Post-Print: Application of Appropriate Technology for Screening, Diagnosis, and Evaluation of Congenital Heart Disease in Neonates at 6 to 72 Hours After Birth in 17 Cities and Counties of Hainan Province

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Abstract

Background Congenital heart disease (CHD) is one of the major types of birth defects globally and a leading cause of death in children. However, the current situation of delayed diagnosis of CHD is not optimistic, and early detection, early diagnosis, and early treatment of CHD in children have become a focus of research.

Objective By establishing and applying an appropriate technical system for newborn CHD screening-diagnosis-assessment in Hainan, to evaluate the operational efficacy of this technology and provide evidence for further promotion of this technology.

Methods In all delivery institutions in 17 cities and counties of Hainan Province, as well as local neonatal departments or NICUs, screening personnel used dual indicators, namely cardiac auscultation and transcutaneous pulse oximetry (POX), to screen live-born neonates at 6 to 72 hours after birth. Neonates with one or more positive results were considered screening-positive. Thirty-one diagnostic institutions certified by the Hainan Provincial Health Commission performed echocardiographic diagnosis on screening-positive live-born neonates. Pediatric cardiovascular physicians and surgeons with appropriate qualifications in six certified tertiary Grade A hospitals reviewed the diagnostic results and conducted necessary re-evaluations, provided corresponding medical intervention recommendations according to the condition, or implemented treatment. Data from screening, diagnosis, assessment, and treatment were networked for reporting, uploading, and management through the Neonatal Congenital Heart Disease Screening Work Information Management System.

Results From January 1, 2020 to December 31, 2021, the number of live-born neonates in Hainan Province was 206761, and 204442 live-born neonates participated in the CHD screening program, with an overall screening rate of 98.87% (204442/206761). There were 5847 screening-positive cases, with a screening positive rate of 2.86% (5847/204442). A total of 527 cases were diagnosed with CHD by echocardiography, with a CHD prevalence of 2.58‰ (527/204442). Atrial septal defect was the most common CHD lesion, with a constituent ratio of 38.14%. There were 291 cases of non-significant CHD, accounting for 55.22%; 142 cases of significant CHD, accounting for 26.94%; 88 cases of severe CHD, accounting for 16.70%; and 6 cases of critical CHD, accounting for 1.14%. The sensitivity of cardiac auscultation, POX, and dual-indicator combined detection for CHD was 67.93%, 37% and 93.35%, respectively; the specificity was 98.07%, 99.28% and 97.3%, respectively. The rate of dual-indicator positivity at initial screening for severe CHD (severe and critical types) was significantly higher than that of single-indicator positivity, with a statistically significant difference (2=13.053, P=0.001). All neonates diagnosed with CHD received assessment, and 94 neonates with severe CHD received timely treatment, with 4 deaths. The standardized mortality rate of CHD in children aged 0-1 years was 1.93/100000 (4/206761), and the case fatality rate of severe CHD was 4.26% (4/94).

Conclusion The dual-indicator method for screening newborn CHD is non-invasive, simple, easy to operate, and reliable, thus facilitating promotion. Establishing an appropriate technical system for newborn CHD screening-diagnosis-assessment is beneficial for timely diagnosis and treatment of CHD, especially timely treatment of severe CHD, and is conducive to reducing mortality. Therefore, the establishment of this appropriate technical system is of great significance.

Full Text

Preamble

Appropriate Technology for Screening, Diagnosis, and Evaluation of Congenital Heart Disease in Neonates in Hainan Province

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Abstract

Background: Congenital heart disease (CHD) represents one of the major types of birth defects globally and constitutes a leading cause of childhood mortality. However, the current situation of delayed CHD diagnosis remains concerning, making early detection, diagnosis, and treatment of pediatric CHD a critical research priority.

Objective: To evaluate the operational effectiveness of an appropriate technology system for neonatal CHD screening-diagnosis-evaluation established and implemented in Hainan, providing evidence for further promotion of this technology.

Methods: At all delivery institutions across 17 cities and counties in Hainan Province, as well as local neonatology departments or NICUs, trained screening personnel employed a dual-indicator approach—cardiac auscultation and pulse oximetry (POX)—to screen live-born neonates within 6–72 hours after birth. Neonates with one or more positive indicators were classified as screen-positive. Thirty-one diagnostic institutions certified by the Hainan Provincial Health Commission performed echocardiographic diagnosis on screen-positive neonates. Qualified pediatric cardiovascular physicians and cardiac surgeons at six certified tertiary hospitals reviewed and re-evaluated the diagnostic results as necessary, providing appropriate medical intervention recommendations or implementing treatment according to condition severity. Screening, diagnosis, evaluation, and treatment data were entered, uploaded, and managed through a networked neonatal CHD screening information management system.

Results: From January 1, 2020, to December 31, 2021, there were 206,761 live births in Hainan Province, of which 204,442 participated in the CHD screening program, yielding an overall screening rate of 98.87% (204,442/206,761). A total of 5,847 neonates screened positive, for a screening positivity rate of 2.86% (5,847/204,442). Echocardiography confirmed CHD in 527 cases, resulting in a CHD prevalence of 2.58‰ (527/204,442). Atrial septal defect was the most common lesion, accounting for 38.14% of cases. Non-significant CHD comprised 291 cases (55.22%); significant CHD, 142 cases (26.94%); serious CHD, 88 cases (16.70%); and critical CHD, 6 cases (1.14%). The sensitivity of cardiac auscultation, POX, and dual-indicator combined screening for CHD detection was 67.93%, 37%, and 93.35%, respectively; specificity was 98.07%, 99.28%, and 97.3%, respectively. The proportion of severe CHD (serious and critical types) with dual-indicator positivity at initial screening was significantly higher than that with single-indicator positivity (^{2} = 13.053, P = 0.001). All diag-

nosed CHD patients received evaluation; 94 severe CHD patients received timely treatment, with 4 deaths occurring. The standardized mortality rate for CHD in children aged 0–1 years was 1.93/100,000 (4/206,761), and the case fatality rate for severe CHD was 4.26% (4/94).

Conclusion: The dual-indicator method for neonatal CHD screening is non-invasive, simple, easy to operate, and reliable, making it suitable for widespread implementation. Establishing an appropriate technology system for neonatal CHD screening-diagnosis-evaluation facilitates timely diagnosis and treatment of CHD, particularly urgent intervention for severe CHD, thereby reducing mortality. This system holds significant practical importance.

Keywords: Congenital heart disease; screening; pulse oximetry; cardiac auscultation; echocardiography

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1. Methods

1.1 Study Design

This project constituted part of the "Neonatal CHD Screening Program Work Plan" [2018] No. 68 issued by the Department of the National Health Commission. The project design comprised: (1) **Screening Procedure:** After obtaining informed consent and signing the "Hainan Province Neonatal CHD Screening Parent Notification" printed by the Hainan Provincial Health Commission Office, trained and qualified physicians or nurses performed CHD screening on live-born neonates at 6–72 hours after birth using the dual-indicator method (cardiac auscultation and pulse oximetry). (2) **Diagnostic Procedure:** Thirty-one medical institutions certified by the Hainan Provincial Health Commission with neonatal CHD diagnostic qualifications performed echocardiographic diagnosis on screen-positive neonates and issued echocardiography reports with result interpretation. Screen-negative neonates who developed CHD symptoms during 3–12 month follow-up also received echocardiography at diagnostic institutions. (3) **Evaluation Procedure:** Qualified pediatric cardiovascular physicians and cardiac surgeons at six tertiary hospitals certified by the Hainan Provincial Health Commission (Hainan Women and Children' s Medical Center, First Affiliated Hospital of Hainan Medical College, Second Affiliated Hospital of Hainan Medical College, Hainan Provincial People's Hospital, Haikou Municipal People' s Hospital, and Sanya Maternal and Child Health Hospital) reviewed and re-evaluated diagnostic results as necessary, providing medical intervention recommendations or implementing treatment based on condition severity. (4) **Evaluation Metrics:** The program assessed screening rate, screening positivity rate, referral completion rate, echocardiography examination rate among screen-positive cases, positive confirmation rate, CHD prevalence, and mortality; it also evaluated the sensitivity and specificity of the two CHD screening indicators across delivery institutions and NICUs in Hainan' s 17 cities and counties.

1.2 Screening Sites

All delivery institutions in 17 cities and counties of Hainan Province (Haikou, Wenchang, Danzhou, Wanning, Wuzhishan, Dongfang, Sanya, Qionghai, Chengmai, Ding' an, Tunchang, Baoting, Qiongzhong, Changjiang, Ledong, Lingao, and Lingshui), as well as local neonatology departments or NICUs.

1.3 Training and Responsibilities of the CHD Screening-Diagnosis-Evaluation System

Led by the Hainan Women and Children' s Medical Center, this project conducted training across all cities and counties according to the "Neonatal CHD Screening Program Work Plan" [2018] No. 68 requirements, providing standardized training on the two CHD screening indicators: cardiac murmur auscultation and POX measurement.

1.3.1 Responsibilities of Screening Institutions Screening personnel performed standardized screening on live-born neonates, entering name, age, ethnicity, residence, and screening results into the dedicated neonatal CHD screening network system. For screen-positive cases, guardians were notified promptly and referral to CHD diagnostic institutions was arranged within one week. For screen-negative cases, guardians were advised to maintain follow-up.

1.3.2 Responsibilities of Diagnostic Institutions Diagnostic institution sonographers performed echocardiographic diagnosis on screen-positive neonates using the "Neonatal CHD Diagnostic Manual (2018 Edition)" issued by the National Neonatal CHD Screening Program Management Office as the diagnostic standard. Examinations combined two-dimensional ultrasound with color Doppler using sequential segmental analysis for congenital heart disease. Diagnostic results were entered into the dedicated neonatal CHD screening network system.

1.3.3 Responsibilities of Evaluation Institutions The six evaluation institutions assessed severity for all neonates diagnosed with CHD via echocardiography across the province, providing appropriate medical intervention recommendations or implementing treatment and entering corresponding treatment outcome information. The flowchart of this appropriate technology is shown in Figure 1.

Figure 1 [Figure 1: see original paper] Protocol of Appropriate Technology for Screening, Diagnosis, and Evaluation of CHD

Note: POX = pulse oximetry; SpO_2 = percutaneous oxygen saturation; CHD = congenital heart disease

1.4 Screening Criteria and CHD Classification

1.4.1 Screening Subjects and Positive Criteria Live-born neonates at 6-72 hours after birth in all delivery institutions across Hainan's 17 cities and counties from January 1, 2020, to December 31, 2021, including those transferred to local neonatology departments or NICUs due to medical conditions, were included for CHD screening. Neonates with positivity in either cardiac murmur auscultation or POX, or both indicators, were classified as screen-positive, while those negative for both indicators were classified as screen-negative [2]. Positivity in any indicator was defined as: (1) **Cardiac murmur auscultation**—detection of grade 2 or higher murmurs in any valve auscultation area during any cardiac cycle (systolic, diastolic, or entire cycle) in a quiet environment; or (2) **POX measurement**—percutaneous oxygen saturation below 90% in either the right hand or any foot; or saturation of 90-94% in the right hand or any foot, or a difference >3% between right hand and any foot, with no change upon repeat measurement after 2-4 hours [2].

1.4.2 CHD Inclusion and Exclusion Criteria Echocardiographic diagnosis served as the gold standard. Included CHD cases were classified by severity using established methods [3,4]: (1) **Non-significant:** CHD without clinical signs or cardiac lesions persisting less than 6 months; (2) **Significant:** Cardiac lesions persisting over 6 months requiring regular monitoring or medication but not classified as serious or critical; (3) **Serious:** Cardiac lesions requiring intervention (surgery or catheterization) before 1 year of age; (4) **Critical:** CHD resulting in death or requiring intervention within 28 days after birth. This study categorized serious and critical types as severe CHD, and significant and non-significant types as mild CHD. Exclusion criteria included: (1) Patent ductus arteriosus (PDA) in premature infants (except those undergoing PDA ligation) or PDA that spontaneously closed within 3 months; (2) Increased pulmonary branch flow velocity without luminal narrowing; (3) Hemodynamically insignificant isolated anomalies (persistent left superior vena cava, fusion of aortic arch branches, bicuspid aortic valve without stenosis).

1.5 Quality Control

(1) The first author maintained close contact with delivery institutions to guide and assess problem resolution during screening and diagnosis; (2) All data were uploaded to the Neonatal CHD Screening Information Management System (https://www.nchd.org.cn/Admin/System/Admins/login); (3) Project team members from the Hainan Women and Children' s Medical Center supervised and managed data for the provincial neonatal CHD screening program. This study was approved by our institutional ethics committee (Approval No. 2021-107).

1.6 Statistical Analysis

SPSS 17.0 software was used for statistical analysis. Count data were expressed as [n (%)], and chi-square (^{2}) tests were performed, with $P < 0.05$ considered statistically significant. Screening rate, screening positivity rate, referral completion rate, echocardiography examination rate among screen-positive cases, positive confirmation rate, CHD prevalence, and mortality were calculated. True positive, true negative, false positive, false negative, sensitivity, specificity, positive predictive value, negative predictive value, and Youden' s index were calculated for different screening indicator combinations.

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2. Results

A total of 204,442 live-born neonates participated in the CHD screening program, including 103,317 males. The overall screening rate was 98.87% (204,442/206,761). Figure 2 shows the number of live births, screened neonates, and screening rates across Hainan' s 17 cities and counties, with all areas meeting the project requirement of >95% screening rate. Among participants, 5,847 screened positive (2.86% positivity rate). Within one week, 5,585 screen-positive neonates were referred for echocardiography, achieving a referral completion rate of 95.5% (5,585/5,847). Due to various reasons (parental attitudes, long travel distances, infant crying precluding examination), 262 screen-positive neonates did not undergo echocardiography within one week but eventually received examination within 1–2 months after birth through follow-up and persuasion by screening institutions, resulting in a 100% echocardiography examination rate among screen-positive cases (5,847/5,847). Echocardiography confirmed CHD in 492 cases, yielding a positive confirmation rate of 8.41% (492/5,847). During 3–12 month follow-up of screen-negative cases, 35 additional CHD cases were identified through symptom-based echocardiography, bringing the total confirmed cases to 527 and the overall CHD prevalence to 2.58‰ (527/204,442).

Figure 2 [**Figure 2: see original paper**] Count of Live Births and Screened Neonates, and Screening Rates of 17 Cities and Counties in Hainan Province

2.1 Diagnosis and Composition of Neonatal CHD

Among the 527 confirmed CHD cases, atrial septal defect (201 cases) was the most common type, accounting for 38.14% of cases. The distribution of neonatal CHD types is shown in Table 1 . Non-significant CHD comprised 291 cases (55.22%); significant CHD, 142 cases (26.94%); serious CHD, 88 cases (16.70%); and critical CHD, 6 cases (1.14%). The 35 CHD cases diagnosed during follow-up included 16 atrial septal defects, 10 patent ductus arteriosus, 4 ventricular septal defects, 3 pulmonary stenosis, 1 coarctation of the aorta, and 1 partial anomalous pulmonary venous connection, all classified as mild CHD.

Table 1 Distribution of CHD Types in Neonates

CHD Type	Cases [n (%)]
Atrial septal defect	201 (38.14)
Ventricular septal defect	135 (25.62)
Patent ductus arteriosus	104 (19.73)
Pulmonary stenosis	17 (3.22)
Partial anomalous pulmonary venous connection	10 (1.89)
Tetralogy of Fallot	9 (1.71)
Partial atrioventricular septal defect	7 (1.33)
Coarctation of the aorta	5 (0.95)
Interrupted aortic arch	5 (0.95)
Total anomalous pulmonary venous connection	4 (0.76)
Complete transposition of great arteries	4 (0.76)
Pulmonary atresia	4 (0.76)
Double outlet right ventricle	3 (0.57)
Complete atrioventricular septal defect	2 (0.38)
Congenital right aortic arch	2 (0.38)
Congenital cleft mitral valve	2 (0.38)
Left ventricular outflow tract stenosis	1 (0.19)
Aortopulmonary septal defect	1 (0.19)
Congenital double aortic arch	1 (0.19)
Pulmonary sling	1 (0.19)
Aortic arch stenosis	1 (0.19)
Double outlet left ventricle	1 (0.19)
Congenital aortic stenosis	1 (0.19)
Congenital bicuspid aortic valve	1 (0.19)
Congenital tricuspid stenosis	1 (0.19)
Congenital pulmonary artery absence	1 (0.19)
Congenital brachiocephalic artery anomaly	1 (0.19)
Congenital pulmonary artery anomaly	1 (0.19)
Total	**527 (100)**

Note: Most patients had only one type of defect. For statistical convenience, only the primary defect was included. The primary defect was defined as the one with the greatest hemodynamic impact or requiring initial treatment. For example, in cases with ventricular septal defect combined with small atrial septal defect, only the ventricular septal defect was counted; in complete transposition of great arteries with ventricular septal defect, only the transposition was counted.

2.2 Value of Screening Indicators

Cardiac auscultation alone screened positive in 4,295 cases, confirming CHD in 358; POX alone screened positive in 1,661 cases, confirming CHD in 195; dual-indicator positivity occurred in 109 cases, confirming CHD in 61; and

dual-indicator combined screening yielded 5,847 positives, confirming CHD in 492 cases. The sensitivity of cardiac auscultation alone, POX alone, and dual-indicator combined screening for CHD was 67.93%, 37%, and 93.35%, respectively; specificity was 98.07%, 99.28%, and 97.3%, respectively. Dual-indicator combined screening demonstrated higher sensitivity than either single indicator with comparable specificity. The screening value of each indicator is shown in Table 2 .

Table 2 Value of Different Indicators for Neonatal CHD Detection

Indicator	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Positive Predictive Value (%) (95% CI)	Negative Predictive Value (%) (95% CI)
Cardiac auscultation	67.93 (63.73–71.87)	98.07 (98.01–98.13)	8.33 (7.53–9.21)	99.91 (99.90–99.93)
POX	37.00 (32.89–41.30)	99.28 (99.24–99.32)	11.74 (10.25–13.41)	99.84 (99.82–99.85)
Dual-indicator combined	93.35 (90.79–95.26)	97.30 (97.30–97.44)	8.42 (7.72–9.16)	99.98 (99.97–99.99)

2.3 Relationship Between Severe CHD and Screening Indicators

Among 94 severe CHD patients, 29 were screen-positive only by cardiac auscultation, 21 only by POX, and 44 by both indicators. Inter-group comparison revealed that the proportion of severe CHD with dual-indicator positivity at initial screening was significantly higher than with single-indicator positivity (^{2} = 13.053, P = 0.001), as shown in Table 3 .

Table 3 Relationship Between Severe CHD and Different Screening Indicators

Group	Severe CHD [n (%)]
Cardiac auscultation-positive only	29 (30.85)
POX-positive only	21 (22.34)
Dual-indicator positive	44 (46.81)

2.4 Treatment and Prognosis

All 94 severe (serious and critical) CHD patients received timely treatment, with 90 undergoing cardiac surgical repair and 4 receiving hybrid cardiac interventions. The 88 serious CHD cases included 37 ventricular septal defects, 11 patent

ductus arteriosus, 7 tetralogy of Fallot, 5 coarctation of the aorta, 4 congenital pulmonary stenosis, 4 pulmonary atresia, 4 total anomalous pulmonary venous connection, 3 interrupted aortic arch, 3 single ventricle, 2 complete atrioventricular septal defect, 2 complete transposition of great arteries, 1 congenital pulmonary artery absence, 1 atrioventricular septal defect, 1 congenital double aortic arch, 1 aortopulmonary septal defect, 1 double outlet right ventricle, and 1 tricuspid stenosis. The 6 critical cases comprised 2 interrupted aortic arch, 2 complete transposition of great arteries, 1 double outlet right ventricle, and 1 patent ductus arteriosus. Among 433 mild (significant and non-significant) CHD cases, 142 significant cases received treatment (42 surgical, 23 interventional, 77 medical therapy or close follow-up), while 291 non-significant cases remained under follow-up observation. Four deaths occurred (2 pulmonary atresia, 1 single ventricle, 1 total anomalous pulmonary venous connection), all in severe CHD patients who died postoperatively due to critical condition. The standardized mortality rate for CHD in children aged 0–1 years was 1.93/100,000 (4/206,761), and the case fatality rate for severe CHD was 4.26% (4/94).

3. Discussion

CHD accounts for nearly one-third of all major congenital anomalies and represents a major global birth defect [5]. However, delayed CHD diagnosis remains a serious concern worldwide, prevalent in both high-income and low-middle-income countries, and CHD is a leading cause of infant mortality. A study in a high-income country reported an 8.9% delayed diagnosis rate for CHD, including 10.4% for acyanotic and 8.7% for cyanotic types [6]. Another study found a 29.5% delayed diagnosis rate for critical CHD [7]. Research in low-middle-income countries indicated an 85.1% delayed diagnosis rate, attributed to inadequate health system training and socioeconomic constraints [8]. Murni IK et al. [9] studied 838 pediatric CHD patients (median age 2.9 years) and found delayed diagnosis rates of 54.9% for acyanotic and 86.2% for cyanotic CHD, with an overall 60.8% delayed diagnosis rate—most commonly due to physician delay, followed by midwifery care, economic factors, referral/follow-up, and social factors. At diagnosis, 49.4% of patients had developed heart failure and 15.8% had pulmonary hypertension, underscoring the importance of early detection and treatment. Stallings EB et al. [10] analyzed population-based surveillance data from 19 U.S. birth defect monitoring programs, identifying 18,587 severe CHD cases with an overall prevalence of 1.96‰, providing insights into risk factors for severe CHD. Experience from developed countries demonstrates that population-based birth defect surveillance systems enable early CHD detection and treatment, reducing mortality. Therefore, implementing a multi-center, large-population CHD monitoring system in China is essential.

Through this screening-diagnosis-evaluation program, we found a CHD prevalence of 2.58‰ in Hainan, similar to reports from other regions [11]. Diagnosed CHD was predominantly mild, with atrial septal defect being the most com-

mon type (38.14%). Severe CHD prevalence was 0.46‰ (94/204,442). Zhang X et al. [12] investigated the Zhejiang Province birth defect monitoring system (2014–2018) and similarly found predominantly mild pediatric CHD with atrial septal defect as the most common type, while severe CHD prevalence remained stable at 1.6‰ over time. Previous studies reported CHD prevalence across Chinese regions ranging from 1.5‰ to 16‰ [11,13–16], with variation primarily reflecting differences in mild CHD prevalence while severe CHD rates remained stable [17]. Regional variation may result from: (1) differences in diagnostic methods, selection criteria, and definitions across institutions; (2) variation in screener skills affecting detection rates; and (3) diverse environmental and genetic factors. Compared with previous Chinese studies, this project employed dual-indicator screening across all participating institutions in Hainan' s diverse geographic regions with a large multi-center sample, achieving near-complete provincial coverage (excluding Sansha City due to distance and transportation limitations), thereby minimizing bias while maintaining long-term follow-up of screen-negative neonates. Notably, the dual-indicator method is non-invasive, simple, and easy to operate, achieving a 98.9% screening rate across Hainan from 2020–2021, with all regions meeting targets—demonstrating its suitability for neonatal CHD screening in remote regions like Hainan.

This project employed cardiac auscultation combined with POX for CHD screening. Cardiac murmur auscultation is an important screening tool; Song J et al. [18] screened 3,327 neonates in Wenzhou, achieving 17.3% sensitivity and 99.7% specificity with murmur screening alone. In our study, cardiac auscultation screened positive in 4,295 cases, confirming CHD in 358, with 67.93% sensitivity and 98.07% specificity. The relatively low sensitivity of isolated cardiac murmur screening may relate to neonatal right ventricular dominance, where minimal pressure differences between left and right heart chambers result in small shunts and absence of high-velocity turbulent flow, making murmurs inaudible or atypical. POX is also crucial for neonatal CHD screening, detecting hypoxemic ductal-dependent or other severe CHD types. Seven severe CHD types have been identified as primary POX screening targets: hypoplastic left heart syndrome, pulmonary atresia, tetralogy of Fallot, anomalous pulmonary venous return, transposition of great arteries, tricuspid atresia, and truncus arteriosus [19]. Hu XJ et al. [2] screened 167,190 neonates at 15 Shanghai hospitals (July 2012–December 2014), finding POX alone had 44.3% sensitivity and 99.9% specificity. A meta-analysis of 22 studies (2002–2016) reported pooled sensitivity and specificity of 69% and 99% for POX screening of severe neonatal CHD [20]. In our study, POX screened positive in 1,661 cases, confirming CHD in 195, with 37% sensitivity and 99.28% specificity. The relatively low sensitivity of isolated POX screening likely reflects the predominance of non-severe CHD in our cohort, as these lesions typically involve small shunts, minor defects, and minimal hypoxemia. Studies show dual-indicator screening significantly improves CHD sensitivity [2,18]. Our study found dual-indicator screening achieved 93.35% sensitivity and 97.37% specificity, similar to Hu XJ et al. [2] (93.7% sensitivity, 98.3% specificity) and Song J et al. [18] (89.9% sensitivity, 94.7% specificity).

The dual-indicator approach showed higher sensitivity than either single indicator with the highest Youden' s index, indicating superior overall performance. We also found that severe CHD patients had significantly higher rates of dual-indicator positivity at initial screening than single-indicator positivity, likely due to more severe hemodynamic abnormalities producing both murmurs and hypoxemia. Therefore, neonates with dual-indicator positivity at initial screening warrant high priority for confirmatory echocardiography. However, some severe CHD may present with single-indicator positivity—for example, large ventricular or atrial septal defects with left-to-right shunting may produce murmurs without hypoxemia at rest, while anomalous pulmonary venous return with small shunts may cause hypoxemia without murmurs. During follow-up of dual-indicator negative cases, 35 mild CHD patients were identified, likely due to subtle murmurs or minimal hypoxemia causing false-negative screens, highlighting the importance of follow-up. In this project, all 94 severe CHD patients received timely treatment, as did most significant CHD patients, with only 4 deaths occurring. The standardized mortality rate for CHD in Hainan' s children aged 0–1 years was 1.93/100,000 during 2020–2021. Reported data [21] show 15,969 Chinese children aged 0–1 years died from congenital heart disease from 2004–2018, with mortality decreasing from 106.81/100,000 to 38.70/100,000. Hainan' s standardized mortality rate is substantially lower. Additionally, reported mortality for delayed severe CHD reaches 27% [22], while Hainan' s severe CHD case fatality rate was 4.26% (4/94), also significantly lower. These results demonstrate that this program facilitates timely CHD diagnosis and treatment, particularly urgent intervention for severe CHD, thereby reducing mortality.

The strengths of this appropriate technology system include: (1) near-complete provincial coverage with large sample size and high screening rate, providing representative data; (2) clear division of labor and good cooperation among screening, diagnostic, and evaluation institutions; (3) use of a dedicated neonatal CHD screening network system for real-time data management and monitoring; and (4) timely treatment of all severe CHD patients. Limitations include: (1) some parental non-participation may have led to underestimation of neonatal CHD prevalence; and (2) despite standardized training, screening application may have varied among individual screeners.

In summary, through implementation of this neonatal CHD screening-diagnosis-evaluation appropriate technology in Hainan, we found the dual-indicator method (cardiac auscultation + POX) to be non-invasive, simple, easy to operate, and highly sensitive and specific, making it suitable for neonatal CHD screening in remote regions. Establishing this appropriate technology system facilitates timely CHD diagnosis and treatment, particularly urgent intervention for severe CHD, thereby reducing mortality and holding significant practical importance.

Author Contributions: ZHANG Dufei conceptualized the research objectives and indicators, designed the study, performed feasibility analysis, conducted

data analysis and statistical processing, drafted the manuscript, and verified data. ZHANG Dufei was responsible for quality control and final approval, taking overall responsibility for the article. ZHANG Dufei, CHEN Renwei, MO Zelai, and YANG Ling jointly conducted screening training, quality management, and supervision. WANG Yazhou and WANG Haifan collected and organized data.

Conflict of Interest: The authors declare no conflict of interest.

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Note: Figure translations are in progress. See original paper for figures.