Perfusion Index and Pulse Oximetry Screening for Congenital Heart Defects

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Objective To evaluate the efficacy of combined pulse oximetry (POX) and perfusion index (PI) neonatal screening for severe congenital heart defects (sCHD) and assess different impacts of screening in tertiary and nontertiary hospitals.

Study design A multicenter, prospective study in 10 tertiary and 6 nontertiary maternity hospitals. A total of 42 169 asymptomatic newborns from among 50 244 neonates were screened; exclusion criteria were antenatal sCHD diagnosis, postnatal clinically suspected sCHD, and neonatal intensive care unit admission. Eligible infants underwent pre- and postductal POX and PI screening after routine discharge examination. Targeted sCHD were anatomically defined. Positivity was defined as postductal oxygen saturation (SpO_2) ≤95%, prepostductal SpO_2 gradient >3%, or PI <0.90. Confirmed positive cases underwent echocardiography for definitive diagnosis. Missed cases were identified by consulting clinical registries at 6 regional pediatric heart centers. Main outcomes were incidence of unexpected sCHD; proportion of undetected sCHD after discharge in tertiary and nontertiary hospitals; and specificity, sensitivity, positive predictive value, and negative predictive value of combined screening.

Results One hundred forty-two sCHD were detected prenatally. Prevalence of unexpected sCHD was 1 in 1115 live births, similar in tertiary and nontertiary hospitals. Screening identified 3 sCHD (low SpO_2, 2; coarctation for low PI, 1). Four cases were missed. In tertiary hospitals, 95% of unsuspected sCHDs were identified clinically, whereas only 28% in nontertiary units; in nontertiary units PI-POX screening increased the detection rate to 71%.

Conclusions PI-POX predischarge screening provided benefits in nontertiary units, where clinical recognition rate was low. PI can help identify coarctation cases missed by POX but requires further evaluation in populations with higher rates of missed cases. *(J Pediatr 2017;183:74-9).*

Congenital heart defects (CHDs) are the most common neonatal malformations, with a prevalence of 0.8%-1%, and are a leading cause of infant death in developed countries. A significant proportion of CHD (1.5/1000 live births) are potentially fatal during the neonatal period.[1] Early recognition of severe CHD (sCHD) is highly important, as surgical correction or palliation is possible for a certain proportion of cases and may improve survival and overall quality of life.

Although advances in prenatal medicine have increased the number of CHD detected through antenatal ultrasound screening, several cases still remain unidentified at birth.[2-4] In addition, as critical CHD often causes subtle symptoms in the early days of life, some cases may be missed during routine neonatal evaluations. Presymptomatic CHD diagnosis is thought to allow better perioperative patient management, reduce hospital stays, and improve survival and prevent neurologic sequelae secondary to hypoxia and acidosis.[5,6]

CHDs	Congenital heart defects	POX	Pulse oximetry
HLHS	Hypoplastic left heart syndrome	sCHD	Severe CHD
HoL	Hours of life	SpO_2	Oxygen saturation
PI	Perfusion index		

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Pulse oximetry (POX) has gained increasing interest in the last decade as an early CHD screening tool in neonates and in 2011 POX screening for critical CHD was included in the recommended uniform screening panel in the US.[7] Other countries are evaluating the potential benefits of implementing this type of screening.[8-12]

The reported sensitivity and specificity of POX vary according to the evaluation timing, adopted cut-off value, use of a single or paired measurement site (postductal only or pre- and postductal), and evaluated target lesion type.[13-18] However, all previous studies described a low sensitivity for left ventricle outflow obstructive defects, including aortic coarctation, interrupted aortic arch, critical aortic stenosis, and hypoplastic left heart syndrome (HLHS), as the main limitation of POX.[14,16-21]

Left-sided heart obstructions are the lesion type most frequently missed by POX and during routine physical examinations.[22,23] Accordingly, POX screening might be ineffective for the very lesions that most require additional diagnostic efforts to improve their detection rate.[24,25]

In 2007, Granelli and Ostman-Smith[26] proposed the peripheral perfusion index (PI) as a possible screening tool for congenital left heart obstruction. PI is a POX-derived, oxygen saturation-independent measure expressed as the ratio of the pulsatile component of the infrared light signal that reaches the sensor (reflected by the arterial blood) to the nonpulsatile component (reflected by the venous blood and tissues) and, thus, represents the relative amount of arterial perfusion in the examined area.[27] In neonates, PI correlates with other measures of peripheral and systemic perfusion obtained via functional echocardiography or near-infrared spectroscopy.[28,29] Granelli and Ostman-Smith[26] observed PI values below the fifth percentile in 6 of 9 infants with a congenital left heart obstruction. However, although promising, the effectiveness of a PI-based screening protocol has not yet been studied prospectively.

Aims of the study were to assess the prevalence of unexpected (not suspected prenatally) sCHD in tertiary and nontertiary hospitals and to evaluate the efficacy of neonatal screening for sCHD using combined POX and PI at the time of patient discharge.

Methods

This study was approved by the ethics committee of the coordinating center. Written consent was obtained from parents at centers where POX screening was not routinely performed.

All neonates who were admitted to well-baby nurseries from June 2011 to November 2013, were asymptomatic at predischarge examination, and had not received a previous echocardiographic assessment were eligible. Patients were enrolled consecutively at each center, with variable starting and ending dates. Infants admitted to the neonatal intensive care unit, suspected prenatally of CHD, or presenting conditions requiring cardiac assessment (genetic syndromes, major extracardiac anomalies, family history of CHD, mother with diabetes) were excluded. Screening occurred at 48-72 hours of life (HoL) at the time of metabolic screening. None of the participating hospitals adopted a policy of early discharge (<48 HoL). Oxygen saturation (SpO_2) and PI were measured in both preductal (right hand) and postductal sites (foot).

To avoid motion artifact effects, PI readings were taken after a regular sinusoidal track was displayed for 10 seconds. Masimo neonatal disposable sensors (Masimo Corporation, Irvine, California) were used along with either the recommended Masimo Rad 7pulse oximeter or Bitmos Sat 805 (Bitmos GmbH, Dusseldorf, Germany) oximeter, which uses Masimo SET technology and displays PI similarly. Positive screening tests met one of the following conditions: postductal SpO_2 ≤95%; >3% difference between pre- and postductal SpO_2; or single-site PI <0.90. Positive screening tests were repeated after 30 minutes for confirmation. Patients who failed the second test were referred for same-day echocardiography.

We selected a higher PI threshold than that originally proposed by Granelli and Ostman-Smith[26] (0.70) based on our preliminary observation that the PI was slightly higher after 48 HoL than during the first 48 hours (data not shown), consistent with previously published data.[30] This threshold was intended to minimize false negative cases while maintaining an acceptable false positive rate. In addition, assuming that combining PI and POX could reduce the number of missed cases from 2.5 to 0.62 per 10 000 neonates (75% reduction), we calculated that 40 000 neonates should be screened to draw statistically significant conclusions (0.80 power, 0.05 alpha error).

Target lesions were anatomically defined severe congenital heart malformations (sCHD; **Table I**). Simple cardiac lesions (eg, isolated ventricular septal defect, atrial septal defect, patent foramen ovale, patent ductus arteriosus, bicuspid aortic valve, mild pulmonary stenosis, and mild aortic stenosis) were excluded. With the aim of exploring the full potential of the new screening protocol the list of potential targets was somewhat broader than those used in other studies.

Table I. Cardiac anomalies defined as target lesions of PI-POX screening

IAA, interrupted aortic arch*
AS, aortic stenosis (moderate to severe)
AVC, atrioventricular canal
CoA, aortic coarctation*
DORV, double outlet right ventricle*
Ebstein anomaly*
HLHS, hypoplastic left heart syndrome*,†
PA/VSD, pulmonary atresia with ventricular septal defect*,†
PA/IVS, pulmonary atresia with intact ventricular septum*,†
PS, pulmonary stenosis (moderate to severe)
PTA, persistent truncus arteriosus*,†
SV, single ventricle*
TA, tricuspid atresia*,†
TAPVR, total anomalous pulmonary venous return*,†
d-TGA*,†
ToF, tetralogy of Fallot*,†
Other complex or rare CHDs with cyanosis and/or low systemic perfusion*

d-TGA, d-transposition of the great arteries.
*Defects indicated as core targets by the Newborn Screening for Critical Congenital Heart Disease Expert Panel (CDC-AAP).[31]
†Defects indicated as pulse oximetry primary target by the US Secretary's Advisory Committee on Heritable Disorders in Newborns.