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Association of vascular stiffness and geriatric syndromes in hypertensive elderly patients

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Aim. To study the relationship of vascular stiffness (cardio-ankle vascular index (CAVI)) with frailty and other geriatric syndromes in hypertensive elderly patients.

Material and methods. The study included 160 patients aged 60 to 101 years with verified stage I-III hypertension. The previous therapy was assessed. A comprehensive geriatric assessment was performed with functional and neuropsychological tests to identify geriatric syndromes. Vascular stiffness was assessed by VaSera-VS-1500 vascular screening system (FUKUDA DENSHI, Japan) with determination of the CAVI.

Results. The mean age of the patients was 77,2±8,1 years (n=160): in the group of patients without frailty — 72,4±6,9 years (n=50), with prefrailty — 76,6±8,1 years (n=50), with frailty — 81,7±6,6 (n=60). Patients with frailty had a higher CAVI than those without frailty and with prefrailty (10,3±1,6 vs 9,3±1,0 and 9,6±1,8, respectively; p=0,002).

In patients with frailty, a negative correlation was found between the vascular stiffness and body mass index (BMI) (Rs=-0,392 (p=0,002)), and a positive correlation between the CAVI and orthostatic response (Rs=0,382 (p=0,003). In patients with prefrailty, negative relationships were found with the dynamometric parameters (Rs=-0,329 (p=0,019)), BMI (Rs=-0,343 (p=0,015) and physical activity (Rs=-0,285 (p=0,047)).

In patients without frailty, the vascular stiffness was associated with an increased total cholesterol level (Rs=0,379 (p=0,009)), a low physical activity (Rs=-0,355 (p=0,015)), as well as negative correlations were found with the clock-drawing test and falls (Rs=-0,458 (p=0,011) and Rs=-0,306 (p=0,031), respectively).

Conclusion. Vascular stiffness in elderly patients with frailty is associated with a decrease in body mass index and orthostatic hypotension. At the stage of prefrailty, the relationship between the vascular stiffness and muscle strength decrease (according to dynamometry) was revealed.

Thus, the vascular stiffness is associated with frailty markers itself.

Relationships and Activities: none.

Keywords: frailty syndrome, vascular stiffness, cardio-ankle vascular index, elderly patients.

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Vascular stiffness parameters are a cardiovascular risk marker, which reflects the relationship with high morbidity and mortality. Due to the low number of studies on elderly patients, this relationship is less reflected in this group, as well as the relationship with geriatric syndromes.

Cardiovascular diseases (CVD) remain the leading cause of death in developed countries, and therefore necessitate novel investigations in clinical practice in high-risk patients. Slowing the vascular stiffening is a way to prevent CVD and heart failure [1].

Measuring the vascular stiffness in routine practice is important for assessing the atherosclerosis progression. So far, many parameters have been proposed for quantifying arterial stiffness. Among them, there is pulse wave velocity (PWV), however, it depends on blood pressure (BP). Therefore, PWV is not suitable for assessing the vascular stiffness in studies with patients with BP changes [2].

The cardio-ankle vascular index (CAVI) was developed on the PWV basis by Japanese scientists to assess the degree of vascular stiffness. The CAVI calculation combines the stiffness and the Bramwell-Hill equation [3]. The most important feature of this method is its independence from BP during examinations. This is important for objective reflection of atherosclerosis severity in individuals with increased BP variability, with resistant hypertension (HTN), or while taking antihypertensive drugs [4].

It is believed that the prevalence of frailty increases with age and increases the risk of adverse outcomes in older people, including mortality, falls and hospital admissions [5].

Diagnosis and assessment of frailty severity is carried out during the implementation of a comprehensive geriatric assessment (CGA). However, is there a relationship between the severity of certain geriatric syndromes and the vascular stiffness?

The vascular stiffness is interrelated with frailty in elderly patients and it can be assumed that it is a risk factor (RF) for the atherosclerosis progression and atherosclerosis-related cardiovascular events [6].

Frailty and atherosclerotic changes have a common pathogenesis and have a mutual cause, but the relationship between them remains unclear. In clinical practice, we observed that the severity of atherosclerosis is more pronounced in the elderly with limited mobility and decreased functional and cognitive status. In this connection, we assume that frailty is associated with atherosclerosis.

The aim was to study the relationship of CAVI with frailty and other geriatric syndromes in hypertensive elderly patients.

Material and methods

The study was approved by the local ethics committee of the Russian Clinical and Research Center of Gerontology in 2017.

All participants signed informed consent prior to enrollment.

We examined 160 patients from 60 to 101 years old with verified stage I-III HTN. For preliminary screening, a short questionnaire was used to identify changes indicative of probable geriatric syndromes. The screening consists of 7 questions related to the following issues: weight loss; limitations in life due to decreased vision/hearing; fall-related injuries; mood swing; memory problems; urinary incontinence; movement disorders. The patients were divided into 3 groups in accordance with the current algorithm for frailty diagnosis [7].

Patients with prior myocardial infarction, stroke, lower limb artery stenosis and occlusions, pulmonary embolism, thromboarteritis, Raynaud's disease, angiitis, permanent atrial fibrillation, acute or exacerbated diseases, severe sensory (deafness and blindness) and cognitive impairments that impede the CGA were excluded.

All patients underwent CGA with determination of functional and cognitive status. The functional status was assessed according to the following parameters: walking speed [8], Timed Up and Go test [9]; Barthel index of activities of daily living [10], Lawton instrumental activities of daily living [11]. Cognitive status was assessed using a mini-mental state examination (MMSE) [12]. To assess the quality of life, a 'Health Status' visual analog scale (VAS) for self-assessment was used [13]. Nutritional assessment was carried out using the Mini Nutritional Assessment (MNA) score [14]. The level of physical activity was assessed for each sex separately [15]. The handgrip strength was determined using a medical dynamometer DMER-120 [16]. Anthropometric measurements included assessment of height, body weight, waist circumference and calculation of body mass index (BMI).

To assess orthostatic response, BP was measured in the supine position and 1, 2, and 3 minutes after the transition to the upright one. Orthostatic hypotension (OH) was diagnosed with a decrease in blood pressure by 20/10 mm Hg and more when moving to the upright position [17].

Evaluation of vascular stiffness by CAVI was carried out using VaSera-VS-1500 vascular screening system (FUKUDA DENSHI, Japan). Determination of CAVI was carried out by simultaneous BP measurement with cuffs placed on the arms and ankles, as well as electrocardiography and phonocardiography.

Statistical analysis. Results are presented as mean values (± standard deviation) or as values

Table 1

Characteristics of three patient groups: patients without frailty (n=50), with prefrailty (n=50), with frailty (n=60)

Parameter	Patients without frailty, n=50	Patients with prefrailty, n=50	Patients with frailty, n=60	p
Age, years	72,4±6,9	76,6±8,1	81,7±6,6	0,003
Women, n (%)	40 (80%)	45 (90%)	54 (90%)	0,221
Education level				0,150
Secondary, n (%)	2 (4%)	8 (16%)	9 (13,6%)	
Secondary vocational, n (%)	20 (40%)	24 (48%)	27 (45,8%)	
Higher, n (%)	28 (56%)	18 (36%)	24 (40,7%)	
Accommodation				<0,001
Alone, n (%)	23 (46,3%)	23 (46%)	32 (53,3%)	
With children, n (%)	5 (10%)	8 (16%)	22 (36,7%)	
With husband/wife, n (%)	22 (44%)	19 (38%)	6 (10%)	
Family status				
Married, n (%)	22 (44%)	21 (42,9%)	7 (11,9%)	
Widower/widow, n (%)	22 (44%)	23 (46,9%)	47 (79,7%)	
Divorced, n (%)	4 (12%)	6 (10,2%)	6 (8,4%)	

Table 2

Characteristics of anthropometric parameters of three patient groups

Anthropometric data	Patients without frailty, n=50	Patients with prefrailty, n=50	Patients with frailty, n=60	P
Height, m	1,59±7,9	1,57±8,5	1,57±7,9	0,535
Weight, kg	71,2±12,9	68,1±14,5	69,9±13,6	0,521
BMI, kg/m^2	28,2±4,6	27,4±5,0	28,7±6,4	0,816
Waist circumference, cm	92,4±13,8	93,3±13,7	94,8±19,3	0,728

Abbreviation: BMI — body mass index.

Table 3

Hemodynamic characteristics of patients in three groups

Parameter	Patients without frailty, n=50	Patients with prefrailty, n=50	Patients with frailty, n=60	P
SBP, mm Hg	142,6±22,6	147,9±22,1	142,6±22,4	0,380
DBP, mm Hg	85,9±10,6	81,6±11,5	81,3±12,9	0,084
Heart rate, bpm	70,5±8,9	70,7±8,6	72,5±10,8	0,500

Abbreviations: DBP — diastolic blood pressure, SBP — systolic blood pressure.

and percentages for qualitative traits. Quantitative variables were compared between groups using Kruskal-Wallis test. If significant differences were found, pairwise comparisons were made using Tukey's test and Dunnett's test. Qualitative variables between groups were compared using Fisher's exact test. If significant differences were found, the source was identified using Fisher's exact test with Holm correction for multiple comparisons. To identify the effect of frailty on CAVI, taking into account age, a general linear model was built with the group as a qualitative factor and with age as a covariate. Spearman's correlation coefficient was used to assess the relationship between the variables. The results were considered significant at $p<0,05$.

Table 4

Prescription rate of antihypertensive drugs in three patient groups

Parameter	Patients without frailty, n=50	Patients with prefrailty, n=50	Patients with frailty, n=60	P
ACE inhibitors	30%	38%	46,7%	0,208
ABR	36%	42%	21,7%	0,060
CCB	26%	26%	31,7%	0,777
Beta-blockers	36%	38%	40%	0,897
Diuretics	26%	26%	33,3%	0,638

Abbreviations: CCB — calcium channel blockers, ARB — angiotensin II receptor blockers, ACE inhibitors — angiotensin-converting enzyme.

Table 5

Prevalence of noncommunicable diseases and geriatric syndromes in three groups of patients

Parameter	Patients without frailty, n=50	Patients with prefrailty, n=50	Patients with frailty, n=60	p	p_1	p_2	p_3
CAD	24%	38%	42%		0,136		
HF	16%	26%	30%		0,215		
Diabetes	8%	16%	15%		0,449		
Knee/hip osteoarthritis	20%	52%	32%		0,200	0,068	0,004
Asthma	6%	2%	5%		0,708		
COPD	8%	2%	5%		0,438		
Cancer	18%	26%	17%		0,482		
Peptic and duodenal ulcer	6%	14%	8,3%		0,385		
Hearing loss	20%	58%	58,3%		<0,001	1	<0,001
Decreased vision	42%	70%	72%		0,006	1	0,016
Prior falls	30%	58%	66,2%	<0,001	0,001	0,431	0,017
Orthostatic hypotension	20%	44%	32%	0,033	0,185	0,433	0,053

Note: p-values are shown for comparing three groups (p) and, if they are significant, p-values for pairwise comparisons: p_1 — comparing groups of patients with frailty and without frailty, p_2 — comparing groups of patients with frailty and with prefrailty, p_3 — comparing groups of patients without frailty and with prefrailty.

Abbreviations: CAD — coronary artery disease, COPD — chronic obstructive pulmonary disease, HF — heart failure.

Results

The age of patients was 77,2±8,1 years (n=160; women, 139 (87%)).

In accordance with the current algorithm for frailty diagnosis, there were no frailty in 50 patients, prefrailty — in 50, and frailty — in 60. Comparative characteristics of patients depending on frailty are shown in Table 1.

All 3 groups significantly differed from each other in age (p=0,003): patients without frailty were younger than patients with frailty. In all three groups, women predominated among the study participants.

There were no significant differences in anthropometric parameters between the three groups of patients (Table 2).

Systolic BP, diastolic BP and heart rate in patients at the inclusion time are shown in Table 3. There were no significant differences in hemodynamic characteristics.

All study participants received antihypertensive therapy. The following main classes of antihypertensive drugs were used: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, β-blockers and diuretics (Table 4). There were no significant differences in the prescription rate of antihypertensives between the groups.

The prevalence of noncommunicable disease is presented in Table 5. There was a high prevalence of morbidity in the surveyed groups, generally typical

Table 6

Parameters of CHA in three groups of patients

Parameter	Patients without frailty, n=50	Patients with prefrailty, n=50	Patients with frailty, n=60	P
Barthel index, points	98,3±3,4a	94,8±7,8a	86,3±4,9b	0,005
Lawton scale, points	7,7±0,7a	7,6±0,8a	6,3±1,8b	<0,0001
Mini nutritional assessment, points	24,3±3,7a	23,7±2,2a	22,6±2,5b	<0,0001
Self-reported health status scale, %	66,4±14,6a	57,5±14,5b	47,8±16,8c	<0,0001
Brief mental health assessment scale, points	27,8±2,1a	27,1±1,9ab	25±4,9b	0,0001
Clock drawing test, points	8,7±1,1a	8,2±1,1ab	7,7±1,6b	0,024
Geriatric depression scale, points	1,6±1,5a	3,0±2,1b	3,7±2,8b	<0,001
Dynamometry, kg	26,7±10,1a	23,9±7,2a	18,8±7,4b	0,0006
Walking speed, m/s	1,0±0,7a	0,9±1,1ab	0,6±0,7b	0,03
Timed Up and Go test, sec	9,1±2,8a	11,2±5,2a	17,2±8,8b	<0,0001

Note: groups that differ significantly in pairwise comparisons have a common letter.

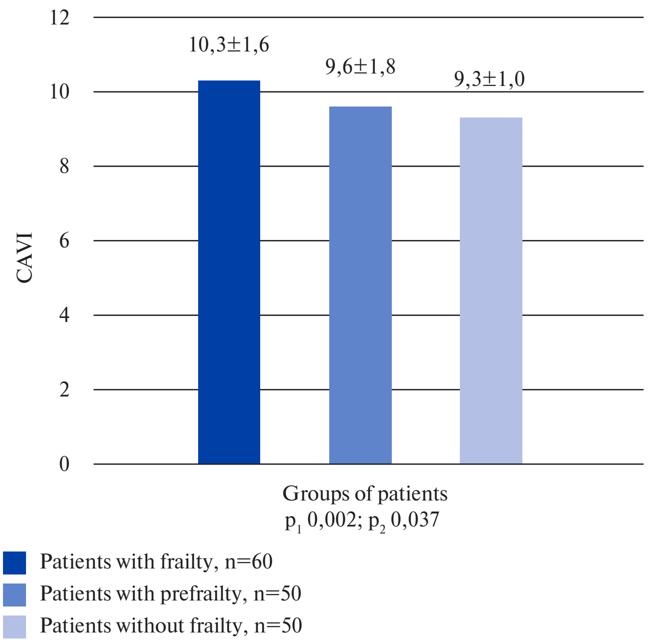

Figure 1. Vascular stiffness in three groups of patients, p=0,002.
Note: p_1 — comparing the group of patients with frailty and without, p_2 — comparing the group of patients with frailty and prefrailty.
Abbreviation: CAVI — cardio-ankle vascular index.

for elderly and senile patients. We found no significant differences in the disease prevalence in groups, with the exception of sensory deficits, the prevalence of which increased significantly with frailty progression. In addition, patients without frailty smoked more often compared to patients with prefrailty and with frailty (28% vs 8,2% and 5%, respectively, p⩽0,001).

The mean values for total cholesterol in the groups were as follows: in the group of patients with frailty, 5,3±1,2 mmol/L; in the group of patients with prefrailty, 5,3±1,5 mmol/L; in the group of patients without frailty, 5,7±1,0 mmol/L (p=0,118).

The CGA revealed significantly worse indicators in frailty group (Table 6).

As for vascular stiffness, significant differences in CAVI between the groups were revealed (p=0,002): patients with frailty had a higher CAVI than patients without frailty and with prefrailty (10,3±1,6 vs 9,3±1,0 and 9,6±1,8, respectively; p=0,002), Figure 1.

Since the groups differed significantly in age, we also performed additional analysis using the general linear model (GLM), including age as a covariate. The GLM revealed a tendency to the effect of frailty on CAVI (p=0,089): at the same age, frailty patients had higher CAVI than in patients without frailty (p=0,0004 in Tukey's test) and with prefrailty (almost reached the significance: p=0,058).

A correlation analysis of vascular stiffness with the RFs of CVD and CGA parameters was carried out (Table 7).

In patients without frailty, there were negative correlations with parameters of physical activity, clock-drawing test, and falls (Rs=-0,355 (p=0,015), Rs=-0,458 (p=0,011), and Rs=-0,306 (p=0,031)) and direct correlations with total cholesterol (Rs=0,379 (p=0,009)). In the group of patients with prefrailty: negative relationships were found with the parameters of dynamometry, BMI and physical activity (Rs=-0,329 (p=0,019), Rs=-0,343 (p=0,015) and Rs=-0,285 (p=0,047), respectively). In the

Table 7

Spearman's rank correlation coefficients between the CAVI and parameters of physical functioning, cognitive status, CVD RFs in three groups of patients

Parameter	Patients without frailty, n=50		Patients with prefrailty, n=50		Patients with frailty, n=60	
Barthel index, points	0,052	p=0,719	-0,037	p=0,799	-0,045	p=0,732
Instrumental activities of daily living, points	-0,046	p=0,747	-0,089	p=0,538	-0,113	p=0,389
Walking speed, m/s	-0,134	p=0,354	-0,209	p=0,145	-0,155	p=0,255
Timed Up and Go test, sec	0,204	p=0,154	0,091	p=0,154	0,120	p=0,379
Brief mental health assessment scale, points	-0,178	p=0,217	-0,113	p=0,433	-0,099	p=0,454
Clock drawing test, points	-0,458	p=0,011	0,016	p=0,909	-0,096	p=0,585
Dynamometry, kg	0,037	p=0,801	-0,329	p=0,019	-0,069	p=0,600
MNA, points	-0,259	p=0,069	-0,054	p=0,707	-0,192	p=0,142
Geriatric depression scale, points	0,089	p=0,539	0,043	p=0,765	0,075	p=0,569
Prior falls	-0,306	p=0,031	0,138	p=0,340	0,163	p=0,217
Orthostatic hypotension	0,173	p=0,229	0,094	p=0,518	0,382	p=0,003
Total cholesterol, mmol/Ll	0,379	p=0,009	-0,143	p=0,321	-0,117	p=0,389
Glucose, mmol/L	0,221	p=0,124	0,174	p=0,226	-0,051	p=0,706
BMI, kg/m^2	0,036	p=0,811	-0,343	p=0,015	-0,392	p=0,002
Smoking	-0,002	p=0,992	-0,145	p=0,319	0,148	p=0,259
Physical activity	-0,355	p=0,015	-0,285	p=0,047	-0,206	p=0,115
Prior diabetes	0,142	p=0,345	0,182	p=0,207	0,032	p=0,806

Abbreviations: BMI — body mass index, MNA — Mini Nutritional Assessment.

group of patients with frailty, inverse correlations were found with BMI (Rs=-0,393 (p=0,002)) and direct correlations with OH (Rs=0,382 (p=0,003)).

Discussion

The relationship between vascular stiffness and severity of CVD RFs is known. The relationship with geriatric syndromes is being actively discussed. Sampaio RA, et al. (2014) suggest that muscle blood supply decreases with age, which is associated with vascular stiffness [18]. Hemodynamic dysfunction may have a predictive effect on muscle loss. This decrease leads to a decrease in body weight, strength and, as a result, to a decrease in the physical functioning of an elderly person, which leads to disability, falls and death.

Aerobic exercise reduces vascular stiffness by increasing nitric oxide levels and decreasing endothelin-1 levels. The study by Son WM, et al. (2017) revealed a positive effect of aerobic exercise on vascular stiffness [19].

Physical activity and improved vascular stiffness are important factors in slowing cognitive decline in older patients.

We found significant differences in CAVI between the groups, as well as different correlations of CAVI with CGA data.

In the group of patients without frailty, the revealed correlations indicate that high vascular stiffness is associated with a decrease in cognitive function and fall rate. Patients in this group require careful analysis and correction of factors associated with these geriatric syndromes, including decrease of total cholesterol levels and increase of exercise.

In patients with prefrailty, an association of high vascular stiffness with sarcopenia signs was revealed — a decrease in muscle strength and, indirectly, a decrease in body weight. Patients in this group should be advised of a protein-rich diet combined with adequate exercise. Weight loss is associated with a decrease in muscle strength and, as a consequence, with a decrease in physical functioning, which contributes to weakness progression [5], which we found in groups of patients with prefrailty and frailty.

In the group of patients with frailty, the association of vascular stiffness with OH was revealed. The relationship between OH and outcomes in the elderly is poorly understood. However, there are works confirming the relationship between orthostatic response and frailty [20].

HTN is a key factor in vascular stiffening. It is necessary to adequately control BP at an earlier age to reduce the risk of OH in the elderly group of patients, when OH becomes a factor that complicates the management of these patients and potentially aggravates the prognosis.

Conclusion

Vascular stiffness in elderly patients with frailty is associated with a decrease in body mass index and orthostatic hypotension. At the stage of prefrailty, the relationship between the vascular stiffness and muscle strength decrease was revealed.

Thus, the vascular stiffness is associated with frailty markers itself.

Relationships and Activities: none.

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