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# Changes in blood flow oscillations associated with COVID-19 as measured by wearable laser Doppler flowmetry

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## ABSTRACT

The paper is aimed at comparing blood microcirculation parameters of conditionally healthy volunteers and patients undergoing rehabilitation after COVID-19 to identify possible blood flow dysregulation that may result from the disease. A system of wearable laser Doppler monitors was used to conduct the study. The study demonstrated an increase in overall oscillatory blood flow activity in the group of patients compared to the control group, with especially pronounced differences in the neurogenic, respiratory and cardiac ranges. It had been shown that optical non-invasive technologies have the potential for further application in the research related to COVID-19.

**Keywords:** laser doppler flowmetry, wearable blood perfusion sensors, COVID-19, SARS-CoV-2, blood flow oscillations, wavelet analysis

## 1. INTRODUCTION

In late 2019, sporadic cases of infection with a new acute respiratory disease called COVID-19 have been reported. Its distribution has resulted in more than 600 million confirmed infections and more than 6 million deaths (according to the Johns Hopkins University Coronavirus Resource Centre). More than 3 years after the virus began to spread, the pandemic is still far from over. Although primarily considered a respiratory disease, coronavirus also affects numerous body systems, including the cardiovascular, nervous, urinary, and gastrointestinal systems.[1] The most common and noticeable symptoms are shortness of breath, general weakness, disturbances in the sense of smell and taste, coughing, and unstable blood pressure. The varied course and outcome of the disease, the possibility of a lethal outcome, and the sudden spikes in the rate of spread, necessitate a more detailed study of its effect on the body's various systems and subsystems, first and foremost on the blood microcirculatory system.

In modern clinical practice, one of the most common methods of noninvasive optical measurement of blood microcirculation parameters is the method of laser Doppler flowmetry (LDF). LDF is used for the diagnosis and subsequent detection of abnormalities in the functioning of the blood microcirculation system in a variety of diseases.[2,3] This method makes it possible to assess the functioning of blood microcirculation regulatory mechanisms based on the analysis of frequency bands, characterizing the contribution of various factors in the reflected signal. There are usually distinguished 5 mechanisms, each of which forms the oscillations of the microvasculature with definite frequencies:[4] endothelial (0.0095-0.021 Hz), neurogenic (0.021-0.052 Hz), myogenic (0.052-0.145 Hz), respiratory (0.145-0.6 Hz) and cardiac (0.6-2 Hz).

This work aimed to compare blood microcirculation parameters of conditionally healthy volunteers and patients undergoing rehabilitation after COVID-19 to identify possible blood flow dysregulation that may result from the disease.

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## 2. MATERIALS AND METHODS

The study was conducted with the participation of two groups of volunteers: the first group consisted of 13 conditionally healthy volunteers who were measured in 2019 even before the spread of the disease (control group). The volunteers in the control group can thus be said to have never experienced COVID-19. The second group consisted of 23 volunteers who were undergoing rehabilitation in a private health facility after suffering an acute coronavirus infection. Three of them had been infected with COVID-19 in a severe form. A distributed system consisting of 4 wireless wearable microcirculatory blood flow analyzers implementing LDF method “LAZMA PF” (LAZMA Ltd, Russia; in EU/UK this device made by Aston Medical Technology Ltd., UK as “FED-1b”)[5] was used for data recording in this study. LDF signal recording was performed for 10 minutes in the supine position with analyzers attached to the wrists and shins in conditions of comfortable ambient temperature for the volunteers. To calculate the amplitudes of blood flow oscillations, a mathematical apparatus of wavelet transform was used.

## 3. RESULTS AND DISCUSSION

Figure 1 shows the results of the analysis of microcirculatory blood flow oscillations in the patient group and the control group, measured in wrists and shins.

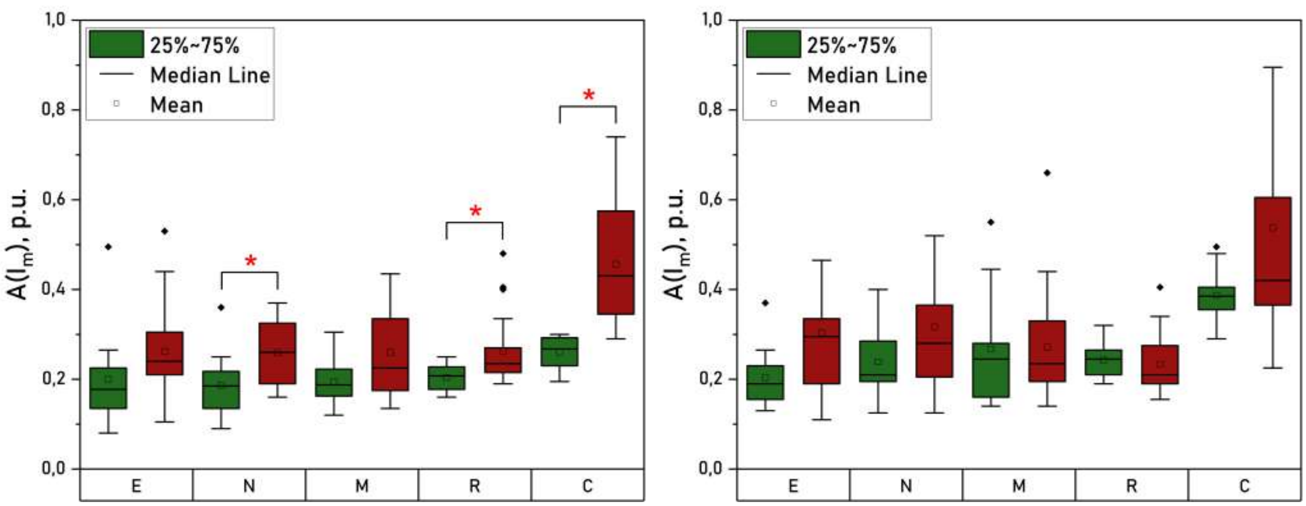


Figure 1. Box plots of blood flow oscillation amplitudes measured in wrists (left panel) and shins (right panel). The green boxes correspond to the data from the control group, the red boxes correspond to the data from the patient group. * - The significance of the difference between the values was confirmed with $p < 0.05$ according to the Mann–Whitney U test.

As can be seen from the data presented, an increase in overall oscillatory blood flow activity was noted in both upper and lower extremities, with statistically significant differences in the neurogenic, respiratory and cardiac ranges in wrists. It should be noted that the patient group was characterised by a reduced level of an index of blood microcirculation, directly measured by LDF.

Since respiratory and cardiac blood flow oscillations are related to the functioning of the venous and arterial sections of the microvascular bed, we suggest that the increase in their amplitudes in the patient group may be related to the dilatation of arterioles and venular overflow due to arterial blood discharge, resulting in more dilated venules. These changes in the microcirculatory system may result from the reduced neurogenic vascular tone recorded in this study.

Indeed it was shown in the works of other authors that patients with COVID-19 are characterized by significantly dilated blood vessels,[6] which, however, decrease over time.[7]

## 4. CONCLUSION

The present work demonstrates the use of laser Doppler flowmetry and peripheral blood flow oscillation analysis for the diagnosis of vascular abnormalities in patients who have undergone COVID-19. The findings confirm changes in microcirculatory blood flow regulation mechanisms after the disease, which may be associated with the persistence of poor patients' well-being in the long term after the recovery. The study has shown that optical non-invasive technologies have the potential for further application in research related to COVID-19.

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