Chapter

Aplication Arterial Oscilography to Study the Adaptive Capacity of Subject with COVID-19 in Primary Care

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Abstract

The aim of study is finding complex pathological process markers occurred in COVID-19. Adaptive capacity, cardiovascular features, autonomic, central nervous systems in 67 patients with severe COVID-19 were studied and evaluated using (suggested by authors) temporal, spectral, correlation analysis of arterial oscillograms (AOG). The method is based on mathematical analysis adaptation of electrocardiographic signal heart rate variability to arterial pulsation variability analysis recorded during blood pressure measurement using an electronic tonometer VAT 41–2. Received results were compared with AOG 480 healthy (including 68 people after exercising) and 26 patients in a closed ward at psychoneurological hospital. Study results showed patients with severe COVID-19 have disorders at (four) cardiovascular system (CVS) regulation levels. It's confirmed by lack of adequate sympathetic-adrenal response to a stressful situation due to severe COVID-19; higher than in healthy, parasympathetic part activity of autonomic nervous system. AOG spectral analysis revealed violation of management centralization, communication and coordination between CVS regulation levels. This leads to functional reserves decrease, low stress resistance of body and finally to a disease severe course and recovery processes. Arterial oscillography can be used to search markers of complex pathological processes occurred in COVID-19 and to improve methods of diagnosis, treatment, control of long-term results in clinical and family medicine.

Keywords: Arterial oscilography, adaptive capacity of the body, heart rate variability, COVID-19, primary care

1. Introduction

The urgency of the work is associated with pandemic COVID-19 [1, 2]. Due to a large-scale pandemic, the SARSCoV-2 virus has become the focus of researchers around the world [3]. To date, the pathogenetic mechanisms of development of COVID-19 are insufficiently studied [4]. Changes in the mental status of patients complicate the course of the disease [5–7]. The search for markers of complex pathological processes that occur in COVID-19 to improve methods of diagnosis, treatment, control of long-term results of this dangerous disease, which course largely depends on the adaptive capacity of the body is continued [3].

The level of adaptability of the body is one of the important health criteria [8]. The circulatory system with its neurohumoral control apparatus and self-regulation is a universal indicator of the adaptive activity of the whole body [9].

An available method for assessing global hemodynamic processes is blood pressure (BP) monitoring [8–16]. The response of blood vessels to compression indicates: the state of coordination between local self-regulatory mechanisms and the central, neurohumoral regulation of the cardiovascular system (CVS) [13–16]; the level of the autonomic nervous system (ANS) [11, 12]; functional ability of the heart, reflex reaction of CVS [14, 15]; the state of the peripheral vascular bed (tone, elasticity, resilience, patency) [15, 16], the activity of the mechanisms of the urgent reaction to compression (baroreceptors, chemoreceptors, ischemia reflex), etc [14–16].

Various invasive and non-invasive devices are used to record the arterial signal [17–22]. The introduction of information technology for its analysis makes it possible to significantly expand the informativeness of blood pressure measurement results [23–28]. The methods used in the mathematical analysis of heart rate variability (HRV) are promising for assessing arterial pulsations [19, 20, 22].

HRV is an integral indicator of the functional state of the body, reflecting the activity of the main physiological systems. It makes it possible to obtain information from 4 levels of CVS regulation activity: peripheral, autonomic, hypothalamic–pituitary, central nervous system [8, 9, 24–26]. A minimum number of levels of the system is involved with optimal regulation to ensure the adaptation of the body. The inclusion of higher levels of regulation is due to the inability of the previous ones to cope with their functions and, if necessary, to coordinate the activities of several subsystems. The higher the body's adaptive capacity, the more reliable the protection, the lower the risk of disease [8, 9, 12, 13, 28–30].

How do adaptation processes occur in patients with COVID-19? To date, the pathogenetic mechanisms of development of COVID-19 are insufficiently studied [4]. Our study is devoted to the determination of the adaptive capacity of the body and the mechanisms of their violation in the severe course of COVID-19 using arterial oscillography AOG.

2. Methods

The studies are based on the results of temporal, spectral, correlation analysis of AOG, registered during the measurement of BP. 67 patients with severe COVID-19 who were treated at the Ternopil Regional Phthisio-Pulmonology Center (main group) were examined. The control group (573 patients) included students of I. Horbachevsky Ternopil National Medical University and Volodymyr Hnatiuk Ternopil National Pedagogical University, as well as 28 patients who were treated in a Closed Department of Ternopil Regional Psychoneurological Hospital.

The main group included 67 patients with COVID-19, who were prescribed intensive care at the Ternopil Regional Phthisio-Pulmonology Center. Among them – 34 (50.7%) men and 33 (49.3%) women. By age – up to 20 years – 1 (1.5%), 21–40 – 19 (28.4%), 41–46 – 29 (43.3%), over 60 years – 18 (26.8%). The most typical complaints of patients on admission: fever and cough (100%), shortness of breath (79.1%), general weakness (71.6%), sore throat (47.8%), loss of smell (38.8%) and taste (23.9%), chest pain (31.3%), hyperhidrosis (28.4%). Complaints of depression or euphoria, insomnia, mood swings with aggression, sometimes psychomotor agitation were observed in 26.8% of patients. The study was conducted from March to September 2020.

The diagnosis was made on the basis of anamnesis, complaints, contact with other patients, laboratory tests, in particular the detection of genetic material (RNA) SARS-CoV-2 by polymerase chain reaction. A positive result of the polymerase chain reaction was observed in 57 (85.1%). Saturation is less than 95% – in 26 (38.8%), changes in the lungs on the radiograph – in 65 (97.0%) patients. Among laboratory indicators lymphopenia (34.3%) and accelerated ESR (41.8%) were noted. Nonspecific flora was found in the sputum of 19 people (28.4%). Among comorbidities, cardiovascular diseaes (46.3%). After performed treatment, patients in satisfactory condition were discharged to continue outpatient treatment.

AOG was recorded during BP measurement when patient's admission and during treatment. 282 AOGs were registered. The article presents an analysis of 68 of them (registered on admission).

The control group included 548 people aged 18–22 without health complaints (CG-1), selected by random, voluntarily, by oral consent. CG-2 included 28 patients treated in a closed department of a psychoneurological hospital. AOG was recorded in them during the BP measurement in the process of treatment. The research results were used for comparative assessment of the adaptive capacity of the cardiovascular, autonomic, central nervous systems of the experimental and control groups.

CG-1 consitsed of 3 groups. CG 1-a – the largest one, included 548 people aged 18–22 without health complaints. AOG was registered in them at rest. The obtained results were used for their general assessment as a standard of indicators of AOG of healthy and comparison with patients with COVID -19 [19].

CG 1-b included 54 persons of the control group, electrocardiogram (ECG) synchronously with AOG was recorded, who were also subjected to temporal and spectral analysis [9, 10, 20, 21]. The obtained results were used for comparative analysis of the correspondence of individual indicators of HRV electrocardiographic signal [8–10, 25] and AOG [19–22].

CG 1-c included 68 members of the control group (45 males and 23 females) aged 18–22 without health complaints. AOG was recorded at rest, immediately after the Ruffier test (30 squats in 45 second, [9, 27] and after 2 minutes of rest). Used to study the dynamics of AOG under the influence of stress (physiological) factors, assessment of adaptation mechanisms at the same time and comparison with indicators of patients with severe COVID-19.

CG-2 included 28 patients (aged 32–65) who were treated at the Ternopil Regional Clinical Psychoneurological Hospital (TRCPH), in a Closed Department for patients with mental disorders. The choice for monitoring CG-2 is due to the appearance in the information sources of indications for the presence of patients with COVID-19 mental disorders in the form of depression, euphoria, insomnia, mood swings with aggression, sometimes psychomotor agitation on the background of severe hypoxia [3, 5–7]. Complaints and indicators of temporal and correlation analysis of AOG in patients of the closed department were closest to AOG in patients with COVID-19 [21].

The CG-2 examination program included clinical and psychological studies (clinical and psychological interview, collection of psychological history). The main range of diagnoses: paranoid schizophrenia, bipolar disorder and severe depressive disorders with psychotic inclusions, requiring systematic and long-term, usually lifelong use of antipsychotropic drugs.

Arterial oscillography. The information technologies of temporal, spectral, correlation analysis of AOG registered at BP measurement (in shoulder compression growth) by means of the electronic tonometer VAT 41–2, ICS Techno [19–21] are developed in the work. For their analysis, the methods, indicators, terminology used in the study and evaluation of the results of mathematical analysis of HRV electrocardiographic signal were used [8, 9, 14, 24–34]. We analyzed both the indicators obtained during the compression of the shoulder, and in its individual (five) periods [19–22] to study and evaluate the process of adaptation of the body to shoulder compression.

Temporal analysis of oscillograms was performed by statistical analysis of the variability of the pulsation duration [19–21]. The values of indicators were studied: SDSD, RMSSD, pNN50, Mo, AMo, BP; IVR, VPR, IN, HVR index. Temporal analysis makes it possible to assess the state of the cardiovascular, autonomic nervous systems and the level of centralization management of their activities [8, 9, 14, 24–34].

Spectral (frequency) analysis of oscillograms. Realization of rhythmic activity of heart is possible only in certain phase relations between oscillating brain and cardiac processes. The control system of these rhythms is functionally and morphologically part of a single adaptive vertical, ensuring the adaptation of the body to conditions of external and internal environment [8, 9, 14, 24–34].

Spectral analysis of AOG was performed by determining the power of the spectrum in the range from 0 to 0.4 Hz: HF – high frequencies, LF, VLF, ULF (low, very low and ultra-low frequencies). Fast, slow, very slow and ultra-slow regulation is controlled by all links (parasympathetic, sympathetic, humoral, thermoregulatory, etc.). The influence of PSL is greater in fast, sympathetic - in slow and very slow, and humoral - in very slow and ultra-slow regulation [8, 9, 14, 24–34]. Due to indicators in the ranges: 0–4 Hz (Delta), 4–8 Hz (Theta), 8–13 Hz (Alpha), 13–25 Hz, 25 Hz and more Hz (Beta) were able to determine the level of brain activity. For this purpose, Fourier and Hilbert-Huang transform methods were used, which reflect the general and instantaneous adaptive response to shoulder compression [24, 34].

Correlation analysis. In the correlation analysis of the arterial oscillogram, the values of the Pearson correlation coefficient from 0.9 to 1 and − 0.9 to −1 were taken into account. The selected correlation values were subject to Cluster analysis (k-means clustering) [35–38], where the calculated correlation values were grouped separately in the middle of one experiment in 12 clusters.

2.1 Statistical methods

Statistical analysis of the data was conducted using the software package "OscEcgReoPuls", which was developed in "Matlab". The statistical significance of differences between the arithmetic average and relative values was estimated by Student's t-test (t) for the normally distributed data set. For samples that differed from the normal distribution, the Wilcoxon method was used. During the comparison of all variants of indicators within the limits of one experiment, we conducted a liaison analysis of the correlation coefficient (r) by the Pearson method [37, 38]. Statistical calculation was additionally processed in Statistica 10 software.

The urgency of the work is associated with the pandemic COVID-19. The obtained results will help doctors to pay attention to possible variants of mechanisms of pathogenetic processes at COVID-19, to plan preventive, diagnostic, medical, rehabilitation process [4].

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3. Results

The results of the temporal analysis of AOG in the main and control groups.

Temporal analysis of oscillograms (by analogy with HRV) reflects the state of the ANS and the level of management centralization of the cardiovascular system.

Healthy persons of CG 1-b. To confirm the reliability of AOG in healthy, the representatives of CG 1-b underwent a temporal analysis of AOG and ECG, recorded synchronously at rest in 54 people aged 18–22 (**Figure 1**).

Cases of strong correlation between Mo, heart rate are obtained. RMSSD (0.97 ± 0.02, p < 0.05) on synchronously recorded ECG and AOG make it possible to conclude that the noted indicators characterize not only the level of control of the cardiac activity, but also blood vessels "peripheral heart" [8, 9, 14, 24–34] and confirm the high informativeness of the selected research methods. Similar results were obtained in the analysis of ECG time indicators from literature sources. So, according to I. V. Babunts [25], the Mo index is (0.8 ± 0.03) s, RMSSD – (0.43 ± 0.19) s, which coincides with our results and confirms the reliability of the indicators obtained in the analysis of AOG registered by us.

The results of the temporal analysis of AOG of healthy, patients with COVID-19 and patients undergoing treatment in a closed department of a psychoneurological hospital (PPNH) separately and in comparison with each other are presented in **Table 1**.

Patients with COVID-19 (main group). As can be seen from **Table 1**, in patients with COVID-19 (compared to healthy) there was an increase in SDSD, pHN50, BP (P < 0.05) and Mo (P > 0.05), a decrease in IVR, IN (P < 0.05) and AMo (p > 0.05). The results obtained (by analogy with the HRV ECG [8, 9, 14, 25, 26]) indicate a slight increase in the activity of the parasympathetic link of the ANS, the lack of sympathetic-adrenal response and management centralization of the body defenses of patients with COVID-19. Homeostasis can be maintained by increasing the activity of the sympathetic division of the ANS [8, 9]. The abovementioned is a vegetative correlator of anxiety and leads to a decrease in functional reserves and stress resilience.

Healthy persons of CG 1-c (Ruffier test). To study the reaction of healthy people to an extreme situation, we used a physiological stress situation – physical activity (30 squats in 45 seconds, Ruffier test). Normally, physical activity promotes the activation

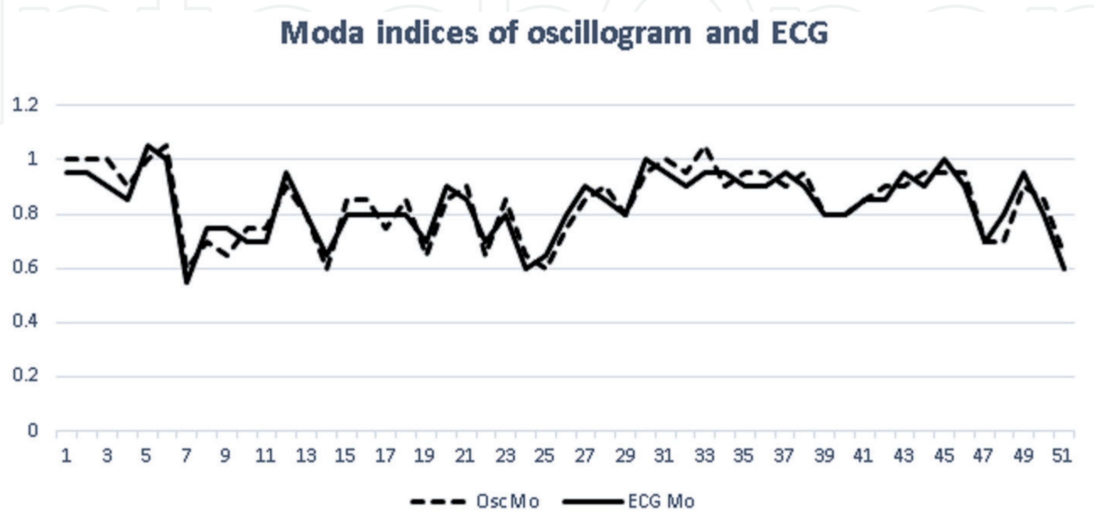

Figure 1.
Mode indicators (Mo), obtained by analysis of AOG and ECG. Note. On the X axis – A representative sample of 30 people, on the Y axis – On the left the duration of R-R intervals (s).

The studied indicator	The impact of growth on the stateANS**	COVID-19	Healthy	COVID-19 - healthy		PPNH	PPNH -3d		COVID-19 – PPNH	
		M±m	M±m	%	P	M±m	%	P	%	P
Mo, (s)	L-PS	0.848 ± 0.003	0.7945 ± 0.002	6.37	>0.05	0.7134+ 0.008	−10.15	>0.05	−15.87	>0.05
pNN50, (%)	L-PS	22.503 ± 0.094	14.894 ± 0.084	33.81	<0.05	26.10+ 0.247	75.24	<0,01	−1.39	>0.05
SDSD, (s)	L-PS	0.381 ± 0.002	0.16966 ± 0.001	55.64	<0.01	0.335+ 0.004	98.22	<0,01	−18.52	>0.05
AMo, (%)	L-S	31.68 ± 0.049	33.49 ± 0.143	−5.88	>0.05	31.19+ 0.407	−6.87	>0,05	−1.39	>0.05
IN, (y.o)	L-S	12.53 ± 0.037	22.80 ± 0.139	−32.04	<0.05	14.07+ 0.167	−38.0	<0,05	−18.52	>0.05
BP, (s)	L-S	0.89 ± 0.001	0.58 ± 0.003	25.64	<0.05	0.857+ 0.006	47.76	<0,01	9.87	>0.05
RMSSD, (s)	L-PS	0.38 ± 0.001	0.40 ± 0.002	−5.26	>0.05	0.335+ 0.004	−16.2	>0,05	−11.84	>0.05

*Note: * - informative value of the studied indicators: Mo (mode) - the range of oscillation duration values, which are most common (s); pHN50 - the percentage of consecutive intervals (separately highs and lows), the difference between which exceeds 50 ms; SDSD - standard deviation of differences between adjacent normal extremes (s); AMo (mode amplitude) - the number of intervals that correspond to the value of the mode (%); IN-voltage index of regulatory systems), BP (variation range) - the difference between the maximum and minimum values of the duration of the intervals between adjacent oscillations (s); RMSSD - the square root of the mean squares of the difference between adjacent extremes (s);*
***- value of increase (B) of indicators concerning activity of sympathetic (S) and parasympathetic (PS) links of ANS. More details are in the following text.*

Table 1.
Indicators of temporal analysis of AOG of healthy, patients with COVID-19 and persons undergoing treatment in a closed department of a psychoneurological hospital and their ratio.

of the central control circuit, accompanied by increased sympathetic activity and manifested by stabilization of the rhythm, reducing the scatter of the duration of cardio intervals, increasing the number of similar intervals [8, 9, 14, 25, 26, 34]. This is confirmed by the results of our research. A significant decrease in SDSD, pHN50 (**Figures 2-1a**), Mo ($P < 0.001$) (**Figures 2-2a**) and an increase in AMo ($P < 0, 01$), IVR, IN and HVR-index, standard deviation of oscillation amplitudes ($P < 0.001$) was registered on AOG in patients of group CG 1-c immediately after exercise. After 2 minutes of rest in most of the examined these indicators returned (or approached) to the initial ones (**Figure 2-b**).

For example, we demonstrate the dynamics of pNN50 and Mo registered in 30 members of group CG 1-c before, after exercise and in 2 minutes of rest (**Figure 2**).

As can be seen from **Figure 2**, after the Ruffier test, an increase in pNN50 (1) and Mo (2) and a return (approach) to the initial data after 2 minutes of rest is recorded. The observed dynamics of the studied indicators (by analogy with HRV on the ECG) indicates an increase in the tone of the sympathetic link of the ANS and increase the level of centralization of circulatory system management [8, 9, 14, 24–26, 34]. Return to the initial level of the studied indicators after 2 minutes of rest indicates a high level of regenerative capacity of the body after stress [27].

In patients with COVID-19, despite the extremely stressful situation, no similar dynamics of the studied parameters was observed. They were even lower than in healthy people at rest [9, 14, 24, 27, 34].

Patients of CG-2 (patients of psychoneurological hospital). As can be seen from **Table 1**, the results obtained of the temporal analysis of AOG in patients of the closed department in most cases had indicators similar to COVID-19, the difference between them was insignificant, had no reliability. This may indicate the same direction of pathological processes in patients with severe COVID-19 and in patients with mental disorders who are taking neuroleptics and are in a closed stay.

Spectral analysis of AOG indicators of the main and control groups.

The results of spectral analysis of AOG of healthy, patients with COVID-19 and PPNH are presented in **Table 2**.

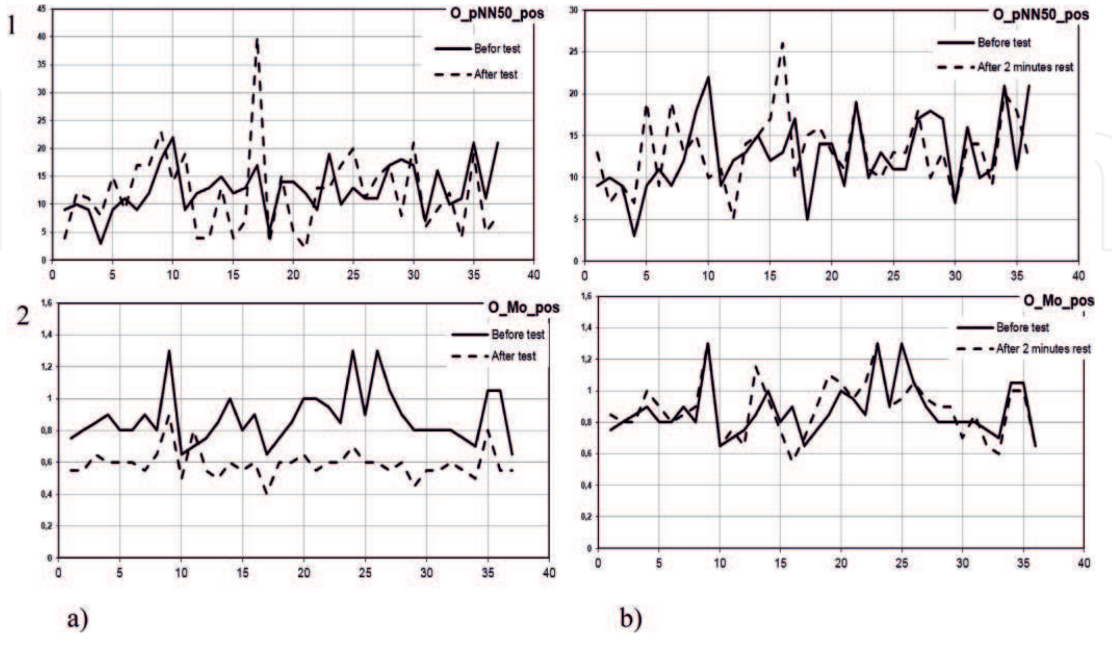

Figure 2.
Dynamics of pNN50 (1) and Mo (2): a) before and after the Ruffier test; b) before the Ruffier test and after 2 minutes of rest. Note. On the X axis – A representative sample of 30 patients; along the Y axis: in figure 2.1– pNN50 (%); figure 2.2. – Mo (s) in each of the patient. The dash line is before the exercise, the solid line is after it.

	Patients with COVID-19 (Co-19)	Healthy			Patients of psychoneurological hospital (PPNH)				
		Index M±m	Co-19-healthy	Co-19-healthy	PPNH				
					Index M±m	PPNH –healthy	PPNH –healthy	Co-19-PPNH	Co-19- PPNH
			%	P		%	P	(%)	P
%ULF	1.15 + 0.019	0.85 + 0.012	+26.1	<0.05	1.443 + 0.030	41.1	<0.01	–25.5	<0.05
%VLF	19.788 + 0.277	20.244 + 0.189	–7.36	>0.05	31/582 + 0.917	48.66	<0.01	–59.60	<0.01
%LF	9.27 + 0.065	10.24 + 0.064	–10.51	>0.05	8.543 + 0.169	–16.57	>0.05	+7.80	>0.05
%HF	69.814 + 0.418	67.64 + 0.349	+3.15	>0.05	57.718 + 1.373	–21.0	>0.05	+17.3	>0.05

*Note. * - informative value of the studied indicators:% HF - measure of high-frequency power,% LF - measure of low-frequency power,% VLF - measure of very low-frequency power,% ULF - measure of power of low-frequency domain in the general frequency spectrum. The influence of parasympathetic activity is greater in fast, sympathetic - in slow and very slow, and humoral - in very slow and ultra-slow regulation [8, 9, 14, 24–34]. These are described in more detail below.*

Table 2.
Indicators of spectral analysis of AOG of healthy, patients with COVID-19, patients of psychoneurological hospital (PPNH) and their ratios.

Patients with COVID-19 (main group). As can be seen from **Table 2**, there is a specific adaptive pattern in patients with COVID-19. A slight increase in the percentage of high-frequency domain power (% HF) in the total frequency spectrum (compared to healthy ones) is noteworthy. This (as well as the results of temporal analysis) indicates a shift in the autonomic balance in the direction of increasing the activity of the parasympathetic division of the ANS. While the degree of its inhibition (not the growth) is an indicator of increase of the tone of the sympathetic link of the ANS, necessary to maintain homeostasis [8, 9].

This was confirmed by the fact that the percentage of power of the LF spectrum was 10% lower than in healthy people. The LF spectrum is an indicator of the activity of the vasomotor center, reflects the sympathetic and parasympathetic effects from the level above the peripheral and to the centers of autonomic innervation in the medulla oblongata [9, 14, 24–26, 34]. They are regulated by the subcortical nodes and the cerebral cortex [8, 9].

% VLF was lower than in healthy. It reflects the influence of higher autonomic centers on the cardiovascular subcortical center. It can be used as a marker of the degree of connection of autonomous (segmental) levels of blood circulation regulation with suprasegmental, including pituitary–hypothalamic (with its nervous and humoral regulation) and cortical level [9, 24, 34].

It should be noted that according to the literature (according to HRV on the ECG) normally the power of % VLF in the total frequency range is 15–30% [9], that also corresponds to the indicators of our studies. The lack of dynamics of %VLF in patients with severe COVID-19 compared to healthy may indicate a violation of the above connections and functions of the corresponding levels of regulation.

At the same time, the %ULF in the total frequency spectrum is higher than in healthy (26%). The latter integrates and adapts the restructuring of the functional state of the body under the influence of external factors [9, 14, 24–26, 34]. The absence of a significant difference in %HF, %LF, %VLF in patients with COVID-19 and healthy may be due to the inability of the central control loop to integrate and adapt the restructuring of functional activity in severe disease. This can be attributed to the lack of necessary connections and coordination between the levels of regulation of the circulatory system in patients with COVID-19.

Since in this vertical the %VLF is already lower than in healthy ones (−3%), it is possible at this level the connection and coordination between the cortex and the lower levels of regulation of the circulatory system are suppressed.

It should be noted that recently there has been an assumption that patients with SARS-CoV-2 the cause of respiratory failure may be not only “damage to the lungs, but the brain stem, where the command center is located, which provides breathing even in unconsciousness” [36]. Probably, the information noted by us is a direction of markers search of the difficult pathological processes arising at COVID-19. Research is ongoing.

Healthy CG 1-c (Ruffier test). Spectral analysis of oscillograms (**Table 2**) showed that fast (HF) waves (indicator of the state of the parasympathetic link of the ANS) also dominated at rest in the general frequency spectrum.

Exercise helped to increase the percentage of spectrum power of low (%LF – $P < 0.01$) and ultra-low (%VLF – $P < 0.01$) frequencies, power of the Theta rhythm spectrum ($P < 0.01$) and reduce the level of high (%HF, $P < 0.01$) frequencies in the total frequency spectrum (**Figure 3**) At the same time, the synchronicity of changes in the %VLF and Theta spectra is noteworthy. This indicates an increase in the activity of the sympathetic division of the ANS after exercise, an increase in the centralization of the impact on the activity of the CVS and high stress resistance of the body in the examined patients [8, 9, 14, 24–26, 34]. After rest (**Figure 3**), the studied indicators returned (or approached) to the initial, which confirm the high

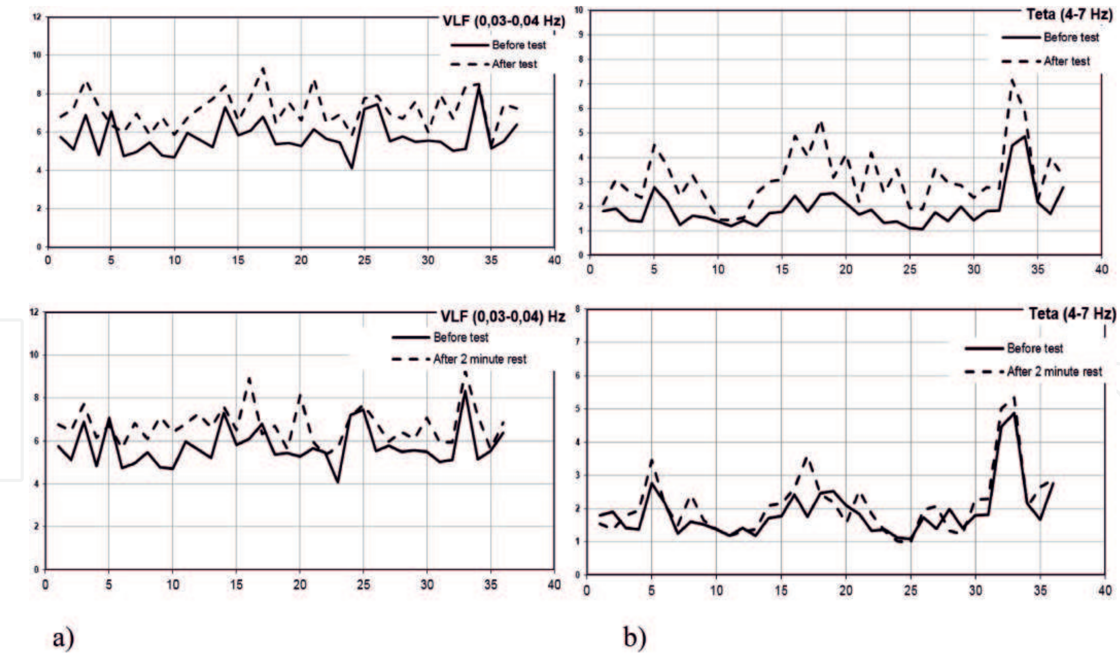

Figure 3.
Dynamics of VLF (left column) and Theta spectrum (right column) before, after the Ruffier test and after 2 minutes of rest. Note. On the X axis – A representative sample of 30 people, on the Y axis – The power of the spectrum (ms^2); top line – Before and after exercise. Bottom line – Before exercise and after 2 minutes of rest. Before exercise – A dash line, after exercise – A solid line.

adaptability of the body of the patients [8, 9, 14, 24–26, 34]. Its slowing down is about the decrease of functional reserves and low stress resistance of the organism, which is a vegetative marker of anxiety [9, 10, 19, 24, 34].

It was noteworthy that (despite the difficult stressful situation due to the severe course of the disease) in patients with COVID-19 the marked direction of the adaptive response of the healthy body was not observed. This confirms the violation of function, coordination and communication in the hierarchical regulation of the circulatory system, which leads to a decrease in functional reserves and low stress resistance of the body.

Patients of CG-2 (PPNH). Frequent analysis of AOG of PPNH (**Table 2**) revealed a slight decrease in the percentage of weight of the spectrum of high (HF), low (LF) and a significant increase in the percentage of VLF (49%) and ULF (41%) frequencies compared to healthy. The last two reflect the activity of the central control circuit by the functional capacity of the cardiovascular system [12, 13, 28–30]. Their activities are closely related to psycho-emotional tensions [9]. It should be noted that in the norm, the power of the central control circuits occurs as a result of the reaction to a stressful situations and disappears in their absence [12, 13, 28–30], confirmed by the results of our (Ruffier test) studies. It is possible to predict that long tension of activity of the central contour of regulation integrating and adapting reorganization of functional activity of the body, can cause mental disorders of the presented group of patients.

When comparing the spectral analysis of patients with COVID-19 and PPNH, the long-term tension of %ULF in the total frequency spectrum was common, which can be associated with the presence of mental disorders.

3.1 Correlation analysis of AOG of the examined patients in main and control groups

Patients with COVID-19 (main group). Analysis of correlations in COVID-19 showed a limitation in their number. If in healthy people (group CG 1-c) 28 pairs of correlates were registered, in patients with COVID-19 – only 10. There were no temporal analysis indicators in the correlation pairs. Waves LF, VLF, HF occurred, respectively, in 15, 15, 5 percent of cases. Among the indicators of brain activity in pairs of correlates Theta rhythm was most common, Alpha, Beta, Gamma (20%, 15%, 10%, 5% – respectively) – less common. The highest aspect that connects the waves of brain activity with human health is the ability to change these states according to the requirements of the situation [24, 34, 39, 40]. In patients with COVID-19, only maximal compression provoked a slight inclusion in the correlations of brain activity, indicating a profound violation of the ability to adapt to external factors.

Healthy, CG 1-c (Ruffier test). Before exersice, correlations were recorded in 28 pairs of correlates, mainly between the temporal parameters of the oscillogram: Mo, AMo, NN50, IVR. In addition, between the waves of high (HF) and the slowest (VLF) frequency of spectral analysis and with temporal parameters in different numerical and percentage values and periods of compression.

Immediately after the Ruffier test, 19 pairs of correlates were recorded. The correlations of rest mostly disappeared. Participation in HF correlates also decreased from 16 to 8 cases. New ones appeared – most often between the absolute and percentage content of Theta, Alpha, Beta, Delta brain rhythms. They occurred (respectively) in 16%, 13%, 8%, 8% of cases and were registered during the entire shoulder compression. Gamma waves were not met.

The obtained results indicate an increase in the rhythms of brain and cardiac activity in healthy people after exercise of coordinated wave activity. Two minutes after the squats, the restoration of the vast majority of correlations inherent in the indicators before exercise was registered in the examined patients.

If we compare the results of the correlation analysis of AOG of healthy people after physiological stress (exercise) and patients with COVID-19, the main differences are that the number of correlates in healthy people is greater, they include indicators of temporal, spectral analysis and brain activity. The reaction in healthy people was manifested from the beginning to the end of compression, in patients – only in its last phases, with maximum compression of the shoulder.

Patients of CG-2 (PPNH). Surveys showed that among the 4 departments of the psycho-neurological hospital on AOG, the fewest correlations were registered in patients treated in a closed department. Actually, they were subject to study. The most common components of 12 correlation pairs were: Beta (20%), Gamma (14%), Delta (11%) rhythms of brain activity. In correlation pairs, Beta and Gamma, VLF and LF were combined. Ultra-low frequencies (VLF) occurred in 20%, %LF and %HF – once. The correlations is noticeable only in the last phases of shoulder compression.

If we compare the correlation portraits of patients with COVID-19 and the closed department, the Theta waves predominate in the first and Beta and the appearance of Gamma waves – in the second. The limited number of correlations between the rhythms of brain and heart activity in both groups was noteworthy. At the same time, they appeared only in the last phases of shoulder compression, which indicates a deep violation of the adaptive capacity to the influence of external factors. According to the results of research, we can predict the common pathogenetic mechanisms of mental disorders in patients with COVID-19 and PPNH [5–7].

4. Discussion

The research is aimed at finding markers of complex pathological processes that occur in COVID-19 and lead to a significant reduction in functional reserves, low stress resistance of the body and as a result - to severe disease and recovery processes in COVID-19. For this purpose (proposed by the authors), the temporal, spectral, correlation analysis of AOG [19–21] was used. The method is based on the adaptation of the mathematical analysis of heart rate variability (HRV) of the electrocardiographic signal [8, 9, 14, 24–34]. to the analysis of variability of the arterial pulsations registered during measurement of arterial pressure by means of the electronic tonometer of BAT 41–2.

The AOG method was developed by the authors for the first time. It is based on the personal experience of scientific researches on morphological, temporal, spectral, correlation analysis of 3500 AOG people of different ages and health conditions. In healthy people AOG was registered at rest and after exposure to various (mechanical, thermal, physical, psychological, etc.) factors. Patients with diseases of the cardiovascular, respiratory and nervous systems were submitted to oscillographic examination [19].

To substantiate the reliability of the results of arterial oscillography, a comparative analysis of the results of mathematical analysis of ECG and AOG synchronously registered at rest (54 people). Cases of strong correlation between Mo, heart rate are obtained. RMSSD (0.97 ± 0.02, $p < 0.05$) on synchronously recorded ECG and AOG make it possible to conclude that the observed indicators characterize not only the level of control of the heart, but also blood vessels “peripheral heart” [8, 9, 14, 24–34] and confirms the high informativeness of the selected research methods which ECG does not register [19–21].

For this study, we used temporal, spectral, correlation analysis of AOG, conducted and evaluated in 67 patients with severe COVID-19. The results compared with AOG of 28 patients at the closed ward of the psychoneurological hospital and 548 healthy (including 68 people after exercise and after 2 minutes of rest).

In patients with COVID-19, dysfunction, coordination and communication at all (four) levels of regulation of CVS activity, which is a universal indicator of adaptive activity of the whole organism [9]. There was a significant decrease in functional reserves and low stress resistance of the body due to the lack of sympathetic-adrenal response and centralization of body defense control, disruption of communication and coordination at all levels of the adaptive vertical. This is confirmed by the following research results.

1. An increase in SDSD, pHN50, BP ($P < 0.05$) and Mo ($P > 0.05$), decrease in IVR, IN ($P < 0.05$) and AMo ($p > 0.05$) compared to healthy people. The results obtained (by analogy with the HRV ECG) [8, 9, 14, 25, 26, 34] indicate the absence of sympathetic-adrenal response and centralization of the defense in patients’ bodies with severe COVID-19. For comparison, the analysis of AOG was performed in 68 people without health complaints before and after exercise (Ruffier Test). After exercise (physiological stress), the statistically significant opposite dynamics of the above indicators was registered. This indicates an increase in the activity of the sympathetic ANS and the centralization of the impact on the CVS after exercise [9] and their recovery after 2 minutes of rest.

2. Examined patients with severe COVID-19 in terms of time and spectral parameters of AOG had the activity of the parasympathetic division of the ANS even higher than in healthy people at rest. While homeostasis can be maintained by increasing the activity of the sympathetic division of the ANS, which can be assessed by the degree of inhibition of its parasympathetic division [8, 9]. And the state of the autonomic response to external influences is the most accurate marker of reactivity and resistance of the organism [9, 14, 24, 27, 34, 39].

3. There was a decrease (compared to healthy) power % VLF, very low-frequency domain in the general frequency spectrum, a marker of the degree of connection of autonomous (segmental) levels of blood circulation regulation with suprasegmental, including pituitary–hypothalamic and cortical levels [9, 34]. Its decrease (compared to healthy) in severe COVID-19 may indicate a violation of the above links and functions of the relevant levels of regulation.

4. The growth of power % ULF, ultra-low-frequency domain in the total frequency spectrum, which integrates and adapts the restructuring of functional activity of the organism under the influence of external factors [9, 14, 24–26, 34] against the background of decreasing% VLF levels suppress the relationship between the cerebral cortex and the lower levels of regulation of CVS activity.

5. Analysis of correlations [35–38] in COVID-19 showed a limitation of their number both separately in the segments of time and spectral indicators, and between them. If 28 pairs of correlates were registered in healthy people (group KG 1-s), then only 10 in patients with COVID-19 were noted. At the same time, they appeared mainly in the last (maximum) phases of shoulder compression. This confirms a significant reduction in the adaptive capacity of the body, when only the maximum compression of the shoulder had the ability to bring them out of this state.

6. The appearance of mental disorders in patients with COVID-19 [5–7]. provoked us to compare the adaptation model which their body builds under the influence of the disease and in patients of a closed ward of a psychoneurological hospital who are constantly taking neuroleptics. At the last ones, it was found most similar to other members of psychiatric wards. There was no significant difference in the results of temporal, correlation analysis of AOG and a significant increase in both cases% ULF in the total frequency spectrum (whose activity is closely related to psycho-emotional stress). This may indicate the same direction of pathological processes in both groups of subjects and justify the presence of mental disorders in patients with COVID-19.

7. The conducted researches gave the chance to reach the set purpose and to inform readers about the following.

    A. At patients with COVID-19 mechanisms of decrease in adaptive ability of an organism, disturbance of a functional condition of cardiovascular, autonomic, central nervous systems, mental frustration are revealed and proved. The obtained results will help doctors to pay attention to possible variants of mechanisms of development of pathogenetic processes at COVID-19 and to consider them at a choice of means of correction of the noted disturbances and to include in the protocol of diagnosis, treatment and rehabilitation of patients with COVID-19 at inpatient and outpatient stages of treatment.

    B. Informative and effective application of arterial oscillography (according to D.V. Vakulenko, L.O. Vakulenko), which can be a mean of finding markers of complex pathological processes that occur in COVID-19. It can be used to improve methods of diagnosis, treatment, rehabilitation, control of long-term results of this dangerous disease in clinical and family medicine.

    C. For implementation in practice new models of electronic blood pressure monitors it is necessary to provide the possibility of using the AOG method (D. Vakulenko, L. Vakulenko). The device has the ability to record the values of cuff pressure during compression and export the values for further analysis. AOG includes: measurement of blood pressure, sending data to the personal account of VEP-service Oranta-AO, obtaining the results of the analysis in the form of values of indicators and recommendations of the expert system for further decision-making by the doctor.

8. The authors continue research in various fields, collaborate with physiologists, cardiologists, neurologists and other specialists for further substantiate AOG methods.

9. Prospects for research on this problem: morphological analysis of AOG, comprehensive analysis of the dynamics of AOG patients with COVID-19, testing of the expert system to support decision-making at the stages of inpatient treatment and rehabilitation after the disease in outpatient treatment, under the supervision of a family doctor.

5. Conclusion bioethics commission

Protocol No. 7, Meeting of the Bioethics Commission of I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine of January 25, 2021.

Resolved: Materials of the article by D.V. Vakulenko L.O. Vakulenko L.A. Hryshchuk I.M. Sas On topic: “The use of arterial oscillography to study the adaptive capacity of the body of patients with COVID-19”, on examination of patients, performing laboratory, scientific researches meets requirements of norms and principles of bioethics.

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Conflict of interest figures and tables

The authors declare no conflict of interest.

Authors’ contributions

Vakulenko D. V. developed the concept and design of the work. Registered AOG downloaded to a PC and subjected to temporal, spectral, correlation analysis using the OscEcgReoPuls program, developed by the authors of the study; conducted statistical processing, analysis, interpretation of the results; participated in the design of the article.

Vakulenko L. O. – co-author of the methods of temporal, spectral, correlation analysis of AOG; made a significant contribution to the concept and design of work; conducted analysis and interpretation of AOG data; participated in the design of the article.

Hryshchuk L. A. conducted examination, treatment, registration of AOG in patients with COVID-19; participated in the analysis and interpretation of AOG data.

Sas L. M. conducted examination, treatment, registration of AOG in patients of the closed department of the psychoneurological hospital; participated in the analysis and interpretation of AOG data.

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