Perfusion index in newborn infants: a noninvasive tool for neonatal monitoring

Carolina Z. Piasek (carozenobi@gmail.com)1, Frank Van Bel2, Augusto Sola3

1. Research Intern at the Orthopaedic Department, Children’s Hospital Los Angeles, Los Angeles, California, USA.
2. Department of Neonatology, University Medical Center Utrecht, Utrecht, Netherlands.
3. Masimo Corporation, Irvine, California, USA

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Correspondence
Carolina Z. Piasek, MD, 9930 Robbins Dr, Apt B, Beverly Hills, California 90212, USA.
Tel: 310-405-1118 | Fax: 310-360-3408 | Email: carozenobi@gmail.com

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ABSTRACT

Aim: To review the utility of perfusion index (PI) in the evaluation of neonatal clinical conditions. Twenty-five manuscripts were reviewed. PI provides information about haemodynamic stability, illness severity, early neonatal respiratory outcome, low superior vena cava flow and subclinical chorioamnionitis.

Conclusion: PI is a valuable tool to assess the newborn’s health condition and could become a standardised measure in clinical evaluation. Different study designs are necessary to provide further validation to this method.

INTRODUCTION

This review intends to examine and discuss the utility of the perfusion index (PI) as a parameter for the evaluation of clinical conditions in term and preterm neonates (preterm neonates defined as newborns with a gestational age ≤36 weeks). Many studies on PI have been done in adults, and the ones on neonates have been focused in establishing correlations that could diagnose and/or early detect life-threatening conditions.

What is perfusion index?
PI is a relative assessment of the pulse strength at a specific monitoring site. It was first described as an index calculated by a pulse oximeter (Masimo signal extraction pulse oximetry) (1). PI is a ratio between pulsatile (DC) and nonpulsatile (AC) signal (AC/DC × 100). Both signals are derived from the amount of infrared light absorbed and their relation reflects the amplitude of the plethysmographic waveform. Alterations of perfusion will change the ratio

Key notes
- This review intends to examine and discuss the utility of the perfusion index (PI) as a parameter for the evaluation of neonates’ clinical condition.
- PI provides essential information on haemodynamic stability, illness severity, early neonatal outcome, low superior vena cava flow and subclinical chorioamnionitis.
- PI proved to be a valuable tool in the clinical practice, along with other objective and subjective parameters. However, further validation to this method is necessary.
and are reflected in real time in the pulse oximeter. Changes in PI are associated with changes in stroke volume, vasomotor tone and skin temperature, being an indirect, noninvasive measure of peripheral perfusion; lower values indicate a lower systemic perfusion.

PI depends on vasomotor tone, which may affect the pulsatile absorption component. Stimulation, such as nociceptive input, can induce changes in vasomotor tone. On the other hand, vasomotor tone is constant during a single respiratory cycle and it does not alter the analysis of the relative changes in PI induced by mechanical ventilation. The measurement of PI is influenced primarily by the amount of blood at the monitoring site, and PI varies in proportion to skin blood flow, provided that local haemoglobin does not change significantly (2). PI has been shown to indicate, reliably, well-established phenomena such as decreased or increased skin blood flow in response to different stimuli such as mechanical restriction, cold/heat, acetylcholine, sodium nitrate and local nerve blockade (3–6). Subtle changes in perfusion are often missed by static displays, but monitoring PI provides the ability to trend and so to capture these changes as they take place. It provides us with a relative capability to report PI in a slightly different way. Although PI is affected by perfusion or motion. There are several papers that show this change significantly (2). PI has been shown to indicate, reliably, well-established phenomena such as decreased or increased skin blood flow in response to different stimuli such as mechanical restriction, cold/heat, acetylcholine, sodium nitrate and local nerve blockade (3–6). Subtle changes in perfusion are often missed by static displays, but monitoring PI provides the ability to trend and so to capture these changes as they take place. It provides us with a relative number that can range from 0.02 to 20% and that varies between monitoring sites and from patient to patient.

PI can be found in just a few SpO2 monitors, but it is not the same as SpO2 monitoring. Most studies on PI have used Masimo Signal extraction technology (SET), where PI was first described and installed, and only two studies with other monitor (Phillips IntelliVue MD70) (7,8) that has the capability to report PI in a slightly different way. Although no studies are performed yet comparing both devices, results of recent studies in preterm infants suggest similar results (7,9). No other SpO2 monitor analyzes or reports PI on their screen. As mentioned, PI is affected by perfusion and this is different to SpO2, which is not affected by low perfusion or motion. There are several papers that show this (10–13).

In the last decade, several research studies have been carried out to determine the utility of PI in different clinical settings as summarised below.

METHODS

For this review, databases such as PubMed were searched for keywords such as ‘perfusion index’, ‘peripheral perfusion index’, ‘peripheral perfusion’ and ‘skin blood flow’. We will use the abbreviation PI indistinctly for the mentioned keywords. From all the manuscripts, we selected those who referred specifically to PI measured with a pulse oximeter in neonates and in adults. 16 manuscripts that targeted this subject in neonates were selected, as well as nine manuscripts in adults. These manuscripts are discussed in this review.

RESULTS

Studies of the perfusion index in Infants

In the adult population, PI studies are mainly focused in evaluating its usefulness in surgical scenarios, more specifically, its efficacy in the detection of nerve blockage (3–6). For example, Klodell et al. (3) tested this in patients undergoing a thoracic sympathectomy. A twofold increase in PI in the ipsilateral arm was considered a positive outcome. An increase >300% (p < 0.0001) was obtained; thus, they concluded that PI would be a valuable tool. There is only one study to detect early clinically significant central hypovolaemia before the onset of cardiovascular decompensation in healthy volunteers (14), and one meaningful study concerning critically ill patients (8). The latter is the only study to give a reference value for adults, being 1.4% (interquartile range 0.7–3.0%) its cut-off PI value to detect abnormal peripheral perfusion in critically ill patients.

Contrarily, in the neonatal population, most of the studies are focused in establishing parameters for the diagnosis and/or early detection of life-threatening conditions (9,11,15,18,22,25).

The studies that reported values in neonates are summarised in Table 1 and Figure 1. In a Swedish study of 10 000 healthy term newborns (15), 1.7% was the median value for PI, with an interquartile range of 1.18–2.50%, being the fifth percentile 0.7% and the 95th percentile 4.5%. Median PI in preterm haemodynamically stable neonates has also been established (16) by a study that evaluated 30 neonates. The PI was registered on the first, third and seventh day of life concluding that the median value was 0.9% on the first day, 1.22% on the third and 1.35% on the seventh. Consequently, they propose that the age of the neonates should be taken into account for its clinical application. A study (9) in preterm neonates with a haemodynamically important persistent ductus arteriosus also established different PI values depending on the neonate age that were not influenced by ductal flow pattern, with a median PI value of 0.7% in the first day of life (0.5–1.05%) and 1.5% (1.0–2.0%) on the seventh (p < 0.01). PI has also been proven to vary, specially in very preterm infants, depending on the placement of the pulse oximeter (7), being higher in the upper limbs (right upper limb = 0.92% vs. lower limb = 0.69%, mean difference = 0.24%, p < 0.001), fact probably related to the transitioning circulation in this population where patent ductus arteriosus is not uncommon, and the position of the low birthweight newborn, presenting a higher PI in prone sleeping position (17) (mean PI value 3.7 ± 0.9% vs. PI 3.1 ± 0.7%).

PI and cardiovascular alterations

Congenital heart disease is one of the most frequent congenital malformations in newborns, 20–40% of deaths in neonates are caused by congenital malformation and 6–10% of all infant deaths. Its diagnosis before birth accounts only for 25–50% (in the United States) of the cases, and many infants are discharged from the hospital without diagnosis. A huge prospective study to evaluate the utility of the perfusion index as a screening tool for critical left heart obstruction took place in Sweden (15). To compare PI values in healthy newborns with those with critical left heart obstruction, 10 000 healthy babies and nine with left
heart obstructive disease (LHOD) had their PI measured from the right hand (preductal) and foot (postductal). The results showed that all the newborns with left obstructive heart disease (LOHD) had pre- or postductal PI’s below the interquartile range, 56% of them had a PI value below the fifth percentile with a cut-off value of 0.7%. From those nine
neonates diagnosed with LOHD, three cases were missed by the neonatal exam, and two of these three were missed by pulse oximetry screening. The authors concluded that a PI value <0.7% indicates cardiac illness, suggesting it might be a useful tool for the detection of congenital heart malformations. Other authors investigating the same subject shared this conclusion (18).

PI has also been studied to assess its accuracy in predicting low superior vena cava (SVC) flow in very low weight preterm newborns (19), which is a risk factor for intraventricular haemorrhage. Superior vena cava flow and PI were obtained in 24 babies, revealing a positive correlation between PI and SVC ($r = 0.509$, $p < 0.001$), and a PI cut-off value for detecting low SVC flow of 0.44%, sensitivity 87.5%, specificity 86.3% and although its positive predictive value was low 38.9%, its negative predictive value was 98.6%.

**PI and illness severity**

De Felice et al. (20) published a study evaluating the correlation between PI and illness severity, if any, in 101 newborns. According to the Score of Neonatal Acute Physiology (SNAP), the children were categorised into two groups: high illness and low illness. An operator, who was unaware of children’s category, registered their PI, SpO$_2$, pulse rate, body temperature and blood pressure. To calculate the accuracy of the PI, SpO$_2$ and pulse rate to predict high illness severity, a receiver operating characteristic (ROC) curve was utilised. PI was the only parameter to demonstrate a predictive accuracy, with a sensitivity, specificity, positive predictive value and negative predictive value all over 90% (95.5, 93.7, 91.2 and 96.8%, respectively). They also established a PI cut-off value of $\leq 1.24\%$ being an accurate predictor of illness severity.

Chorioamnionitis in term newborns is associated with neonatal morbidity and mortality and preoccupies neonatologists especially because a big part of these neonates remain subclinical. Hence, a study was performed to evaluate PI as a predictor of subclinical chorioamnionitis (21). The study was divided into two phases: the first one to establish cut-off values of term newborns with chorioamnionitis and a matched control population; the second phase consisted of testing newborns with these cut-off values. A cut-off value of $\leq 1.74\%$ at one minute and $\leq 2.18\%$ at five minutes was evaluated in 329 infants. The results showed 30 true positive (9.12%), two false positive (0.61%), zero false negative (0%) and 297 true negatives (90.27%). Hence, they demonstrated 100% sensitivity, 99.4% specificity, 93.7% positive predictive value and 100% negative predictive value for chorioamnionitis. The two neonates with false-positive results after further evaluation were diagnosed with congenital heart defect and vascular malformation. Thus, the authors concluded that PI accurately identifies subclinical chorioamnionitis, which may decrease morbidity and mortality in these newborns.

These authors also demonstrated that a maternal PI $\leq 1.9\%$ (lower quartile) during the pre-anaesthesia phase of the elective caesarean section was an independent predictor of early adverse neonatal respiratory outcome (odds ratio 68.0, 95% confidence interval 6.02–767.72; $p < .0001$) (22).

Another study proposed PI and oxygen assessment as parameters of indirect information on the circulatory failure of vital organs during circulatory shock in critically ill newborns (23). Sometimes this circulatory failure information is provided through near-infrared spectroscopy (NIRS), which measures the calf muscle perfusion and the oxygen consumption. Thus, the study in 43 neonates was designed to compare foot PI to the parameters measured by NIRS. They established a mean PI value of 1.26 $\pm$ 0.59%. This correlated positively with calf muscle blood flow and oxygen delivery ($p = 0.03$), but had no correlation with oxygen consumption or fractional oxygen extraction. They concluded that monitoring PI would be a simple bedside clinical tool for evaluating circulatory status in newborns and that it could become a customary tool in the intensive care unit.

**DISCUSSION**

Under stress-free circumstances, newborns skin perfusion is higher than its oxygen demand, thus when illness is present cardiac output is redistributed to provide the necessary oxygen to critical organs such as brain, heart and adrenal glands (24). Consequently, monitoring PI could be of great value in assessing newborn’s condition (health/illness).

Pulse oximeter waveform contains additional information that has been underexploited despite potential useful clinical applications. PI as measured by Masimo$^\text{TM}$ is a very simple, easily applicable, noninvasive tool to measure peripheral perfusion in various clinical settings. For example, in anaesthetised adults and children, an increased PI (compared with the baseline PI measured before the application of anaesthesia) is a parameter that indicates the proper functioning of the anaesthesia (3–6).

In critically ill patients, a decreased PI underlines severity of illness (8). In newborns (preterm or term), if this parameter is combined with others such as oxygen saturation and pulse rate, a decreased measure indicates a worsening state of neonatal health (20). In subclinical chorioamnionitis, PI accurately identifies affected newborns and by that influences the immediate outcome (21).

A decreased PI has also been used to detect congenital heart malformations, especially those with left heart obstructive disease, but more research is needed here (15,18,19,25). In cardiovascular alterations, it is likely to be very useful as an indicator of low superior vena cava flow (risk factor for intraventricular haemorrhage) (19). Therefore, PI is being increasingly recognised as an effective parameter to increase the sensitivity for the detection of important neonatal complications (25).

With available neonatal studies, it is yet not possible to determine with certainty, which are clear ‘cut-off’ values for severe illness in all cases. This may be due, at least in part, to different methods and subjects used in collecting the data reported. For example, one study (20) suggested...
1.24% as such value, while in another study (15) 1.18% separated the first and second quartiles. Until such information becomes clearer, caution is recommended when interpreting a low PI determination and value in an individual baby. Monitoring and assessing changes or stability over a period of at least several minutes and the evaluation of trends over time may be of greater value in clinical practice.

We therefore share, with caution, the concept that some authors (7,15,18,20,21,23,25) have suggested: this method could become a standardised, objective measure in addition to the already established objective and subjective means to assess the clinical condition of a neonate. We consider that, thus far, studies of PI have proven that it could be an extremely valuable tool for the assessment of newborns’ health condition and that the future application of PI in neonatal intensive care is broad. However, it cannot be yet considered as standard of care and future research with large samples, and different study designs are needed to provide further validation for its use in clinical practice. Of significance is that one value of PI could be truly meaningless, but monitoring its trend can provide us with important clinical information, especially because the PI is obviously affected by perfusion which can change in a brief period of time just by bending or moving an extremity, even when using monitors with SET. For this reason, it only makes sense to design studies with continuous monitoring and to choose epochs to record PI, for example 15–30 sec or even 2–3 min or more, and then averaging the PI value for that epoch to make comparisons with the next epoch.

Potential future applications of PI in neonates could be as a predictor of illnesses, to estimate volume status, assess the restoration of peripheral perfusion in various clinical conditions and to indicate circulatory function. Furthermore, it could become a useful tool to be used in delivery room resuscitation, in congenital heart disease screening and in continuous routine monitoring of ill (preterm) newborn infants. PI may be found to be a good noninvasive and simple tool to be used in the assessment of neonatal hemodynamics. Further research may reveal that PI can also be a reliable surrogate for left ventricular cardiac output, tissue oxygenation and cerebral perfusion.

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CONFLICT OF INTEREST
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