Cardiology in the Young

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Perfusion index in newborns with CHD without clinical signs of hypoperfusion and heart failure: comparison with healthy newborns

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Original Article

Cite this article: Argun M, Sunkak S, Elmalı F, Keskin Ş, and Narin N (2023) Perfusion index in newborns with CHD without clinical signs of hypoperfusion and heart failure: comparison with healthy newborns. *Cardiology in the Young* **33**: 1092–1096. doi: 10.1017/S1047951123002469

Received: 20 September 2022
Revised: 13 May 2023
Accepted: 14 June 2023
First published online: 17 July 2023

Keywords:
Peripheral perfusion index; saturation; CHD; newborn

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Abstract

Introduction: Peripheral perfusion index has been proposed as a possible method for detecting circulatory impairment. We aimed to determine the normal range of peripheral perfusion index in healthy newborns and compare it with that of newborns with CHD. *Methods:* Right-hand saturation and right-hand peripheral perfusion index levels were recorded, and physical examination and echocardiography were performed in newborns who were 0–28 days old and whom were evaluated in our paediatric cardiology outpatient clinic. The saturation and peripheral perfusion index levels of newborns with normal heart anatomy and function were compared with those of newborns with CHD. *Results:* Out of 358 newborns (238 mature and 75 premature) enrolled in the study, 39 had CHD (20 mild CHD, 13 moderate CHD, and 6 severe CHD), of which 29 had CHD with left-to-right shunting, 5 had obstructive CHD, and 5 had cyanotic CHD. No newborn had clinical signs of hypoperfusion or heart failure, such as prolonged capillary refill, weakened pulses, or coldness of extremities. Peripheral perfusion index level was median (interquartile range) 1.7 (0.6) in healthy newborns, 1.8 (0.7) in newborns with mild CHD, and 1.8 (0.4) in newborns with moderate and severe CHD, and there was no significant difference between the groups regarding peripheral perfusion index level. *Conclusion:* Peripheral perfusion index remains unchanged in newborns with CHD without the clinical signs of hypoperfusion or heart failure. Larger studies with repeated peripheral perfusion index measurements can determine how valuable this method will be in the follow-up of newborns with CHD.

The incidence of moderate and severe CHD is approximately 6/1.000 live births. When small ventricular septal defects and other insignificant lesions are also included, the combined incidence of CHD rises to 75/1.000 live births.[1] When newborns and infants with CHD are not diagnosed early enough, both mortality and morbidity rates increase. It is essential to use laboratory findings in addition to clinical signs in the diagnosis, interpretation, follow-up, and treatment of CHD.

Pulse oximetry, which is very practical and widely used today, calculates the percentage of oxygenated haemoglobin measured transcutaneously by estimating the absorption of light at two different wavelengths, corresponding to oxygenated and deoxygenated haemoglobin.[2] With the routine use of a screening programme with pulse oximetry in the newborn, the rate early diagnosed critical CHD in newborns has increased, which in turn has reduced newborn mortality and morbidity resulting from critical CHD.[3]

It is of importance to recognise a newborn with CHD, whether it is critical or not, before heart failure and signs of hypoperfusion develop, or if these clinical conditions have already developed, before the clinical state progresses to a decompensated state. In this sense, besides the existing mortality risk prediction models, efforts are being undertaken to develop novel models devised by artificial intelligence. These models include many clinical and laboratory parameters.[4] The predictive power of these models can be increased with the addition of some routinely use parameters like lactate, which indicate tissue hypoperfusion, to these models. Novel technologies, on the other hand, are introduced to clinical practice to predict the degree of haemodynamic instability. In this sense, compensatory reserve index can be given as an example as a non-invasive tool designed to use the pulse photoplethysmogram waveform. It has been reported that compensatory reserve index can accurately reflect haemodynamic changes in children with CHD at risk of decompensation.[5]

Thanks to technological advances in pulse oximetry devices in recent years, it has become possible to calculate the perfusion index, a parameter that is derived from the ratio between

pulsatile and non-pulsatile signals of the absorbed light.[6] Perfusion index is a novel, easy-to-use, non-invasive, continuous parameter derived from pulse oximetry. It is displayed in new-generation pulse oximetry monitors. Perfusion index is not affected by the oxygen saturation level of arterial blood but primarily affected by the amount of blood in the monitored area.

It has been reported that low perfusion index levels are particularly an accurate predictor of increased disease severity in newborns. It has also been reported that it reflects real-time changes in peripheral blood flow and determines inadequate peripheral perfusion in newborns suffering critical disease.[7,8] Therefore, when there is a decrease in arterial circulation due to reduced stroke volume, decreased perfusion index is expected. Monitoring the perfusion of less vital organs such as skin, subcutaneous tissue, and muscle will give an idea about how more vital tissues are perfused.[9] In addition, there may be a decrease in peripheral circulation due to an increase in systemic vascular resistance in infants with CHD whose cardiac output is less affected. For all these reasons, in addition to clinical examination and saturation, perfusion index may contribute to the diagnosis and follow-up of newborns with CHD.

We aimed to determine the perfusion index levels of healthy newborns that we evaluated with saturation, physical examination, and echocardiography at the paediatric cardiology outpatient clinic and also to determine if the perfusion index levels would be altered in newborns with CHD without clinical signs of hypoperfusion and heart failure.

Material and methods

Ethical approval and consent to participate

This study was approved by Kayseri City Hospital clinical research ethics committee (February/2021; no.302). The study was conducted in accordance with the declaration of Helsinki.

Subjects

Newborns aged 0–28 days that were evaluated in Health Sciences University Kayseri Medical Faculty Kayseri City Hospital paediatric cardiology outpatient clinic between February 2021 and June 2022 were prospectively enrolled. The newborns were referred to the outpatient clinic for various reasons such as murmur, cyanosis, prematurity, diabetic mother's infant, and history of CHD in a first-degree relative. The newborns' birth week, maturity, gender, postnatal days, birth weight, and current body weight were recorded.

Exclusion criteria

The study design excluded newborns who were currently admitted to the newborn ICU, who had infection, dehydration, or nutritional problems, and those who were still using medications for heart failure or tachyarrhythmia.

Saturation and perfusion index

Perfusion index measurements were performed using a Philips Efficia CM12 monitor (Andover, USA). The sensor was placed to the right hand. After it was confirmed that the pulse tracing showed a smooth curve on the monitor for 5 seconds, the saturation and perfusion index readings were recorded.

Echocardiography

After all newborns were physically examined, a transthoracic echocardiographic examination was performed by the same experienced paediatric cardiologist using the GE Vivid 7 Pro echocardiography device.

Classification of CHDs

Echocardiographically diagnosed CHDs were classified by severity as mild, moderate, and severe, and by the pathophysiological basis as being with left-to-right shunting, obstructive, and cyanotic. Infants with mild CHD are asymptomatic. Small ventricular septal defect, small patent ductus arteriosus, mild pulmonary stenosis, and bicuspid aortic valve are in this group. Moderate CHD requires specialist care. This group includes mild or moderate aortic stenosis or aortic regurgitation, moderate pulmonary stenosis or regurgitation, non-critical aortic coarctation, large atrial septal defect, and medium-sized ventricular septal defect. Severe CHD patients present with severe illness in the neonatal period or early infancy. All cyanotic CHDs are in this group. Severe non-cyanotic CHD includes atrioventricular septal defect, large ventricular septal defect, large patent ductus arteriosus, critical or severe aortic stenosis, severe pulmonary stenosis, and critical aortic coarctation.[1]

A ventricular septal defect was defined as "small" when it was smaller than 3 mm, "medium" when 3–5 mm, and "large" when greater than 5 mm.[10] An atrial septal defect larger than 8 mm was defined as "large." A patent ductus arteriosus was defined as "small" if it did not cause clinical symptoms and if the pulmonary artery side of the duct was restrictive. A haemodynamically significant and larger patent ductus arteriosus was defined as "large." Aortic stenosis was classified according to peak Doppler gradient, and graded as "trivial" when the latter was < 25 mm Hg, "mild" when it was 25–50 mmHg, "moderate" when it was > 50 and < 70–80 mmHg, and "severe" when it was > 70–80 mmHg. Pulmonary stenosis was classified according to peak Doppler gradient and graded as "mild" when it was < 25 mm Hg, "moderate" when it was 25–40 mm Hg and "severe" when it was > 50 mm Hg.[11]

Statistical analysis

The study data were evaluated with IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA) statistical software package. Descriptive statistics included number of units (n), percent (%), mean±standard deviation ($\bar{x}$ ±sd), median (M), minimum (min), maximum (max), and interquartile range. Normality of the distribution of numerical variables was evaluated with the Kolmogorov–Smirnov test. Perfusion indexes of normal, mild, and moderate patients, and the perfusion indexes of normal, left–right shunt, obstructive, and cyanotic patients were compared using Kruskal–Wallis test. If the result of Kruskal–Wallis analysis was found to be significant, subgroup analyses were performed with the Dunn–Bonferroni test. Perfusion indexes of mature and premature patients were compared with Mann–Whitney *U*-test. A p value of < 0.05 was considered statistically significant.

Results

There were 358 infants (184 boys, 51.4%; 174 girls, 48.6%), who had a mean birth week of 38.03 ± 1.99 (31–41.4) weeks (mature 283, 79.1%; premature 75, 20.9%), a mean age of 10.62 ± 8 days, and a mean body weight of 3241.0 ± 771.7 (1270–5900) grams.

https://doi.org/10.1017/S1047951123002469 Published online by Cambridge University Press

Table 1. Comparison of saturation and perfusion index values in terms of the severity of CHDs

	Saturation median (interquartile range)	Perfusion index median (interquartile range)
Normal (n: 319)	98.0 (3.0)	1.7 (0.6)
Mild CHD (n: 20)	97.0 (3.5)	1.8 (0.7)
Moderate and severe CHD (n: 19)	97.0 (3.0)	1.8 (0.4)

p-Value = 0.129 for saturation; p-value = 0.835 for perfusion index.

Table 2. Comparison of saturation and perfusion index values in terms of pathophysiology of CHDs

	Saturation median (interquartile range)	Perfusion index median (interquartile range)
Normal (n:319)	98.0 (3.0)	1.70 (0.60)
CHD with left–right shunt (n: 29)	97.0 (3.5)	1,82 (0,85)
Obstructive CHD (n: 5)	95.0 (3.5)	1,80 (0,55)
Cyanotic CHD (n: 5)	96.0 (20.5)	1,70 (0,35)

p-Value = 0.636 for the comparison of normal and CHD saturation values with left–right shunt, p-value = 0.117 for comparison of normal and obstructive CHD saturation values, p-value = 0.018 for the comparison of normal and cyanotic CHD saturation values, p-value = 0.044 for comparison of left–right shunt and cyanotic CHD saturation values, p-value = 0.933 for the perfusion index between groups. Subgroup analyzes were performed using the Dunn–Bonferroni test.

Thirty-nine newborns were diagnosed with CHD (20 mild CHD, 13 moderate CHD, and 6 severe CHD). The infants with CHD had a similar mean age with the healthy infants (mean age of 9.71 ± 7.66 days) (p = 0.471). All newborns with CHD had a good overall health condition. No newborn had the clinical signs of hypoperfusion or heart failure, such as prolonged capillary refill, weak peripheral pulses, and cold extremities. The patients were categorised on the basis of the severity and pathophysiology of CHD, and the number of newborns with CHD was determined (Supplementary Figure).[1]

There was no significant difference between the perfusion index levels of the mature newborns median (interquartile range) 1,7 (0.6), (min–max; 0.7–3.3) and the premature newborns median (interquartile range), 1.7 (0.5) (min–max; 0.7–2.9) (p = 0.322). Healthy newborns were divided into weekly age groups. There was no difference in healthy newborns' perfusion index between 0 and 7 days median (interquartile range) (1.6 (0.7)), 8–14 days (1.8 (0.5)), 15–21 days (1.8 (0.7)), and 22–28 days (1.8 (0.8)) (p = 0.064).

There was no significant difference between the saturation and perfusion index levels of the healthy newborns, newborns with mild CHD, and newborns with moderate–severe CHD (Table 1). There was a significant difference between the saturation levels of the healthy newborns and the newborns with cyanotic CHD (p = 0.018). There was also a significant difference between the saturation levels of the newborns having CHD with left-to-right shunting and the newborns with cyanotic CHD (p = 0.044). The difference between the perfusion index levels of the healthy newborns, newborns with CHD with left-to-right shunting, obstructive CHD, and cyanotic CHD was not significantly different (Table 2).

Discussion

We found a median perfusion index level of 1.7 and a minimum perfusion index level of 0.7 in healthy newborns with a mean age of 10 days. The perfusion index level did not change in mild, moderate, or severe CHD without the clinical signs of hypoperfusion or heart failure. Perfusion index level does not change in the newborns with CHD with left-to-right shunting, obstructive CHD, or cyanotic CHD without the clinical signs of hypoperfusion or heart failure.

The newborn critical CHD screening programme with the measurement of arterial saturation in the right hand and foot has made it possible to detect many CHDs earlier in their course.[12,13] However, saturation is not expected to decrease in heart diseases with left-to-right shunt and cyanotic CHDs with an increased pulmonary flow. While these CHDs may cause pulmonary congestion, it may also cause a decrease in systemic perfusion.

Corsini et al.[14] examined 48-hour-old healthy newborns with perfusion index and echocardiography in addition to the measurement of saturation. The perfusion index level of the right hand and foot were 1.9 ± 0.6 and 1.9 ± 0.8, respectively. Perfusion index was significantly correlated to left ventricular output, and this finding was interpreted by the authors as supportive to the theoretical potential role of perfusion index in the critical CHD screening programme. Zaramella P. et al.[6] reported that continuous perfusion index measurement with pulse oximetry appeared to be a clinically more practical, rapid, and inexpensive method than near infrared spectroscopy for monitoring peripheral perfusion in healthy newborns.

Jegatheesan et al.[15] reported a similar range for pre-ductus and post-ductus perfusion index levels and reported a fifth percentile perfusion index value of 0.7 in 2768 healthy newborns that were approximately 24 hours old. Schena et al.[16] reported a higher perfusion index value with a cut-off level of 0.9 in a study including more than 42,000 asymptomatic newborns screened 48 hours after birth. Cresi F et al.[7] found a median perfusion index value of 0.9 on the first day, 1.1 on the third day, and 1.3 on the seventh day in 30 haemodynamically stable preterm newborns, with the perfusion index level showing a significant increase between the first and third days. The authors suggested that this change in the first week of life may indicate the necessity of considering patient's age in clinical practice. In our study, there was no difference in perfusion indices when newborns were divided into four groups by age.

Osman AA. et al.[17] reported that a perfusion index below 0.4 was correlated to most echocardiographic parameters of haemodynamically significant patent ductus arteriosus. Furthermore, the authors derived a 24-hour perfusion index histogram data. Low (perfusion index < 0.4) and high (perfusion index > 2) perfusion episodes were significantly longer in the newborns with patent ductus arteriosus prior to treatment compared to those during or after treatment. They suggested that this finding reflected the dynamic nature of the shunt volume passing through the ductus in premature newborns younger than 29 weeks who had a patent ductus arteriosus requiring treatment. In our mild disease group, we had six patients with haemodynamically insignificant patent

https://doi.org/10.1017/S1047951123002469 Published online by Cambridge University Press

ductus arteriosus. The perfusion index did not change in these patients. We think the right-hand and foot perfusion indices and the difference between them can yield significant results in preterm infants with haemodynamically important patent ductus arteriosus.

It is important to assess perfusion in critical aortic coarctation, interrupted aortic arch, and critical aortic stenosis showing signs of hypoperfusion and ductus-dependent systemic circulation.[3] Hypoplastic left heart syndrome, another important disease, is characterised by the clinical signs of hypoperfusion and mild cyanosis. Hypoperfusion becomes prominent with narrowing of the ductus. In this case, perfusion index in addition to clinical signs and lactate level may provide valuable information. In a comprehensive study of 10,000 newborns, Granelli A. et al.[18] found a median perfusion index value of 1.70, an interquartile range of 1.18–2.50, a 5th percentile of 0.7, and a 95th percentile of 4.5 between 1 and 120 hours of life. In all of nine newborns with left-sided obstructive disease, the pre-ductus or post-ductus perfusion index levels were below 1.18, and five (56%) newborns had a perfusion index below 0.7. Uygur O. et al.[19] reported that the addition of perfusion index measurements to pulse oximetry as part of the newborn critical CHD screening programme may be helpful in preventing delays in the diagnosis of critical CHD. They found that the measurement of perfusion index was particularly helpful in obstructive left heart lesions where pulse oximetry screening offers a limited diagnostic efficacy. Lannering K. et al.[20] reported a reduced false positivity rate by using a cut-off level of 0.7 and employing repeated measurements instead of a single measurement in newborns with aortic coarctation.

However, several studies have reported unacceptably high false-positive rates for the perfusion index as a screening test.[21] Perfusion index changes can also occur as a result of local vasoconstriction (decrease in perfusion index) or vasodilation (increase in perfusion index) in the skin at the monitoring site. Potential limitations of the perfusion index may include hypothermia and local vasospasm.[22] These conditions may be considered among the reasons of false positives.

It is obvious that the diagnostic value of the perfusion index may be higher in the obstructive diseases of the left heart, particularly those with a ductus-dependent systemic circulation. Moreover, increased systemic vascular resistance due to the activation of the renin angiotensin aldosterone system and the sympathetic nervous system can reduce peripheral perfusion in patients with severe heart failure. The perfusion index did not change in our newborn patients with CHD without the clinical signs of hypoperfusion or heart failure. We did not have a newborn patient with CHD resulting in the signs of hypoperfusion associated with a low stroke volume. Most of our patients are expected to have an increased pulmonary artery blood flow (CHD with left–right shunt and cyanotic CHD with increased pulmonary artery flow). However, physiologically elevated pulmonary vascular resistance in the neonatal period prevents heart failure in this period. Therefore, we did not have any patients in our heart failure clinic. In newborns, the perfusion index does not seem to have a role in CHD without signs of hypoperfusion nor in CHD without heart failure.

Study limitations

The number of our newborn CHD cases was limited. When the classification of the patients was based on CHD severity and pathophysiology, the number of patients in each group was quite small. We had no patient with ductus-dependent systemic circulation. As a final limitation, only a single perfusion index measurement was done.

Conclusions

Perfusion index is an indirect marker of circulation that can be easily obtained using new-generation pulse oximetry devices. Perfusion index remains unchanged in newborns with CHD without the clinical signs of hypoperfusion and heart failure. Clinical correlation can be made with large-scale studies and repeated perfusion index measurements in children with CHD with and without signs of hypoperfusion and heart failure. By this way, the most accurate age- and disease-specific cut-off level of perfusion index can be determined.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1047951123002469

Acknowledgements. None.

Author contribution. The contributions of all authors must be described in the following manner: The authors confirm contribution to the paper as follows: study conception and design: M.A.; data collection: M.A., Author; analysis and interpretation of results: M.A., S.S., and F.E.; draft manuscript preparation: M.A., Ş.K., F.E., and N.N. All authors reviewed the results and approved the final version of the manuscript.

Financial support. This research received no specific grant from any funding agency, commercial, or not-for-profit sectors.

Competing interests. None.

Ethical standard. This study was approved by local clinical research ethics committee (February/2021; no.302). The study was conducted in accordance with the declaration of Helsinki. Informed consent was obtained from the parents of all patients.

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