Ascertaining the Prevalence of Heart Malformations in Neonates: A Novel Clinically Approved Solution

Arash Bordbar
Iran University of Medical Sciences (IUMS)
Mandana Kashaki
Iran University of Medical Sciences (IUMS)
Maryam Vafapour
Pediatrician, Ali-Asghar Hospital, Iran University of Medical Sciences
Amir A. Sepehri (sepehri@capis.be)
CAPIS Biomedical R&D Director
Elaheh Partovi
GSN Pars

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Abstract

Background: Screening for critical congenital heart defects should be done as early as possible and is essential to save lives and reduce the incidence of undetected adult congenital heart diseases. Over 50% of neonates with heart malformations remain unrecognized at birth. Accurate screening for congenital heart malformations is achievable using a certified and internationally patented digital intelligent phonocardiography machine. This study aimed to assess the actual incidence of newborn heart defects in a well-baby nursery and evaluate digital intelligent phonocardiogram screening for critical congenital heart defects.

Methods: We conducted the "Neonates Cardiac Monitoring Research Project" (ethics approval number: IR-IUMS-FMD. REC.1398.098) at the Shahid Akbarabadi Maternity Hospital. This study is a retrospective analysis of screening congenital heart malformation in 840 neonates. Randomly, 840 neonates from the well-baby nursery underwent standard clinical examinations at birth and digital intelligent phonocardiogram examination in a double-blinded format. A pediatric cardiologist performed echocardiography for each neonate classified as abnormal using the intelligent machine or routine medical examinations. If a follow up was demanded by the pediatric cardiologist, the neonate was considered as having a congenital heart malformation and the cumulative incidence proportion was calculated accordingly.

Results: The incidence of heart malformations in the well-baby nursery was 5%, and 44% of neonates with heart malformations were unrecognized at birth based on the standard medical examination results, including those with critical congenital heart defects (CCHD). An intelligent phonocardiogram recognized 100% of neonates with heart malformations.

Conclusion: We accurately and cost-effectively screened for congenital heart malformations in all neonates in our hospital using a digital intelligent phonocardiogram. We detected neonates with CCHD and congenital heart defects using an intelligent machine; these could not be detected using standard medical examinations. In addition, the intelligent machine interpreted innocent murmurs as healthy heart sounds.

Introduction

Congenital heart malformations are grouped in the following categories: congenital heart defects (CHD) and critical congenital heart defects (CCHD). CHD and CCHD are leading causes of birth defect-associated infant illness and death (1, 2) and account for 10% of all congenital anomalies (3). However, approximately 30% of mortalities due to congenital malformations are caused by CCHD and CHD (4). The occurrence of CCHD and severe CHD is approximately 3 in 1000 neonates (5, 6). Despite antenatal screening processes using fetal echocardiography, more than 50% of neonates with heart malformations remain unrecognized at birth (7, 8). Previous studies have shown that the number of adult patients with CHD is remarkably high, and we are facing a “tsunami” in terms of adult CHD cases (9, 10, 11). Consequently, timely screening of neonates’ cardiac health is vital (12, 13).

Owing to the limitations of the human auditory system (e.g., masking effect), and existence of clicks and non-pathological extra heart sounds, some heart abnormalities may not produce an audible murmur (14, 15); thus, screening the heart malformations using conventional auscultation is not accurate. Doppler echocardiography is an accurate screening modality; however, it requires intervention by a pediatric cardiologist, and diagnostic timing is relatively long. In addition, performing Doppler ultrasound screening for every neonate is not practical, and it remains a subject of debate in as much as screening all neonates for congenital heart malformations is concerned (5,16, 17).

Screening for CHD in neonates is essential to save lives and reduce the incidence of undetected pediatric and adult congenital heart diseases. Most heart sounds in neonates are inherent additional sounds, which are not indications of any disease; they are merely sounds rooted in the physiology of newborns’ hearts called innocent murmurs (15). High pulmonary pressure, high heart rate, and innocent murmurs, among other factors, make screening for congenital heart malformations in neonates inaccurate when using standard medical examinations, rendering high positive and negative errors (2, 18). Occasionally, babies with healthy hearts are referred to the subspecialist medical department for safety. Referring children to pediatric subspecialist cardiovascular centers is a significant concern and source of worry for parents (19). It is vital to screen for severe and critical congenital heart defects in neonates as early as possible (19). CCHD screening by pulse oximetry could detect approximately 50% of CCHD malformations, whereas the other 50% of neonates with CCHD (such as coarctation of the aorta or transposition of the great arteries) are less likely to be detected by pulse oximetry (20, 21). Mandated critical CHD screening by pulse oximetry reduces early infant deaths from critical CHD by 33% (22). There are also other limitations in using pulse oximetry screening, such as the effect of the altitude of the location on the oxygen level and the timing of the procedure, which is recommended to be done 24 h after birth (23).

Based on our internationally patented technology, we have developed the first accurate intelligent digital phonocardiogram for screening congenital heart defects in children from 28 days after birth up to 12 years in 2008 (24). The first version required simultaneous acquisition of electrocardiogram signal in order to be able to segment children’s heart sounds correctly. We have developed a new algorithm for automatic segmentation of children’s heart sounds without using electrocardiogram signal (25). Efficiency, sensitivity and specificity of the intelligent machine for detection and discrimination of cardiac murmur was first published in a medical journal in 2013 (3). The first robust and commercialized intelligent phonocardiogram for automatic screening children’s congenital heart malformations (from 28 days up to 12 years), was presented on the market in 2015 (26).. After the publication of our internationally patented mathematical modeling of children heart’s sound production and its specifications, some medical universities, in conjunction with engineering schools, have developed research versions of the intelligent phonocardiogram and validated its proper functioning (27, 28, 29, 30, 31, 3).

The actual incidence of heart malformations (CHD and CCHD) in neonates is subject to social and economic factors in different societies, e.g. mothers with gestational diabetes carry a risk of causing heart malformations in their children. To date, the only known solution for accurate screening of neonatal congenital heart malformations is Doppler ultrasound; however, it is expensive and not practical, especially in less privileged areas. Accurate screening for congenital heart malformations in neonates is now achievable using a neonatal version of the certified and internationally patented digital intelligent phonocardiography machine, known as Pouya Heart.

This study aimed to assess the actual incidence of newborn heart malformations in a well-baby nursery and evaluate the neonatal version of the digital intelligent phonocardiogram screening for critical congenital heart defects. This is the first study to evaluate the incidence of heart malformation in neonates using intelligent phonocardiography.

Materials And Methods

Study setting

The obstetrics and gynecology departments of our hospital are accredited for the four-year residency period, and are considered the largest specialized centers in the field in Iran. Our hospital is a tertiary referral center for gynecological and neonatal patients, with the largest and most advanced neonatal intensive care unit in the country, with sixty active beds. Approximately 15 babies are born daily at our hospital. Each neonate undergoes routine medical examination. Newborns with possible CCHD or any other types of diseases requiring special care are taken directly to the neonatal intensive care unit, whereas healthy neonates are taken to the well-baby nursery. Those with possible CHD are also taken to the well-baby nursery for an echocardiography examination. Echocardiography is also performed in neonates with gestational age <34 weeks, weighing < 1,500 g, and whose mothers had gestational diabetes or any other illness that carries a risk of causing heart malformations in their children.

Study design and population

This is a retrospective analysis in 840 neonates. Overall, neonates randomly selected from the well-baby nursery underwent intelligent phonocardiogram screening in a double-blinded manner. Informed consent was obtained from their legal guardians according to the study protocol. The local ethics committee of the Shahid Akbarabadi Clinical Research & Development Unit approved the study (approval number: IR.IUMS.FMD.REC.1398.098), and the study was conducted according to the guidelines of the World Medical Association and Declaration of Helsinki.

A pediatric cardiologist with at least 12 years of expertise in the field performed echocardiography diagnosis for each neonate classified as abnormal by the intelligent machine. The dataset included the following data: rate and strength of the pulse, neonatologist auscultation, pulse oximetry testing of four limbs, family records, intelligent phonocardiography examination results, echocardiography diagnosis results, echocardiography follow-up, and notes on family records screening.

Intelligent Phonocardiography Machine

The intelligent phonocardiogram comprises an electronic stethoscope, medical computer cart, and medical monitor (25). It is run by an operator, who is required to have a bachelor's degree in applied science and should have passed 60 hours of training on the machine. The technician recorded 10 s of heart sounds from two different sites of either one of the four thoracic sites of a newborn using the digital stethoscope of the intelligent machine. The result appeared on the screen as normal or abnormal in real-time and in a printout. Recording of the heart sound was performed in a room with reduced background noise; there was no timing limitation for performing intelligent machine examination. On an average, it took approximately 6 minutes between two consecutive examinations. The machine considers a neonate's heart sound healthy if the diagnostic results from both thoracic sites are healthy. The intelligent machine automatically interprets innocent murmurs as healthy sounds (3, 24, 25).

Neonatal version of the intelligent phonocardiography machine: Pouya Heart

The intelligent phonocardiogram, Pouya Heart (designed and developed by CAPIS in Mons, Belgium, www.capis.be), is a passive technology for accurate CHD and CCHD screening in neonates. It is based on our internationally patented technology (European patent number: 2249707, US patent number: 8,649,854, Indian patent number: 333694, Iranian patent number: 139/02/25-69899, Russian patent number: 2512794, and Chinese patent number: 1045312; The *Patent* Cooperation Treaty (PCT) number EP2009/051410) using spectral mathematical modeling of a neonate's heart sound generation, in conjunction with advanced artificial intelligence and machine learning techniques. We have defined a power spectral density function for normal heart sounds. A discriminative frequency band is attributed with each congenital heart malformation named Arash-Band. The Arash-Band for a heart malformation is defined as the band for which spectral energy provides the maximum of discrimination with respect to the normal spectral density function (24). The intelligent machine groups heart sounds into two classes: normal or abnormal in real-time. The machine has obtained approval and certifications from the Iranian Society of Neonatology and the Ministry of Health and Medical Education.

The incidence of small patent foramen ovale (PFO) is relatively high in newborns (32, 33). The Pouya Heart screens for all heart defects, including small PFOs, and we selected the option of not detecting small PFOs in this study.

Results

Screening 840 neonates, with a median age of 30.85 h and median weight of 3.12 kg, for congenital heart malformations using Pouya Heart resulted in the detection of 43 neonates with abnormal heart sounds, including one case of CCHD, one case of severe CHD, and one false-positive error. The types of the 42 congenital heart malformations identified by echocardiography are shown in Table 1.

Table 1. Echocardiogram findings of the intelligent machine (n=42)

Row no.	Echocardiography findings	Number of patients
1	small ASD	5
2	small ASD/mild TR	1
3	small VSD	1
4	PDA with significant shunt	1
5	large PFO/mid mmc VSD/LR shunt	1
6	PDA with continuous shunt	1
7	PDA with the mild left to right shunt	1
8	small PDA	5
9	PFO/small PDA	5
10	PFO	2
11	PDA/PFO	2
12	PDA/mil TR	2
13	PFO/small PDA/mild IHSS	2
14	PFO/mil IHSS	2
15	PDA/LVH/IHSS	1
16	PFO/LVH	1
17	mild TR	1
18	LVH	2
19	mild LVH/mild IHSS	2
20	mild LPA stenosis	2
21	IHSS/IVC	1
22	COA (CCHD)	1

ASD: Atrial Septal Defect; VSD: Ventricular Septal Defect; PDA: Patent Duct Arteriosus; COA: Coarctation PFO: Patent Froramen Ovale; TR: Tricuspid valve Regurgitation; IHSS: Idiopathies Hypertrophic Subaortic Stenosis; IVC: Inferior Vena Cava; LPA: Left Pulmonary Artery; LVH: Left Ventricular Hypertrophic

Table 2 shows that based on the routine medical examinations, 44% of the 42 abnormal cases were unrecognized at birth. The incidence of congenital heart malformations in our well-baby nursery was 5% (Table 2).

Table 2. Data of neonates included in this study (N=840)

Median age	30.85 h
Timing of the intelligent machine examination	1 to 192 h after birth
Median weight	3.12 kg
Number of female neonates	414
Number of male neonates	426
Heart malformations Detected	42 (Male: 29; Female 13)
Auscultation (human ear), false-negative error	79%
Standard medical examination, including auscultation, false-negative errors	44%
Intelligent machine, false-negative error	0%
Auscultation (human ear), false-negative error	79%
Intelligent machine, CHD & CCHD, correct detection rate	100%

CHD: Congenital Heart Defects; CCHA: Critical CHD

Table 2 shows that the neonate with CCHD was undiagnosed at birth by routine medical examination. The routine medical examination results of this neonate with CCHD included a pulse oximetry of 96%, healthy auscultation, and no abnormal family history. Table 2 shows that standard medical examinations diagnosed only 56% of neonates with heart malformations at birth. Simultaneously, the digital intelligent phonocardiogram examination recognized 100% of the 42 abnormal cases, including one neonate with CCHD and one with severe CHD, which were not recognized through standard examination. Screening by the Pouya Heart takes 6 minutes on average and is operated by a technician. Echocardiography takes approximately 30 minutes and is performed by a pediatric cardiologist. The price of the Pouya Heart and the maintenance costs are much lower than that of the echocardiogram. Therefore, comparing the cost of conducting 43 echocardiography scans and 840 intelligent phonocardiogram examinations to that of conducting 840 echocardiography scans shows that our study was highly cost-effective. The dataset showed that intelligent machine examinations were performed from 1 h to 192 h after birth, and Doppler echocardiography was performed from 2 to 72 h after Pouya Heart screening. Tables 1 and 2 present detailed data on the 42 abnormal cases recognized by the Pouya Heart.

Discussion

The dataset showed that the Pouya Heart detected 43 neonates with heart malformations. Of these, 42 had heart defects as confirmed by echocardiography. The pediatric cardiologist requested follow-up for all 42 cases. Therefore, the false-positive error rate of Pouya Heart was 0.1%. However, the pediatric cardiologist performed echocardiography 48 h after Pouya Heart auscultation. Consequently, it is possible that Pouya Heart detected trivial heart defects, which self-recovered after 48 h. Self-recovery of trivial CHD after 48 h is probable. The complete screening process using Pouya Heart took approximately six minutes, and a trained technician operated the Pouya Heart. The main cost of this study included screening 840 neonates with Pouya Heart and echocardiography diagnosis of 43 neonates. The other alternative to reaching such a result was performing 840 echocardiography using pediatric cardiologists.

This study had some limitations. First, screening newborn CHD and CCHD using Pouya Heart is novel consequently, not all families followed the recommended echocardiography examinations for their newborns that were recommended by the Pouya Heart examination. The second limitation was, according to the study design, we needed to replace neonates who did not undergo the echocardiography examination randomly with neonates from the well-baby nursery; 11 neonates with abnormal heart sounds detected by Pouya Heart did not undergo echocardiography; consequently, we replaced them with new neonates from the well-baby nursery. Therefore, there is a possibility that the number of neonates with congenital heart malformations undetected by standard medical examination would have increased to 58%, if the 11 neonates had undergone echocardiography or if other newborns in the well-baby nursery were unavailable to replace them, or if we replaced the 11 neonates by those who had been recognized as having abnormal heart sounds by the Pouya Heart examination. Third, we did not examine for small PFOs (32, 33). However, precise prevalence of heart malformation in neonates can be reached if small PFOs are chosen to be detected by Pouya Heart examination. The fourth limitation is that Pouya Heart screening is based on heart sound analysis (3, 26). Therefore, it is important to reduce the interference of background noise, such as artefact, air conditioner noise, and ringing of the telephone. Adult congenital heart defects increase by 5% annually (9). Combining screening by Pouya Heart and routine medical examinations not only allow the timely detection of all neonates with congenital heart malformations but also considerably lowers the number of adult patients with CHD.

In summary, we introduced a novel, practical, and cost-effective method for screening CHD and CCHD in newborns that can be performed immediately after birth. Pouya Heart detected neonates with heart malformations, including CCHD and CHD cases, who were unrecognized at birth by routine medical examinations in our hospital. Moreover, Pouya Heart interpreted innocent murmurs as healthy heart sounds.

Timely screening of neonates' cardiac health is vital. Screening for CCHD should be done as early as possible. Screening for CHD in neonates is essential to save lives and reduce the incidence of undetected pediatric and adult congenital heart diseases. Therefore, screening newborns for heart malformations using Pouya Heart will significantly affect pediatric heart healthcare and eliminate unrecognized adult CHD cases. The intelligent machine should be tested at various hospitals in different countries to validate its accuracy across population types.

Declarations

Conflict 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.

Author Contributions

AB was the principal author of the study and contributed to the design of the study, performed data verification and analyses and drafted the first version of the manuscript. MK contributed to the design of the study and drafted the first version of the manuscript. MV performed data collection, verification and analyses, and drafted the first version of the manuscript. AS, the principal inventor of the Pouya Heart, performed technical supervision and drafted the first version of the manuscript. All authors provided substantial conceptual and intellectual contribution and approved the final version of the manuscript.

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Data Availability Statement

The datasets generated and analyzed and the printout for this study can be found in the CAPIS repository; the dataset link is: https://capis.be/media/hstlreco/840-neonates-examination-result.pdf and the printout can be found here: https://capis.be/media/gznagtbc/pouya-heart-printouts.rar

Abbreviations

CHD, congenital heart disease; CCHD, critical CHD.

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