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Evaluation of the pleth variability index, perfusion index, and other physiological parameters after COVID-19

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Abstract. – OBJECTIVE: The aim of this study was to observe the changes in pleth variability index (PVI), perfusion index (PI) and other hemodynamic parameters in adult individuals who had had Coronavirus disease 2019 (COVID-19) and were currently living a normal life. A further aim was to draw attention to the fact that some hemodynamic changes after COVID-19 may cause long-term health problems.

PATIENTS AND METHODS: A total of 174 adult individuals who had had COVID-19 and were currently living a normal life and 56 healthy individuals with similar demographic characteristics who had not had COVID-19 were included in the study. The PI, PVI, oxygen saturation (SpO_2), pulse rate (PR), total hemoglobin (Hgb), oxygen reserve index (ORI), and blood pressure values were measured by Masimo Radical 7. The data of individuals who had and did not have COVID-19 before were compared.

RESULTS: The mean PVI ($p = 0.008$) and PI ($p < 0.001$) were significantly lower in people who had been exposed to COVID-19. Likewise, the mean of ORI, SpO_2, and SpOC values was observed to be significantly lower in participants exposed to COVID-19 disease ($p < 0.001$, $p < 0.001$, and $p = 0.006$, respectively). The PVI had a positive correlation with body mass index (BMI) (r = 0.263, $p < 0.001$) and a negative correlation with SpO_2 (r = -0.194, $p = 0.003$) and PR (r = 0.190, $p = 0.004$).

CONCLUSIONS: The PVI, PI, and other physiological parameters could potentially be useful for monitoring COVID-19 patients and evaluating their response to therapy. We believe that people who have been exposed to COVID-19 may be more susceptible to other diseases; therefore, they should be subjected to regular clinical checks.

Key Words:
Coronavirus disease 2019, Pleth variability index, Perfusion index, Physiologic parameters.

Introduction

Coronavirus disease 2019 (COVID-19) is a viral infection that can affect many different systems and organs. Some people with this disease develop symptoms and complications related to the respiratory system. However, COVID-19 has other effects and may cause changes in a number of physiological parameters in some patients, including the heart, circulatory system, and other organs[1,2].

COVID-19 is a severe immunological consequence of SARS-CoV-2 infection, which is considered to be responsible not only for lung disease but also for multiple organ dysfunction syndrome1. A great concern is that, among people infected with COVID-19, the effects have lasted much longer than what was expected from a typical airborne viral illness. The causes of these "post-COVID" symptoms and clinical development, which has recently been called the "post-acute sequelae of COVID-19", remain unknown[3,4].

Vital signs show the physiological state of an individual's vital organs, namely the brain, the heart, and the lungs. In order to evaluate the physiological functions of the patients, vital signs should be evaluated at regular intervals. In recent years, noninvasive monitoring methods have increasingly been preferred to invasive methods. Since its inception, pulse oximetry has proven indispensable in measuring tissue oxygenation and monitoring the heart rate.

The pleth variability index (PVI) and the perfusion index (PI) measure patients' clinical status and monitor their response to treatment. The PVI is a value based on the ripple pattern of the pulse wave as measured by pulse oximetry. This value provides information about a person's blood circulating volume and fluid status[2,5].

The PVI is one of the new, noninvasive, easily applied, and easily interpreted monitoring methods. It is a noninvasive oximetric indicator of PI variability and has been used as an alternative to predict vascular tone and the intravascular fluid requirement. The PVI is shown as a percentage; the lower the number, the less variability in PI in respiratory cycles[6]. The PI is a measure used

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in many pulse oximeters and is a relative assessment of the pulse strength in the specific applied area. Its advantages are that it is non-invasive and can yield continuous measurement[7]. PI changes are due to various causes, such as epidural blocks, pain stimuli, sympathetic discharges, and decreased peripheral perfusion. Cyclic changes in blood pressure and in the pleth waveform may also occur owing to changes in intrathoracic pressure associated with intravascular volume. Cyclic changes in blood pressure and pulse oximetry pleth waveform are observed during airway obstruction; the severity of obstruction correlates with the magnitude of the cyclic waveform[8]. In COVID-19 patients, conditions such as lung injury and breathing difficulties can affect fluid balance, so monitoring by the PVI and the PI may be important.

The aim of this study was to observe the changes in the PVI, PI and other hemodynamic parameters in adult individuals who had had COVID-19 and were currently living a normal life. A further aim was to draw attention to the fact that some hemodynamic changes after COVID-19 may cause long-term health problems.

Patients and Methods

Ethics

Ethical approval of our study was obtained from the Clinical Research Ethics Committee of Mardin Artuklu University (Consent number: 2023/5-30, Consent date: 03.05.2023). Demographic, and clinical data records were obtained with the consent of the participants between 4 May 2023 and 5 June 2023. All subjects included in the study were voluntary participants. Before the study, the participants were informed about all the details of the study, both orally and in writing. Informed consent forms were signed by the volunteers who agreed to participate.

Study Design and Population

Our study was a prospective, cross-sectional, and observational study. The minimum sample size required, based on similar work in this country, was at least 100 participants to achieve 80% statistical power with a 5% margin of error and a 95% confidence interval. Thus, 174 adult individuals between the ages of 18 and 80 who had COVID-19 and were currently living a normal life (Group 1: 94 females and 80 males) and 56 healthy individuals with similar demographic characteristics (Group 2: 28 females and 28 males) who had not had COVID-19 were included in the study, making a total of 230 participants. Patients who were found to be negative in all COVID-19 tests performed on their health cards, who were not diagnosed with COVID-19 and who did not have a history of febrile illness during the pandemic period were included in group 2.

Exclusion Criteria

A non-invasive procedure was used for the study. The study was carried out in Mardin City. Patients with liver and/or kidney failure, tuberculosis, or chronic obstructive pulmonary disease (COPD), obese patients [body mass index (BMI) 30 and above], patients with trauma, cancer, uncontrolled diabetes, or decompensated heart failure, and those with a history of chronic pain were excluded from the study.

Study Tool

The Masimo Radical-7® Pulse CO-Oximeter (Masimo Corp., Irvine, CA, USA) device was used for the study. Necessary training in the use of non-invasive devices was given beforehand by the relevant company staff. The tool measured the PI, PVI, oxygen saturation (SpO_2), pulse rate (PR), total hemoglobin (Hgb), oxygen reserve index (ORI), and blood pressure values. PI describes the ratio of fluid blood to other non-fluid blood, when using infrared rays on the body. The PI value is the value calculated by looking at the absorption of infrared rays with a pulse oximeter. It can be measured from the patient's fingertip, hand, toe, or ear. It also gives information about the peripheral vasomotor tone. It shows the perfusion status of the continuous tissue in the PI-applied area for an instant and a certain time interval.

With the saturation probe of the Masimo oximetry device, the PVI, PI, ORI, SpO_2, and SpOC were non-invasively measured from the fourth distal phalanx of the non-dominant hand with the hand at heart level and recorded as primary data, after waiting for 10 minutes. Age, gender, pulse, blood pressure, and hemoglobin values were recorded as simultaneous secondary data. The BMI was calculated by measuring the weight of each individual with a portable scale and the height with a tape measure.

Statistical Analysis

The data were statistically analyzed using SPSS (version 26.0; IBM Corp., Armonk, NY, USA). Power analysis was used to determine the total number of cases that would be included in the study. Comparisons were made between the

PVI, PI, ORI, and other hemodynamic and demographic variables of the groups. Under conditions $\alpha = 0.05$ of PVI standard deviation with 80% power, the number of people needed was calculated as 50 for each group. The normal distribution was determined using the Shapiro-Wilk test. Mean ± standard deviation for continuous variables, frequency, and percentage for categorical variables were evaluated. The continuous variables were analyzed using the Student *t*-test, while categorical variables were analyzed by the Chi-square tests. The Pearson's correlation test was used to determine the relationship between the variables. *p*-values of the tests below 0.05 were considered statistically significant.

Results

Table I shows the distribution of age, BMI, PVI, PI, ORI, and other independent variables of the participants with and without COVID-19. The mean age of the participants who had had COVID-19 was 45.82 ± 12.71 years, and the mean age of the participants who had not had the disease was 43.57 ± 12.42 years ($p = 0.249$). The BMI for the two groups was 26.40 ± 3.20 and 25.89 ± 2.94 ($p = 0.201$), respectively. 80 (46%) men and 94 (54%) women had had COVID-19 disease, while 28 (50%) men and 28 (50%) women had not had COVID-19 ($p = 0.646$).

The mean PVI was 25.45 ± 8.73 in participants who had had COVID-19, while it was 27.76 ± 4.24 in those who had not (Figure 1). The PVI was found to be significantly lower in people who had been exposed to the disease ($p = 0.008$). The mean of PI values was 0.95 ± 0.57 in the COVID-19 patients and 3.36 ± 0.69 in the non-COVID-19 patients (Figure 2), and the difference was significant ($p < 0.001$). Likewise, the mean of ORI, SpO_2, and SpOC values was observed to be significantly lower in participants exposed to COVID-19 disease ($p < 0.001$, $p < 0.001$, and $p = 0.006$, respectively).

Table I. PVI, PI, and other noninvasive physiological parameters and demographic characteristics of the participants.

Parameters	Group 1 (n = 174, %) [N, % or Mean ± SD]	Group 2 (n = 56, %) [N, % or Mean ± SD]	*p**
Gender, Men/Women	80 (46%)/94 (54%)	28 (50%)/28 (50%)	0.646
Smoking, Yes/No	74 (42.5%)/100 (57.5%)	26 (46.4%)/30 (53.6%)	0.535
Age, year	45.82 ± 12.71	43.57 ± 12.42	0.249
BMI, kg/m^2	26.40 ± 3.20	25.89 ± 2.94	0.201
PR, beat/min	82.22 ± 9.74	82.96 ± 11.99	0.639
SpHb	12.47 ± 1.35	12.75 ± 1.80	0.405
PVI	25.45 ± 8.73	27.76 ± 4.24	0.008
PI	0.95 ± 0.57	3.36 ± 0.69	< 0.001
ORI	0.05 ± 0.03	0.14 ± 0.09	< 0.001
SpO_2	96.46 ± 1.31	97.64 ± 2.02	< 0.001
SpOC	15.64 ± 1.84	16.46 ± 2.23	0.006

*$p < 0.05$ considered statistically significant for Student *t*-test. BMI: Body mass index, ORI: Oxygen Reserve Index, PI: Perfusion Index, SpO_2: Oxygen Saturation, PVI: Pleth Variability Index, PR: Pulse Rate, SpOC: Oxygen Content SpHb: Total Hemoglobin.

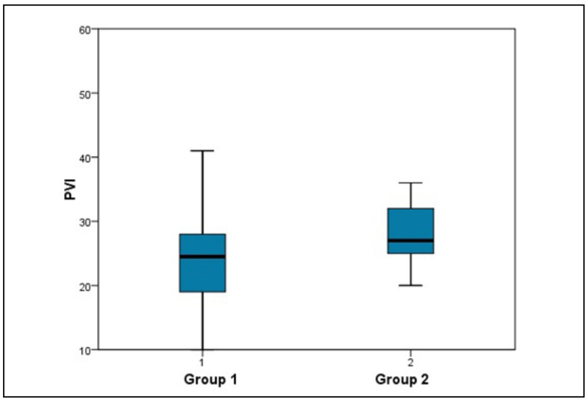

Figure 1. The mean of PVI values in participants who have had COVID-19, and in those who had not.

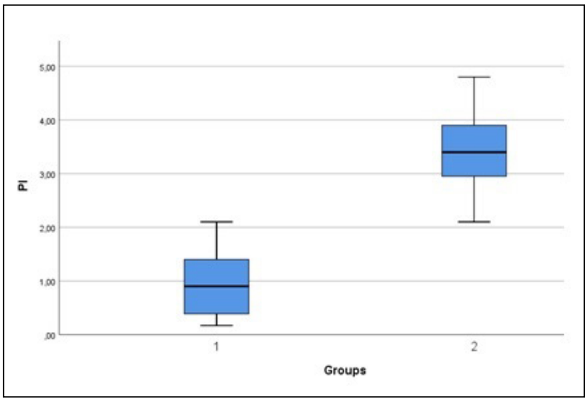

Figure 2. The mean of PI values participants who have had COVID-19, and those who have not.

Table II. Correlation of PVI and PI with other parameters.

	Age	BMI	SpO_2	SpHg	ORI	PR	SpOC
PVI							
r	0.029	0.263	-0.194	0.059	-0.102	-0.190	0,013
*p***	0.660	< 0.001	0,003	0.375	0.122	0.004	0.847
PI							
r	-0.096	-0.122	0.365	0.188	-0.109	-0.30	0.257
*p***	0.148	0.065	< 0.001	0.004	0.098	0.656	< 0.001

*p*** < 0.05 considered statistically significant for Pearson's correlation test; r: correlation coefficient, BMI: Body mass index, ORI: Oxygen Reserve Index, PI: Perfusion Index, SpO_2: Oxygen Saturation, PVI: Pleth Variability Index, PR: Pulse Rate, SpOC: Oxygen Content SpHb: Total Hemoglobin.

The correlation between the PVI and the PI with other independent variables is shown in Table II. The PVI had a positive correlation with BMI (r = 0.263, $p < 0.001$) and a negative correlation with SpO_2 (r = -0.194, $p = 0.003$) and PR (r = 0.190, $p = 0.004$). In addition, the PI had a significant positive correlation with SpO_2 (r = 0.365, $p < 0.001$), Hgb (r = 0.188, $p = 0.004$), and SpOC (r = 0.257, $p < 0.001$).

Discussion

Our study showed that the averages of the PVI, PI and ORI values were significantly lower in the 174 adult individuals who had previously experienced COVID-19. Likewise, in these individuals, the average of SpO_2 and SpOC values was observed to be significantly lower than among those who had not had the disease.

Studies[9,10] have shown that measurements such as static hemodynamic central venous pressure and mean arterial pressure are weaker in evaluating volume status than dynamic indices such as arterial pressure waveform and stroke volume in patients who will or may not respond to volume expansion. However, the operator-dependent, more invasive nature of dynamic indices has made the PVI preferable in recent years.

Cyclic changes have been shown[10] to reflect changes in the patient's intravascular volume level. Cyclic changes in blood pressure and in the pleth waveform may also occur because of changes in intrathoracic pressure associated with intravascular volume. Steele et al[11] noninvasively showed that cyclic changes in blood pressure and in the pulse oximetry pleth waveform are seen in airway obstructions and that the size of the cyclic waveform correlates with the severity of the airway obstruction.

Demirci et al[9], in their study on healthy volunteers, showed that there was a statistically significant change in PVI values for the supine position and working position in both passive leg lift and Trendelenburg position groups. While a decrease in PVI values was predicted at the beginning of their study, the results showed an increase in PVI values after the working position in both groups.

In another study[12], the relationship between PVI values, attack severity and response to treatment was investigated in the management of acute obstructive airway disease in children. In this study, it was stated that PVI, which was measured blindly from clinical severity scoring in triage, increased with the severity of attacks and there was a significant difference in PVI values between the groups. Hospital protocols such as targeted therapy and enhanced recovery after surgery are used in many healthcare settings, including our hospital, with non-invasively PVI and PI parameters for fluid management as part of larger interventions designed to improve patient care and safety. In a study[13] conducted in France, a blood transfusion protocol based on SpHb was used together with a targeted therapy protocol with PVI, and monitoring with SpHb and PVI integrated into the vascular filling algorithm was reported to be associated with earlier transfusion. In this study, it was shown that 30- and 90-day mortality at the whole hospital scale decreased by 33% and 29%, respectively.

Patients who have had COVID-19 may experience chronic lung fibrosis and proliferation, as well as damage to alveolar epithelium and endothelial cells[14]. In one study[15], it was reported that there was a deterioration in diffusion capacity, following restrictive ventilation defects in the lung, which was associated with the severity of the disease. Studies[16,17] on pre-COVID-19 coronavirus infections have reported that patients may experience permanent organ deterioration in months or even years after discharge. Unfortunately, there is not enough literature reporting post-COVID-19 pulmonary capacity or cardiovascular physiological parameters. In COVID-19 patients, oxygen levels may drop, and adequate oxygen delivery to tissues may be impaired owing to lung damage and breathing difficulties. Therefore, monitoring parameters such as the PI is important to assess patients' oxygenation status and to see if they are responding appropriately to treatment[10,18,19]. Saini et al[20], in their study on infants with neonatal sepsis, emphasized that PI values were significantly lower in non-survivors than in survivors and that PI should be interpreted together with other vital signs in order to make clinical decisions.

In our study, the averages of PVI and PI values were found to be clearly low. Likewise, the averages of ORI, SpO_2, and SpOC values were found to be significantly lower in participants who had had COVID-19. In the literature, there is, to our knowledge, no similar study of post-COVID-19 patients. Although there are studies[10,17,18] on the PVI and PI in different patient groups, such as intensive care patients, pre-operative patients, and emergency room patients, our study appears to be the first cross-sectional and observational study on patients who have maintained their normal daily activities. We think the study is important for this reason.

However, more research is needed to evaluate the PVI, PI, ORI, and other physiological parameters after COVID-19. COVID-19 is a complex disease and, owing to the diversity of the systems it affects, may have different effects on each individual. Therefore, care should be taken in the use and interpretation of these parameters, which should be considered together with a comprehensive clinical evaluation.

Limitations of the Study

Undoubtedly, our study has many limitations. The study was non-invasive, blood gas and some other laboratory parameters were not included. The study would have had more validity if it had included more participants or been multicenter. Moreover, the participants were living normal daily lives, a cohort that has not yet been examined in the literature.

Conclusions

According to our results, non-invasive measures showing physiological values such as PVI, ORI and PI were lower in participants who had had COVID-19 and continued their daily activities after discharge. Although our results need further corroboration, we think that they are important even in their current form and contribute to the literature. We believe that people who have been exposed to COVID-19 may be more susceptible to other diseases; therefore, they should be subjected to regular clinical checks. The PVI, PI, and other physiological parameters could potentially be useful for monitoring COVID-19 patients and evaluating their response to therapy. However, more research is needed on the correct use and interpretation of these parameters. Each patient should be evaluated individually, and the evaluation should be used in conjunction with a comprehensive clinical assessment.

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Availability of Data and Materials

The datasets generated during and/or analyzed during the current study are not publicly available because it contain private personal information, but are available from the corresponding author on reasonable request.

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Conflict of Interests

The authors declare there are no conflicts of interest.

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Infomed Consent

An informed consent form was obtained from the participants before participating in the study.

Ethics Approval

Ethical approval of our study was obtained from the Clinical Research Ethics Committee of Mardin Artuklu University (Consent number: 2023/5-30, Consent date: 03.05.2023).

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