An Ideal Neonatal Congenital Heart Disease Screening Plan by Pulse Oximeter and Auscultation in a Large Single Center

Yuqiang Huang

Linyi Maternal and Child Healthcare Hospital

Shiqing Zhong

Linyi Maternal and Child Healthcare Hospital

Xianmei Zhang

Linyi Maternal and Child Healthcare Hospital

Linghui Kong

Linyi Maternal and Child Healthcare Hospital

Wenli Wu

Linyi Maternal and Child Healthcare Hospital

Shixia Yue

Linyi Maternal and Child Healthcare Hospital

Ning Tian

Linyi Maternal and Child Healthcare Hospital

Guanghua Zhu

Linyi Maternal and Child Healthcare Hospital

Aiqin Hu

Linyi Maternal and Child Healthcare Hospital

Juan Xu

Linyi Maternal and Child Healthcare Hospital

Haijan Zhu

Linyi Maternal and Child Healthcare Hospital

Airong Sun

Linyi Maternal and Child Healthcare Hospital

Fangling Qin

Linyi Maternal and Child Healthcare Hospital

Ziwen Wang

Linyi Maternal and Child Healthcare Hospital

Shiqiang Wu (✉ 604287252@qq.com)

Linyi Maternal and Child Healthcare Hospital

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Abstract

Purpose

To investigate the feasibility and reliability of pulse oximeter (POX) as a fast-screening device for congenital heart disease (CHD) through comparing performances of cardiac auscultation and POX in a large retrospective single center study.

Methods

Every newborn received auscultation and POX tests separately. When an abnormal murmur or SpO₂ level is detected, an echocardiogram will be ordered to confirm the diagnosis of CHD in the newborn.

Results

From January 1, 2018 to December 31, 2019, there were 44,147 livebirths at the studied hospital where 498 newborns were diagnosed with CHD: 27 newborns by POX screening and 471 by cardiac auscultation. The diagnosis was further confirmed in 458 neonates through echocardiogram. This result puts forth an overall diagnosis rate of 91.97%. Cardiac auscultation detected the majority of CHD cases 438 (95.6%) while POX only screened 20 (4.4%) cases. Interestingly, no CHD case was detected by both auscultation examination and POX screening. Auscultation detected most of the common types of CHD, but POX excelled in identifying rare and critical cases. POX screening alone had a very low accuracy of 3.41% in positive predict value (PPV). On the other hand, auscultation can function well in terms of PPV and negative predict value (NPV) (92.99% and 99.95%, respectively), but the addition of POX could improve the overall screening performance and reach NPV to 100%. We also validate the finding with the data six months after the study period.

Conclusion

Auscultation screening operates well in detecting common CHDs whereas POX screening excels in distinguishing rare, yet critical, cases of CHDs. Therefore, an ideal CHD screening plan should combine cardiac auscultation and POX screening.

What Is Known

- Pulse-oximetry is safe, acceptable, non-invasive and effective.
- Pulse oximetry screening increases early diagnosis of major CHD as well as other important pathology with a very low false positive rate and minimal requirement for extra echocardiograms.

- Pulse-oximetry plus cardiac auscultation significantly improved the detection rate of major CHD in the early neonatal stage, with high sensitivity and a reasonable false-positive rate.

What is new

- No CHD case was detected by both auscultation examination and Pulse-oximetry screening.
- Auscultation can function well in terms of positive predict value and negative predict value (92.99% and 99.95%, respectively), but the addition of POX could improve the overall screening performance and reach NPV to 100%.

1. Introduction

Congenital heart disease (CHD) is the most common type of congenital malformations, with an overall prevalence of 6-10‰ in newborns (among which 2-3‰ cases are considered severe). [1] About a quarter of CHD patients require surgery or catheterization in neonatal period, or early infancy. [2] Timely diagnosis and treatment can greatly improve the prognosis of patients. [3] Conversely, delayed diagnosis often leads to serious hypoxia, shock, acidosis, pneumonia, and other complications including death. Studies have reported that delayed diagnosis of critical congenital heart disease (CCHD) led to death in 1-2 of every 100,000 live births in the United States. [4] Prenatal obstetric ultrasound can detect about 30% fetuses with CHD [5], but early neonatal diagnosis is still a big challenge.

Although echocardiography is the gold standard to validate cases of CHD, it usually takes more than 10 minutes to perform. Hence, performing echocardiography for every newborn in areas with limited resources is not practical. As an alternative, pulse oximetry (POX) is easy to operate and requires only 2 to 3 minutes to analyze the results. Besides, POX as an adjunct to current routine practice is likely to be a cost-effective strategy in the light of currently accepted thresholds. [6]

It is highly specific in detecting CCHD with moderate sensitivity, and had been widely employed.[7] Since Dr. Guoying Huang introduced and established CHD screening system via POX to China in 2018, it has been adopted in nationwide clinical routines. [8]

As a large maternal and child healthcare facility, the hospital of study delivers more than 20,000 babies annually. Consequently, offering quick, convenient, and accurate screening tools for CHD detection among newborns are crucial for the local community in the absence of echocardiologist. This health center has combined auscultation and POX in CHD diagnostic tests among newborns since 2018. When babies are recognized with CHD by POX or auscultation, an echocardiography will be requested for confirmation. This study aims to compare and report the performances of auscultation and POX screenings for the first time.

2. Methods

2.1 Study design and participants

We conducted this retrospective study; from January 1, 2018 to December 31, 2019 at Linyi Maternal and Child Healthcare Hospital, where more than 20,000 infants were delivered annually, to confirm the applicability and accuracy of pulse oximetry combined cardio-auscultation in determining congenital heart disease among neonates.

All consecutive newborns were eligible, irrespective of gestational age, NICU admission, symptom presence or prenatal diagnosis.

This study was approved by institutional ethical review board of Linyi Maternal and Child Healthcare Hospital. Verbal, informed consent was obtained from the participants' parents. The registry number is NCT05105880 (<https://register.clinicaltrials.gov>).

2.2 Procedures

2.2.1 Cardio-auscultation

Pediatricians from Departments of Neonatal Medicine and Developmental Medicine are responsible for auscultation screening. A standard pediatric stethoscope (Model 3200, 3M Littmann) was used. Cardiac auscultation was performed on the five points of auscultation (pulmonic, aorta, Erb's point, tricuspid, and mitral) for each newborn under typical conditions of the general maternity ward, and the duration lasted 60 seconds per neonate. When abnormal murmur occurred, an echocardiography would be requested to confirm if the newborn has CHD or not.

2.2.2 Pulse oximetry

Physicians from obstetrics department and nursing staff from neonatal department examined POX measurements using a pulse oximeter (Masimo, Irvine, CA, USA), with a multisite reusable or disposable sensor (Model 2329, Masimo). All babies should be screened within 72 hours after birth. Pulse oximeter oxygen saturation (SpO₂) was measured from the right hand and on either foot. SpO₂ levels is recorded on the nursing report sheet. If the measurement was less than 90% or the difference between two extremities was more than 3%, the baby would be referred for echocardiography immediately. If one extremity's measurement ranged between 90% and 94%, the clinician would repeat the test on the baby 4 hours later. If measurements on both extremities were between 90% and 94%, the baby would be referred for echocardiography.

2.2.3 Echocardiography

Physicians from Department of Ultrasonography confirmed the diagnosis of CHD among newborns diagnosed by auscultation or POX through directing echocardiography. Pediatricians then refer the CHD results to cardiology center. On the basis of the severity classification of congenital heart disease recommended by Hoffman's method, we divided cases of the disease into severe, moderate and mild groups, and prescribed treatment plans accordingly. [9]

3. Results

From January 1, 2018 to December 31, 2019, there were 44,147 livebirths in the studied hospital. The demographic characteristics of the screened population were summarized in *Table 1*. The majority of the newborns were full term births delivered between 37 and 40 gestational weeks, with a median gestational age of 39 weeks. The median birth weight for newborn is 3,420 g, which was consistent with the gestational age of the mother. Three quarters of the babies underwent screening within 24 hours after birth and cesarean section rate was 45.2%. As the study center undertakes the child healthcare in the study region, there is no additional CHD case found among these infants up to 2022.

There were 498 newborns diagnosed with CHD initially – 27 by POX screening and 471 by cardiac auscultation – with an overall diagnostic rate of 1.13% among all 44,147 livebirths. Of these cases, 458 neonates were confirmed by echocardiography, making the overall diagnostic rate of CHD via echocardiogram 91.97% (including 253 male babies and 245 female babies). The screen results are presented in Table 2. The most common types of CHD were PDA (34.3%), ASD (20.5%), VSD (8.3%), and combined complications (34.5%). Rare CHD included COA, CTA PAPVC, TAPVC, TGA, and TOF, accounting for a total of 2.2% cases. Mild CHD accounted for 74% of all cases, followed by moderate CHD (15.3%), and severe CHD (10.7%). Among all CHD cases, 37 cases were already identified by prenatal screening with ultrasonography.

Of the 458 confirmed CHD subjects, cardiac auscultation alone detected majority of CHD cases 438 (95.6%) and POX only screened 20 (4.4%) cases. However, not a single incidence of CHD is recognized by both auscultation and POX screening (Table 3). A potential explanation for this result is that auscultation detected most of the common types of CHD neonates, but POX detected the rare, yet critical CHD types, including COA, CTA, PAPVC, TAPVC, TGA, and TOF. The same observation was made in a new set of data from 2020.

POX screening alone has a very low accuracy of 3.41% in positive predict value (PPV). Auscultation alone can function well in terms of PPV and negative predict value (NPV) (92.99% and 99.95%, respectively), but the addition of POX could improve the overall screening performance and reach NPV to 100% (Table 4).

As PDA and ASD were not included in prenatal screening by ultrasonography, they were excluded when tracing back prenatal ultrasound screening. Of the remaining 108 cases, 37 fetuses were diagnosed with CHD, including 35 cases of VSD, 1 case of COA, and 1 case of TOF (Table 5).

4. Discussion

In this large single-center retrospective study, we applied combined POX and auscultation in routine CHD screening for all newborn infants within 24 hours after delivery. Within a two-year period, we identified 458 CHD neonates from 44,147 live births, of which 74% neonates are diagnosed with mild CHD, 15.3% with moderate CHD, and 10.7% with major CHD. Although POX can not detect slight CHD accurately, this

inexpensive and quick screening technique in conjunction with clinical auscultation can result in a high detection rate of serious CHD.

The most intriguing finding in this screening was that there was no overlap of CHD spectrums between POX detection and auscultation detection. In contrast to common CHDs detected by auscultation, POX-detected CHDs were rare and critical, including COA, CTA, PAPVC, TAPVC, TGA, and TOF, which were consistent with the primary and second target lesions presenting at least mild hypoxemia during the neonatal period.[10] This observation is quite different from two previous research with significant overlaps between two screening techniques.[8, 11] The dynamic changes of pulmonary arterial pressure in newborns in combination of all screenings conducted within the first 24 hours after delivery likely contributed to the difference between our observation and the observations made by previous researches. In fetal period, pulmonary circulation was not in use. Instead, it is occupied by amniotic fluid and full of pressure. After birth, because postnatal circulation requires inhalation of air, lung aeration initiates and clears the airway fluid, accompanied by decreasing pulmonary arterial pressure. The pressure is 60 mmHg at birth and drops to about 30 mmHg at 24 hours of age. [12-14] Since all of the screenings were conducted within the first 24 hours of delivery, which was different from the 72-hour window used in previous studies, it might be difficult to detect abnormal heart murmur when pulmonary arterial pressure still maintained relatively high. Moreover, in one of two previous studies with a large population of 167,190 asymptomatic newborn infants, most POX-recognizable cases of CHD were only detected via auscultation.[11] Considering this current, early-stage, multicenter study investigated the accuracy and feasibility of implementing cardiac auscultation and POX as a screening method in China, there might be large variations in the POX measurement among different hospitals studied for different researches, resulting in low detection rate by POX in other studies. This study's finding manifests the complementary aspects of POX and auscultation in preliminary diagnosis of CHD among newborns, shedding light on the effectiveness of combined use of both methods in comprehensive neonatal screening, especially regions lacking echocardiologists.

Meanwhile, the commonality of certain types of CHD was different: PDA, VSD, and ASD accounting for 97.6% of total CHD cases in our study and ~91.1% in previous studies. The difference in incidence rate and the CHD spectrum could be explained by differences in prenatal management among different hospitals. Tertiary referral hospitals have more medical resources and better prenatal screening and management systems. Pregnant women registered at these hospitals usually received additional prenatal ultrasound screening, which can increase the chance of prenatal diagnosis of major CHD, usually followed with termination of pregnancy. Contrasting to previous multicenter researches which collected data from a wide range of hospitals, our study was conducted at a single, tertiary referral hospital which had better prenatal management systems, prenatal screenings and adequately trained medical staffs.[15]

Some mild congenital defects, including small muscular VSD, ASD and PDA, would become less noticeable or even close spontaneously without intervention.[16] Owing to the natural closure, these neonates should not be included when calculating CHD incidence, or if counted, it will increase the incidence rate at different stages. Moreover, due to limited resources, our study only considered

observable CHD cases before discharge, whereas other studies offered follow up statistics among neonates after discharge. Thus, previously misdiagnosed or undiagnosed neonates would be determined to have CHD and added to the total CHD incidence later in the study. Furthermore, some studies would exclude CHD cases that were screened out in prenatal ultrasonography and confirmed in postnatal echocardiography, and symptomatic CHD neonates such as cyanotic subjects would not be included, either. As a whole, these limitations explain the observable differences in overall CHD occurrence and the major type of diagnosed CHD between our study and the previous studies.

5. Conclusions

Our study demonstrates that within the first 24 hours after birth, auscultation screening functions well in detecting common CHDs, whereas POX screening excels in differentiating rare and critical CHDs. When combined in CHD screening, these two techniques can generate quick and accurate outcomes in an economic way, which can benefit facilities in low-income area and hospitals short of ward resource. More cohort studies will be established for these infants.

Abbreviations

ASD: atrial septal defect

CCHD: critical congenital heart disease

CHD: congenital heart disease

COA: coarctation of the aorta

CTA: cor triatriatum

NPV: negative predict value

PAPVC: partial anomalous pulmonary venous connection

PDA: patent ductus arteriosus

POX: pulse oximeter

PPV: positive predict value

SpO₂: oxygen saturation

TAPVC: total anomalous pulmonary venous connection

TGA: transposition of the great arteries

TOF: tetralogy of Fallot

VSD: ventricular septal defect

Declarations

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Conflicts of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Availability of data and material: Not available.

Code availability: Not applicable.

Authors' contributions: Yuqiang Huang designed the study and drafted the manuscript; Shiqiang Wu, Shiqiang Zhong, Ziwen Wang conducted auscultation and collected data; Xianmei Zhang, Linghui Kong undertook echocardiography; Wenli Wu, Shixia Yue, Ning Tian, Guanghua Zhu, Aiqin Hu, Juan Xu, Haijian Zhu, Airong Sun, Fangling Qin undertook pulse oximeter tests.

Ethics approval: This study was approved by institutional ethical review board of Linyi Maternal and Child Healthcare Hospital. Verbal, informed consent was obtained from the participants' parents. The registry number is NCT05105880 (<https://register.clinicaltrials.gov>).

Consent to participate: Not applicable.

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Tables

Table 1. Demographic characteristic of newborns

Variables	Total N=44,147	Normal N=43,689	Mild CHD N=339	Moderate CHD N=70	Severe CHD N=49
Gestational age (weeks)					
<37	2,691 (6.1%)	2,668 (6.1%)	14 (4.1%)	6 (8.6%)	3 (6.1%)
37-40	37,229 (84.3%)	36,841 (84.3%)	290 (85.6%)	57 (81.4%)	41 (83.7%)
>40	4,227 (9.6%)	4,180 (9.6%)	35 (10.3%)	7 (10.0%)	5 (10.2)
Gestational age (weeks)	39 (38-40)	39 (38-40)	39 (39-40)	39 (38-39)	39 (39-40)
Birth Weight (g)	3,420 (3,130- 3,720)	3,420 (3,130- 3,720)	3480 (3170- 3800)	3245 (3000- 3515)	3440 (3160- 3790)
Age at screening (hours)	20 (15.0- 24.0)	20 (15.0- 24.0)	20 (16.0- 24.0)	19.5 (15.8- 24.0)	19 (15.5- 24.0)
Delivery method					
Natural birth	24,159 (54.7%)	23,894 (54.7%)	205 (60.4%)	35 (50.0%)	25 (51.0%)
Cesarean section	19,946 (45.2%)	19,754 (45.2%)	133 (39.2%)	35 (50.0%)	24 (49.0%)
Natural birth to cesarean section	42 (0.1%)	41 (0.1%)	1 (0.2%)	0	0

Table 2. Result of CHD cases

CHD Type	Mild CHD	Moderate CHD	Severe CHD	
	Case counts (%)	Case counts (%)	Case counts (%)	Total case counts (%)
ASD	70 (15.3)	24 (5.2)	0 (0)	94 (20.5)
ASD&PDA	76 (16.6)	13 (2.8)	10 (2.2)	99 (21.6)
COA	0	1 (0.2)	0	1 (0.2)
CTA	0	1 (0.2)	0	1 (0.2)
PAPVC	0	2 (0.4)	0	2 (0.4)
PDA	127 (27.7)	9 (2.0)	21 (4.6)	157 (34.3)
TAPVC	0	0	3 (0.7)	3 (0.6)
TGA	0	0	2 (0.4)	2 (0.4)
TOF	0	0	2 (0.4)	2 (0.4)
VSD	27 (5.9)	7 (1.5)	4 (0.9)	38 (8.3)
VSD&ASD	14 (3.1)	5 (1.1)	2 (0.4)	21 (4.6)
VSD&ASD&PDA	9 (2.0)	3 (0.7)	2 (0.4)	14 (3.1)
VSD&PDA	16 (3.5)	5 (1.1)	3 (0.7)	24 (5.2)
Total	339 (74.0)	70 (15.3)	49 (10.7)	458 (100)

Table 3. Detection rate for CHD types

		Detection rate		
CHD types	N	Auscultation alone	Pulse oximetry alone	Auscultation or pulse oximetry
Study Period Data				
ASD	94	94	0	0
ASD&PDA	99	99	0	0
COA	1	0	1	0
CTA	1	0	1	0
PAPVC	2	0	2	0
PDA	157	154	3	0
TAPVC	3	0	3	0
TGA	2	0	2	0
TOF	2	0	2	0
VSD	38	35	3	0
VSD&ASD	21	20	1	0
VSD&ASD&PDA	14	12	2	0
VSD&PDA	24	24	0	0
In Total	458	438	20	0
First Half of 2020 Data				
ASD	6	6	0	0
VSD	8	8	0	0
PDA	10	10	0	0
ASD&VSD	2	2	0	0
VSD&PDA	2	2	0	0
TOF	1	0	1	0
TAPVC	1	0	1	0
In total	30	28	2	0

Table 4. Screening accuracy for CHD new born (n=44,147)

	Pulse oximetry alone	Auscultation alone	Auscultation or pulse oximetry
True positives	31	438	458
False negatives	427	20	0
False positives	877	33	40
True negatives	42,812	43,656	43,649
Sensitivity	6.77%	95.63%	100.00%
Specificity	97.99%	99.92%	99.91%
Positive Predict Value	3.41%	92.99%	91.97%
Negative Predict Value	99.01%	99.95%	100%

Table 5. Prenatal trace back of confirmed CHD cases excluding PDA and ASD cases (n=108)

Conditions	Case counts	Percentage (%)
Prenatal identification of CHD		
VSD	35	32.41
COA	1	0.93
TOF	1	0.93
Prenatal identification of non-CHD	51	47.22
Unclear ultrasound image	3	2.78
No prenatal screening	14	12.96
Lost to trace back	3	2.78

Figures

Figure 1

Screening process