UDC 616.12-008.331.1:616.13/.14-072.7]-055.1/.3-053
DOI: 10.15587/2519-4798.2024.306857

GENDER DIFFERENCES IN THE ELASTIC PROPERTIES OF THE ARTERIAL WALL IN PATIENTS WITH ARTERIAL HYPERTENSION DURING THE AGE-RELATED EVOLUTION

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Age-related changes in the elastic properties of the arterial wall in patients with arterial hypertension increase the risk of CV events. Additional CV risk factors in women lead to gender differences in vascular stiffness.
The aim: *to determine changes in the elastic properties of the arterial wall in patients with hypertension depending on gender, with considering of the age-related changes.*
Materials and methods: *258 patients with arterial hypertension stage II were examined: 132 women (55.56±7.69 years) and 126 men (51.75±8.42 years). By age, patients were divided into 5 subgroups (37–45, 45–49, 49–54, 54–58 and 58–69 years). The following were assessed: pulse wave velocity in the aorta (PWVao), central systolic blood pressure in the aorta (SBPao), central pulse blood pressure (cPBP), augmentation index in the aorta (Aix ao) and on the brachial artery (Aix br), PWV index (PWVind), amplification blood pressure (BPamp), pulse blood pressure index (C/B indPBP).*
Results: *In the absence of differences in peripheral hemodynamics in all groups, women aged 49-54 years had a magnification of the PWV by 2 m/s, and, in comparison with men, this difference was 1.65 m/s ($p<0.05$). Aix br and Aix ao were also superior to men in all groups, and in 49-54 years old, this difference was greatest and amounted to 39 % and 20 %, respectively. At this age, SBPao was also significantly raised in women, with a difference of 15 mmHg relative to men ($p=0.038$). In all age groups, women had negative values of the BPamp in contrast to men. In women, PWV correlated with the duration of hypertension ($r=0.21$; $p<0.05$), SBP ($r=0.40$), DBP ($r=0.35$), cPBP ($r=0.43$), in contrast to men, where PWVao was associated only with the heart rate ($r=0.30$).*
Conclusion: *In women with hypertension, changes in vascular wall stiffness occur earlier than in men with significant growth at 49–54 years. In women, the elastic properties of arteries are associated with the level of blood pressure and duration of the disease, and in men - with the level of the heart rate*
Keywords: *arterial hypertension, arterial wall stiffness, gender features, females, age*

How to cite:
Yehorov, K. (2024). Gender differences in the elastic properties of the arterial wall in patients with arterial hypertension during the age-related evolution. ScienceRise: Medical Science, 2 (59), 4–13. http://doi.org/10.15587/2519-4798.2024.306857

1. Introduction

The vascular wall is one of the first structures that reacts to any changes in the environment by contraction or dilation. The walls of arteries, especially vessels of the elastic type, carry out hemodynamic balance inside the body. Therefore, it is important to know the features of such a reaction and consider the degree of pathological changes in the management of patients with arterial hypertension (AH).

The level of blood pressure (BP) is determined by two main physiological processes – the volume of blood ejected by the left ventricle during systole into the vascular bed and the resistance exerted by the same vessels (peripheral resistance). A normal or optimal level of blood pressure is the result of such a natural balance produced by nature in the process of evolution. Moreover, changes in any component of this equation are a trigger of arterial hypertension, especially in the presence of such cardiovascular risk factors as gender and age.

The process of changes in the elastic properties of arteries is quite physiologically observed during the ageing of the body. A decrease in the number of elastic and an increase in rigid collagen fibers, especially in the medial layer, leads to a violation of the vascular regulation of blood pressure. These changes are more pronounced in large arteries but are also observed in the peripheral vascular bed [1, 2]. All of this is due to genetic predisposition and a number of other factors, such as nutritional characteristics, hypodynamism, smoking status, and concomitant diseases (diabetes, inflammatory diseases of the arteries), which lead to an increase in vascular stiffness [3, 4].

According to the results of recent studies, the increase in arterial stiffness associated with the development of hypertension leads to an increase in cardiovascu-

lar risk [5, 6] and is an early marker of organ damage caused by hypertension [7]. Analysis of the Framingham Heart Study showed that an increase in the stiffness of the arterial wall, as assessed by pulse wave velocity (PWV), was associated with a rise in blood pressure and the appearance of new cases of hypertension during the next 7 years of observation [8].

The process of age-related changes in arterial stiffness is non-linear and accelerates after the age of 60. The dissociation between the chronological and biological age of vessels is at the basis of the theory of early vascular ageing (EVA), which predicts the acceleration of the development of cardiovascular diseases with the increase in the stiffness of the arterial wall, both in men and in women [9]. When the stiffness of the arterial wall increases, blood flow accelerates and returns to the heart faster, which leads to increased afterload and inadequate blood supply to the myocardium. This contributes to the development of left ventricular hypertrophy, myocardial ischemia, and heart failure [10, 11]. Reduction or prevention of reduction in arterial wall elasticity is associated with significant cardiovascular protection in hypertensive patients, suggesting an additional goal of antihypertensive treatment [12].

Nevertheless, there are a sufficient number of factors that cause gender differences in the properties of the vascular wall. First, these are estrogenic hormones that can directly affect arterial distensibility [13], the level of which fluctuates significantly during pregnancy and menopause [14, 15]. There are also non-hormonal causes, including anthropometric characteristics, heart rate (HR), stroke volume, arterial compliance, and distensibility.

These and other studies convincingly prove the need for a thorough and in-depth study of the gender characteristics of the elastic-elastic properties of the arterial wall.

The aim: determination of changes in the elastic properties of the arterial wall in patients with arterial hypertension, depending on gender, considering age changes.

2. Materials and methods

The study was conducted at the clinical base of the Department of Internal Medicine 3 of the Dnipro State Medical University from 2014 to 2019.

The study included 322 patients with essential arterial hypertension II stage 1-3 degree of hypertension. The diagnosis of "hypertensive disease" was established in accordance with the recommendations of the Ukrainian Association of Cardiologists (Clinical Guidelines of 2017 [16] and Order of the Ministry of Health of Ukraine No. 384 of 05/24/2012 [17]) and the European Society of Cardiologists on the Treatment of Arterial Hypertension 2023 [18]. Verification of arterial hypertension was carried out based on the results of daily automatic blood pressure monitoring. None of the patients was taking regular antihypertensive therapy (AHT) and statins at the time of inclusion in the study.

The conduct of the study was approved by the Local Ethics Committee at the Dnipropetrovsk State Medical Academy of the Ministry of Health of Ukraine with a conclusion on compliance with the requirements of moral and ethical norms of bioethics (protocol No. 1 dated January 20, 2014). The work was carried out in accordance with the basic bioethical norms of the Helsinki Declaration of the World Medical Association on methodological principles of conducting scientific and medical research with amendments (2000, 2008) in accordance with the rules of ISN/GCP, the Council of Europe Convention on Human Rights and Biomedicine (1997), as well as the current legislation of Ukraine. Before the study, all patients received informed consent and, after careful reading, agreed in writing to participate in the study.

Patients with oncological pathology, diabetes, renal failure, other secondary forms of arterial hypertension and heart failure of III, IV functional class or in the stage of decompensation were excluded from the study. 3 days before the study, planned antihypertensive therapy (if any) was cancelled for patients with the recommendation to use short-acting drugs as needed.

All examined patients were divided into 2 groups based on gender (men and women). Each group was also divided by age into 5 subgroups. For women, it was 37–45 years, 45–49 years, 49–54 years, 54–58 years and 58–69 years. The selection of age categories was carried out according to the quartile principle proposed by Smulyan H. et al. [19], where age periods were reduced after removing from the analysis patients who were below the 10th and above the 90th percentiles for women with preserved reproductive function and menopausal separately. Thus, in the first and second age groups, there were only women of childbearing age (15 and 9 patients, respectively); in the fourth and fifth groups - women only in menopause (30 and 49 patients, respectively), and in the 3rd group there were women with both preserved and absent reproductive function (10 and 19 people, respectively).

In men, after excluding patients with age less than 10 and more than 90 percentiles, as well as selection of 50 percentiles, the division by age categories coincided with the female group.

Thus, according to the age classification, the analysis of the received data was carried out in 258 patients: 132 women, whose average age was 55.56±7.69 years and 126 men, with an average age of 51.75±8.42 years.

Office blood pressure measurements and analysis of elastic-elastic properties of the arterial wall were performed using an **Arteriograph** oscillometric device (Tensiomed, Hungary) using a cuff of the appropriate size according to the volume of the patient's arm. The study was conducted by a single operator from 9:00 a.m. to 10:00 a.m. according to the manufacturer's instructions in a quiet, temperature-controlled environment after a minimum 10-minute rest period. During the examination, the patient was not allowed to speak or move. Alcohol, caffeine, and smoking were prohibited 10 hours before the study [20]. Measurements were made of the speed of propagation of the pulse wave in the aorta (PWVao), central systolic blood pressure in the aorta (SBPao), central pulse blood pressure (cPBP), augmentation index in the aorta (Aix ao) and in the brachial artery (Aix br), as well as the humeral index (Hi). Additional indicators were evaluated: PWV index (PWV ind), which is the difference between the measured and "theoretical" pulse wave speed; SBPao ind. – the difference between the real

SBPao and the expected normal level for each specific patient; amplification BP (BPamp) – the difference between the pressure in the brachial artery and the aorta; pulse BP index (C/B indPBP), which is the ratio of central and peripheral PBP. Office BP values were assessed as systolic BP (SBP), diastolic (DBP), average BP (avBP) and pulse arterial pressure (PBP).

Statistical analysis. Results were expressed as mean ± standard deviation or median (25th and 75th percentiles) for quantitative variables and as a percentage (%) for categorical variables. Statistical analysis was performed in STATISTICA v 10.0 using the paired Student's t-test and the Mann-Whitney U-test for between-group comparisons on parametric and nonparametric variables, respectively.

The potential relationship between variables was assessed using the Pearson correlation coefficient. A value of $p<0.05$ was considered the threshold of statistical significance.

3. Results

In women in the general group, arterial hypertension developed at an older age and, accordingly, they sought medical help later than men, which is expressed in a significant difference in age by 4 years and the duration of the disease – by more than 2 years, which corresponds to global development statistics arterial hypertension. Corresponding gender differences in current smoking status were also observed in the examined patients. However, in the general group, women and men had the same indicators of obesity – they were comparable according to the body mass index (Table 1).

Indicators of peripheral hemodynamics also did not differ by gender in the general group. Systolic, diastolic, average and pulse BP, HR did not have a significant difference between the male and female groups, which allows us to talk only about the differences in the properties of the vascular wall, which are related to gender characteristics (Table 1).

Table 1

Demographic data, indicators of peripheral hemodynamics and elasticity of arteries in the general group (M±m)

Indicator	Women	Men	p
Age	55.56±7.69	51.75±8.42	0.002
BMI	29.98±5.67	30.29±5.53	0.658
AH duration (years)	8.32±6.95	6.09±5.54	0.005
Smoking	13.64 %	38.1 %	<0.05
SBP (mmHg)	143.14±20.98	142.51±19.01	0.799
DBP (mmHg)	87.27±12.35	89.40±11.94	0.162
AvBP (mmHg)	105.89±14.62	106.87±13.64	0.576
PBP (mmHg)	55.94±12.48	53.43±13.17	0.117
Aix brachial: (%)	10.20±2.41	-19.60±2.70	<0.001
Aix in aorta: (%)	42.80±1.22	27.72±1.36	<0.001
PWVao (m/s)	10.42±2.06	9.45±1.71	<0.001
PWV ind (m/s)	1.33±0.17	0.64±0.16	0.003
SBPao (mmHg)	146.42±23.99	138.37±22.48	0.006
SBPao ind	13.82±0.82	6.72±1.04	<0.001
BPamp	–3.28±0.54	4.14±0.77	<0.001
cPBP	59.15±14.94	48.97±14.06	<0.001
C/B indPBP	105.59±11.18	92.08±15.51	<0.001
HR (1/min)	66.87±9.92	66.12±10.42	0.553
Hi (%)	1.24±0.14	1.25±0.12	0.787

Note: p – the reliability of the difference between women and men

A comparative analysis of gender characteristics of indicators of the elastic-elastic properties of the arterial wall in general in the examined patients showed that the augmentation index in the brachial artery and aorta was significantly higher in women than in men, Δ was 29.4 for Aix br and 15.08 for Aix ao. The pulse wave propagation speed in women was also significantly (Δ=0.97 m/s) higher than that in men. In addition, the PWV index in women exceeded the similar indicator in men by 0.69 m/s.

Central hemodynamic parameters also had significant gender differences. Thus, the central SBP was 8.05 mm Hg. higher in women than in men, the SBPao index in women was also significantly higher than the examined men (Δ=7.06 mmHg, $p<0.001$). In addition, the amplification BP in the female group was much lower than in the male group and acquired negative values. Central pulse blood pressure in examined women was also reliably and significantly higher than in men by 10.18 mm Hg.

The examined patients in each age subgroup (men and women) did not differ by age criteria, had approximately the same duration of the disease and excessive body weight bordering on obesity of the 1st degree. The exception is the "youngest" subgroup, where men had a significantly higher body weight. Current smoking status in each subgroup also corresponds to the overall indicator (Table 2).

In the examined patients, peripheral blood pressure (SBP, DBP, AvBP) increased with age in both men and women, reaching a maximum in the average age group of 49–54 years, then maintaining this level (Table 3). Moreover, no significant difference in the parameters of peripheral hemodynamics (including HR) was found between men and women in all age subgroups. Pulse blood pressure measured on the brachial

artery is one of the easiest to determine and, at the same time, prognostically significant indicators of arterial stiffness. In the examined patients, no significant gender differences in PBP were found in all age subgroups, although in the 3rd and 4th groups, women's pulse BP was still higher by 5 and 6 mmHg, respectively. It should be noted that the tendency to increase PBP was noted in all patients, regardless of gender, at the age of 49–54 years, with the preservation of this level in the future.

Table 2

Clinical characteristics of the examined patients (Me (25 %; 75 %)) when distributed by age groups

Indicator	Group 1 (37–45 years)		Group 2 (45–49 years)		Group 3 (49–54 years)		Group 4 (54–58 years)		Group 5 (58–69 years)	
	M (n=34)	W (n=15)	M (n=24)	W (n=9)	M (n=20)	W (n=29)	M (n=18)	W (n=30)	M (n=30)	W (n=49)
Age (years)	42.39 (40.00; 43.42)	42.41 (38.47; 43.58)	46.95 (46.05; 48.03)	47.41 (47.02; 48.43)	52.03 (50.85; 53.57)	51.63 (50.06; 52.56)	56.18 (55.08; 57.01)	56.34 (55.34; 56.69)	63.49 (62.16; 65.61)	62.80 (60.91; 65.96)
	p=0.575		p=0.343		p=0.194		p=0.848		p=0.616	
Duration (ages)	3.00 (1.00; 6.00)	4.00 (1.00; 5.00)	2.50 (1.00; 9.00)	4.00 (1.00; 10.00)	5.00 (2.00; 10.00)	5.00 (3.00; 10.00)	5.00 (1.00; 9.00)	6.00 (3.00; 11.00)	9.00 (5.00; 15.00)	10.00 (7.00; 17.00)
	p=0.583		p=0.653		p=0.898		p=0.269		p=0.157	
BMI (kg/m^2)	29.32 (27.75; 31.70)	26.18 (20.82; 31.89)	30.25 (27.45; 33.67)	28.63 (25.86; 29.76)	29.03 (27.27; 30.34)	30.48 (26.06; 35.32)	30.39 (25.17; 31.14)	29.72 (27.24; 33.46)	29.70 (26.47; 33.59)	29.43 (27.05; 34.29)
	p=0.010		p=0.145		p=0.118		p=0.355		p=0.539	
Smoking (%)	50.0	11.11	50.0	22.22	30.0	17.24	38.89	10.0	20.0	8.16

Note: p – the reliability of differences between women and men

Table 3

Indicators of peripheral hemodynamics (Me (25 %; 75 %)) when distributed by age groups

Indicator	Group 1 (37–45 years)		Group 2 (45–49 years)		Group 3 (49–54 years)		Group 4 (54–58 years)		Group 5 (58–69 years)	
	M (n=34)	W (n=15)	M (n=24)	W (n=9)	M (n=20)	W (n=29)	M (n=18)	W (n=30)	M (n=30)	W (n=49)
SBP (mmHg)	141 (125; 150)	133 (124; 143)	134 (127; 147)	127 (125; 139)	141 (126.5; 159.5)	146 (131; 163)	144 (126; 148)	138 (129; 156)	141,5 (133; 158)	139 (130; 153)
	p=0.409		p=0.392		p=0.404		p=0.757		p=0.396	
DBP (mmHg)	86.50 (81.00; 93.00)	82 (78; 87)	85.50 (82.00; 93.50)	82.00 (80.00; 88.00)	90.00 (81.00; 100.50)	91 (82; 104)	92 (83; 99)	88 (77; 99)	85,50 (81,00; 96,00)	86 (78; 93)
	p=0.312		p=0.222		p=0.911		p=0.291		p=0.413	
AvBP (mmHg)	103.50 (97.00; 111.00)	99 (93; 106)	102.00 (97.50; 109.00)	97.00 (96.00; 105.00)	109.00 (96.50; 118.00)	109,00 (98,00; 123,00)	108,00 (99,00; 117,00)	106,00 (91,00; 114,00)	104,50 (99,00; 115,00)	105,00 (96,00; 114,00)
	p=0.415		p=0.254		p=0.684		p=0.631		p=0.433	
PBP (mmHg)	52.00 (44.00; 60.00)	50 (46; 56)	48.00 (41.00; 53.00)	49.00 (47.00; 51.00)	51.50 (44.00; 57.00)	56,00 (49,00; 69,00)	48 (42; 54)	54 (46; 63)	55,50 (50,00; 64,00)	56 (49; 63)
	p=0.922		p=0.706		p=0.089		p=0.061		p=0.678	
HR (1/min)	66.50 (61.00; 75.00)	69 (63; 75)	63.50 (58.50; 71.50)	61.00 (56.00; 68.00)	68.00 (62.50; 73.00)	65,00 (61,00; 70,00)	62 (57; 65)	68,00 (60; 75)	67,00 (60,00; 74,00)	66 (60; 74)
	p=0.367		p=0.512		p=0.387		p=0.084		p=0.686	

Note: p – the reliability of differences between women and men

Considering the properties of the pulse wave (Table 4), it was found that the Aix augmentation index in both the brachial artery and the aorta was the highest in the oldest age group among both sexes. But this indicator was statistically significantly different by gender in all age categories, and at the age of 49–54, this difference was the largest and amounted to 39 % for the brachial and 20 % for the aortic augmentation index.

Table 4

Indicators of spring-elastic properties of the vascular wall depending on age (Me (25 %; 75 %))

Indicator	Group 1 (37–45 years)		Group 2 (45–49 years)		Group 3 (49–54 years)		Group 4 (54–58 years)		Group 5 (58–69 years)	
	M (n=34)	W (n=15)	M (n=24)	W (n=9)	M (n=20)	W (n=29)	M (n=18)	W (n=30)	M (n=30)	W (n=49)
Aix br: (%)	-37.05 (-54.70; 13.40)	-6.30 (-43.20; 26.40)	-17.60 (-39.30; 1.50)	12.50 (-19.90; 36.30)	-26.30 (-39.00; -10.10)	13,70 (-0,70; 37,20)	-24,45 (-34,30; 12,70)	3,90 (-7,70; 22,90)	-8,70 (-28,70; 9,70)	20,60 (-2,50; 34,70)
	p=0.033		p=0.036		p=0.001		p=0.049		p=0.001	
Aix ao: (%)	18.90 (10.00; 30.90)	34.50 (18.50; 46.10)	28.70 (17.75; 38.40)	44.00 (27.60; 56.00)	24.35 (17.85; 32.55)	44,60 (37,30; 56,50)	25,25 (20,30; 44,10)	39,65 (33,70; 49,20)	33,25 (23,10; 42,60)	48,00 (36,40; 55,20)
	p=0.027		p=0.036		p=0.001		p=0.049		p=0.001	
PWVao (m/s)	8.30 (7.50; 9.50)	9.00 (7.60; 10.10)	9.30 (7.80; 10.90)	8.50 (7.80; 10.80)	8.55 (8.30; 9.60)	10,20 (8,80; 12,10)	9,90 (7,90; 10,70)	10,25 (8,80; 11,30)	10,80 (1,20; 11,40)	10,70 (9,70; 12,30)
	p=0.241		p=0.706		p=0.015		p=0.212		p=0.393	
PWV ind	0.50 (-0.50; 1.90)	1.30 (0.90; 1.90)	1.10 (0.40; 2.35)	1.10 (0.20; 2.70)	0.20 (-0.75; 1.15)	1,70 (-0,10; 2,90)	0,85 (-0,30; 1,40)	1,35 (0,10; 2,50)	0,15 (-1,50; 1,20)	0,50 (-0,80; 2,30)
	p=0.101		p=1.000		p=0.006		p=0.072		p=0.091	
BPamp (mmHg)	10.00 (1.80; 13.00)	-0.90 (-7.00; 9.10)	2.95 (-3.00; 9.10)	-6.00 (-6.90; 4.40)	7.00 (0.50; 8.50)	-7,00 (-8,00; -2,60)	4,05 (-6,80; 10,00)	-5,20 (-7,70; -0,30)	0,00 (-7,00; 7,00)	-6,70 (-7,40; -3,00)
	p=0.013		p=0.036		p=0.001		p=0.020		p=0.019	
Hi (%)	1.25 (1.20; 1.33)	1.20 (1.10; 1.33)	1.25 (1.19; 1.30)	1.27 (1.20; 1.28)	1.24 (1.10; 1.32)	1,20 (1,10; 1,31)	1,29 (1,20; 1,40)	1,27 (1,20; 1,36)	1,20 (1,10; 1,30)	1,23 (1,17; 1,32)
	p=0.535		p=0.706		p=0.407		p=0.484		p=0.127	
SBPao (mmHg)	130.50 (119.40; 142.00)	125.00 (120.50; 150.00)	129.00 (123.40; 141.40)	133.30 (130.90; 144.90)	136.00 (119.30; 150.50)	151,00 (134,00; 171,00)	136,00 (121,00; 149,00)	141,85 (126,80; 161,70)	141,00 (130,00; 152,60)	145,90 (132,00; 159,60)
	p=0.712		p=0.512		p=0.038		p=0.229		p=0.582	
SBPao ind (mmHg)	2.65 (-2.00; 8.00)	8.90 (-0.10; 11.80)	5.30 (-0.40; 13.50)	15.00 (7.00; 17.30)	3.00 (-2.70; 11.00)	16,00 (11,00; 19,00)	6,00 (0,00; 8,00)	13,20 (9,30; 20,90)	12,00 (4,00; 19,60)	15,00 (10,80; 18,00)
	p=0.362		p=0.026		p=0.001		p=0.001		p=0.284	
cPBP (mmHg)	43.50 (36.80; 51.20)	44.00 (40.50; 62.00)	43.60 (39.40; 49.80)	52.00 (48.00; 56.30)	44.00 (36.00; 57.50)	60,00 (54,00; 70,00)	43,50 (38,00; 53,00)	55,00 (49,40; 65,00)	55,00 (49,00; 64,70)	59,00 (50,70; 70,00)
	p=0.228		p=0.029		p=0.001		p=0.002		p=0.208	
C/B indPBP (%)	82.27 (73.40; 96.60)	99.70 (81.80; 111.76)	93.54 (81.66; 107.32)	112.32 (91.23; 113.53)	88.64 (80.91; 98.98)	111,76 (105,58; 113,39)	89,45 (83,67; 114,36)	109,72 (100,56; 113,79)	100,00 (86,15; 111,54)	111,69 (105,26; 113,40)
	p=0.045		p=0.036		p=0.001		p=0.075		p=0.005	

Note: p – the reliability of the difference between women and men

It should be noted that in women already at the age of 37–45 years (I group), the pulse wave propagation speed was somewhat higher than in men (Fig. 1, a). And during the period of hormonal adjustment (49–54 years), a sharp rise in PWV by 2 m/s was observed, and in comparison, with men, this difference was 1.65 m/s ($p<0.05$). With increasing age, this difference decreased and by the age of 70, it practically disappeared. Also, women had a higher level of PWV index than men aged 37–45 years, but a reliable and significant difference was observed only in the middle age group (49–54 years). In older age groups, these differences decreased.

In men and women of the first and second age groups, the central systolic BP (Fig. 1, b) had no reliably significant differences, and with age, the level of SBPao increased in both men and women. However, it is noteworthy that in women aged 49-54, a sharp rise in SBPao was noted, and compared to men, this difference acquired reliable and significant values. The trend towards a higher level of SBPao in the female group than in the male group continued.

The difference between the actual central SBP and the predicted calculated SBPao – the SBPao index in women in all age groups of the examined patients exceeded that in the male part of the patients. Moreover, this index was the largest at the age of 49–54.

Amplified BP in women already in the 1st group had negative values and was significantly different from the male group, where central SBP was lower than peripheral (Fig. 1, c). With age, BPamp gradually decreased in men and was close to zero in the oldest age group. In women, there was a decrease in BPamp with the achievement of minimum values at the age of 49-54 and further preservation of this level. A statistically significant gender difference, according to this indicator, was observed in all age categories.

The central pulse pressure (Fig. 1, d) also increased with age, but in men, this increase was gradual and reached a maximum in the older age group (58-69 years). In women, a significant increase in cPBP was noted as early as 45-49 years, with a sharp rise in the middle age group and further maintenance of this level in the future.

In the 3rd and 4th groups, the difference in this indicator between men and women was significant and statistically significant.

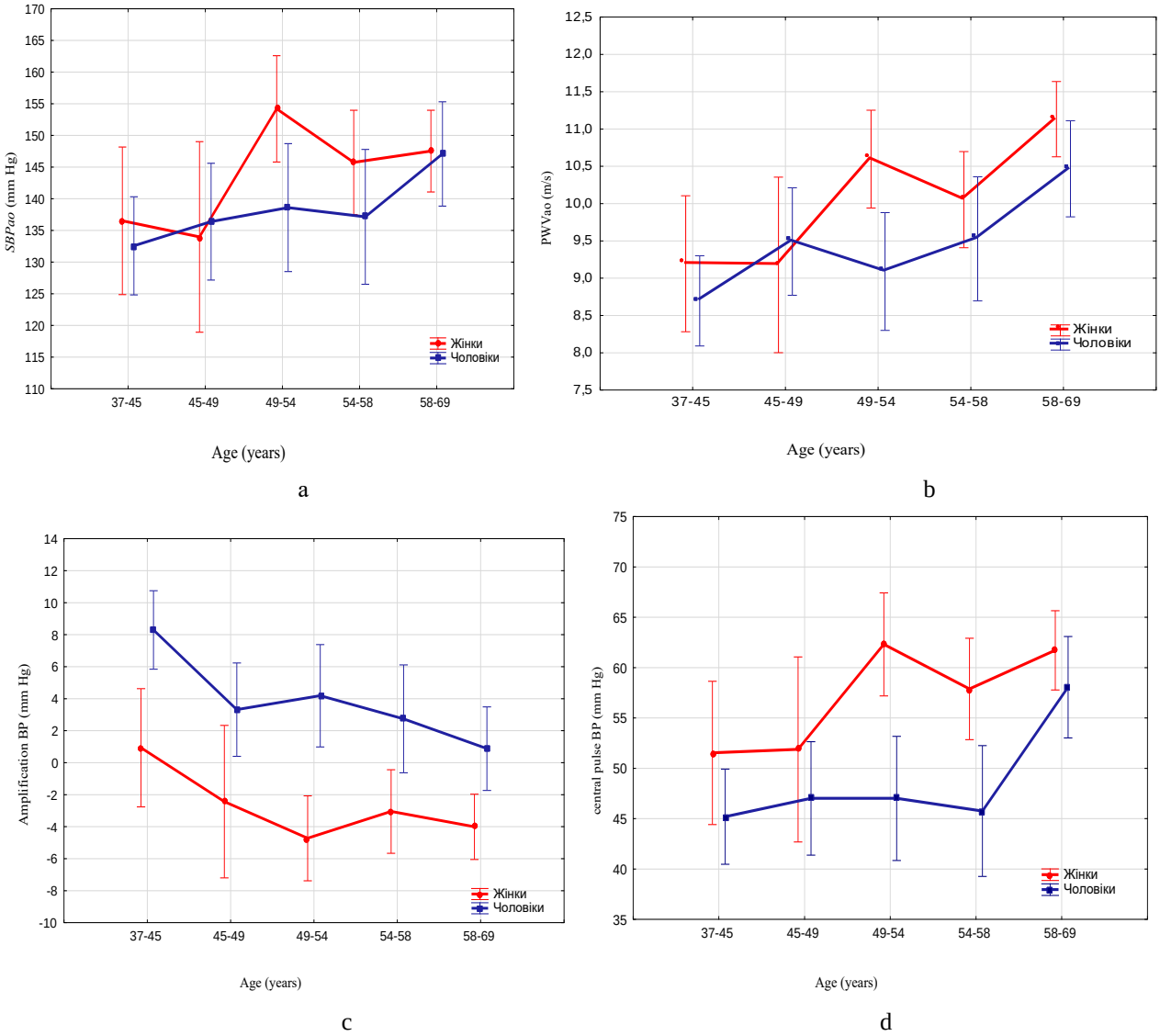

Fig. 1. Progression of changes in vascular wall properties depending on age and gender: *a* – age-related evolution of central systolic BP; *b* – pulse wave propagation speed in the aorta; *c* – amplification BP; *d* – central pulse BP. Vertical lines are 0.95 CI

Correlation analysis revealed that arterial wall stiffness and central pressure were associated with age, and this association was more pronounced in men. Thus, the correlation index (r) in men was 0.36 for PWVao and 0.25 for SBPao ($p<0.05$), and in women r was equal to 0.31 and 0.14 for the corresponding indicators. The duration of the disease also led to deterioration of the elastic properties of arteries in both groups, but the speed of pulse wave propagation and SBPao mainly depended on the history of hypertension in women (r=0.21 for PWVao; r=0.27 for SBPao ($p<0.05$)). Although the difference with the male group was not statistically significant, in men the correlation with the history of hypertension was lower and was 0.16 for PWVao and 0.21 for SBPao. Body weight was not associated with the studied parameters in either men or women.

The speed of propagation of the pulse wave directly and significantly depended on the level of peripheral BP in women, while in men, this relationship was weak and significantly different from the female group. Thus, Δr SBP was 0.25 (p=0.036); by DBP – Δr=0.23 (p=0.066); AvBP – Δr=0.24 (p=0.038); PBP – Δr=0.25 (p=0.042). The association of PWVao with central PBP was also more pronounced in women than in men (Δr=0.34; p=0.036).

In men, in contrast to women, a direct correlation dependence of PWVao on HR was found (Fig. 2).

The augmentation index in the aorta and brachial artery was directly correlated with the level of peripheral blood pressure without pronounced gender differences, except for PBP, where women had a more pronounced association compared to men (r=0.25; p=0.04).

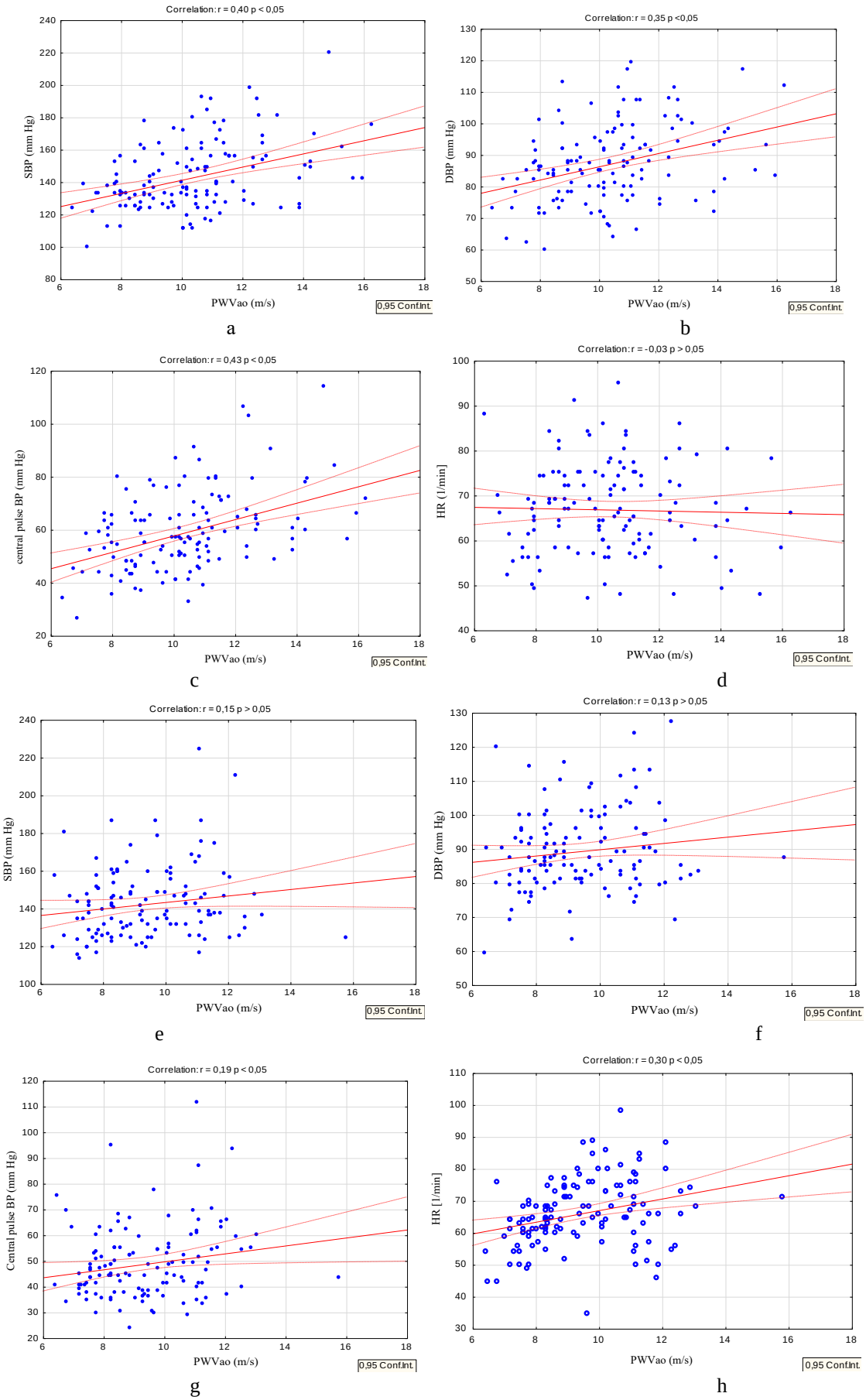

Fig. 2. Correlations of the speed of pulse wave propagation in the aorta with parameters of peripheral hemodynamics in women: *a* – with systolic blood pressure; *b* – with diastolic blood pressure; *c* – central pulse blood pressure; *d* – with HR; in men: *e* – with systolic blood pressure; *f* – with diastolic blood pressure; *g* – central pulse blood pressure; *h* – with HR

4. Discussion of research results

Research in recent years shows that the state of stiffness of the arterial wall significantly increases the risk of cardiovascular events, especially in patients with hypertension [21, 22].

In healthy women, menopause worsens the age-related increase in stiffness of the arterial wall [23]. Other studies have also confirmed that early menopause and estrogen deficiency negatively affect the elastic properties of arteries [24]. In this regard, we studied changes in the pulse wave propagation speed, augmentation indices, central hemodynamics indicators and other calculated indicators of vascular wall properties. For this purpose, we divided the examined patients by gender and age categories. By age, groups of women with preserved reproductive function, postmenopause, climacteric period were selected, and correspondingly similar age periods were used for men. This allocation of age periods is expedient in connection with the influence of hormonal changes on many functions of the body, including vascular regulation, not only in women but also in men.

To date, carotid-femoral PWV is the gold standard for the analysis of arterial stiffness, and a velocity greater than 10 mm/s is an indicator of increased arterial wall stiffness in patients with essential hypertension [25]. Assessment of pulse wave velocity is effective not only in specific clinical situations but can also be effectively used to predict cardiovascular risk [26]. According to the NHANES study, which included more than 14,000 participants, elevated PWV was positively correlated with all-cause and most-cause mortality, independent of traditional risk factors. Moreover, PWV demonstrates high accuracy in predicting all-cause mortality over 5 and 10 years, surpassing the Framingham Risk Score [27]. In the same Framingham study, among 7898 participants, elevated PWV was the most common feature of ODMH [28].

To estimate individual values of PWV, considering age, gender, and blood pressure level, standardized ranks proposed in 2010 based on a study of more than 16,000 people in the European population are used [29]. The difference between the measured PWV and the "theoretical" is called the PWV index. In a study of patients with renal failure, this index proved to be a strong predictor of cardiovascular and total mortality. Moreover, in patients with a positive index, in comparison with patients who had a negative value, a two-fold increase in mortality was observed [30].

In our study, a gradual increase in pulse wave speed was noted in men and women aged 33 to 49 years. But at the age of 49–54 years, a sharp increase in PWV was noted in the female group, in contrast to men. In the next age group, men "caught up" with women, and by the age of 70 this difference levelled off. Such dynamics of PWV are confirmed by the data of other studies [31]. The PWV index in women also significantly exceeded that in male patients, especially increasing in the middle-aged subgroup, that is, in the period of menopause.

The importance of analyzing the properties of the central pulse wave was shown in the CAFE study [32]. Central augmentation index (Aix ao) and central pulse BP (cPBP) were independent predictors of all-cause mortality in patients with essential AH, severe renal impairment, and cardiovascular events in patients after coronary interventions. In addition, it was shown that central systolic BP (SBP ao) and central PBP depend not only on the stiffness of the aorta but also on the geometry and vascular tone of small arteries. Therefore, the analysis of hemodynamics should be performed both at the peripheral and at the central level, which reflects the real load experienced by the left ventricle and the walls of the central large arteries [33]. In addition, a meta-analysis showed that parameters of central hemodynamics are predictors of future cardiovascular events and total mortality [34].

In the examined patients, SBP in the aorta and central pulse BP increased with age, which is a natural process of the age-related evolution of the vascular wall. However, in women, there was a sharp increase in the level of central systolic BP in the middle age group with a significant difference from the male group. SBPao index and central pulse BP were also significantly higher in women, but already in a wider age range (from 45 to 58 years). Indices of augmentation in the aorta and brachial artery in women also significantly exceeded the corresponding indicators of the male group in all age categories. Other studies (Costa-Hong VA et al., 2018) also showed a significant superiority of augmentation indices, central SBP and PBP in women over men [35]. In the Framingham study, based on the study of central hemodynamics, it was also concluded that the aortic wall was stiffer in women [36]. In addition, in our study, amplification BP and the ratio of central and brachial PBP in women differed significantly from men regardless of age, which indicates more pronounced violations of the physiological regulation of BP in women in connection with arterial hypertension. The results of research by other authors also indicate that the increase in stiffness of the arterial wall in women begins at an earlier age than in men, reaching the peak of growth up to 54 years [37]. Attention is drawn to the fact that such pronounced differences in the characteristics of elastic-elastic properties of the arterial wall and indicators of central hemodynamics were observed with a minimal difference in peripheral blood pressure indicators between the sexes.

When analyzing the influence of individual factors on the stiffness of the vascular wall in hypertension, certain gender differences were also revealed. With age, the elastic-elastic properties of the vascular wall deteriorated in both groups, which is consistent with physiological age evolution, but this dependence was stronger in men. In women, it was the duration of increased hemodynamic pressure on the arterial wall that led to an increase in arterial stiffness. Also, the elasticity of the vascular wall in both groups did not depend on obesity, especially in the first three age groups, which is consistent with the data of other authors [38]. In women, there was a pronounced correlation dependence of the marker of vascular stiffness – PWV on the level of peripheral BP, especially central pulse pressure, in contrast to men, where pulse wave speed was associated with heart rate.

Study limitations. This study has several limitations. First, the study evaluated only the level of office blood pressure, although daily BP monitoring allows a more thorough and qualitative diagnosis of AH and not only that. Second, we did not evaluate the dynamics of

changes in arterial stiffness under the influence of various antihypertensive drugs during long-term follow-up. Finally, the study included patients who live only in the industrial centre – the city of Dnipro. A harmful environment can also have an additional negative effect on the elasticity of the arterial wall.

Prospects for further studies. Therefore, it is advisable to further study the relationship between the properties of the vascular wall and the data of automatic daily monitoring of AH (circadian rhythm, variability of AH, etc.) and other cardiovascular risk factors. There is controversy in the literature regarding the effect of different classes of antihypertensive drugs on the regression of arterial stiffness, which is a promising further study, especially taking into account gender differences and age.

5. Conclusions

In patients with arterial hypertension, one of the early subclinical signs of organ damage is increased stiffness of the arterial wall, which is a risk factor for cardiovascular complications. However, changes in the elastic properties of arteries have gender differences associated with age-related changes, especially in conditions of increased hemodynamic load in hypertension.

1. In women, the change in the elastic-elastic properties of the vascular wall occurs earlier than in men and is characterized by a significant increase in all stiffness indicators at the age of 49–54, when PWVao increased by 2 m/s relative to the previous age group and by 1.65 m/s compared to men, and the level of SBPao by 18 and 15 mm Hg, respectively. In men, the trend of increasing stiffness of blood vessels with age has a gentler appearance compared to women under 60 years of age.

2. In women, there is an earlier and, in comparison with men, a significant violation of the physiological ratio of central and brachial blood pressure in hypertension, which is reflected in the presence of a negative value of amplification BP for all age groups.

3. In women, arterial elastic properties are associated with blood pressure level and disease duration, where the correlation with SBP, DBP and central PAT for PWVao in women was 0.40; 0.35; 0.43, while in the male group r was equal to 0.15; 0.13 and 0.19, respectively. But in men, a significant level of correlation of PWVao with HR was observed (r=0.30 in contrast to women, where r=-0.03).

Conflict of interest

The author declares that he has no conflict of interest in relation to this research, including financial, personal, authorship or other nature, which could affect the research and its results presented in this article.

Funding

The study was conducted without financial support.

Data availability

Data will be provided upon reasonable request.

Use of artificial intelligence technologies

The authors confirm that they did not use artificial intelligence technologies when creating the presented work.

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Received date 02.04.2024
Accepted date 23.05.2024
Published date 31.05.2024

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