value
Male, n (%)	17 (25.4%)
Age, yr	84.1 ± 3.1
Smoking, n (%)	4 (6%)
BMI, kg/m^2	29.2 ± 4.7
Obesity I-III degree, n (%)	20 (29.85%)
AO*, n (%)	57 (85.1%)
Dyslipidaemia**, n (%)	56 (83.6%)
Fasting plasma glucose, mmol/L	6.28 (5.68. 7.23)
SBP, mm Hg	134.8 ± 23.2
DBP, mm Hg	73.1 ± 11.8
eGFR, ml/min/1.73 м^2	52.76 ± 15.52
GFR 45–60 ml/min/1.73 м^2, n (%)	27 (40.3%)
GFR 30–45 ml/min/1.73 м^2, n (%)	12 (17.9%)
CHF I–II FC, n (%)	52 (77.6%)
DM, n (%)	21 (31.3%)

Note: BMI — body mass index; AO — abdominal obesity; SBP — systolic blood pressure; DBP — diastolic blood pressure; eGFR — estimated glomerular filtration rate; CHF — chronic heart failure; FC — functional class; DM — diabetes mellitus; AO* — abdominal obesity (waist circumference: men ≥ 102 cm; women ≥ 88 cm); ** — low-density lipoprotein cholesterol > 3.0 mmol/L, and/or high-density lipoprotein cholesterol: men < 1.0 mmol/L, women < 1.2 mmol/L, and/or triglycerides > 1.7 mmol/L, and/or total cholesterol > 4.9 mmol/L

DBP — from 46 to 93 mm Hg. Based on clinical BP measurement on the brachial artery, controlled HTN (SBP < 150 mm Hg and DBP < 90 mm Hg) was found in 47 patients (70 %), isolated SBP increase — in 16 (24 %) patients; isolated DBP increase was not found. Uncontrolled HTN in terms of both SBP and DBP was found in 4 patients (6 %).

Average clinical SBP on the brachial artery was 134.8 ± 23.2 mm Hg, clinical DBP on the brachial artery — 73.1 ± 11.8 mm Hg. Average pulse pressure (PP) on the brachial artery equaled 61.8 ± 19.3 mm Hg. Mean heart rate was 67.5 ± 7.8 bpm.

For the analysis of the association between BP and studied parameters, the patients were divided in tertiles depending on their SBP level in sitting position: tertile I included readings from 94 to 127.4 mm Hg, tertile II — from 127.5 to 140.9 mm Hg; tertile III — from 141 to 175 mm Hg. Patients in the subgroups differed by their body mass index (BMI) and waist circumference (WC), and maximum values were found in patients with the highest SBP level (Table 2). No statistically significant differences in the lipid profile parameters were found.

Analysis of the differences between blood pressure in the right and in the left arm

Median of SBP differences (Δ) between the arms was 4.00 (2.50, 9.00) mm Hg, DBP — 3.00 (2.00, 5.00) mm Hg, PP — 4.00 (1.50, 8.00) mm Hg. Δ SBP values varied from 0 to 30 mm Hg, DBP — from 0 to 24 mm Hg, PP — from 0 to 32 mm Hg. The proportion of patients with Δ SBP ≥ 10 mm Hg was 25.4 % (n = 17). Patients with higher Δ SBP between the arms were characterized by notably higher BMI and WC values, whereas no relevant differences in metabolic parameters were found (Table 3).

Statistically significant correlation of Δ SBP with WC was found: r = 0.2827 (p < 0.05).

Comparison of the pulse wave readings revealed the differences between the subgroups in aortic PWV and the reflected wave transmission time. No relevant differences of aortic augmentation index between the subgroups were found (Table 3), as well as there were no differences in parameters characterizing the state of other target organs — kidneys (glomerular filtration rate) and heart (LVMI).

Analysis of relationships of the differences in SBP and PP between the arms with the pulse wave parameters demonstrated negative correlation between the reflected wave transmission time normalized to the heart rate of 75 bpm and the differences of both SBP and PP between the arms. In the latter case the correlation was stronger (r = –0.267, r = –0.315; p < 0.05, p < 0.01, respectively). Positive correlation between aortic augmentation index, also normalized to the heart rate, and BP level differences between the arms was found (r = 0.277 and 0.246, p < 0.05 for SBP and PP, respectively) (Table 4). No relevant relationships of arterial stiffness parameters with BMI or WC were found.

Table 2

MAIN CLINICAL, DEMOGRAPHICAL AND LABORATORY PARAMETERS DEPENDING ON THE TERCILE OF PERIPHERAL SYSTOLIC BLOOD PRESSURE

Category	I tercile n = 22	II tercile n = 22	III tercile n = 23	p-value
Male, n (%)	8 (36.4 %)	4 (18.2 %)	5 (21.7 %)	0.339
Age, yr	84.3 ± 4.4	83.3 ± 2.1	83.4 ± 2.2	0.988
BMI, kg/m^2	27.09 ± 3.69	29.42 ± 4.22	31.06 ± 5.34	< 0.05*
WC, cm	103.8 ± 9.4	110.5 ± 11.0	115.2 ± 13.9	< 0.01*
Triglycerides, mmol/L	1.46 ± 0.84	1.56 ± 0.72	1.68 ± 0.62	0.422
Total cholesterol, mmol/L	5.11 ± 1.62	5.43 ± 1.38	5.36 ± 0.99	0.749
LDL cholesterol, mmol/L	3.58 ± 0.91	3.41 ± 0.86	3.23 ± 1.04	0.79
HDL cholesterol, mmol/L	1.37 ± 0.36	1.11 ± 0.37	1.38 ± 0.58	0.358
eGFR, ml/min/1.73 м^2	55.45 ± 11.55	52.75 ± 16.38	50.09 ± 18.15	0.526
SBP, mm Hg	113.8 ± 9.08	133.6 ± 4.0	151.7 ± 10.5	< 0.0001*

Note: BMI — body mass index; WC — waist circumference; HDL cholesterol — high-density lipoprotein cholesterol; LDL cholesterol — low-density lipoprotein cholesterol; eGFR — estimated glomerular filtration rate; SBP — systolic blood pressure; DBP — diastolic blood pressure; PP — pulse pressure; * — statistically significant.

Table 3

PATIENTS CHARACTERISTICS DEPENDING ON THE DIFFERENCE IN SYSTOLIC BLOOD PRESSURE LEVEL BETWEEN THE ARMS

Category	Δ SBP < 10 mm Hg (n = 50)	Δ SBP ≥ 10 mm Hg (n = 17)	p-value
Male, n (%)	14 (28)	3 (17,6)	0,3209
Age, yr	83 (81; 86)	83 (81; 85)	0,6949
BMI, kg/m^2	28,48 ± 4,11	31,39 ± 5,73	< 0,05*
WC, cm	107,7 ± 11,3	116,3 ± 13,6	< 0,05*
Total cholesterol, mmol/L	5,39 ± 1,41	5,00 ± 1,06	0,3433
Triglycerides, mmol/L	1,39 (1,03; 2,14)	1,62 (0,91; 1,87)	0,6920
Fasting plasma glucose, mmol/L	6,1 (5,53; 7,55)	6,6 (5,87; 7,07)	0,5756
eGFR, ml/min/1.73 м^2	53,41 ± 13,88	47,86 ± 19,01	0,23
SBP, mm Hg	131,5 ± 18,1	138,6 ± 15,7	0,1547
DBP, mm Hg	67,0 ± 9,4	70,1 ± 10,6	0,2524
PP, mm Hg	64,5 ± 15,0	68,5 ± 14,7	0,3444
SBP ao, mm Hg	122,8 ± 16,1	126,3 ± 12,5	0,4145
DBP ao, mm Hg	69,8 ± 9,6	71,5 ± 10,7	0,5603
PP ao, mm Hg	51,0 (42,5; 64,0)	56,0 (47,5; 61,5)	0,4904
AIxao@HR 75 bpm, %	37,0 (26,0; 47,0)	41,0 (27,0; 49,0)	0,7404
PWV in aorta, m/s	10,75 ± 1,71	11,65 ± 1,46	< 0,05*
RWTT@HR 75 bpm, ms	131,2 ± 17,6	121,0 ± 14,2	< 0,05*
LVMI, g/m^2	125,2 ± 29,07	139,5 ± 25,53	0,1308

Note: Δ SBP — difference systolic blood pressure between the arms; BMI — body mass index; WC — waist circumference; GFR — glomerular filtration rate; SBP — systolic blood pressure; DBP — diastolic blood pressure; PP — pulse pressure; ao — aorta; AIxao@HR75 — aortic blood pressure augmentation index standardized against heart rate 75 beats per minute; RWTT — reflected wave transit time; PWV — pulse wave velocity; LVMI — left ventricular mass index; * — statistically significant differences between the groups.

Table 4

CORRELATION OF THE ARM-TO-ARM DIFFERENCES IN BLOOD PRESSURE WITH ARTERIAL STIFFNESS AND CENTRAL PULSE WAVE VELOCITY

Category	Δ SBP		Δ PP	
	r	p	r	p
RWTT	–0.267*	< 0.05	–0.315**	< 0.01
PWVao	0.329	0.108	0.191	0.128
AIxao@HR75	0.277*	< 0.05	0.246*	< 0.05
SBPao	0.011	0.928	0.045	0.72

Note: ΔSBP/ΔPP — difference systolic/pulse blood pressure between the arms; RWTT — Reflected wave transit time; PWVao — pulse wave velocity in aorta; AIxao@HR75 — aortic blood pressure augmentation index standardized against heart rate 75 beats per minute; SBPao — systolic blood pressure in aorta; r — correlation coefficient; * — statistically significant differences between the groups.

Therefore, our data provide evidence of association of arm-to-arm SBP differences with anthropometric signs of obesity and arterial stiffness characteristics.

Blood pressure changes during tilt-test

During the orthostatic test, the SBP on the brachial artery (2 minutes after the tilt-test of a patient) increased in 26 patients (maximum pressure increase was 27 mm Hg), and in 8 (11.9%) of them — by more than 20 mm Hg; it did not change in 4 subjects and decreased in 37 patients (maximum SBP decrease — 37 mm Hg). In 15 persons (22.4%) the decrease achieved more than 20 mm Hg. In all patients orthostatic SBP decrease ≥ 20 mm Hg was asymptomatic.

Table 5

COMPARATIVE ANALYSIS OF PATIENTS DEPENDING ON THE ORTHOSTATIC RESPONSE OF SYSTOLIC BLOOD PRESSURE

Category	Orthostatic decline SBP ≥ 20 mm Hg (n = 15)	Changes SBP within ± 19 mm Hg (n = 44)	Orthostatic increase SBP > 20 mm Hg (n = 8)	p-value
Male, n (%)	6 (40)	9 (17.3)	2 (25)	0.323
Age, yr	84 (81; 86)	83 (81; 86)	83 (81.5; 86.3)	0.741
BMI, kg/m²	27.9 (24.5; 29.8)	29.0 (26.1; 33.6)	27.3 (24.9; 28.7)	0.357
WC, cm	107.1 ± 8.4	109.6 ± 12.7	114.9 ± 16.8	0.367
Total cholesterol, mmol/L	5.53 ± 1.11	5.33 ± 1.34	4.65 ± 1.48	0.410
LDL cholesterol, mmol/L	4.05 ± 0.48	3.21 ± 0.79	3.19 ± 0.89	< 0.05*
Triglycerides, mmol/L	1.17 (0.82; 1.77)	1.55 (1.04; 2.26)	1.45 (1.13; 2.08)	0.252
Fasting plasma glucose, mmol/L	6.70 (5.51; 7.90)	6.10 (5.59; 6.87)	7.13 (6.25; 10.98)	0.418
SBP, mm Hg	145.9 ± 28.7	132.2 ± 20.2	121.8 ± 10.1	< 0.05*
DBP, mm Hg	73.2 ± 12.0	74.7 ± 11.1	64.1 ± 12.2	0.064
PP, mm Hg	72.7 ± 24.7	58.8 ± 17.5	57.6 ± 8.3	< 0.05*
Central SBP, mm Hg	125.2 ± 11.8	122.6 ± 16.9	122.9 ± 10.2	0.851
Central DBP, mm Hg	69.0 ± 8.9	71.6 ± 10.5	65.0 ± 6.7	0.197
Central PP, mm Hg	57.0 (50.0; 63.0)	47.5 (41.8; 61.8)	53.3 (59.5; 63.8)	0.148
AIxao@HR 75 bpm, %	43.0 (36.0; 50)	36.0 (24.0; 47.5)	42.0 (24.8; 56.8)	0.240
PWVao, m/s	11.13 ± 1.64	10.80 ± 1.78	11.63 ± 1.30	0.430

Note: BP — systolic blood pressure; BMI — body mass index; WC — waist circumference; LDL cholesterol — low-density lipoprotein cholesterol; DBP — diastolic blood pressure; PP — pulse pressure; AIxao@HR 75 bts/min — augmentation index in aorta, all indicators are standardized against heart rate of 75 beats per minute; PWVao — pulse wave velocity in aorta; * — statistically significant differences between the groups.

The comparison of patient subgroups that were formed according to OH or hypertension diagnosed in patients (Table 5) showed that, in patients with the greater SBP decrease the initial values of peripheral SBP and PP were notably higher but the central SBP levels did not differ. This can be an evidence of possible association of the degree of SBP decrease with its amplification. However, no differences in the groups were found in other indirect (augmentation index) or direct (PWV) parameters of arterial stiffness.

Thus, no correlation of the orthostatic BP response with the clinical parameters or arterial stiffness characteristics was found.

Discussion

In the present study phenomena associated with clinical BP measurement: OH, orthostatic hypertension and SBP arm-to-arm differences were studied in very old patients.

SBP arm-to-arm differences of more than 10 mm Hg may be an evidence of supraaortic artery lesions. Initially ultrasound study was carried out to exclude this factor.

The proportion of the patients with Δ SBP ≥ 10 mm Hg constituted 25.4 %. The increase in SBP arm-to-arm difference was associated both with direct (PWV) and indirect (reflected pulse wave transmission time, augmentation index, PP) signs of arterial rigidity. In patients with differences between the arms > 10 %, higher parameters of general and abdominal obesity (BMI and WC) were found.

SBP differences between the arms ≥ 10 mm Hg are considered to be a specific (although not sensitive enough) sign of supraaortic artery stenosis and is independently associated with the development of coronary heart disease in the future, increase of stroke risk and cardiovascular mortality [2, 9, 10, 11]. Researchers from the Baltimore Longitudinal Study of Aging assumed that the associations of the marked differences in BP level between the arms with the cardiovascular risk were partially due to arterial stiffness and, indeed, they proved the association of the SBP arm-to-arm difference with the carotid-femoral PWV [12]. A number of studies demonstrated independent correlation of the arm-to-arm differences in BP level of more than 10 mm Hg with the age, BMI, dyslipidemia, ankle-brachial index, and HTN [12–14].

Our results are consistent with the findings of the Baltimore Longitudinal Study of Aging (n = 1045, average age — 66 ± 13 years old), which showed that in patients with considerable SBP arm-to-arm difference (> 10%) carotid-femoral PWV increased notably: 8.2 ± 2 versus 7.3 ± 1.3 m/s, $p < 0.01$ (like in our study, in which the difference in average PWV in the groups was 0.9 m/s), and BMI and WC were relevantly higher in the group with great SBP differences (31 ± 6 versus 27 ± 4 kg/m2, $p < 0.0001$ and 100 ± 14 versus 91 ± 12 cm, $p < 0.0001$, respectively) [12]. Some authors assume that extreme BP differences between the arms may not only evidence the arterial stenosis but also reflect endothelial dysfunction and significant arterial rigidity leading to the failure of functional compensation of normal differences in anatomical organization of the right and left subclavian arteries [12, 15].

OH is associated with increased risk of cerebrovascular disease, myocardial infarction and increase in total mortality [7]. In elderly patients OH contributes to the total mortality and is of particular importance as a prognostic factor, since many risk factors applicable to the total population lose their predictive value in very old patients [16]. Many factors are involved in OH development, such as the decreased baroreflex sensitivity, autonomic nervous system impairment, arterial rigidity and others [3].

Less attention is paid to the phenomenon of orthostatic hypertension compared to OH, although recent data showed that this type of orthostatic response is also associated with unfavourable prognosis and 2.5-fold increase in risk of ischemic stroke. Orthostatic hypertension in elderly persons is associated with the increased incidence of silent strokes and left ventricular hypertrophy [8]. In elderly patients orthostatic hypertension is associated with albuminuria independent of BP level in the sitting position; moreover, treatment with doxazosin caused the decrease of albuminuria and orthostatic hypertension while the average daily BP registered in the sitting position remained unchanged [17]. Correlations of orthostatic hypertension with such cardiovascular risk factors as age, HTN, diabetes mellitus, and dyslipidemia were found [8]. There are findings evidencing that orthostatic hypertension can be considered as a prehypertension marker and predictor of future HTN development (relative risk is 2.17–4.74 depending on the gender and race) as well as a marker of latent hypertension. Due to the latter, orthostatic hypertension is of particular importance. The involvement of arterial stiffness in the pathogenesis of this condition in elderly patients is evidenced by the fact that in young patients during tilt-test the increase of DBP and heart rate is registered, whereas in elderly patients SBP increases more often. The correlation of orthostatic BP response with the types of biphasic rhythm was stated: in "over-dippers" orthostatic hypertension is much more common, whereas in "night-peakers" the OH prevails. There is an evident U-shaped association between cardiovascular risk and the type of orthostatic response [8]. Several studies confirmed the correlation of orthostatic response intensity with the BP level, and it should be possibly considered in the context of antihypertensive treatment optimization [3].

The prevalence of asymptomatic OH in our study was 22.4%, of hypertension — 11.9%. The prevalence of the first phenomenon did not differ from the results of the previous findings (from 8.9 to 30% according to various data). Our findings show that asymptomatic OH in very old patients is associated with higher SBP and PP in the brachial artery. Interpretation of higher SBP amplification in patients with higher initial SBP in case of no differences in arterial stiffness is problematic. The exclusion of the drug-induced factor seems to be possible, since all patients received beta-blockers — drugs with the largest modifying effect on SBP amplification [18].

No relevant clinical associations were found for orthostatic hypertension.

Conclusions

Thus, the value of BP differences between the arms and the type of orthostatic response may potentially be of great clinical importance in elderly persons. Pathophysiology of these conditions, their real contribution to the disease development, and reference values have not been definitely determined yet, so further research is required.

Conflict of interest

The authors declare no conflict of interest.

Список литературы / References

1. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2013;34(28):2159–2219.

2. Clark CE, Taylor RS, Shore AC, Ukoumunne OC, Campbell JL. Association of a difference in systolic blood pressure between arms with vascular disease and mortality: a systematic review and meta-analysis. Lancet. 2012;379(9819):905–914.

3. Bouhanick B, Meliani S, Doucet J, Bauduceau B, Verny C, Chamontin B et al. Gerodiab Study group. Orthostatic hypotension is associated with more severe hypertension in elderly autonomous diabetic patients from the French Gerodiab study at inclusion. Ann Cardiol Angeiol (Paris). 2014;63(3):176–182.

4. Finucane C, O'Connell MD, Fan CW, Savva GM, Soraghan CJ, Nolan H et al. Age-related normative changes in phasic orthostatic blood pressure in a large population study: findings from the Irish Longitudinal Study on Ageing (TILDA). Circulation. 2014;130(20):1780–1789.

5. Fedorowski A, Stavenow L, Hedblad B, Berglund G, Nilsson PM, Melander O. Orthostatic hypotension predicts all-cause mortality and coronary events in middle-aged individuals (The Malmo Preventive Project). Eur Heart J. 2010;31(1):85–91.

6. Fagard RH, De Cort P. Orthostatic hypotension is a more robust predictor of cardiovascular events than night-time reverse dipping in elderly. Hypertension. 2010;56(1):56–61.

7. Verwoert GC, Matace-Raso FU, Hofman A, Heeringa J, Stricker BH, Breteler MM et al. Orthostatic hypotension and risk of cardiovascular disease in elderly people: the Rotterdam study. J Am Geriatr Soc. 2008;56(10):1816–1820.

8. Kario K. Orthostatic hypertension — a new haemodynamic cardiovascular risk factor. Nat Rev Nephrol. 2013;9(12):726–738.

9. English JA, Carell ES, Guidera SA, Tripp HF. Angiographic prevalence and clinical predictors of left subclavian stenosis in patients undergoing diagnostic cardiac catheterization. Catheter Cardiovasc Interv. 2001;54(1):8–11.

10. Agarwal R, Bunaye Z, Bekele DM. Prognostic significance of between-arm blood pressure differences. Hypertension. 2008;51(3):657–662.

11. Verberk WJ, Kessels AG, Thien T. Blood pressure measurement method and inter-arm differences: a meta-analysis. Am J Hypertens. 2011;24(11):1201–1208.

12. Canepa M., Milaneschi Y, Ameri P, AlGhatrif M, Leoncini G, Spallarossa P et al. Relationship between inter-arm difference in systolic blood pressure and arterial stiffness in community-dwelling older adults. J Clin Hypertens (Greenwich). 2013;15(12):880–887.

13. Kimura A, Hashimoto J, Watabe D, Takahashi H, Ohkubo T, Kikuya M et al. Patient characteristics and factors associated with inter-arm difference of blood pressure measurements in a general population in Ohasama, Japan. J Hypertens. 2004;22(12):2277–83.

14. Khokhlov RA, Gaydashev AE, Akhmedzhanov NM. Predictors of atherosclerotic lesions of limb arteries according to cardioangiological screening of the adult population. Ratsional'naya Farmakoterapiya v Kardiologii = Rational Pharmacotherapy in Cardiology. 2015;11(5):470–476. In Russian.

15. Hu W, Li J, Su H, Wang J, Xu J, Liu Y et al. The inter-arm diastolic blood pressure difference induced by one arm ischemia: a new approach to assess vascular endothelia function. PLoS One. 2014;13(9): e84765.

16. Jacobs JM, Stessman J, Ein-Mor E, Byrsztun M. Hypertension and 5-year mortality among 85-years-olds: the Jerusalem Longitudinal Study. J Am Med Dir Assoc 2012;13(8):1–6.

17. Hoshide S, Parati G, Matsui Y, Shibazaki S, Eguchi K, Kario K. Orthostatic hypertension: home blood pressure monitoring for detection and assessment of treatment with doxazosin. Hypertens Res. 2012;35(1):100–106.

18. Avolio AP, Van Bortel LM, Boutouyrie P, Cockcroft JR, McEniery CM, Protogerou AD et al. Role of pulse pressure amplification in arterial hypertension: experts' opinion and review of the data. Hypertension. 2009;54(2):375–383.

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