





Can Peripheral Perfusion Index (PPI) Predict Disease Severity in COVID-19 Patients in the Emergency Department?

Mustafa Korkut¹  Cihan Bedel¹ Fatih Selvi¹ Ökkeş Zortuk¹ 

¹Department of Emergency Medicine, Health Science University, Antalya Training and Research Hospital, Antalya, Turkey

Address for correspondence Mustafa Korkut, MD, Department of Emergency Medicine, Health Science University, Antalya Training and Research Hospital, Kazım Karabekir Street, postal zip code: 07100, Muratpaşa, Antalya, Turkey (e-mail: drmustafakorkut@gmail.com).

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Abstract

Background Coronavirus disease 2019 (COVID-19) causes significant mortality and morbidity in severe patients.

Objective In this study, we aimed to examine the relationship between COVID-19 disease severity and peripheral perfusion index (PPI).

Patients and Methods This prospective observational study included COVID-19 patients admitted to the tertiary hospital emergency department. Basal clinical and demographic data of the patients and PPI values at the time of admission were recorded. The patients were categorized to severe and nonsevere groups according to clinical severity. The relationship between COVID-19 severity and PPI was examined in comparison with the control group.

Results A total of 324 patients who met the inclusion criteria were analyzed. COVID-19 (+) was detected in 180 of these patients. Ninety-two of the COVID-19 (+) patients were in the severe group, and 88 of them were in the non severe group. Note that 164 COVID-19 (–) patients were in the control group. PPI average was found to be 1.44 ± 1.12 in the severe group, and 3.69 ± 2.51 in the nonsevere group. PPI average was found to be significantly lower in the severe group than the nonsevere group ($p < 0.01$) As for the nonsevere group and control group, PPI averages were found to be 3.69 ± 2.51 and 3.54 ± 2.32 , respectively, and a significant difference was determined between the two groups ($p < 0.05$). PPI COVID-19 severity predicting activity was calculated as area under the curve: 0.833, sensitivity: 70.4%, and specificity: 71% ($p = 0.025$) at 2.2 cutoff value.

Conclusion The results of our study showed that PPI is an easy-to-apply and useful parameter in the emergency department in determining the severity of COVID-19 patients.

Keywords

- ▶ COVID-19 severity
- ▶ peripheral perfusion index
- ▶ emergency department

Introduction

Coronavirus disease 2019 (COVID-19) pandemic caused severe morbidity and mortality across the world.^{1,2} COVID-19 is an

infectious disease that has high incidence and infectivity, and 81% mild, 14% severe, and 5% critical clinic rates. Sepsis, septic shock, and multiple organ failure may develop in severe and critical patients, and it can cause poor prognosis and

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mortality.³⁻⁵ Therefore, it is important to predict, which patients are at high-risk of severe disease and mortality.⁶ When the literature is examined, there have been many studies on the risk factors and clinical parameters showing the level of seriousness of COVID-19.⁷ In recent years, innovative improvements have emerged on pulse oximetry devices to understand the disease severity and the continuous monitoring of COVID-19 patients.⁸ Peripheral perfusion index (PPI), one of these indicators, is a noninvasive simple procedure measured by a pulse oximetry device that is used in patient care and provides continuous perfusion monitoring.⁹ PPI changes can take part in patients receiving early critical care.⁸ In the clinical evaluation of PPI microcirculation, photoelectric plethysmography is the measurement-based estimated value. It is the measurement of pulsatile and non-pulsatile flows connected to the liquid in the peripheral tissue on the body.¹⁰ It also provides information about peripheral vasomotor tonus. It shows the instantaneous and fixed time perfusion status of the permanent tissue on the PPI applied area. It can be easily monitored as noninvasive by pulse oximetry probe from fingertip, hand, toe, and ear lobe.¹¹ There are studies in the literature showing that the PPI changes are closely associated with the cardiac output dynamic changes.¹² Therefore, in the cases that cardiac output cannot be monitored, PPI, which can be monitored as noninvasive as a pulse oximetry method, can be a guide in the critical patient care.⁸ As far as we know in the literature, there are no studies on PPI showing the severity of the disease in COVID-19 patients. Therefore, in this study, we aimed to investigate the relevance of the severity of COVID-19 with the PPI value.

Patients and Methods

Study Design and Participants

This is a prospective observational study conducted at a single center. Patients with COVID-19 suspicion or diagnosis were also admitted to the tertiary university hospital between January and July, 2021. COVID-19 was diagnosed based on World Health Organization guidelines.¹³ Clinical classification is done based on the international guideline and categorized as mild and severe. Mild (defined in this study as no pneumonia) and severe (defined as dyspnea, respiratory frequency ≥ 30 breaths/min, oxygen saturation $SpO_2 \leq 93\%$), are based on the use of a high-flow nasal cannula, non-rebreather mask, noninvasive mechanical ventilation, or lung infiltrates $>50\%$ in thoracic computed tomography (CT).¹⁴ Patients were divided into three groups according to the clinical classification as group 1 severe, group 2 as nonsevere, and group 3 as the control group. According to the clinical classification, the mild group was included in the nonsevere group. COVID-19 quantitative reverse transcription-polymerase chain reaction (RT-PCR) control group was made from negative patients. Data of the patients were obtained who match the criteria to be included in the study with COVID-19 suspicion or diagnosis aged ≥ 18 . All the patients who do not have clinical COVID-19 suspicion (trauma, cardiac arrest, aortic dissection, pulmo-

nary embolism, decompensated heart failure), patients whose PPI cannot be measured (peripheral vascular disease, autonomous neuropathy, center hypothermia, nail deformity), all the patients aged <18 , patients with no obtained data, and negative patients synonymous with thorax CT COVID-19 (RT-PCR) were accepted as exclusion criteria.

Data Collection and Measurements of Variable

Patient demographic data, laboratory, and thorax CT results were recorded in a data form with a study protocol. After the first evaluation of the patient by an emergency specialist, ground class and/or pneumonic infiltration presence was evaluated as COVID-19 pneumonic symptom as a thorax CT screening method.

For the identification of severe acute respiratory syndrome coronavirus 2, RT-PCR was performed on samples taken from the upper respiratory tract (nasopharyngeal and oropharyngeal secretions). In accordance with the recommendations of the Turkish Republic Ministry of Health's Diagnostic Treatment Guide, Coronex COVID-19 QPCR (DS BIO and NANO Tech. Inc., Ankara, Turkey) was used as a standard method.

Heart rate (HR), respiration rate (RR), systolic (SBP), and diastolic blood pressure (DBP) were measured by the emergency nurses who took the patients during the appeal. It was measured with BP oscillometric noninvasive technique in the supine position after 5-minute rest. Bedside thorax motion was counted with inspiration for RR 1 minute HR, PPI was measured after the patient had a rest for 5 minutes in the supine position. The PPI, HR bedside was measured with Masimo Radical-7 pulse oximetry device (Masimo Corporation, Irvine, California, United States) by pulse oximetry probe from the dominant hand's 2nd or 3rd fingertip. After waiting for 30 seconds, a constant value seen on the monitor was recorded. Shock index was measured with HR/SBP , and mean arterial pressure (MAP) was measured with $[(DBP \times 2) + SBP]/3$ formula technique.

Statistical Analysis

Standard deviation and mean values were calculated for continuous variables; median and interquartile range were calculated for nonparametric data. Each of the independent variables was compared by applying the chi-square test and, if suitable, with an independent *t*-test. Dependence power of statistically meaningful ($p < 0.05$) independent variables with the disease severity was evaluated by using regression. All the variables in the data form were analyzed using descriptive statistics. Descriptive statistical analysis of all variables was studied using SPSS 21.0. The optimum cutoff value of immature granulocyte count, which shows the diagnostic relationship in COVID-19 patients, was examined by receiver operating characteristic (ROC) analysis.

Results

A total of 324 patients who met the inclusion criteria were analyzed. COVID-19 (+) was detected in 180 of these patients. Ninety-two of the COVID-19 (+) patients were in

the severe group, and 88 of them were in the nonsevere group. Note that 164 COVID-19 (-) patients were in the control group. The age average of the patients was found to be 59.83 ± 15.58 for the severe group, 44.09 ± 17.08 for the nonsevere group, and 41.83 ± 15.36 for the control group and there was a significant difference between the groups ($p < 0.001$). Fifty-seven (62%) of the male patients were in the severe group, 43 (48.9%) in the nonsevere group, and 91 (55.5%) in the control group. There was no significant difference between the groups in terms of gender ($p = 0.210$). The most common comorbid diseases were hypertension, diabetes mellitus, coronary heart disease, and chronic kidney failure; and a significant difference between the groups was found. The baseline characteristics of the patients are shown in ►Table 1. Sixty-three (68.5%) of the patients in the severe group were accepted to the intensive care unit, and in 20 (21.7%) patients, inpatient mortality was seen. The average hospitalization time (length of stay) was found to be 10 days.

PPI average was found to be 1.44 ± 1.12 in the severe group and 3.69 ± 2.51 in the nonsevere group. PPI average

was found to be significantly lower in the severe group than the nonsevere group ($p < 0.01$). As for the nonsevere group and control group, PPI averages were found to be 3.69 ± 2.51 and 3.54 ± 2.32 , respectively, and a significant difference was determined between the two groups ($p < 0.05$). However, there was no significant relationship between the severe group and the control group. While DBP and MAP averages were determined to be significantly lower in the severe group than the nonsevere group, a significant difference could not be found when compared with the control group. However, when the nonsevere group was compared with the control group, a significant relationship was determined. While SBP and RR averages were determined to be significantly higher in the severe group than the nonsevere group, a significant difference could not be found when compared with the control group. However, when the nonsevere group was compared with the control group, a significant relationship was determined. PPI and other vital parameters and their relations with the groups are shown in ►Table 2.

In multivariate logistic regression analysis age (odds ratio [OR] 1.243, 95% confidence interval [CI] 1.168 to 1.319,

Table 1 Baseline characteristics of patients

Variables	Severe group 1 (n = 92)	Nonsevere group 2 (n = 88)	Control group 3 (n = 164)	p
Age (y)	59.83 ± 15.58	44.09 ± 17.08	41.83 ± 15.36	<0.001 ^{ab}
Male gender, n(%)	57 (62)	43 (48.9)	91 (55.5)	0.210
Previous history, n(%)				
Hypertension	29 (31.5)	7 (8.0)	17 (10.4)	<0.001 ^{ab}
Diabetes mellitus	21 (22.8)	7 (8.0)	20 (12.2)	0.011 ^{ab}
Cerebrovascular diseases	4 (4.3)	1 (1.1)	1 (0.6)	0.080
Coronary heart disease	18 (19.6)	1 (1.1)	6 (3.7)	<0.001 ^{ab}
COPD	3 (3.3)	2 (2.3)	1 (0.6)	0.271
Chronic kidney failure	6 (6.5)	0 (0)	1 (0.6)	0.002 ^b
Liver disease	0 (0)	0 (0)	1 (0.6)	0.577
Presenting symptoms				
Fever	20 (21.7)	22 (25.0)	33 (20.1)	0.670
Cough	59 (64.1)	43 (48.9)	60 (36.6)	<0.001 ^{ab}
Dyspnea	71 (77.2)	13 (14.8)	17 (10.4)	<0.001 ^{ab}
Generalized pain	38 (41.3)	50 (56.8)	93 (56.7)	0.040 ^{ab}
Fatigue	38 (41.3)	62 (70.5)	110 (67.1)	<0.001 ^{ab}
Loss of appetite	14 (15.2)	14 (15.9)	11 (6.7)	0.035 ^a
Nausea	8 (8.7)	19 (21.6)	23 (14.0)	0.048 ^a
Diarrhea	5 (5.4)	9 (10.2)	17 (10.4)	0.375
Vomiting	3 (3.3)	13 (14.8)	9 (5.5)	0.006 ^{ac}
Anosmia	1 (1.1)	9 (10.2)	4 (2.4)	0.003 ^{ac}
Loss of taste	2 (2.2)	9 (10.2)	11 (6.7)	0.085
Discharge from ED	19 (20.7)	82 (93.2)	164 (100)	<0.001 ^{abc}

Abbreviations: COPD, chronic obstructive pulmonary disease; ED, emergency department.

^ap, compared with the 1–2.

^bp, compared with the 1–3.

^cp, compared with the 2–3.

Table 2 Comparison of PPI and other vital parameters of patients with COVID-19 between the groups

Variables	Group 1 Severe (n=92)	Group 2 Nonsevere (n=88)	Group 3 Control (n=164)
Perfusion index ^{a,c}	1.44 ± 1.12	3.69 ± 2.51	3.54 ± 2.32
Shock index	0.78 ± 0.25	0.70 ± 0.17	0.70 ± 0.14
Vital signs at ED presentation			
Heart rate (beat/min)	95 (31)	90 (23)	92.5 (20)
Respiratory rate ^{a,c}	25.85 ± 10.71	11.97 ± 1.15	11.84 ± 0.86
SBP (mmHg) ^{a,c}	122.5 ± 22.9	130.4 ± 18.1	132.9 ± 19.1
DBP (mmHg) ^{a,c}	73.21 ± 14.99	80.83 ± 16.49	83.18 ± 15.31
MAP (mmHg) ^{a,c}	105.83 ± 18.66	114.41 ± 15.55	116.15 ± 16.56
Temperature (°C)	36.4 (0.8)	36 (0.6)	36 (0.2)

Abbreviations: COVID-19, coronavirus disease 2019; DBP, diastolic blood pressure; ED, emergency department; MAP, mean arterial pressure; PPI, peripheral perfusion index; SBP, systolic blood pressure.

^a*p* < 0.01 compared with the 1–2.

^b*p* < 0.01 compared with the 1–3.

^c*p* < 0.05 compared with the 2–3.

Table 3 Logistic regression analysis of the risk factors affected the severity of COVID-19 patients

Variables	Logistic regression analysis	
	OR (95% CI)	<i>p</i>
Age	1.243 (1.168–1.319)	<0.001
Male	0.525 (0.431–0.619)	0.448
Diabetes mellitus	2.130 (1.084–4.183)	0.028
Dyspnea	1.499 (1.051–3.250)	<0.001
Perfusion index	0.934 (0.895–0.937)	<0.001

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; OR, odds ratio.

p < 0.001), PPI (OR 0.0934, 95% CI 0.895 to 0.93, *p* 0.001), dyspnea (OR 0.470, 95% CI 0.218 to 1.010, *p* 0.001), and diabetes mellitus (OR 2.130, 95% CI 1.1084 to 4.183, *p* = 0.028) were defined as independent predictors that could predict diagnostic associations in COVID-19 patients (► **Table 3**).

PPI COVID-19 severity predicting activity was calculated by drawing a ROC curve. For PPI, it was calculated as area under the curve: 0.833, sensitivity: 70.4%, and specificity: 71% (*p* = 0.025) at 2.2 cutoff value (► **Fig. 1**, ► **Table 4**).

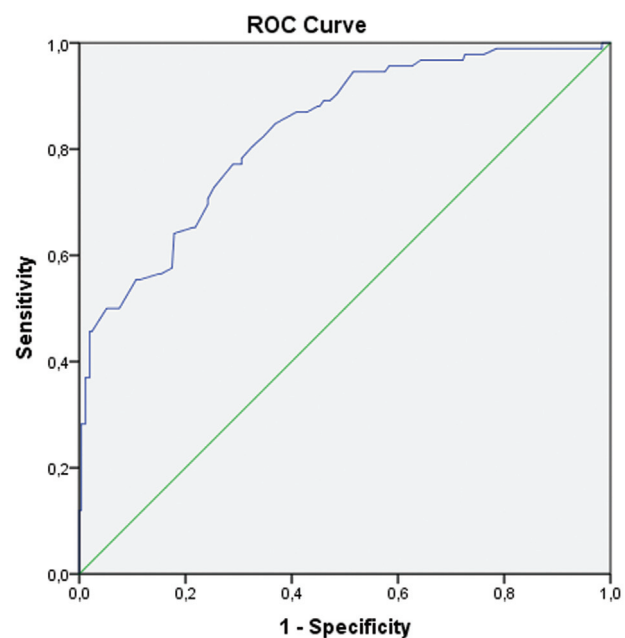
Discussion

COVID-19 overwhelmed health systems around the world by spreading rapidly. There are many studies in the literature

Table 4 Perfusion index as diagnostic accuracy of prognostic parameter with the best predictive cutoff in severe COVID-19 patients

	AUC	Cutoff value	Sensitivity (%)	Specificity (%)	95% CI	<i>p</i> -Value
Perfusion index	0.833	2.2	70.4	71	0.784–0.881	0.025

Abbreviations: AUC, area under the curve; CI, confidence interval; COVID-19, coronavirus disease 2019.

**Fig. 1** Receiver operating characteristic curve analysis of the peripheral perfusion index (PPI) to show predicting activity in the severity of coronavirus disease 2019 (COVID-19).

on clinical, laboratory, and radiologic findings to understand the seriousness and mortality of the infected patients.¹⁵ Premature recognition and early treatment of severe COVID-19 patients in the emergency services is important for emergency specialists.¹⁶ However, making decisions in a

limited time and recognizing major COVID-19 patients can be a difficult situation in emergency services. In some studies, PPI has been shown as a parameter that can be used in the triage field for patient acceptance and mortality predictor of major patients in emergency services.^{17,18} Thereby, in this study, we wanted to show that PPI can predict the seriousness of COVID-19 in emergency services since it can be measured with an easy and fast method during the appliance. In our study, we found that PPI is a parameter that is measured during the appliance at emergency service and shows the seriousness level of COVID-19.

In the literature, some demographic data has shown that COVID-19 has higher severity of the clinical course. Advanced age is an important parameter between the clinical seriousness scores.^{15,19} In a retrospective study done in Italy, the average age of 1,591 severe COVID-19 patients were found to be 63.²⁰ In our study, similarly, mean age in the severe group was found to be 59.83 ± 15.58 . Studies in the literature show that obesity, hypertension, and diabetes poses a risk for severe COVID-19.²¹ Similarly, in our study, hypertension, diabetes mellitus, coronary heart disease, and chronic kidney failure are seen mainly in the severe group. In the studies in the literature, COVID-19 mortality rates of inpatients vary between 4.3 and 15%.^{5,22} Therefore, high mortality rates in severe patients suggest that early diagnosis and early treatment are needed. In our study, we found the inpatient mortality rate was found to be high in severe patients (21.7%). We believe that comorbid situations in the patients of our study may have affected this result.

Fluid overload in the patients who developed sepsis and septic shock should be avoided and the treatment should be balanced with sufficient liquid to provide tissue perfusion and cardiac output. Hence, Surviving Sepsis Campaign guideline also suggests using the parameters that estimate preload in COVID-19 patients since they can recover septic shock results.²³ PPI is the reflection of pulsatile blood flow that shows the blood flow ability to tissues in the circulation. If there is high pulsatile flow, pulse intensity increases and a higher PPI value is monitored. Therefore, local blood flow fluctuations can be seen on the monitor as a reflection of tissue perfusion continuously by PPI.²⁴ Resuscitative liquid treatment in COVID-19 patients and that PPI changes can be used for the monitoring of intensive care patients is reported in some studies.⁸ It is also shown in the studies that PPI is a prognostic marker in critical patients. In their study on PPI's prognostic performance on hospital outcome prediction, Daş et al found that PPI average of 2.70 (1.2–5.00) is significant to show hospitalization and 30-day mortality.²⁵ There was no known study on COVID-19 seriousness and PPI relevance when we planned this study. Therefore, we thought that we can foresee COVID-19 seriousness by measuring the PPI value during the appeal in the emergency service. In a study done in a critical patient department with 202 resuscitative patients, when <0.6 cutoff value of PPI is calculated, it was found that it is related with poor results of resuscitative and 30-day mortality with sensitivity of 61% and specificity of 90%.²⁶ Also, the study done by Lima et al on intensive care patients shows that $PPI < 1.4$ (sensitivity 81% and specificity

86%) is a strong indicator of damaged tissue perfusion.¹⁰ Again, in another study done in emergency service, it was found that PPI is at the normal range when used with synthetic cannabinoid (SC) (3.16 ± 3.26 [0.19–14]). But, it was shown that it has predictivity in the group who used SC more than 2 hours at the PPI 1.99 cutoff value with 81.4% sensitivity and 83.3% specificity.²⁷ In the study done by Akdur et al, PPI relevance with predicting mortality in COVID-19 patients was analyzed and it was found that it has significant relevance in predicting 14- and 90-day mortality at the <1.5 cutoff value.²⁸ Similar to the literature, in our study, PPI was found to be significant to show COVID-19 seriousness with 70.4% sensitivity and 71% specificity at the 2.2 cutoff value.

Even though we determined that PPI can show COVID-19 seriousness, there were some restrictions. First, the PPI value can change according to the blood flow fluctuations since it reflects tissue perfusion continuously. Only one PPI measurement was done in our study, and since we do not know the duration until the application, it may have affected our results. Furthermore, PPI value after discharge was not measured in the study. This created a limitation for us in terms of understanding the safety of the parameter. Second, since it is hard to find a control group in emergency service, COVID-19 (-) were accepted as the control group from the applicants and it may have affected the PPI value. Therefore, we suggest to researchers to find a cutoff PPI value with periodical and repetitive measurements in broad-populated and multicentered further studies. And, we also believe that it would be helpful to create a healthy volunteer control group, have a PPI value, and make comparisons.

Conclusion

The outcomes of our study have shown that the monitoring of PPI value is an easy and fast method to be used in the emergency service during the application. It also shows that it can be used as a parameter to predict COVID-19.

Availability of Data and Materials

All data, tables, and figures used in the manuscript were prepared originally by the authors; if otherwise, the sources are cited. Furthermore, the authors can share any data and materials that are reported in the study.

Informed Consent

Written informed consent was obtained from the patients or their family members.

Human Rights

This research does not harm human rights regarding Ethical Principles for Medical Research Involving Human Subjects.

Authors' Contributions

The authors conducted the study and developed the manuscript and approved its final version.

Medical practices: C.B., M.K., Concept: C.B., M.K., F.S., Design: C.B., M.K., Data collection or processing: F.S., O.Z., Analysis or interpretation: C.B., M.K., Literature search: C.B., F.S., M.K., O.Z., Writing: C.B., M.K.

Ethical Approval

Permission was obtained from the local ethics committee for the study at Health Science University Antalya Education and Research Hospital with decision date and number was 04.03.2021 and 1/35.

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None.

Conflict of Interest

None declared.

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