Microvascular Research 144 (2022) 104419

Contents lists available at ScienceDirect

Microvascular Research

journal homepage: www.elsevier.com/locate/ymvre

Skin microcirculation in middle-aged men with newly diagnosed arterial hypertension according to remote laser Doppler flowmetry data

A.A. Fedorovich [a,b], Y.I. Loktionova [c], E.V. Zharkikh [c,d], A.Yu. Gorshkov [a], A.I. Korolev [a], V.A. Dadaeva [a], O.M. Drapkina [a], E.A. Zherebtsov [d,*]

[a] FSBI "National Health and Research Center of Preventive Healthcare" of the Ministry of Health of Russia, Moscow, Russia
[b] FSBI SRC RF "Institute of Biomedical Problems" RAS, Moscow, Russia
[c] Research & Development Center of Biomedical Photonics, Orel State University, Orel, Russia
[d] Optoelectronics and Measurement Techniques, University of Oulu, Oulu, Finland

ARTICLE INFO

Keywords:
Portable laser Doppler flowmetry
VECSEL
Newly diagnosed arterial hypertension
Daily blood pressure monitoring
Echocardiography
Skin blood perfusion
Blood perfusion oscillations
Resistive skin microvessels
Vasomotor activity

ABSTRACT

Objective: This work aims to study the functional state of resistive skin microvessels in patients with newly diagnosed arterial hypertension (AH), using portable laser Doppler flowmetry (LDF) devices.

Materials and methods: The study included 89 men aged 30 to 60 years (44.4 ± 8.5) who had no known medical complaints, subjectively considered themselves healthy, and did not take medications on a regular basis. All the men underwent LDF on the left forearm, daily blood pressure (BP) monitoring (DBPM) on the left arm, echocardiography, and laboratory tests. According to DBPM data, the men were divided into two groups. The control group (CG) consisted of 30 men with normal BP, and 59 men were included in the AH group.

Results: According to LDF data, in men with AH, there is a decrease in the amplitude (tone increase) of neurogenic and myogenic vasomotion, a decrease in the amplitude of pulse oscillations of microcirculatory flow, a decrease in perfusion efficiency of endothelial, neurogenic, myogenic and pulse mechanisms of tissue perfusion regulation. Of all tone-forming mechanisms, only the myogenic mechanism has a weak negative correlation with systolic blood pressure level. The amplitude of pulse oscillations demonstrates the highest degree of correlation with blood pressure parameters.

Conclusion: The functional disorders of vasomotor activity of resistive skin microvessels revealed in men with AH have minor correlations with the level of blood pressure. Despite this, the use of portable devices for remote LDF may be a useful method for the dynamic monitoring of patients with hypertension, which requires further research.

1. Introduction

Arterial hypertension (AH) is the most common chronic non-infectious human disease (Salem et al., 2018; Balanova et al., 2019) and the leading risk factor for cardiovascular disease, cerebrovascular disease and kidney damage. Despite the available study data on the causes and mechanisms of essential hypertension, its pathogenesis has not been definitively determined.

As defined by E.D. Frohlich and H.O. Ventura, AH is a hemodynamic disease in which an increase in arterial pressure is caused by an increase in cardiac output and/or an increase in total peripheral vascular resistance (TPVR) (Frohlich and Ventura, 2009). TPVR is formed at the level of resistive microvessels and depends on their functional and structural state, tone and lumen size (Struijker Boudier et al., 1992; Vicaut, 1992; Frohlich and Ventura, 2009; Rosei et al., 1995; Antonios et al., 1999; Feihl et al., 2006; Fedorovich et al., 2014).

The most convenient object for microvascular bed (MVB) research is skin, which is due to its availability and the possibility of carrying out a wide range of functional and pharmacological tests reflecting the reactions of microvessels to various stimuli, both in norm and in pathology. Available data indicate that skin MVB may reflect the state of microcirculation in other organs and systems (Rossi et al., 1997a, 1997b; Shamin-Uzzaman et al., 2002; Stewart et al., 2004; Holovatz et al., 2008; Goltsov et al., 2017).

Today, of all noninvasive methods of human MVB study, laser Doppler flowmetry (LDF) with amplitude-frequency analysis of tissue

* Corresponding author.
E-mail address: evgenii.zherebtsov@oulu.fi (E.A. Zherebtsov).

https://doi.org/10.1016/j.mvr.2022.104419
Received 28 March 2022; Received in revised form 11 July 2022; Accepted 2 August 2022
Available online 5 August 2022

perfusion fluctuations is the most widely used. The LDF method with amplitude-frequency analysis provides information on the functional state of the skin's resistive precapillary arterioles, assessing separately myogenic, neurogenic and endothelial mechanisms of vascular tone formation, and is a promising method (Martini and Bagno, 2018). Despite the high prevalence of arterial hypertension and the high social significance of the pathology, there are very few works on LDF with amplitude-frequency analysis in AH (Rossi et al., 1997a, 1997b, 2011; Gryglewska et al., 2010; Vasilyev et al., 2011; Podzolkov et al., 2012; Fedorovich et al., 2014).

Modern technical solutions for blood perfusion measurements made it possible to abandon the fiber optic data transmission channel and miniaturize the device to the size of a compact wrist-mounted LDF monitor (Zherebtsov et al., 2019). Standard wireless protocols (Bluetooth, Wi-Fi) are used to transmit tissue perfusion data, allowing researchers to study microcirculation in the convenient remote monitoring mode. The implemented fibreless technique significantly reduces the motion artefacts in the registered blood perfusion signal. In addition, an accelerometer installed in the sensor systems provides complete annotation of all mechanical movements during the recording session assisting in the selection of utterly artefact-free blood perfusion recordings at the stage of the signal post-processing. As a result of the measures, the blood perfusion measurements by the devices provide comparable or better sensitivity and signal-to-noise ratio compared with known table-top laser Doppler flowmetry systems. Such wrist-mounted LDF monitors recently have been used to study relative alterations in average perfusion and blood flow oscillations measured in the skin during postural changes of body position (Fedorovich et al., 2021), as well as to characterize systemic effects of cigarette smoking (Saha et al., 2020).

The study aimed to investigate the functional state of resistive skin microvessels in men with newly diagnosed arterial hypertension using portable wrist-mounted LDF devices.

2. Materials and methods

The study enrolled 89 men aged 30 to 60 years (44.4 ± 8.5) who subjectively considered themselves healthy, had no known medical complaints and were not taking medications on a regular basis. The study was conducted in accordance with the standards of Good Clinical Practice (GCP) and the principles of the Declaration of Helsinki. The study protocol was approved by an Independent Ethics Committee of the Federal State Budgetary Institution “National Medical Research Center for Therapy and Preventive Medicine” of the Ministry of Health care of the Russian Federation (Moscow, Russia). Protocol No. 01-01/19 of February 12, 2019. All subjects gave written consent to participate in the study.

The day before the study, intensive physical activity and alcohol intake were excluded, as well as night shift work. The intake of tonic drinks (tea, coffee, etc.) was excluded 6 h before the study, as was smoking – at least 2 h before the study. A set of examinations was performed in the first half of the day (9:00–12:00) in the following sequence: 1) examination, anthropometry (body weight, height, calculation of body mass index (BMI) according to the Ketle formula, waist circumference, hip circumference), collection of medical history, three-time BP measurement in sitting position (office BP); 2) LDF measurement on the left forearm; 3) venous blood sampling for laboratory studies; 4) glucose tolerance test; 5) echocardiography; 6) 24-hour ambulatory blood pressure monitoring (ABPM). The first two stages of the examination were conducted in a laboratory with a constantly maintained microclimate - temperature + 23 ± 1 °C, humidity 40–60 %. Office BP values were measured with an automatic analyzer “OMRON M10-IT” (OMRON HEALTHCARE Co., Ltd., Japan).

Following the first stage, we studied microcirculation in the supine position after a 15-minute adaptation period. To record skin perfusion, we used a portable wrist-mounted laser analyzer “LAZMA-PF” (Lazma Ltd., Russia). The device has built-in channels for recording blood perfusion that allow simultaneous measurements at several points of the body. The wavelength of the laser radiation in the sensors is 850 nm, and the power is about 1 mW. Each analyzer also has a built-in skin temperature sensor and accelerometer to monitor and eliminate possible artefacts. The probe was placed on the outer surface of the left forearm, 5–6 cm proximal to the wrist joint (Fig. 1).

Skin microcirculation was recorded for 10 min. The average level of cutaneous perfusion (M) was assessed. The initial LDF-gram (Fig. 2A) was subjected to amplitude-frequency wavelet transformation, using complex-valued Morlet wavelet (Fig. 2B). The time-averaged vasomotion amplitude was estimated from the maximum values (Ai) in the corresponding frequency range for endothelial (Ae), 0.0095–0.02 Hz, neurogenic (An) - 0.021-0.052 Hz, myogenic (Am) - 0.052-0.145 Hz, venular (respiratory-associated rhythm, Av) - 0.145 − 0.6 Hz, and cardiac (Ac) - 0.6-2.0 Hz blood flow modulation pathways (Stefanovska et al., 1999; Bernjak et al., 2008). Due to the impossibility of expressing the average perfusion level in microcirculation in absolute units, for example, in ml/s/mm^3 (Stefanovska and Bracic, 1999), M and Ai values were estimated in arbitrary perfusion units (PU). In addition to absolute values of vasomotion amplitude, the functional contribution of each regulatory mechanism to the total level of tissue perfusion was assessed according to the formula:

$$\mathrm{Ai}/\mathrm{M} \times 100\%,$$

where Ai is the vasomotion amplitude of the regulatory mechanism, M is the average level of tissue perfusion.

Clinical blood tests were performed on an MEK-8222 K automatic hematology analyzer (Nihon Kohden, Japan). Levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), uric acid (UA), C-reactive protein (CRP), and glucose were determined in blood serum, using an automatic analyzer, Architect C8000 (Abbott, USA); fibrinogen level was determined using an automatic analyzer, ACL Elite (Instrumentation Laboratory, USA). After venous blood sampling, all men took 75 g of glucose with 0.5 l of water, and 2 h later, blood sampling was repeated from the vein to assess response to carbohydrate load.

After oral glucose administration, echocardiography was performed on an expert class machine, Toshiba Xario SSA 660A (Japan) in M- and B-mode. The following parameters were assessed: left atrium (LA); left atrium volume (LAV); left ventricular end-diastolic dimension (LVEDD); left ventricular end-systolic dimension (LVESD); left ventricular end-diastolic volume (LVEDV); left ventricular end-systolic volume (LVESV); stroke volume (SV); cardiac output (CO); interventricular septum thickness (IVST); left ventricular mass (LVM); left ventricular mass index (LVMI).

In the last stage of the examination, ABPM was performed using a BpLab apparatus. The tonometer cuff was placed on the left shoulder. Blood pressure measurement intervals were 20 min during the active time of the day, and 40 min during night hours.

Statistical processing was performed using SPSS Statistics 17.0 software (StatSoft Inc., USA). The Shapiro-Wilk criterion was used to

Fig. 1. Portable LDF monitor on the left forearm.

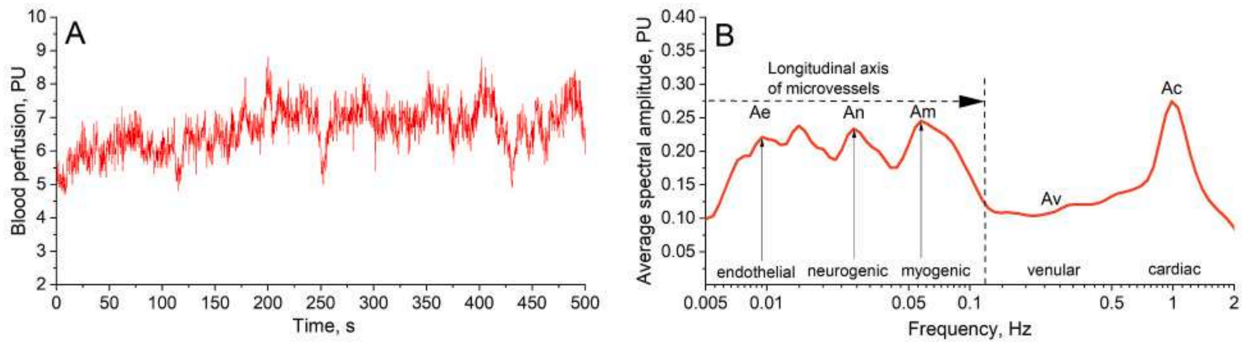

Fig. 2. Typical example of blood perfusion time-series recording obtained by the used wrist-mounted LDF monitor. A - tissue blood perfusion; B - amplitude-frequency wavelet analysis. Dotted lines indicate the projection of the precapillary arteriole.

estimate the type of feature distribution. The data obtained were presented as median and interquartile intervals (Me [Q_{25}; Q_{75}]). The Mann-Whitney test was used to determine differences between the groups. Differences were considered significant at $p < 0.05$. The Spearman rank correlation coefficient was used to evaluate the relationship between the variables. Relations were considered reliable at $p < 0.05$.

3. Results

According to ABPM results, the subjects were divided into 2 groups. The first group (CG) included 30 men with mean daily BP <130/80 mmHg and office BP <140/90 mmHg. The second group (AH) consisted of 59 men who were diagnosed with AH - mean daily BP ≥130/80 mmHg in accordance with the 2018 European Society of Cardiology guidelines (Williams et al., 2018). The main clinical characteristics of the groups are shown in Tables 1-3.

From the data obtained, we can see that the men in the analyzed groups are comparable only in age and height, and in other parameters the patients with AH have higher values. The results of laboratory tests revealed higher values of triglycerides and glucose in the AH group. The results of the glucose tolerance test did not reveal carbohydrate metabolism disorders in any of the 89 men.

According to transthoracic echocardiography, higher values of left atrial size, interventricular septal thickness, LV myocardial mass and LV myocardial mass index, as well as increased circulatory minute volume were noted in AH group.

The LDF results are shown in Figs. 3 and 4. The average skin temperature in the study area during 10 min of LDF registration was 31.4 ± 1.5 °C in the CG group and 31.7 ± 1.5 °C in the AH group.

Fig. 3 shows the amplitudes of the regulatory mechanisms of blood flow modulation and the level of tissue perfusion. It follows from the data obtained that, in AH patients, there is a decrease in the amplitude of neurogenic and myogenic vasomotions, the amplitude of pulse blood flow oscillations, with the preserved level of tissue perfusion. Fig. 4 shows the perfusion efficiency (Ai/M) of regulatory mechanisms. In patients with AH the contribution of regulatory mechanisms in tissue, perfusion is decreased by endothelial, neurogenic, myogenic, and pulse modulation mechanisms.

The results of correlation analysis of the functional activity of regulatory mechanisms of tissue perfusion and DBPM parameters for the whole group ($n = 89$) are shown in Table 4.

The data obtained show that pulse and myogenic mechanisms of

Table 1
Clinical characteristics of the analyzed groups.

Parameters	CG ($n = 30$)	AH ($n = 59$)	p
Age (years)	41 [35,5; 49,5]	44,5 [38; 52]	n/s
Height (cm)	180,5 [175,5; 183]	178,9 [174; 184]	n/s
Weight (kg)	81,5 [74,8; 88]	91,5 [83; 104]	<0,00005
BMI (kg/m^2)	24,8 [22,9; 28,2]	28,8 [26,5; 32]	<0,001
WC (cm)	92,5 [88,5; 97,5]	103 [98; 110]	<0,00001
HC (cm)	104 [99; 107]	107 [103; 114]	<0,01
Office BP and HR			
SBP (mm Hg)	120 [110; 127]	134,8 [130; 142]	<0,000001
DBP (mm Hg)	80 [70; 85]	90 [80; 92]	<0,000001
HR (bpm)	63 [49; 83]	69 [50; 103]	<0,005

Table 2
Results of laboratory research methods.

Parameters	CG ($n = 30$)	AH ($n = 59$)	p
WBC (10^9/L)	6,55 [5; 7,3]	6,55 [5,7; 7,4]	n/s
Platelets (10^9/L)	220 [184; 232]	226,5 [191, 257]	n/s
RBC (10^{12}/L)	4,94 [4,69; 5,28]	5,04 [4,78; 5,27]	n/s
Hemoglobin (g/L)	152,5 [146; 157]	155 [149; 163]	n/s
Hematocrit (%)	44,1 [42,6; 45,3]	44,9 [43,5; 46,8]	n/s
TC (mmol/L)	5,1 [4,8; 5,7]	5,7 [4,8; 6,4]	n/s
HDL-C (mmol/L)	1,29 [1,16; 1,54]	1,22 [1,05; 1,44]	n/s
LDL-C (mmol/L)	3,35 [2,9; 3,74]	3,61 [2,76; 4,22]	n/s
TG (mmol/L)	1,04 [0,77; 1,49]	1,42 [1,05; 2,1]	<0,001
UA (mg/dL)	5,85 [4,85; 6,75]	6,2 [5,6; 7]	n/s
Fibrinogen (g/L)	3,4 [3,2; 3,8]	3,6 [3,2; 3,9]	n/s
Glucose (mmol/L)	5,9 [5,68; 6,17]	6,2 [5,75; 6,6]	<0,05
CRP (mg/L)	0,9 [0,52; 1,51]	1,04 [0,61; 2,43]	n/s
Creatinine (μmol/L)	82 [71; 93]	81,5 [76; 91]	n/s

Table 3
Results of instrumental methods of investigation.

Parameters		CG (n = 30)	AH (n = 59)	p
Echocardiography				
LA (cm)		3,3 [3,1; 3,6]	3,6 [3,4; 3,9]	<0,005
LA volume (mL)		49 [44,5; 54]	57 [47; 68]	<0,05
LV EDD (cm)		4,8 [4,45; 5,3]	5 [4,6; 5,2]	n/s
LV ESD (cm)		2,8 [2,45; 2,9]	2,8 [2,6; 3]	n/s
LV EDV (mL)		107,5 [97; 124]	114 [99; 132,5]	n/s
LV ESV (mL)		36,5 [30,5; 41,5]	36,5 [31; 42]	n/s
SV (mL)		74,5 [62; 85,5]	76 [63,5; 93]	n/s
CO (L/min)		4,66 [4,19; 5,25]	5,23 [4,47; 6,18]	<0,5
IVST (cm)		1 [0,9; 1,1]	1,1 [1; 1,2]	<0,01
LVM (g)		158 [138; 173]	180 [158; 209]	<0,005
LVMI (g/m^2)		80 [72,5; 87,5]	85 [73; 95]	n/s
24-hour ambulatory blood pressure monitoring				
Daytime	SBP (mm Hg)	121 [114; 127]	136,4 [130; 143]	<0,000001
	DBP (mm Hg)	78 [74; 81]	89,5 [84; 94]	<0,000001
	HR (bpm)	70,5 [67; 80,5]	78,5 [76; 84]	<0,001
Night	SBP (mm Hg)	103,5 [100; 107,5]	120 [110; 131]	<0,000001
	DBP (mm Hg)	65 [63; 68]	75 [70; 85]	<0,000001
	HR (bpm)	59 [56; 64]	65 [58; 71]	<0,01

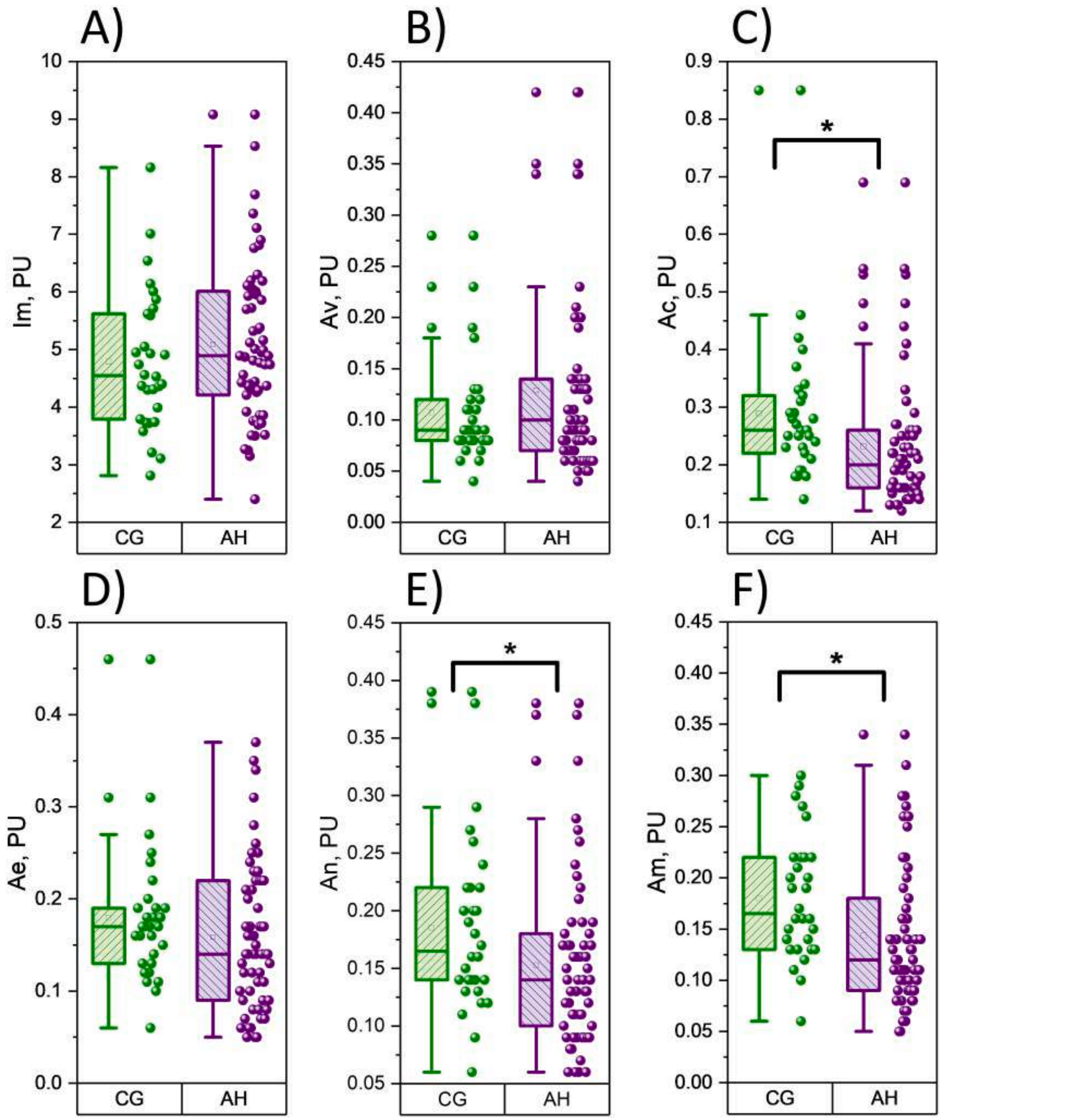

Fig. 3. A – level of tissue perfusion (M); B – amplitude of respiratory-driven blood flow oscillations (Av); C – amplitude of pulse oscillations of blood flow (Ac); D – amplitude of endothelial vasomotion (Ae); E – amplitude of neurogenic vasomotion (An); F – amplitude of myogenic vasomotions (Am). * – $p < 0,05$.

microcirculatory blood flow modulation demonstrate weak correlations with BP and HR. The activity of the endothelial mechanism is negatively correlated only with heart rate in daytime hours, and the neurogenic mechanism with heart rate in both daytime and nighttime hours.

4. Discussion

The study included men who, at the time of the examination, did not have any known medical complaints, subjectively considered themselves healthy, and did not take any pharmacological drugs on a regular basis. In the course of the study, it became evident that 66 % of the men had AH, i.e., two out of three men of working age were unaware of their pathology, despite their subjective well-being.

This group of men is characterized by higher values of body weight, BMI, WC and HC (Table 1). In normotensive men, 15 people (50 %) in the CG and only 6 (10 %) in the AH group had a BMI <25.3 people (10 %) in the CG and 23 (39 %) in the AH group were obese (BMI ≥30). Signs of abdominal obesity (FROM ≥94 cm) existed in 11 men (37 %) in the CG and 47 (80 %) in the AH group.

Despite significant differences in body weight, the indicators of laboratory research methods between the groups did not differ significantly, except for the level of triglycerides and glucose (Table 2), but glucose tolerance disorders were not detected by any of the subjects. In men with AH, there was a tendency to increase the values of all laboratory parameters and some of them went beyond the upper limits of reference values (total cholesterol, triglycerides, glucose).

According to echocardiography, all indicators in both groups were within the reference values, but in men with hypertension there was a trend towards an increase in almost all structural and functional parameters of the heart, with significant differences in LA size, LVM

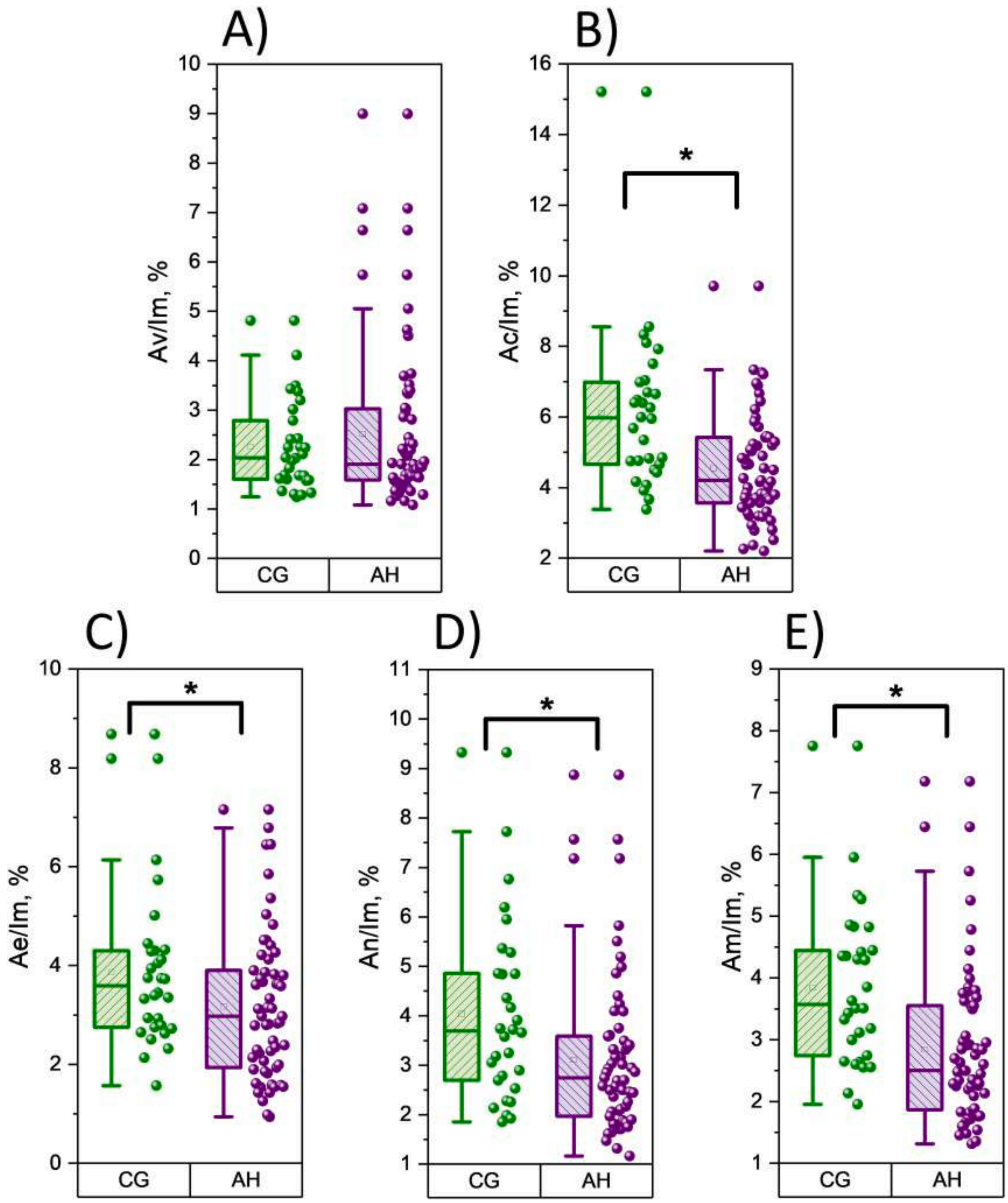

Fig. 4. A – perfusion efficiency of the venular mechanism (Av/M); B – perfusion efficiency of pulse mechanism (Ac/M); C – perfusion efficiency of endothelial mechanism (Ae/M); D – perfusion efficiency of neurogenic mechanism (An/M); E – efficiency of myogenic mechanism of tissue perfusion regulation (Am/M). * – p < 0,05.

myocardial mass and LVMI (Table 3).

According to LDF data, the level of skin perfusion (M) was comparable in both groups. In patients with AH, there was a decrease in the amplitude of pulse oscillations (Ac), which can be interpreted as a decrease in arterial blood flow to precapillary arterioles and capillaries. The amplitude of respiratory-induced fluctuations in blood flow (Av), which reflects the degree of blood filling of the venular (postcapillary) MVB, is comparable to CG (Fig. 3).

Vasomotor activity of the tone-forming mechanisms demonstrated a significant decrease in the amplitude of myogenic and neurogenic vasomotion in the AH group (Fig. 3). A decrease in the amplitude of vasomotion indicates an increase in tone on the part of these regulatory mechanisms (Fedorovich et al., 2014). If we imagine the zero value of the amplitude for the longitudinal axis of the microvessel, and the magnitude of vasomotion for the vessel wall, then it is clear that the lower the amplitude of vasomotion, the higher the tone and the smaller the lumen of the precapillary arterioles (Fig. 2B).

The calculated perfusion efficiency parameter (Ai/M) makes it possible to evaluate the contribution of the regulatory mechanism to the total trophic provision of tissue. The functional task of vasomotor tone-forming mechanisms (Ae, An, Am) is to modulate the incoming volume of arterial blood (Ac) to optimal values for transcapillary exchange, and the Av parameter reflects the functional state of the blood outflow pathways from the capillary bed. The results obtained in this study demonstrate a decrease in the perfusion efficiency of all three tone-forming mechanisms and a decrease in the perfusion contribution of pulse fluctuations in blood flow in men with hypertension (Fig. 4).

Summing up the data obtained, it can be concluded that, in men of

Table 4
Correlation coefficients of BP and HR with LDF parameters.

ABPM		M	Ae		An		Am		Av		Ac	
			Ae	Ae/M	An	An/M	Am	Am/M	Av	Av/M	Ac	Ac/M
Day	SBP	0,12	−0,03	−0,09	−0,05	−0,12	−0,23[1]	−0,32[3]	0,11	0,05	−0,25[2]	−0,34[4]
	DBP	0,12	−0,1	−0,19	−0,11	−0,19	−0,2	−0,29[3]	0,13	0,07	−0,27[2]	−0,36[5]
	HR	−0,08	−0,23[1]	−0,23	−0,26[2]	−0,27[2]	−0,27[2]	−0,27[2]	−0,05	0,03	−0,41[6]	−0,32[3]
Night	SBP	0,05	−0,11	−0,13	−0,08	−0,11	−0,25[2]	−0,27[2]	0,05	0,03	−0,3[3]	−0,34[4]
	DBP	0,11	−0,1	−0,15	−0,1	−0,16	−0,2	−0,27[2]	0,17	0,12	−0,23[1]	−0,29[2]
	HR	0,11	−0,08	−0,15	−0,2	−0,28[2]	−0,12	-0,18	0,09	0,1	-0,38[5]	-0,39[6]

[1] $p < 0,05$.
[2] $p < 0,01$.
[3] $p < 0,005$.
[4] $p < 0,001$.
[5] $p < 0,0005$.
[6] $p < 0,0001$.

working age at the initial stage of hypertension, the vasomotor function of the endothelium is not impaired, which is consistent with the previously published results of assessing the morpho-functional properties of subcutaneous fat microvessels (Rizzoni et al., 2006), but there is an increase in neurogenic and myogenic tone with a decrease in arterial blood flow to the metabolic microvessels. Despite the absence of violations of the vasomotor function of the endothelium, the perfusion efficiency of this regulation mechanism is reduced. The perfusion efficiency of other regulatory mechanisms is also reduced, with the exception of respiratory-induced fluctuations in blood flow.

Of particular interest is the relationship of the activity of the tone-forming mechanisms with the parameters of blood pressure. If the tone is elevated (low Ai values), then it is logical to expect an increase in blood pressure due to an increase in peripheral vascular resistance. As was shown in the study by Rosei et al., the media:lumen ratio and media thickness of subcutaneous microvessels are interrelated with both blood pressure and minimal vascular resistance (Rosei et al., 1995). The results obtained in this study (Table 4) show that only the myogenic component of vascular tone formation has negative correlations with SAD during daytime and night hours. The relationship is logical but very weak. The endothelial and neurogenic mechanisms of tone formation have not demonstrated reliable correlations with blood pressure levels. The amplitude of the tone-forming mechanisms has a reliable relationship only with the heart rate during the daytime. Unlike the tone-forming mechanisms, the amplitude of pulse fluctuations of the blood flow has a weak relationship with all the parameters of ABPM in the daytime and at night.

The Ai parameter, which reflects the vasomotor activity of the regulatory mechanism, the perfusion efficiency index (Ai/M), demonstrates significant negative relationships with a large number of parameters of central hemodynamics. Considering the fact that the main physiological role of microcirculation is in the trophic provision of tissues, the identified relationships are logical – the higher the perfusion efficiency of the regulatory mechanism (Ai/M), the lower the BP and HR.

5. Conclusion

This study showed the possibility of performing LDF using a portable device in patients with AH. According to remote LDF data, in men of working age with newly identified AH, there is an increase in the neurogenic and myogenic mechanisms of the tone formation of precapillary arterioles, a decrease in the amplitude of pulse oscillations, and a decrease in the perfusion efficiency of all regulatory mechanisms, with the exception of those related to respiration. Of all the tone-forming mechanisms (endothelial, neurogenic, myogenic), only the myogenic has weak negative correlations with the level of BP, which does not allow consideration of the LDF method as optimal for the study of peripheral vascular resistance. It can be assumed that the revealed violations of the functional state of the resistive microvessels of the skin at the onset of hypertension are due to systemic shifts of a metabolic nature and/or the action of circulating vasoactive agents, which requires further research.

CRediT authorship contribution statement

A.A. Fedorovich: Conceptualization, Methodology, Investigation, Writing- Original draft preparation.
Y.I. Loktionova: Data curation, Visualization, Writing- Original draft preparation.
E.V. Zharkikh: Data curation, Visualization, Writing- Original draft preparation.
A.Yu. Gorshkov: Investigation, Data curation.
A.I. Korolev: Investigation, Data curation.
V.A. Dadaeva: Investigation, Data curation.
O.M. Drapkina: Writing- Reviewing, Funding acquisition and Editing.
E.A. Zherebtsov: Conceptualization, Writing- Reviewing, Funding acquisition and Editing.

Funding

The reported study was funded by the Russian Foundation for Basic Research (RFBR), grant number 20-08-01153. E. Zherebtsov acknowledges the funding from the Academy of Finland, grant number 318281.

Declaration of competing interest

The authors declare that there is no conflict of interest.

References

Antonios, T.F., Singer, D.R., Markandu, N.D., Mortimer, P.S., MacGregor, G.A., 1999. Rarefaction of skin capillaries in borderline essential hypertension suggests an early structural abnormality. Hypertension 34 (4–1), 655–658. https://doi.org/10.1161/01.hyp.34.4.655.

Balanova, Y.A., Shalnova, S.A., Imaeva, A.E., Kapustina, A.V., Muromtseva, G.A., Evstifeeva, S.V., et al., 2019. Prevalence, awareness, treatment and control of hypertension in russian federation (data of observational ESSERF-2 study). Ration. Pharmacother. Card. 15 (4), 450–466. https://doi.org/10.20996/1819-6446-2019-15-4-450-466 (In Russian).

Bernjak, A., Clarkson, P.B.M., McClintock, P.V.E., Stefanovska, A., 2008. Low-frequency blood flow oscillations in congestive heart failure and after β1-blocade treatment. Microvasc. Res. 76 (3), 224–232. https://doi.org/10.1016/j.mvr.2008.07.006.

Fedorovich, A.A., Rogoza, A.N., Chikhladze, N.M., 2014. Characteristics of functional state of arteriolar and venular skin microvessels in patients with essential arterial hypertension. Microvasc. Res. 93, 105–113. https://doi.org/10.1016/j.mvr.2014.04.005.

Fedorovich, A.A., Loktionova, Y.I., Zharkikh, E.V., Mikhailova, M.A., Popova, J.A., Suvorov, A.V., Zherebtsov, E.A., 2021. Body position affects capillary blood flow regulation measured with wearable blood flow sensors. Diagnostics 11 (3), 436. https://doi.org/10.3390/diagnostics11030436.

Feihl, F., Liaudet, L., Waeber, B., Levy, B.I., 2006. Hypertension: a disease of the microcirculation? Hypertension 48 (6), 1012–1017. https://doi.org/10.1161/01.HYP.0000249510.20326.72.
Frohlich, E.D., Ventura, H.O., 2009. Pathophysiology: disease mechanisms. In: Hypertension. Clinical Publishing Oxford.
Goltsov, A., Anisimova, A.V., Zakharkina, M., Krupatkin, A.I., Sidorov, A.V., Sokolovski, S.G., Rafailov, E., 2017. Bifurcation in blood oscillatory rhythms for patients with ischemic stroke: a small scale clinical trial using laser doppler flowmetry and computational modeling of vasomotion. Front. Physiol. 8, 160. https://doi.org/10.3389/fphys.2017.00160.
Gryglewska, B., Necki, M., Cwynar, M., Baron, T., Grodzicki, T., 2010. Neurogenic and myogenic resting skin blood flowmotion in subjects with masked hypertension. J. Physiol. Pharmacol. 61 (5), 551–558. https://doi.org/10.1097/01.hjh.0000378766.31971.ab.
Holovatz, L.A., Thompson-Torgerson, C.S., Kenney, W.L., 2008. The human cutaneous circulation as model of generalized microvascular function. J. Appl. Physiol. 105, 370–372. https://doi.org/10.1152/JAPPLPHYSIOL.00858.2007.
Martini, R., Bagno, A., 2018. The wavelet analysis for the assessment of microvascular function with the laser doppler fluxmetry over the last 20 years. Looking for hidden informations. Clin. Hemorheol. Microcirc. 70 (2), 213–229. https://doi.org/10.3233/CH-189903.
Podzolkov, V.I., Vasil'eva, L.V., Matveev, V.V., Kolesnichenko, N.A., 2012. Sex characteristics of the microcirculation in healthy subjects and patients with the first degree arterial hypertension. Ration. Pharmacother. Card. 8 (6), 746–751. https://doi.org/10.20996/1819-6446-2012-8-6-746-451 (In Russian).
Rizzoni, D., Porteri, E., DeCiuceis, C., Boari, G.E.M., Zani, F., Miclini, M., et al., 2006. Lack of prognostic role of endothelial dysfunction in subcutaneous small arteries of hypertensive patients. J. Hypertens. 24 (5), 867–873. https://doi.org/10.1097/01.hjh.0000222756.76982.53.
Rosei, E.A., Rizzoni, D., Castellano, M., Porteri, E., Zulli, R., Muiesan, M.L., et al., 1995. Media: lumen ratio in human small resistance arteries is related to forearm minimal vascular resistance. J. Hypertens. 13 (3), 341–347. https://doi.org/10.1097/00004872-199503000-00010.
Rossi, M., Taddei, S., Fabbri, A., Tintiri, G., Credidio, L., Virdis, A., et al., 1997. Cutaneous vasodilation to acetylcholine in patients with essential hypertension. J. Cardiovasc. Pharmacol. 29, 406–411. https://doi.org/10.1097/00005344-199703000-00015.
Rossi, M., Taddei, S., Fabbri, A., Tintori, G., Credidio, L., Virdis, A., et al., 1997. Cutaneous vasodilation to acetylcholine in patients with essential hypertension. J. Cardiovasc. Pharmacol. 29, 406–411. https://doi.org/10.1097/00005344-199703000-00015.
Rossi, M., Bradbury, A., Magagna, A., Pesce, M., Taddei, S., Stefanovska, A., 2011. Investigation of skin vasoreactivity and blood flow oscillations in hypertensive patients: effect of short-term antihypertensive treatment. J. Hypertens. 29, 1569–1576. https://doi.org/10.1097/HJH.0b013e328348b653.
Saha, M., Dremin, V., Rafailov, I., Dunaev, A., Sokolovski, S., Rafailov, E., 2020. Wearable laser Doppler flowmetry sensor: a feasibility study with smoker and non-smoker volunteers. Biosensors 10 (12), 201. https://doi.org/10.3390/bios10120201.
Salem, H., Hasan, D.M., Eameash, A., El-Mageed, H., Hasan, S., Ali, R.F.M., 2018. Worldwide prevalence of hypertension: a pooled meta-analysis of 1670 studies in 71 countries with 29.5 million participants. JACC 71 (11). https://doi.org/10.1016/S0735-1097(18)32360-X. Suppl.
Shamin-Uzzaman, Q.A., Pfenninger, D., Kehrer, C., Chakrabarti, A., Kacirotti, N., Rubenfire, M., et al., 2002. Altered cutaneous microvascular responses to reactive hyperemia in coronary artery disease: a comparative study with conduit vessel responses. Clin. Sci. 103, 267–273. https://doi.org/10.1042/CS1030267.
Stefanovska, A., Bracic, M., 1999. Physics of the human cardiovascular system. Contemp. Phys. 40 (1), 31–35. https://doi.org/10.1080/001075199181693.
Stefanovska, A., Bracic, M., Kvernmo, H.D., 1999. Wavelet analysis of oscillations in peripheral blood circulation measured by doppler technique. IEEE Trans. Biomed. Eng. 46 (10), 1230–1239. https://doi.org/10.1109/10/790500.
Stewart, J., Kohen, A., Brouder, D., Rahim, F., Adler, S., Garrick, R., Goligorsky, M., 2004. Noninvasive interrogation of microvasculature for signs of endothelial dysfunction in patients with chronic renal failure. Am. J. Physiol. Heart Circ. Physiol. 287, H2687–H2696. https://doi.org/10.1152/AJPHEART.00287.2004.
Struijker Boudier, H.A., Le Noble, J.L., Messing, M.W., Huijberts, M.S., Le Noble, F.A., Van Essen, H., 1992. The microcirculation and hypertension. J. Hypertens. Suppl. 10 (7), S147–S156. https://doi.org/10.1097/00004872-199212007-00016.
Vasilyev, A.P., Streltsova, N.N., Sekisova, M.A., Malishevskyi, M.V., Samoylova, I.V., 2011. Functional characteristics of microcirculation and their prognostic value in patients with arterial hypertension. Cardiovacs. Ther. Prev. 10 (5), 14–19. https://doi.org/10.15829/1728-8800-2011-5-14-19 (In Russian).
Vicaut, E., 1992. Hypertension and the microcirculation: a brief overview of experimental studies. J. Hypertens. Suppl. 10 (5), S59–S68. https://doi.org/10.1097/00004872-199207005-00009.
Williams, B., Mancia, G., Spiering, W., Rosei, E.A., Azizi, M., Burnier, M., et al., 2018. ESC/ESH guidelines for the management of arterial hypertension. Eur. Heart J. 39 (33), 3021–3104. https://doi.org/10.1093/eurheartj/ehy339.
Zherebtsov, E.A., Zharkikh, E.V., Kozlov, I.O., Zherebtsova, A.I., Loktionova, Y.I., Chichkov, N.B., Rafailov, I.E., Sidorov, V.V., Sokolovski, S.G., Dunaev, A.V., Rafailov, E.U., 2019. Novel wearable VCSEL-based sensors for multipoint measurements of blood perfusion. In: Proc. SPIE 10877, Dynamics and Fluctuations in Biomedical Photonics XVI, 1087708. https://doi.org/10.1117/12.2509578.