Comparative Analysis of Methods of Laser Doppler Flowmetry and Doppler Ultrasound Measurement of Blood Flow during the Procedure of Intermittent Pneumatic Compression

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Abstract. The results of the analysis of microcirculation of the blood flow of the toe and ultrasound Doppler measurement of blood flow in the femoral artery during the intermittent pneumatic compression procedure are presented. A professional device "Doctor Life Mark 400" (South Korea) was used for the pressotherapy procedure. Microcirculation was measured using a portable laser Doppler flowmeter "LAZMA PF" (Russia). Ultrasonic Dopplerograms were obtained using the device "Edan U50" (China) with a linear sensor model L15-7b with a frequency in pulsed Doppler mode (PW) 7.2 MHz. The study involved a group of 11 subjects without identified vascular disorders, the age of the group was from 23 to 42 years. The method of calculating the average speed and volume of blood flow over the period of the cardiac cycle was used for ultrasound Dopplerograms. Arterial resistance was evaluated, which was compared with the dynamics of perfusion in the limb. In the studies, approximately half of the test subjects had an increase in perfusion of the microcirculatory bed and a decrease in resistance of arterial vessels. At the same time, with an increase in the perfusion of the microcirculatory bed, a decrease in the resistance of arterial vessels was observed.

Keywords: laser Doppler flowmetry; ultrasound Dopplerography; volumetric blood flow; microcirculatory bed; intermittent pneumatic compression.

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1 Introduction

Measurement of microcirculation readings using Laser Doppler Flowmetry (LDF) is one of the non-invasive methods for assessing the effect of intermittent pneumatic compression (IPC) on hemodynamics in human limb vessels. External rhythmic compression of the limbs can increase the probability of improving the result of treatment of patients with peripheral vascular diseases. This fact has been statistically recognized for many decades [1]. There are a number of publications stating that the procedure of pressotherapy has a positive effect on the perfusion of the tissues of the lower extremities, improves arterial and venous hemodynamics [2–15]. Repeated attempts have been made by researchers to describe the body's reaction to compression effects [16–18]. At the moment, there are areas of uncertainty in the full understanding of what processes occur during IPC and how this fully affects the characteristics of the LDF-gram and Dopplerogram, since there are many different factors whose contribution must be taken into account, for example, the individual characteristics of the test subject, physiological and molecular reactions.

In Ref. [19], IPC procedure was performed on 20 patients with an average age of 74 years with critical limb ischemia. One pneumatic cuff was placed on the foot, and the other on the calf muscle. The maximum pumping pressure was 120 mm Hg. The data were evaluated using duplex ultrasound scanning and LDF in a semi-standing position before, during and after the IPC procedure. Perfusion measured on the back of the foot increased significantly. There was an increase in blood flow during the application of pressure therapy in all three arteries (popliteal, calf and collateral) compared with the initial values, which was associated with an increase in the average velocity over time, since the diameter of the arteries remained unchanged. After the termination of the IPC, the flow returned to the initial level. Significant popliteal vein reflux was detected in two test subjects without an increase in arterial or cutaneous blood flow.

The article [16] reviewed the literature concerning the use of compression methods of treatment. It has been shown that special devices that create short phases of pressure waves up to 180 mm Hg increase arterial flow even in patients with occlusive artery disease and in severe stages of ischemia. Other studies have described an increase in capillary perfusion and tissue oxygenation in response to IPC procedure, which is a consequence of increased release of nitric oxide [11, 12] and increased regulation of the fibrinolytic potential of endothelial cells (the mechanism of gradual dissolution of the thrombus and normalization of blood circulation), and additionally with suppression of activation of the procoagulant (the mechanism of reducing blood clotting) [13]. In some reports, there was no increase in fibrinolytic activity after IPC [14, 20].

A review [21] shows that in the period from 1966 to 2001, 26 reports of IPC procedure were found, in which arterial blood flow of the lower extremities in the popliteal, anterior and posterior tibial and fibular arteries noticeably increases. This is explained by several mechanisms of the effect of IPC on positive changes in perfusion of the tissues of the lower extremities. These include emptying of the plantar venous plexus, a decrease in venous pressure in the legs, an increase in arteriovenous pressure gradients in dependent patients, an increase in arterial flow, the release of vasodilators (nitric oxide – NO, prostacyclines), as well as a decrease in local vascular resistance and temporary cessation of the arteriovenous reflux [8, 22].

The article [23] shows that the use of IPC reduces venous congestion and increases the rate of blood flow in deep veins, which leads to favorable hemodynamic changes, such as a decrease in venous pressure and interstitial edema. Pressotherapy leads to an increase in the volume of venous flow and an increase in the velocity of venous flow, causing increased shear stress. Animal studies have shown that these mechanical effects lead to endothelial cell reactions that promote profibrinolytic, vasodilating and antithrombotic effects after the use of IPC.

An additional method for analyzing the effect of IPC on vascular hemodynamics in the lower extremities can be the combination in time of the parameters of peripheral vascular microcirculation and the data of Dopplerograms of arterial vessels during and after the procedure of pressotherapy. This data synchronization allows us to better understand and describe the body is reaction to compression effects.

This study presents the results of Doppler ultrasound examination of the volume blood flow of the femoral artery and LDF analysis of the perfusion of the phalanx of the toe before, during and after pressotherapy.

2 Methods and Equipment

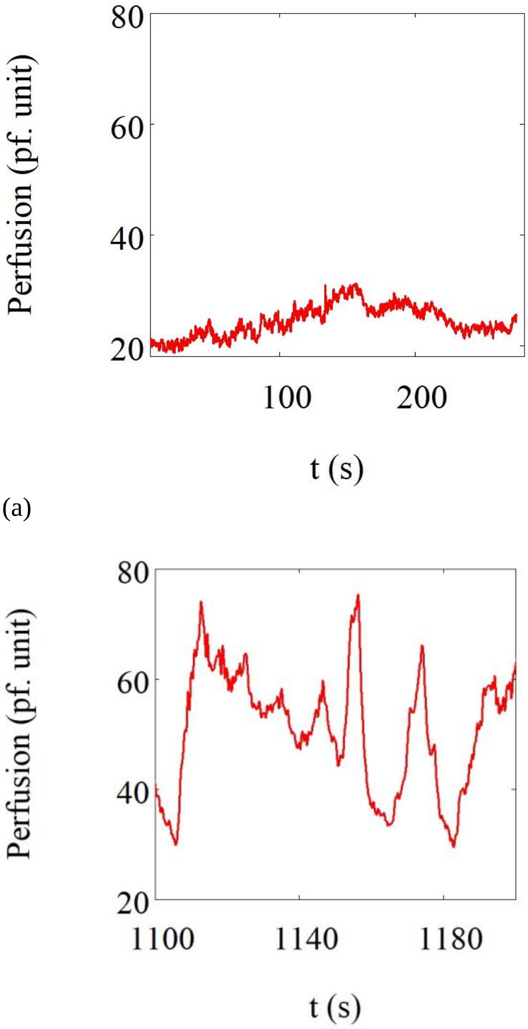
The study used an ultrasound device “Edan U50” (China) with a linear sensor model L15-7b with frequencies 10.0/12.0/14.0 MHz, 128 elements, in pulse Doppler mode (PW) 7.2 MHz. Mode B was used to visualize the arteries, and color coding mode CD was used to find arterial blood flow. Pulse-wave Doppler mode was used to measure arterial blood flow dopplerograms. The screen resolution of the ultrasound device was 1024×768 pixels. Grayscale 256 was used when capturing the image.

Microcirculation readings were measured using a portable LDF device “LAZMA PF” (Russia). The “LAZMA PF” device uses a single-frequency laser with a radiation power of 0.7 mW and a wavelength of 850 nm, the depth of penetration into the skin of which is about 1–1.2 mm [24]. With the help of laser Doppler flowmetry, fluctuations in blood volume caused by the activity of vascular smooth muscles are recorded [25].

The LDF-gram obtained during the experiment was divided into its constituent frequency components using wavelet analysis, as recognized as the most suitable for these calculations. The following factors of microcirculation regulation were distinguished: “passive” and “active” mechanisms [26]. Making a common contribution to vascular hemodynamics, these factors form five non-overlapping frequency ranges from 0.005 to 3 Hz: 0.007–0.017 Hz is the range of endothelial activity; 0.023–0.046 Hz is the range of neurogenic activity; 0.05–0.145 Hz is the range of myogenic activity; 0.2–0.4 Hz is the range of respiratory rhythm; 0.8–1.6 Hz is the range of cardiac rhythm [24].

The professional device “Doctor Life Mark 400” (South Korea) was used for the procedure of pressotherapy (lymphatic drainage). The cuffs of the Mark 400 device were put on a person’s legs, each of them consists of six separate internal air chambers. The lowest cameras on the feet were turned off so that they did not affect the operation of the LDF device. The pressotherapy procedure lasted 30 min at a pressure of 200 mm Hg in the “C” mode: the chambers are consistently inflated and deflated from the bottom up.

The LDF device was fixed on the large phalanx of the toe, data was recorded by the device for 4 min before the pressotherapy procedure, during the procedure and for 4 min after the IPC. Ultrasound Dopplerograms from the femoral artery were taken at the time corresponding to the beginning and end of the presstorapy procedure, as well as during the occlusion of the lower limb in the interval of 5 min from the beginning of the experiment (I occlusion) and 5 min before the end of the study (penultimate occlusion).



(a)

(b)

Fig. 1 LDF-gram before pressotherapy (a), LDF-gram after pressotherapy (b).

The image processing program "ImageJ", which has no license restrictions, was used to analyze the received Dopplerograms. Doppler images were converted from RGB format to 8-bit. Using the built-in tools, the area of interest in the image was highlighted. As such, the direct and reverse blood flow, denoted by "A" and "B", respectively, was selected. By applying the coordinate saving function, we get a ready-made file with pixel coordinates and the corresponding intensity for them in grayscale (0–255). The increase in intensity on the Dopplerogram corresponds to an increase in the number of blood cells from which the ultrasound radiation is reflected. Using the zoom setting function, it was calculated what one pixel is equal to by the velocity coordinate. For images with different speed intervals, the pixel value was normalized by speed. This technique allows you to compare Dopplerograms with an unequal range along the velocity axis. This technique made it possible to calculate the average speed and volumetric blood flow for the selected period of the cardiac cycle, to build the intensity distribution by speed. The diameter of the femoral artery was considered unchanged throughout the experiment and was chosen to be 0.76 cm [27].

The average speed over the period of the cardiac cycle was calculated using the following Eq.:

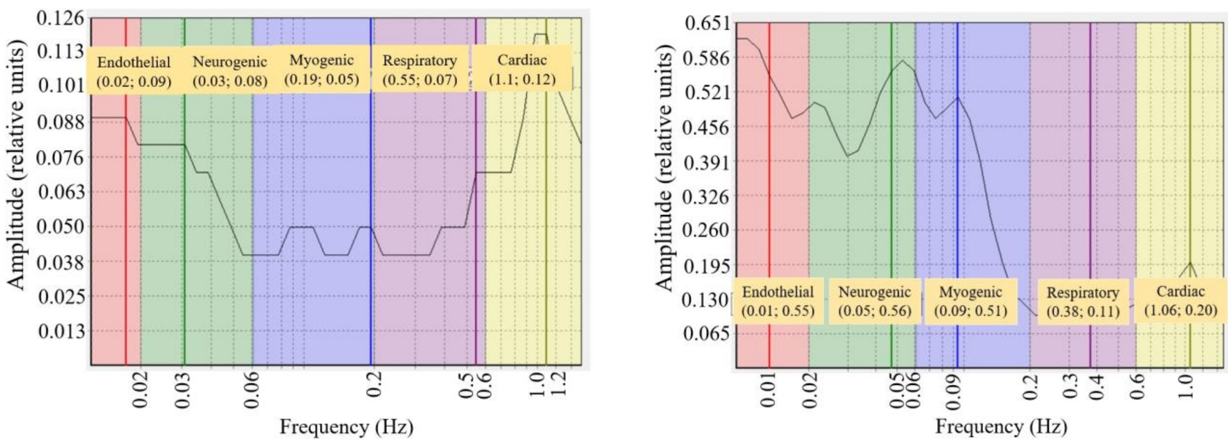
$$\mathrm{v}_{as} = \frac{\sum \text{Pixel Intensity} * \text{The speed of this pixel}}{\sum \text{Pixel intensity}}. \quad (1)$$

Volumetric blood flow over the period of the cardiac cycle has the form:

$$Q = S * \mathrm{v}_{as}, \quad (2)$$

where S is the cross sectional area of the vessel. The dimensionless vascular resistance coefficient was introduced:

$$R = \frac{\mathrm{v}_{max_B}}{\mathrm{v}_{max_A}}. \quad (3)$$

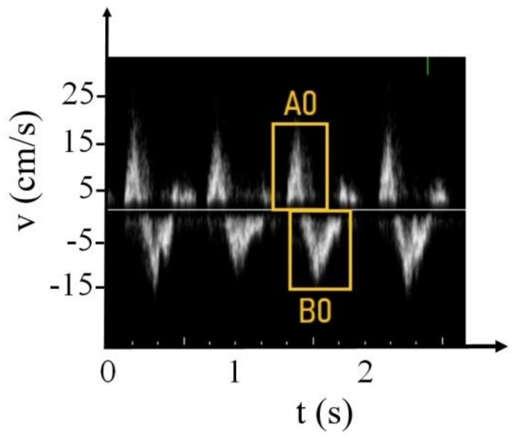


(a) (b)

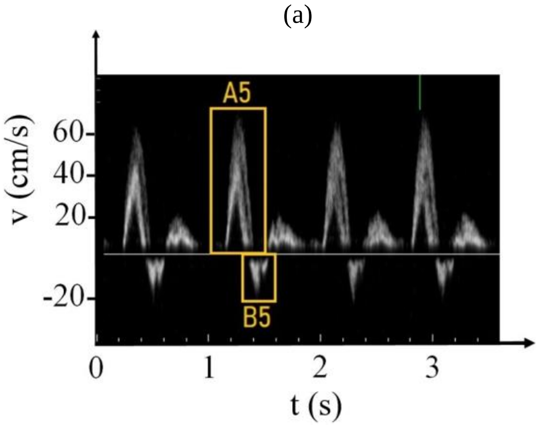
Fig. 2 The wavelet spectrum of the LDF-gram before the pressotherapy (a), the wavelet spectrum of the LDF-gram after the pressotherapy (b).

Table 1 Values of average velocity, volume blood flow and vascular resistance before and after IPC.

Parameter	Before pressotherapy	After pressotherapy
Average speed direct/reverse blood flow (cm/s)	6.2 / –6.2	25.8 / –7.9
Direct/reverse volumetric blood flow (ml/min)	197.5 / –195.6	821.4 / –249.7
Vascular resistance	0.88	0.39



(a)



(b)

Fig. 3 Dopplerogram before pressotherapy with selected areas of interest (a), Dopplerogram after pressotherapy with selected areas of interest (b). Areas “A0” and “A5” – direct blood flow, “B0” and “B5” – reverse blood flow.

where v_{max_B} is the maximum speed of reverse blood flow, v_{max_A} is the maximum speed of direct blood flow. The closer the value of the resistance coefficient R is to 1, the more pronounced the local vascular resistance.

3 Comparison Results for One Test Subject

IPC procedure was performed on a 23-year-old test subject who did not have cardiovascular diseases.

Figs. 3(a) and 3(b) show ultrasound Dopplerograms corresponding to LDF-grams before and after the IPC procedure, respectively. There was an increase in the maximum rate of direct blood flow from 17 to 51 cm/s. The maximum rate of reverse blood flow increased after the procedure from –15 to –20 cm/s. Before IPC, there is a large reverse blood flow, shown in Fig. 3(a), the amplitude of which is almost equal in magnitude to the direct blood flow. According to the Dopplerogram in Fig. 3(b), it can be seen that after the pressotherapy procedure, the amplitude of the direct blood flow increased noticeably, the reverse one decreased.

Table 1 shows the measured parameters of blood flow before and after the pressotherapy procedure. The average rate of direct blood flow increased significantly after IPC in comparison with reverse blood flow. The volumetric blood flow during the period of the cardiac cycle increased in a similar way. The value of the dimensionless coefficient of vascular resistance decreased markedly after pressure therapy, which indicates a decrease in local vascular resistance.

Fig. 4 shows the LDF-gram with marked interval areas corresponding in time to the Dopplerogram readings during and after I occlusion. The figure in the range from 30 to 45 perfusion units (pf. units) shows an increase in perfusion after occlusion.

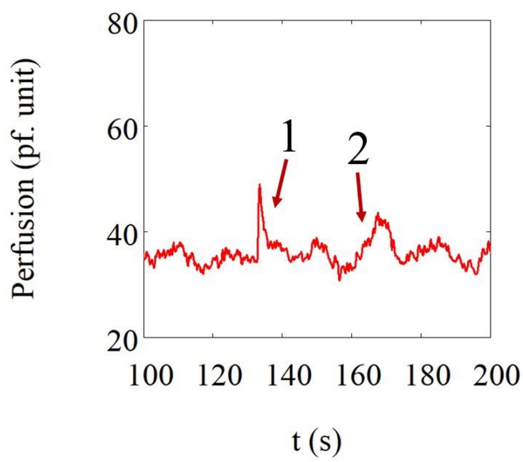


Fig. 4 LDF-gram with data of the selected areas of interest of Dopplerograms during and after I occlusions. 1 – the beginning of occlusion, 2 – after occlusion.

Table 2 Values of average velocity, volume blood flow, and vascular resistance during and after I occlusion.

Parameter	During I occlusion	After I occlusion
Average speed direct / reverse blood flow (cm/s)	11 / –8.8	10.1 / –5.6
Direct / reverse volumetric blood flow (ml/min)	348.9 / –280.3	322.7 / –178.5
Vascular resistance	0.71	0.44

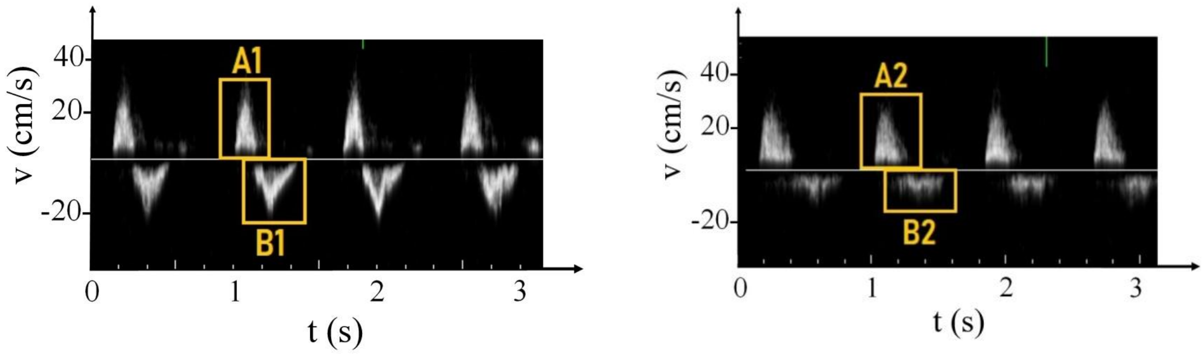


Fig. 5 Dopplerogram during occlusion with selected areas of interest (a), Dopplerogram after occlusion with selected areas of interest (b). Areas “A1” and “A2” – direct blood flow, “B1” and “B2” – reverse blood flow.

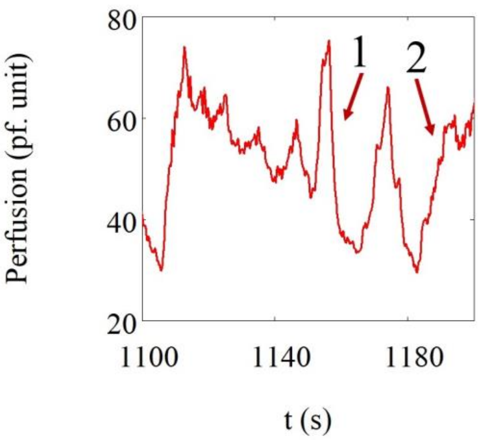


Fig. 6 LDF-gram with data of the selected zones of interest of Dopplerograms during and after the penultimate IPC occlusion. 1 – the beginning of occlusion, 2 – after occlusion.

In Fig. 5, Dopplerograms during and after occlusion, corresponding to the interval from 130 to 170 s on the LDF-gram are shown in Fig. 4. There was a slight decrease in the maximum rate of direct blood flow from 35 to 33 cm/s after occlusion. The maximum rate of reverse blood flow decreased from –25 to –14 cm/s. During occlusion, the blood flow becomes turbulent, since there is no clearly defined “window” in Fig. 5(a). After occlusion, the return blood flow became more stretched along the time axis, as shown in Fig. 5(b).

Table 2 shows the measured parameters of blood flow during and after I occlusion during the pressotherapy procedure. According to the table, it follows that the average rate of direct blood flow after occlusion has almost returned to its previous values. The amount of reverse volumetric blood flow has changed more pronounced. The value of the dimensionless vascular resistance coefficient decreased after IPC.

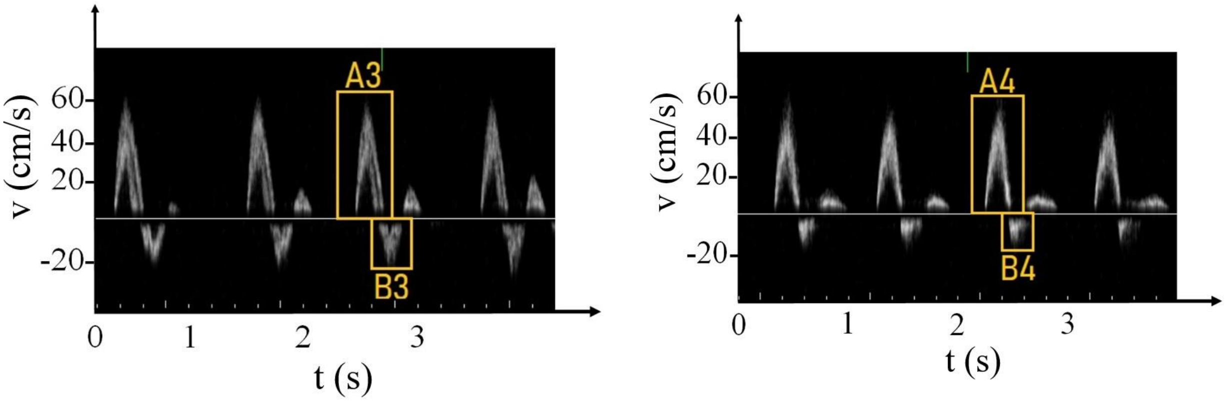
Fig. 6 shows an LDF-gram with marked interval zones corresponding in time to the Dopplerogram readings during and after the penultimate occlusion. The amount of perfusion by the end of the procedure increased to 75 pf. units. During occlusion, there is a significant decrease in perfusion, and after occlusion, a non-monotonic increase in perfusion to a value of 80 pf. units is recorded.

Fig. 7 show Dopplerograms during and after the penultimate IPC occlusion, corresponding to the interval from 1150 to 1190 s on the LDF-gram shown in Fig. 6. The maximum velocity of direct blood flow remained almost unchanged and was in the region of 53 cm/s after occlusion. The maximum rate of reverse blood flow decreased from –21 to –15 cm/s. On Dopplerograms shown in Figs. 7(a) and 7 (b), a clearly defined “window” is observed, indicating a laminar flow.

Table 3 shows the measured parameters of blood flow during and after the penultimate occlusion of the pressotherapy procedure. It can be seen from the table data that the blood flow parameters change slightly, while their average values have increased relative to the I occlusion.

Table 3 Values of average velocity, volume blood flow, and vascular resistance during and after the penultimate occlusion.

Parameter	During the penultimate occlusion	After the penultimate occlusion
Average speed direct / reverse blood flow (cm/s)	25 / –9.7	25.5 / –6.6
Direct / reverse volumetric blood flow (ml/min)	795 / –308.46	810.9 / –209.88
Vascular resistance	0.4	0.28



(a) (b)

Fig. 7 Dopplerogram during the penultimate occlusion with selected areas of interest (a), Dopplerogram during the reset of the penultimate occlusion with selected areas of interest (b). Areas "A3" and "A4" – direct blood flow, "B3" and "B4" – reverse blood flow.

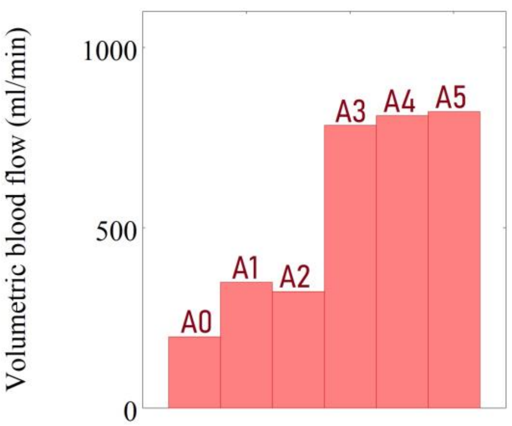
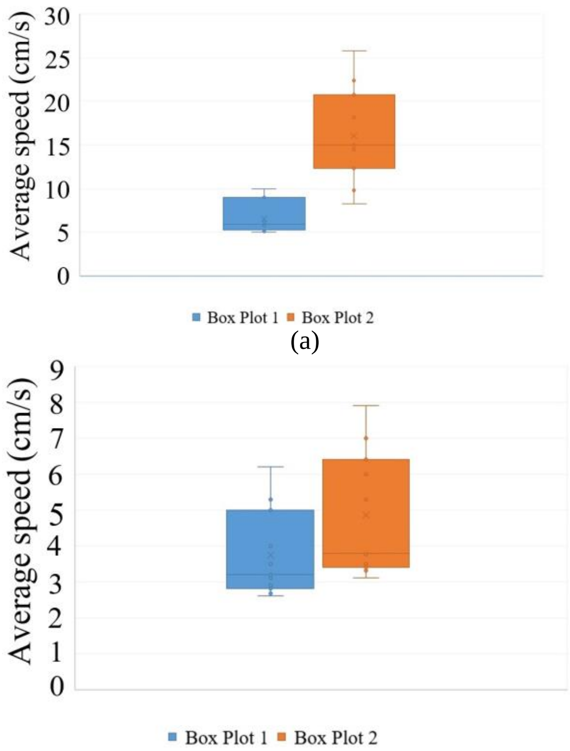


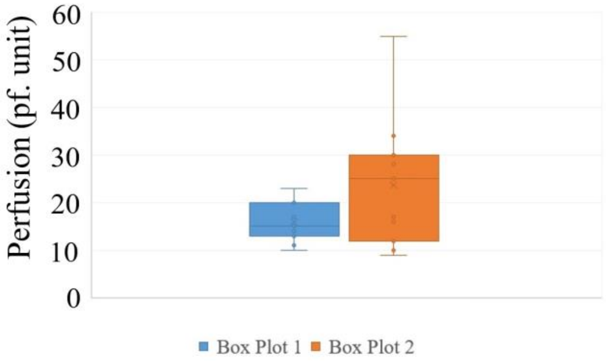
Fig. 8 Volumetric blood flow by areas of interest.

The change in volumetric blood flow in all selected areas of the Dopplerograms of the test subject is shown in Fig. 8. After the IPC procedure, the volume blood flow, as well as perfusion, increased markedly relative to the initial values. At the same time, the resistance coefficient as the ratio of reverse blood flow to direct decreased, which indicates a decrease in vascular resistance of the femoral artery. During a sharp decline in perfusion of the peripheral bed of the toe, observed on the LDF-gram during occlusion, volumetric blood flow in the femoral artery increases.

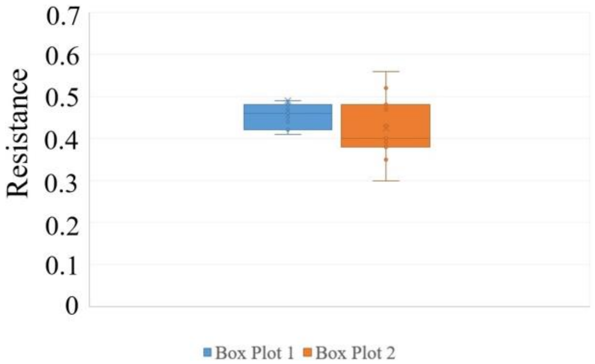


(b)

Fig. 9 The spread of the average blood flow rate over the period of the cardiac cycle before (Box Plot 1) and after (Box plot 2) pressotherapy: (a) direct blood flow, (b) reverse blood flow.



(a)



(b)

Fig. 10 The spread of microcirculatory perfusion (a) and arterial vascular resistance (b) before (Boxplot 1) and after (Boxplot 2) pressotherapy.

The study involved a group of 11 test subjects without identified vascular disorders, the age of the group was from 23 to 42 years. All test subjects signed an informed consent to conduct the study before participating. The studies were conducted during the daytime in conditions of physical and mental rest with preliminary adaptation of the test subjects to the room temperature of 20–23 °C.

The values of the following parameters were measured before and after the procedure of pneumatic compression: the average speed and volume of blood flow during the cardiac cycle, resistance of arterial vessels and the amount of perfusion of the microcirculatory bed. Fig. 9 shows diagrams of the spread of the average blood flow rate over the period of the cardiac cycle before and after pressotherapy. As follows from the data shown in Fig. 9, the procedure of pneumatic compression leads to an increase in direct and reverse blood flow.

Fig. 10 shows diagrams of microcirculatory perfusion and arterial vascular resistance before and after pressotherapy. As follows from the data shown in Fig. 10, the procedure of pneumatic compression leads to an increase in the perfusion of the microcirculatory bed and a decrease in the resistance of arterial vessels.

Fig. 11 shows diagrams of changes in microcirculatory perfusion and arterial vascular resistance for all subjects based on the indications of LDF-grams and ultrasound Dopplerograms before and after the pressotherapy procedure.

As follows from the data shown in Fig. 11, the procedure of pneumatic compression for healthy subjects does not always increase the perfusion of the microcirculatory bed and reduces the resistance of arterial vessels. In the studies, an increase in microcirculatory perfusion was observed in about half of the subjects, which may be due to the choice of a group of healthy and relatively young test subjects. However, a correlation between an increase in microcirculatory perfusion and a decrease in arterial vascular resistance was observed in all cases.

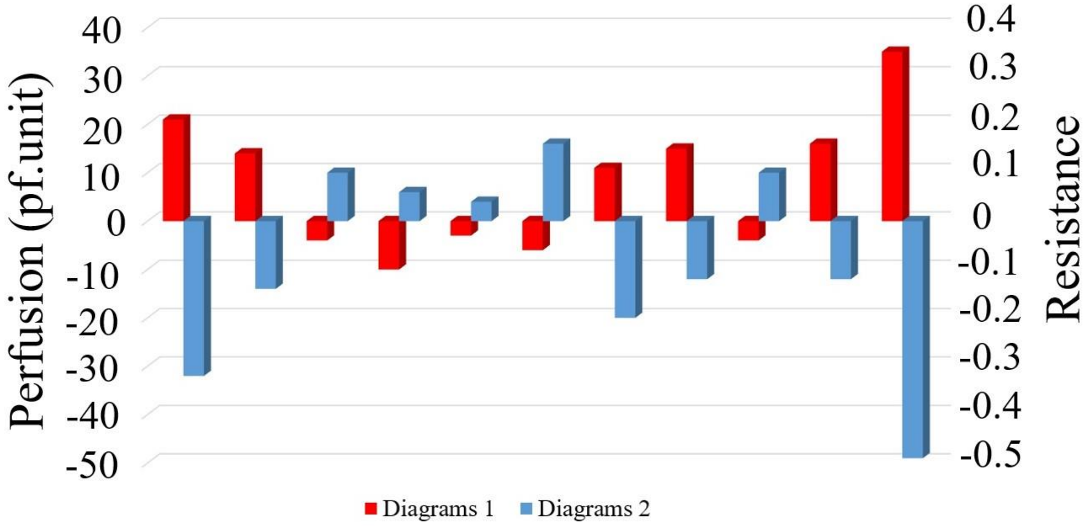


Fig. 11 Diagrams of changes in microcirculatory perfusion and arterial vascular resistance for all subjects: Diagrams 1 shows the difference between the indications of average perfusion before and after the pressotherapy procedure for each test subject according to LDF-gram. Diagrams 2 shows the difference between the indications of resistance before and after the pressotherapy procedure for each test subject according to ultrasound dopplerograms.

4 Discussion

The blood flow in the vessels is a constant stimulus for the production of substances involved in the autoregulation of vascular tone. Endothelial cells, in response to changes in shear stress, produce nitric oxide (NO), which contributes to the expansion of arteries, arterioles and veins. Suppression of sensitivity to blood flow leads to vasoconstriction and an increase in blood pressure [28, 29, 30]. Nitric oxide (NO) is the main endothelial relaxation factor, relaxing the smooth muscles of the vessels that maintain the tone of the vascular wall. Activation of endothelial cells in the body can occur both under the action of NO and of vasoactive substances and under the action of mechanical stimuli, for example, stretching or squeezing of the vessel during the IPC procedure. Under physiologically normal conditions, the activation of vasodilatory mechanisms is associated with the influence of shear stress [31–36].

Measurement of microcirculatory perfusion parameters with a laser Doppler flowmeter and blood flow velocity in arterial vessels with an ultrasound device performed on a group of healthy subjects aged 23 to 42 years showed an ambiguous change in these parameters after the pressotherapy procedure. Perhaps this is due to the high adaptation of blood vessels at a young age and the physical fitness of the vascular system in some of the test subjects.

In the studies, approximately half of the test subjects had an increase in perfusion of the microcirculatory bed and a decrease in resistance of arterial vessels. At the same time, with an increase in the perfusion of the microcirculatory bed, a decrease in the resistance of arterial vessels was observed. This pattern correlates well with the data on changes in the regulatory mechanisms of blood flow control. With an increase in the value of microcirculatory perfusion and an increase in the amplitudes of the endothelial, neurogenic and myogenic components of the LDF spectrum, a decrease in arterial vascular resistance is observed after pressotherapy, which indicates a decrease in vascular tone. Conversely, with a decrease in the perfusion of the microcirculatory bed, an increase in the resistance of arterial vessels was observed, which indicates an increase in vascular tone.

5 Conclusions

This study supplemented previously known facts about the effect of pneumatic compression on vascular hemodynamics based on the analysis of the signal of the laser Doppler flowmeter of the blood flow of the toe and Doppler ultrasound measurement of blood flow in the femoral artery.

The parameters of microcirculation of peripheral vessels and blood flow of arterial vessels at different time intervals, differing in occlusion modes, were compared. The results of measurements of the dynamics of vascular tone of the peripheral system of the leg corresponded to the dynamics of changes in the resistance of the arterial bed.

As follows from the measurements, the LDF-gram makes it possible to assess well enough the change in the nature of blood flow in the microcirculatory bed. However, to assess changes in the tone and resistance of the vascular system, a long time period of LDF recording is required. For a short-term assessment of the nature of blood flow in the microcirculatory bed (for the period of one cardiocycle), it is preferable to use ultrasound Dopplerograms, by changing the parameters of which it is also possible to assess changes in the tone and resistance of the vascular system

The experimental data presented in the article expand the information about hemodynamics in arterial vessels and microcirculation, allow us to better understand the relationship between the processes occurring in large vessels and capillaries during intermittent pneumatic compression, and can also become the basis for identifying patterns of diseases of the cardiovascular system.

Disclosures

The authors declare no conflict of interest.

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