Correlation between Perfusion Index and Left Ventricular Output in Healthy Late Preterm Infants

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Abstract

Objective The perfusion index (PI) is a noninvasive marker derived from photoelectric plethysmographic signals in pulse oximetry in the evaluation of peripheral perfusion. This study was aimed to determine the correlation between PI and left ventricular output (LVO) in healthy late preterm infants at 48th hour of life.

Study Design With new generation pulse oximeter (MASIMO Rad 7 Oximeter) pre- and post-ductal PI values were recorded from healthy late preterm babies at the 48th hour of life. PI was determined simultaneously with LVO as measured by transthoracic echocardiography.

Results A total of 50 late preterm babies were included in the study. The mean gestational age of the cases was 35.4 ± 0.7 weeks and the birth weight was 2,586 ± 362 g. Mean pre- and post-ductal PI values at the postnatal 48th hour of babies’ life were found to be 2.0 ± 0.9 and 1.7 ± 1.1. The mean LVO value was 438 ± 124, LVO/kg 175 ± 50. When the LVO value was normalized according to the babies’ body weight, there was no statistically significant correlation between the pre- and post-ductal PI and the LVO/kg value (r <0.2, p >0.05 in both comparisons).

Conclusion There was no correlation between pre- and post-ductal PI and LVO values in healthy late preterm infants. This may be due to the failure of the LVO, a systemic hemodynamic parameter, to accurately reflect microvascular blood flow due to incomplete maturation of the sympathetic nervous system involved in the regulation of peripheral tissue perfusion in preterm babies.

Key Points
- No correlation found between PI and LOV in preterm babies.
- LVO cannot adequately reflect peripheral blood flow.
- Sympathetic nervous system is immature in preterm infants.

Keywords
- perfusion index
- left ventricular output
- late preterm infants
- echocardiography

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Congenital heart diseases (CHD) are the most common birth defects, with a prevalence of approximately 1% percent of births. About 25% of these babies have a critical CHD that requires catheter-based intervention or surgery in the first year of life, and late diagnosis is associated with higher mortality and morbidity. Therefore, peripheral capillary oxygen saturation (SpO2) should be determined by pulse oximeter from pre- and postductal regions in infants who are approximately 48 hours old for early diagnosis of critical CHD as a universal neonatal screening strategy in line with the recommendations of the American Academy of Pediatrics, the American Heart Association, and the American College of Cardiology. A major disadvantage of this screening method is that it cannot detect CHD even if it is at a critical level in patients with low left ventricular output (LVO). To detect these cases, it is recommended that SpO2 measurement be supplemented with perfusion index (PI) during screening.

PI is an easy-to-apply, inexpensive, and noninvasive method used in clinical practice to evaluate peripheral perfusion of critical patients. Peripheral PI derived from photoelectric plethysmographic signals in a new generation pulse oximeter has been reported to show real-time changes in peripheral blood flow, and is a numerical value that occurs when infrared signals at the monitored location are reflected relative to different tissue components. It is achieved by the ratio of variable light absorption (AC) due to pulsatile arterial blood flow to constant light absorption (DC) due to non-pulsatile blood flow in venous blood, connective tissue, skin, bone, and other tissues. Changes in PI are thought to be related to changes in peripheral vascular tone and cardiac output. It is suggested that PI may be a possible marker for screening critical CHD with low LVO. But it is not known whether there is a correlation between PI and LVO in late preterm infants. A literature review showed that there was only one study in term infants on this topic, but no study in late preterm infants.

The aim of this study is to determine whether there is a correlation between PI and LVO in healthy late preterm infants.

**Materials and Methods**

This study included clinically and hemodynamically stable late preterm infants (34^(0/7)~ and 36^(0/7)~ week gestational age) born in a university hospital between August 2019 and February 2020. Study was approved by Muğla, Şitki Koçman University Ethics Committee (date: May 02, 2019 and decision no: 08/II). The babies were considered hemodynamically stable according to the following criteria: normal skin color, respiratory pattern and cry, normal postural, muscle tone and movements, and no need for fraction of inspired oxygen (FiO₂) ≥0.25, heart rate (HR) 100 to 160 beats/min, respiratory rate 40 to 60 breaths/min, absence of >20-second apnea episodes. During the first 12 hours after birth, the clinical and laboratory evaluations were performed to assess Score for Neonatal Acute Physiology—Perinatal Extension (SNAPPE-II). Neonates with a SNAPPE-II score of >18 were excluded from the present study. In addition, exclusion criteria were as follows: maternal gestational diabetes, pregnancy hypertensive disorders, premature rupture of membranes, Apgar score <6 at 1 minute, FiO₂ requirement ≥25%, and need for mechanical ventilation, and invasive procedures at birth, intracardiac shunt with the exception of patent foramen ovale and non-hemodynamically significant ductus arteriosus, intrauterine growth restriction, and congenital malformations (congenital diaphragmatic hernia, neural tube defect, etc.).

Along with demographic and clinical information of infants, PI, SpO2, HR, body temperature, blood pressure (BP), and cardiac output (CO) values measured at the 48th hour of life were recorded into previously prepared forms. The pre ductal (right hand) and the post ductal (foot) PI, SpO2, and HR were measured by Masimo Radical 7 pulse oximetry (Masimo Corp., Irvine, CA). The PI value was recorded during the echocardiographic examination after a period in which the signal was stable and artifact-free with an average time setting of 3 minutes. The median PI for each measurement was obtained from the average of PI values recorded signal at 10-second intervals. Transthoracic echocardiographic (TTE) examination was performed by a single pediatric cardiologist using Philips EPIQ7C Ultrasound System (Philips Healthcare, Best, The Netherlands), with 12S transducer (S12-4 Sector Array Transducer), and CO value was calculated with “pulse wave” Doppler echocardiography. Simultaneously measured PI value was not reported to the pediatric cardiologist. Right ventricular output (RVO), LVO, superior vena cava (SVC) flow, right and left ventricular outflow tract velocity time integral (VTI) values were measured by two-dimensional (2D) and pulsed-wave Doppler echocardiography. LVO was evaluated, using the following formula as previously reported by European Society of Pediatric Cardiology: LVO (mL/min) = LVO VTI (cm) × π × (LVO diameter/2)^2 (cm^2) × HR (bpm).

LVO diameter was measured just below the aortic valve during five consecutive systoles in a cardiac long axis view with 2D mode TTE, and averaged. LVO VTI was measured with “pulse wave” Doppler echocardiography tracing in a five-chamber apical view with the box positioned inside the LVO tract and with an angle <15 degrees.

RVO was evaluated in agreement with van Vonderen et al. using the following formula: RVO (mL/min) = RVO VTI (cm) × π × (RVO diameter/2)^2 (cm^2) × HR (bpm). By the same method, the RVO diameter was measured from the adhesion site of the pulmonary valves during five consecutive systoles in a cardiac transthoracic short axis and averaged. RVO VTI was measured with pulse Doppler tracing in a cardiac view with the box positioned inside the RVO tract and with an angle <15 degrees.

The superior vena cava flow (SVCf) was evaluated in agreement with Kluckow and Evans using the following formula: SVCf (mL/min) = (mean SVC VTI × π × mean SVC diameter^2)/4 (cm^2) × HR (bpm). In subcostal view, the maximum and minimum SVC inner diameters were measured from the right atrium—SVC connection area during three consecutive cycles with 2D mode TTE and averaged. SVC VTI was
was measured with pulse Doppler tracing in the box positioned at the junction of the SVC and the right atrium with an angle < 15 degrees. The mean velocity of SVCf was averaged from five consecutive cardiac cycles with “pulsed wave” Doppler echocardiography.

LVO, RVO, and SVCf values were standardized by proportioning the baby’s weight at the time of echocardiographic study (LVO/kg, RVO/kg, and SVCf/kg).

**Statistical Analysis**

SPSS 22.0 (SPSS, Chicago, IL) was used for the statistical analysis. The data was expressed as mean (standard deviation, SD) or median (interquartile range [IQR]), frequency, percentage, minimum, maximum as appropriate. The suitability of quantitative data for normal distribution was tested by the Shapiro-Wilk test and graphical assessment. Differences between two groups were tested by using Student’s t-test or Mann-Whitney U-test. Pearson Chi-square test and Fisher’s exact test were used to compare qualitative data. Spearman correlation analysis and Pearson correlation analysis were used to evaluate the relationships between quantitative variables. A two-tailed *p*-value of < 0.05 was accepted as significant.

**Results**

Overall, 50 late preterm babies with negative CHD screening were studied, and the clinical characteristics of these babies were shown in **Table 1**. Of these babies, 14% (n: 7) were at 34th week of gestation, 24% (n: 12) at 35th week of gestation, and 62% (n: 31) at 36th week of gestation. Among them, 17 (34%) were hospitalized infants with a SNAPPE-II score of ≥ 18. None of them showed any evidence of cardiac pathology and/or required blood transfusions or pharmacological treatments.

**Table 2** shows PI, SpO₂, HR, BP, and body temperature mean ± (SD) or median (IQR) values of cases at the 48th hour of life. All infants had normal echocardiographic findings, none had hemodynamically significant patent ductus arteriosus (PDA). LVO, RVO, SVC diameter and VTI values measured by echocardiography are shown in **Table 3**. Mean values of LVO, RVO, and SVCf were 4,438 ± (SD) 124, 626 ± 213, and 343 ± 139 mL/min, respectively. Mean values of LVO/kg, RVO/kg, and SVCf/kg were 175 ± 50, 250 ± 83, and 136 ± 52 mL/kg/min, respectively.

Precordial PI was not significantly correlated LVO, LVO/kg, SVCf, and SVCf/kg (*p* < 0.2 and *p* > 0.05 for all comparisons).

**Table 1** Demographic and clinical characteristics of cases

| Variables                      | n = 50          |
|--------------------------------|-----------------|
| Gestational age (weeks, [mean ± SD]) | 35.4 ± 0.7 |
| Birth weight (g, [mean ± SD])     | 2,586 ± 362    |
| Cesarean section (n, %)           | 40 (80)        |
| Female/Male (n, %)                | 27 (54)/23 (46) |
| Apgar score at 5th min. (median, range) | 9 (8–10) |

**Table 2** PI, SpO₂, heart rate, blood pressure, and body temperature of cases

| Variables                      | n = 50          |
|--------------------------------|-----------------|
| PI Preductal (mean ± SD)       | 2.0 ± 0.9       |
| PI Post ductal (mean ± SD)     | 1.7 ± 1.1       |
| SpO₂ Preductal (%)             | 97 (90–100)     |
| SpO₂ Post ductal (%)           | 97 (91–100)     |
| HR (median, IQR)               | 137 (102–170)   |
| Body temperature (°C, [median, IQR]) | 36.6 (36.4–36.9) |
| Systolic BP (mm Hg, [median, IQR]) | 78 (63–108)   |
| Diastolic BP (mm Hg, [median, IQR]) | 47 (28–80)  |
| Mean BP (mm Hg, [median, IQR]) | 56 (32–85)     |

**Table 3** LVO, RVO, SVC diameter, and VTI values of infants evaluated with TTE

| Variables                      | n = 50 (mean ± SD) |
|--------------------------------|------------------|
| LVO diameter (cm)              | 0.65 ± 0.08      |
| LVO VTI (cm)                   | 9.55 ± 1.46      |
| RVO diameter (cm)              | 0.68 ± 0.09      |
| RVO VTI (cm)                   | 12.9 ± 2.44      |
| SVC diameter (cm)              | 0.43 ± 0.06      |
| SVC VTI (cm)                   | 16.0 ± 3.4       |

**Discussion**

In this study, the relationship between LVO and PI derived from a new generation pulse oximeters in healthy late preterm infants was investigated for the first time. It is believed that PI may be a direct predictor of peripheral perfusion, as well as a useful and practical method for determining critical patients in NICU and evaluating the effect of treatment on peripheral perfusion.15,16 Normal

Abbreviations: BP, blood pressure; HR, heart rate; IQR, interquartile range; PI, perfusion index; SD, standard deviation; SpO₂, oxygen saturation.
values of PI were evaluated during the postnatal transition period and early neonatal period in healthy term infants. Cresi et al investigated the PI reference values in clinically and hemodynamically stable preterm infants during the first week of life. They reported average PI values measured from the feet of infants at 28 to 36 gestational weeks (mean 32.5 weeks) as 0.90 on the postnatal 1st day, 1.22 on the 3rd day, and 1.36 on the 7th day. Although they found a significant difference in PI values between 1st day and 3rd day, there was no significant difference between 3rd day and 7th day. They suggested that this trend of change in peripheral PI values reflects physiological changes in peripheral microvascular blood flow that begin immediately after birth and may be associated with intrinsic hemodynamic adaptation that occurs on the first day of life. A study of systemic blood flow in preterm infants reported that perfusion is achieved even in the presence of low blood flow and high vascular resistance within the first 24 hours of life. In the following days, it was noted that vascular resistance decreased due to vasodilation and blood flow returned to normal. In our study, the median PI value measured from the preterm babies’ feet at the 48th hour of life was higher than the PI values from the study of Cresi et al. This may have been caused by the fact that the gestation age of preterm infants in our study was higher than that of infants in the study of Cresi et al., and the completion of physiological changes in peripheral microvascular blood flow within the first 24 hours in our cases.

In a study conducted by Granelli and Ostman Smith, pre- and post-ductal PI reference values were investigated in 10,000 healthy newborns whose postnatal ages ranged from 1 hour to 120 hours. In this study, the measured PI fifth percentile value of both the right hand and foot was reported as 0.7. It is noted that a PI value of <0.7 can be a critical CHD indicator. They suggested that only pre-and post-ductal arterial oxygen saturation screening can miss the diagnosis of infants with left ventricular obstruction, and that this screening method may be insufficient in the diagnosis of critical CHD associated with low systemic perfusion. But as far as we know, there is only one study in the English literature that evaluates the correlation between PI and LVO in the newborn. Corsini et al showed for the first time that there is a correlation between PI and LVO in healthy term infants. In their study on 49 healthy term infants at the day 2 of life, when postnatal transition circulation was completed, the average PI value of both preductal and post-ductal was 1.9. In our study, the preductal PI value was similar to the Corsini et al study, but the post-ductal PI value was lower. Corsini et al reported the LVO/kg, RVO/kg, and SVCf/kg as 139, 160, and 132 mL/kg/min, respectively. In our study, LVO/kg, RVO/kg, and SVCf/kg values were higher than those reported by Corsini et al. They reported that there was a positive correlation between pre-/post-ductal PI and LVO in term infants, and also the correlation between PI and LVO/kg continued when LVO was normalized according to

**Table 4** Correlation between PI value and LVO, RVO, SVCf values, and PI value and LVO/kg, RVO/kg, SVCf/kg values of infants

| Total (n: 50) | LVO (mL/min) | RVO (mL/min) | SVCf (mL/min) | LVO/kg | RVO/kg | SVCf/kg |
|--------------|-------------|--------------|---------------|--------|--------|---------|
| Preductal PI |             |              |               |        |        |         |
| r            | 0.02        | -0.27        | -0.08         | 0.01   | -0.29  | -0.06   |
| p            | 0.89        | 0.04         | 0.55          | 0.89   | 0.03   | 0.63    |
| Post ductal PI |           |              |               |        |        |         |
| r            | -0.01       | 0.07         | -0.04         | 0.09   | 0.06   | -0.01   |
| p            | 0.95        | 0.62         | 0.77          | 0.49   | 0.66   | 0.92    |

Abbreviations: LVO, left ventricular output; PI, perfusion index; r, Spearman’s correlation coefficient; RVO, right ventricular output; SVCf, superior vena cava flow.

* p < 0.05.
to body weight (LVO/kg). Therefore, they noted that PI may have a role in detecting critical CHD with low perfusion. Contrary to the findings of Corsini et al.,¹⁰ our study found no correlation between pre-/post-ductal PI and LVO in healthy late preterm infants. There was also no correlation between PI and LVO/kg when LVO was normalized according to body weight (LVO/kg). These data suggested that LVO, as a hemodynamic parameter, in healthy late preterm infants was not sufficiently sensitive to reflect peripheral microvascular blood flow. It has been thought that this difference between term and preterm infants may be due to the fact that the maturation of the sympathetic nervous system, which plays a role in the regulation of peripheral perfusion, in preterm infants is not yet complete. Although studies in adult patients on this topic are limited, a study conducted by Lima et al. in adult patients reported no association between changes in CO and peripheral PI or clinical signs of poor peripheral perfusion.

In our study, there was a weak negative correlation between pre-/post-ductal PI and RVO or RVO/kg. This may be because the foramen ovale has not yet been closed. Similar to the results of Corsini et al.,¹⁰ there was no association between pre-/post-ductal PI and SVCf or SVCf/kg in our study. Takahashi et al.²¹ reported that they found a correlation between PI and SVC flow in their cohort of preterm infants. They noted that SVC flow reflects systemic blood flow, especially in small preterm infants with PDA. In our study, there was a moderate correlation between SVC flow and LVO/kg. The reason why our study result differs with the findings of Takahashi et al.²¹ may be that our study population does not cover very low birth weight babies with PDA.

As a result of observations, it has been reported that PI shows circadian rhythm, and can be affected by nutrition, intravenous therapy, jaundice, sleep–awake status, and sleep position.¹¹,²² A study conducted by Sahni et al.²² in low birthweight infants reported that the PI value measured in the supine sleep position was higher than in the supine position. In our study, peripheral perfusion in all infants was evaluated after feeding, in supine position and while awake. Although the infants with physiological jaundice were included in the study, the infants with hyperbilirubinemia requiring phototherapy were not included in the study. In our study, circadian rhythm was not taken into account in the time period during which the measurement was performed, due to the fact that babies had different birth times. It has been reported that PI measurement is not affected by physiological variables such as HR, SpO₂, oxygen consumption, BP, and body temperature.²³ Similarly, no association between PI and HR, SpO₂, body temperature, and BP (systolic, diastolic, and mean BP) was found in our study.

Our study had some limitations: (1) the number of babies included in the study was small, and (2) we did not examine whether there was a relationship between PI and LVO in infants with CHD.

**Conclusion**

In conclusion, a correlation between pre-/post-ductal PI and LVO in healthy late preterm infants was not found in our study. We believe that a systemic hemodynamic parameter such as LVO cannot adequately reflect peripheral microvascular blood flow due to incomplete maturation of the sympathetic nervous system in preterm infants, which is involved in regulating peripheral perfusion. New studies with larger populations are needed to determine the actual role of the synergistic effect of SpO₂ with PI in screening for critical CHD, especially in preterm infants.

**Authors’ Contributions**

N.H. and H.O. contributed toward concept of the study. N.H. and A.A. designed the study. M.A. and H.O. did the supervision. Ö.I. and A.A. collected the materials. A.A., Ö.I., and H.O. did the data collection and/or processing. A.A., Ö.I., and M.A. did the literature review. A.A., N.H., and Ö.I. wrote the manuscript. H.O. did the echocardiographic evaluation. N.H., M.A., and H.O. did the critical review.

**Ethical Approval**

The study was approved by our faculty of ethics committee (date: May 02, 2019 and decision no: 08/II).

**Consent to Participate**

Formal and written consents were obtained from the study subjects’ parent.

**Funding**

None.

**Conflict of Interest**

None declared.

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