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Changes in peripheral perfusion index within 72 h of life in a cohort of very low birth weight infants

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To the Editor: The latest generation of pulse oximeters are equipped with technology allowing for monitoring of the peripheral perfusion index (PI), the percentage of the amount of light absorbed by pulsatile tissue (variable arterial blood flow) over non-pulsatile tissue (venous blood, muscle, and other tissues) at a wavelength of 940 nm as a signal.[1] A low PI usually indicates that the peripheral perfusion is poor at the time of monitoring, which is conducive to the early detection of hypoperfusion of vital organs and has the advantages of being continuous, stable, sensitive, convenient, and non-invasive.[2,3] PI may have a certain value in predicting neonatal diseases and outcomes, including in preterm infants. However, before applying this indicator, its normal range needs to be established. Numerous studies have investigated the normal range of PI in neonates. Nevertheless, the sample sizes of studies on preterm infants were very small, with none reporting the PI values of very low birth weight (VLBW) infants (birth weight <1500 g) within 72 h of life. This study aimed to evaluate PI value in a cohort of VLBW infants and to explore its changes within 72 h postpartum.

From January 1, 2018, to December 31, 2019, a prospective cohort study was conducted in the level III neonatal intensive care unit (NICU) of a tertiary children's hospital with no obstetric unit, with all VLBW infants outborn and transported from maternity hospitals in Shanghai. All infants with a birth weight <1500 g required NICU admission and were subjects for this study. This study was approved by the institutional review board at the hospital (No. 2017-147), with verbal informed consent obtained from parents. The inclusion criteria were infants born <32 weeks gestational age (GA) and <1500 g. Exclusion criteria included patients with severe hypothermia (temperature <32°C), sepsis, severe congenital malformations (including congenital heart diseases) or patent ductus arteriosus >2 mm, surgical issues, severe edema, requiring prostaglandins or vasoactive drugs during admission, those who were admitted at >72 h of age, those with maternal chorioamnionitis, and infants who were deemed palliative after discussion with their parents.

The VLBW infants transferred to the NICU within 72 h of age underwent oxygenation index (OI) evaluation starting at the time of admission. Study participants were monitored using a Masimo Radical 7 pulse oximeter (Masimo Corp, Irvine, CA, USA). Professionally trained data collectors who were blinded to the purpose of the study placed the probe on the right hand of the infant for at least 30 s to obtain the pre-ductal PI. After the signal was stable, five PI values were continuously recorded to obtain the mean value. The probe was then removed and placed on either lower limb (post-ductal PI) to obtain the mean value as with the right hand. Pre- and post-ductal PI values were measured at 0 to 24 h, 24 to 48 h, and 48 to 72 h of life for each participant. Infants underwent treatment and nursing care as per guidelines for preterm infants. Episodes of infection, survival, or death were monitored and recorded when applicable. Infection was defined as septicemia or localized infections with positive cultures (blood or other specimens, for example, septicemia, meningitis, and pulmonary abscess).

Means and standard deviations (SDs) or medians and interquartile ranges (IQRs) were reported for variables with normal and skewed distributions, respectively. One-factor analysis of variance, Kruskal–Wallis test, Pearson's chi-squared test, and Fisher's exact test were used to compare differences between measurement variables

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across time points as appropriate. Correlations between pre- and post-ductal PI values measured at 0 to 24 h, 24 to 48 h, and 48 to 72 h were examined by using the Spearman correlation. Multiple linear regression with robust standard error was used to evaluate associations between baseline and measurement factors and the (log-transformed) pre- or post-ductal PI values at 48 to 72 h postpartum. Variables that showed a relation ($P < 0.20$) with the pre- or post-ductal PI values in the unadjusted analyses were entered into the model. We chose to examine the associations at this time point because measurement data were available for all infants ($n = 180$). Separate linear mixed models were used to explore the effect of advancing hours within 72 h postpartum on the (log) pre-and post-ductal PI values after controlling for potential confounders identified from the literature and univariate analyses (body temperature, measurement position, heart rate, and ventilation modes). We used the actual measurement hour instead of time range (ie, 0–24, 24–48, and 48–72 h) for our analysis because this yielded more information for each infant; the range was 2 to 72 h. A linear mixed model was necessary to make maximum use of the available information because some subjects had missing data. The models also included random effects with random coefficients at the individual level (ie, intercept and measure time). This required estimating three extra variables: one variance each for the two random coefficients plus a covariance term. The standardized residuals at levels 1 (within infants) and 2 (between infants) were visually assessed for normality. We estimated the multivariable-adjusted geometric mean ratios of the pre- and post-ductal PI values for each increasing postpartum hour.

Additionally, we analyzed the respective associations of pre- and post-ductal PI measured at the three-time periods with the risk of infection or death using Poisson regression for infection as the outcome and logistic regression for death as the outcome. Adjustments were for gestational age, birth weight, and temperature at measurement. Significance was set at $P < 0.05$. All analyses were conducted by using Stata 16.0 (Stata Corp LP, College Station, TX, USA). One hundred and eighty participants meeting the inclusion criteria were included. The median (IQR) age of infants at enrollment was 3.0 (2.0–4.0) h, mean (SD) gestational age was 28.9 (1.7) weeks, and 47.2% were female. The mean (SD) birth weight was 1174.2 (219.9) g, 1 min Apgar score was 7.1 (2.0), median fraction of inspired oxygen (FiO_2) on admission was 21.0 (IQR 21.0–30.0)%, and OI was 310.5 (170.8). There were no missing cases for baseline variables [Supplementary Table 1, http://links.lww.com/CM9/A965]. In total, 501 measurements were collected from all infants and at all time points.

The median pre- and post-ductal PI values of these 501 measurements were 2.2% (IQR 1.5%–3.1%) and 2.0% (IQR 1.4% –3.0%), respectively. Pre- and post-ductal PI values were collected from 141, 180, and 180 infants at 0 to 24 h, 24 to 48 h, and 48 to 72 h postpartum, respectively. Because some VLBW infants were older than 24 h of life on NICU admission, a total of 141 infants provided three time-point measurements. Table 1 presents pre- and post-ductal PI values, temperature, heart rate, FiO_2, position, and ventilation mode at each point. Although both PI values tended to be higher, only post-ductal PI values reached statistical significance ($P = 0.013$). There were significant, moderate correlations

Table 1: Comparison of measurement results in the three-time periods.

Parameters	0–24 h ($n = 141$)	24–48 h ($n = 180$)	48–72 h ($n = 180$)	P values
Post-natal time (h)	22.0 (2.0, 24.0)	45.0 (25.0, 48.0)	69.0 (49.0, 72.0)	<0.001
Temperature (°C)	36.5 ± 0.4	36.6 ± 0.4	36.5 ± 0.3	0.59
FiO_2 (%)	21.0 (21.0–23.0)	21.0 (21.0–23.0)	21.0 (21.0–23.0)	0.44
Heart rate (beats/min)	149.1 ± 13.2	153.3 ± 13.2	155.6 ± 13.3	<0.001
Pre-ductal SpO_2 (%)	97.0 (95.0–99.0)	98.0 (95.0–99.0)	97.0 (95.0–99.0)	0.87
Pre-ductal PI (%)*	2.0 ± 1.9	2.3 ± 1.8	2.3 ± 1.7	0.056
Post-ductal SpO_2 (%)	98.0 (96.0–99.0)	97.0 (95.0–99.0)	97.0 (95.0–99.0)	0.004
Post-ductal PI (%)	1.8 ± 1.7	2.1 ± 1.8	2.2 ± 1.7	0.013
Position				0.067
Supine	102 (72.3)	110 (61.1)	105 (58.3)	
Prone	0 (0.0)	1 (0.6)	1 (0.6)	
Right side lying	19 (13.5)	24 (13.3)	25 (13.9)	
Left side lying	20 (14.2)	45 (25.0)	49 (27.2)	
Ventilation mode				0.96
None	8 (5.7)	10 (5.6)	13 (7.2)	
CPAP	92 (65.2)	110 (61.1)	108 (60.0)	
CMV	34 (24.1)	54 (30.0)	52 (28.9)	
BIPAP	3 (2.1)	3 (1.7)	3 (1.7)	
HFV	4 (2.8)	3 (1.7)	4 (2.2)	

Data are presented as mean ± standard deviation (SD), median (range), or median (interquartile) for continuous variables, and n (%) for categorical variables until otherwise stated. * Geometric mean ± geometric SD. BIPAP: Biphasic positive airway pressure; CPAP: Continuous positive airway pressure; CMV: Conventional mechanical ventilation; FiO_2: Fraction of inspired oxygen; HFV: High frequency ventilation; IQR: Interquartile range; PI: Perfusion index; SpO_2: Saturation of peripheral capillary oxygen.

between pre-ductal PI measured at 0 to 24 h and 24 to 48 h (Spearman $r = 0.269$, $P < 0.01$), 0 to 24 h and 48 to 72 h ($r = 0.232$, $P < 0.001$), and 24 to 48 h and 48 to 72 h ($r = 0.343$, $P < 0.01$) postpartum. There were significant, moderate correlations between post-ductal PI measured at 0 to 24 h and 24 to 48 h (Spearman $r = 0.212$, $P < 0.01$), and 24 to 48 h and 48 to 72 h post-natal ($r = 0.261$, $P < 0.01$).

Among the baseline factors investigated, only temperature, measurement position, and ventilation mode were associated with pre-ductal PI measured within 48 to 72 h postpartum in the univariate linear regression models ($P < 0.20$; Supplementary Table 2, http://links.lww.com/CM9/A965). On the other hand, ventilation mode, gestational age, and birth weight were significantly associated with post-ductal PI measured within 48–72 h postpartum in the univariate linear regression models ($P < 0.20$; Supplementary Table 2, http://links.lww.com/CM9/A965). Linear mixed models exploring the effect of post-natal time within 72 h and pre-ductal PI and post-ductal PI measurements showed that temperature and postnatal time of measurement were significantly associated with pre-ductal PI and post-ductal PI, which are presented in Supplementary Table 3, http://links.lww.com/CM9/A965.

We explored the effect of time on pre- or post-ductal PI values using a linear mixed model in 180 infants, adjusting for covariates significant at $P < 0.2$ from the univariate analyses [Supplementary Table 3, http://links.lww.com/CM9/A965]. Post-natal time at which the PI was measured was significantly associated with both increased pre-ductal PI (geometric mean ratio 1.002, 95% confidence interval [CI] 1.000–1.005, $P = 0.029$) and post-ductal PI (geometric mean ratio 1.004, 95% CI 1.001–1.006, $P = 0.001$). When extrapolating these values over 24 h, the pre-ductal PI increased by 1.12 times within 24 to 48 h. The corresponding values were 1.15 times and 1.19 times for post-ductal PI within 24 to 48 and 48 to 72 h (all $P < 0.05$).

Supplementary Table 4, http://links.lww.com/CM9/A965 presents the associations between pre- and post-ductal PI measured at the three-time periods with the risk of infection or death. We found pre- and post-ductal PI values had no predictive effect for infection and death, but this was not the main purpose of this study, so further studies on this specific effect will be needed.

This study obtained the range of pre- and post-ductal PI values of VLBW infants within 72 h of life. It is often presumed that VLBW infants are particularly vulnerable to hemodynamic instability at birth, as at birth, the left ventricle is immediately stressed, including a sharp increase in pulmonary blood flow and systemic vascular resistance, insufficient blood volume, and insufficient cardiac contractility makes it more difficult for them to adapt to extra-uterine life.[4,5] In this case, the PI value may be very low. The infants included in the current study were preterm infants who were stable from a cardiorespiratory perspective, so the PI values obtained were relatively stable. This study further confirms that all factors that affect vascular tone will subsequently affect PI value. The current study found that position and temperature were important influencing factors for pre-ductal PI. The lateral decubitus position and increased body temperature led to local vasodilation of the skin at the monitoring site, resulting in an increased PI. These changes were due to changes in microvascular skin perfusion.[6] The main factor affecting post-ductal PI was post-natal age. For each 1-h increase in postpartum age, pre- and post-ductal PI values increased by a factor of 1.002 (95% CI: 1.000–1.005) and 1.004 (95% CI: 1.001–1.006), respectively. This study did not find that PI value had an impact on infection and death of VLBW infants. PI values within 72 h of life were not related to infection or death, although a more targeted research design and a larger sample size would facilitate further observation and analysis.

In summary, PI values of VLBW infants increase gradually with post-natal age. Influencing factors such as body temperature must be taken into consideration when interpreting PI values. PI values can be used as a conventional indicator in routine clinical monitoring for VLBW infants.

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Conflicts of interest

None.

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