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Accuracy of cardiac auscultation in detection of neonatal congenital heart disease by general paediatricians

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Abstract

Background: Challenges remain in the judgement of pathological murmurs in newborns at maternity hospitals, and there are still many simple major CHD patients in developing countries who are not diagnosed in a timely fashion. This study aimed to evaluate the accuracy of cardiac auscultation on neonatal CHD by general paediatricians. *Methods:* We conducted a prospective study at three hospitals. All asymptomatic newborns underwent auscultation, pulse oximetry monitoring, and echocardiography. Major CHD was classified and confirmed through follow-up. We evaluated the accuracy of various degrees of murmurs for detecting major CHD to determine the most appropriate standards and time of auscultation. *Results:* A total of 6750 newborns were included. The median age of auscultation was 43 hours. Cardiac murmurs were identified in 6.6% of newborns. For all CHD, 44.4% had varying degrees of murmurs. A murmur of grade ≥2 used as a reference standard for major CHD had a sensitivity of 89.58%. The false positive rate of murmurs of grade ≥2 for detecting major CHD was significantly negatively related to auscultation time, with 84.4% of false positives requiring follow-up for non-major CHD cardiac issues. Auscultation after 27 hours of life could reduce the false positive rate of major CHD from 2.7 to 0.9%. *Conclusions:* With appropriate training, maternity hospital's paediatricians can detect major CHD with high detection rates with an acceptable false positive rate.

Introduction

Pulse oximetry (POX) has been confirmed as an effective and reliable screening method for critical congenital heart disease (CCHD) in newborns.[1–4] A number of developed countries have enacted recommendations to use POX as a screening tool for newborns.[5,6] While we are committed to improving the detection rate of CCHD through POX, it is imperative that we understand that there are still many simple major CHD patients (e.g. those with large septal defects, defined as defects that require intervention in the first year of life) in developing countries who are not diagnosed in a timely fashion due to insufficiencies in training of clinicians with regards to auscultation, thus leading to Eisenmenger syndrome or heart failure.[7–11] Thus, the importance of cardiac auscultation should be emphasised, highlighting the need to improve the ability of paediatricians to accurately discern a heart murmur. This not only decreases the need for unnecessary echocardiographic studies, but can ensure that major CHD can be detected during the neonatal period as many as possible. However, it may be difficult even for experienced paediatric cardiologists to accurately distinguish an innocent murmur from a pathologic one in the early neonatal period.[12–17] Targeting the same study population as that of our previous multicenter pilot study in 2011,[2] we evaluated the accuracy of cardiac auscultation by general paediatricians. It also provides a reference for the understanding of neonatal murmurs in the maternity hospital setting.

Methods

Study design and participants

Five general paediatricians from three secondary maternity facilities participated in the study (three from Songjiang Maternity Hospital, one from Minhang Maternity Hospital, and one from Songjiang District Central Hospital). These paediatricians had between 3 and 15 years of paediatric clinical experience. Resource allocation and the number of annual births at these three hospitals are typical of most maternity facilities in China.

We conducted a prospective study at three hospitals. All deliveries of asymptomatic newborns during this period, with the exception of those who were diagnosed with CHD prenatally, underwent cardiac auscultation, POX measurement, and echocardiography. We made a data collection plan before we started to recruit study participants at all sites.

This study was approved by the Ethics Committee of the Children's Hospital of Fudan University (CHFU). Verbal informed consent was obtained from parents of participating newborns.

Procedures

Cardiac auscultation. Prior to the study, five paediatricians simultaneously underwent simple cardiac auscultation simulation training at CHFU. Training tools included audio files of normal heart sounds, standard murmurs from common CHD, and of different intensity heart murmurs, as well as a newborn manikin labelled with standard auscultation sites. The character and phase of the murmur was also introduced in the training but were not used as criteria for judgement in the study. The objectives of training were to discern the presence or absence of the murmur, the intensity of the murmur, and to identify standard auscultatory sites. During the study, a standard paediatric stethoscope (Jiangsu Yuwell Medical, Nanjing, China), the most common model used in community hospitals, was used. Auscultation took place in five auscultation areas (pulmonic, aorta, Erb's point, tricuspid, and mitral) for each newborn under typical conditions of the general maternity ward. It was imperative for the newborn to be quiet during auscultation, and that duration of auscultation be no less than 20 seconds. After auscultation, the grade of murmur was recorded as follows: 0 for no murmur; 1 for barely discernable murmur; 2 for soft but easily noticeable murmur; and ≥3 for murmurs that are noticeably loud or those with thrill. Five doctors auscultated and carried out POX measurements in their respective hospitals for all asymptomatic newborn infants during the study period.

Echocardiographic diagnosis. The first author, a paediatric cardiologist with 5 years' experience in paediatric echocardiography, visited each of the study sites daily and carried out echocardiographic scans for each participant. Auscultation of each asymptomatic participant occurred only after the first author was on site. All echocardiographic scans were completed at the bedside with a Vivid Q Ultrasound Machine, ensuring echocardiography was completed within 1 hour of cardiac auscultation. The paediatric cardiologist was blinded to auscultatory findings of the infant.

Determination of CHD and severity. The following conditions were not included in the scope of CHD: (1) patent ductus arteriosus (PDA) which spontaneously closed within 3 months; (2) atrial septal defect (ASD) <5 mm diameter after 3 months; (3) physiological pulmonary branch stenosis which had resolved at follow-up; (4) Pulmonary stenosis (PS) or aortic stenosis (AS) with pressure gradient of <20 mmHg with no further deterioration during follow-up; (5) simple patent foramen ovale (PFO). The main outcomes analysed for this study were major CHD, including all cyanotic heart disease and other acyanotic lesions determined to require intervention during infancy (e.g. atrioventricular septal defect, large VSD, large PDA, large ASD, severe PS, and critical coarctation). All CHD were followed up with repeat echocardiography at 3 months, 6 months, 1 year, and 2 years to confirm severity. For those that were unable to be followed up at CHFU, parents were contacted by telephone to gain an understanding of echocardiographic findings from other institutions and for presence of CHD symptoms and whether interventions had been carried out.

Table 1. The prevalence of CHD and each specific CHD subtype by severity

Predominant Defect	All CHD No. (%)	All CHD Prevalence (‰)	Major CHD No. (%)	Major CHD Prevalence (‰)
Ventricular septal defect	113	16.7	30	4.4
Perimembranous	35	5.2	23	3.4
Muscular	72	10.7	1	0
Subarterial†	6	0.9	6	0.9
Atrial septal defect	40	5.9	2	0.3
Patent ductus arteriosus	11	1.6	4	1
Pulmonary stenosis	5	0.7	2	0
Tetralogy of fallot	2	0.3	2	0
Single ventricle	2	0.3	2	0
Pulmonary atresia	1	0.1	1	0
Transposition of the great arteries	1	0.1	1	0
Atrioventricular septal defect	2	0.3	2	0
Double outlet right ventricle	2	0.3	2	0
Coronary fistula	1	0.1	0	0
Total	180	26.7	48	7.1

†Three newborns were diagnosed as subarterial ventricular septal defect combined with coarctation of the aorta.

Statistical analysis

Sample size calculations were explained in the previous study[2]: On the basis of a prevalence of CHD of eight per 1000 livebirths (and assuming a 50% sensitivity and 90% specificity of routine clinical assessment), and with a sample size of 6700 (including 54 cases of CHD), the study had 99% power to prove the sensitivity was at least 80% with a two-sided test with type-I error of 5%. The sample size needed to detect a 5% increase in specificity from 90% was 552 on the basis of a two-sided test with type-I error of 5% (99% power).

The sensitivity, specificity, and positive and negative predictive values were calculated for different murmur grades. The Wilson method was used to calculate the 95% CI of sensitivity and specificity. Spearman's correlation analysis was used to evaluate the relationship between the FPR from the murmur and auscultation time in 1-hour increments. Using false positive and true negative murmur findings from raw data during each auscultation time in 1-hour increments, the optimal auscultation time for minimising false positives was derived from the ROC curve. $P<0.05$ was considered statistically significant.

Results

A total of 6785 newborns were born in the three participating hospitals during the study period, of which 6750 were asymptomatic at the time of clinical assessment and included in the study. Median age at auscultation was 43 hours (2–97 hours). A total of 180 infants were diagnosed with CHD (incidence rate of 26.7‰), of which 48(0.71%)were classified as major CHD. The types and incidence of CHD are shown in Table 1.

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Table 2. Accuracy of cardiac murmurs for detection of major CHD in asymptomatic newborn babies

	Grade ≥1	Grade ≥2	Grade ≥3
True positives	43	43	40
False negatives	5	5	8
False positives	402	181	21
True negatives	6300	6521	6681
False positive rate	6.00	2.70	0.31
Sensitivity (%)	89.58 (77.83–95.47)	89.58 (77.83–95.47)	83.33 (70.42–91.30)
Specificity (%)	94.00 (93.41–94.55)	97.3 (96.88–97.66)	99.69 (99.52–99.79)
Positive predictive value (%)	9.66 (7.25–12.76)	19.20 (14.58–24.86)	65.57 (53.05–76.25)
Negative predictive value (%)	99.92 (99.81–99.97)	99.92 (99.82–99.97)	99.88 (99.76–99.94)
Positive likelihood ratio	14.94 (14.78–15.09)	33.17 (32.64–33.71)	266 (239.9–294.8)
Negative likelihood ratio	0.11 (0.07–0.16)	0.11 (0.07–0.16)	0.17 (0.13–0.21)
Odds ratio	134.8 (53.09–342.1)	309.8 (121.3–791.4)	1591 (665.3–3803)

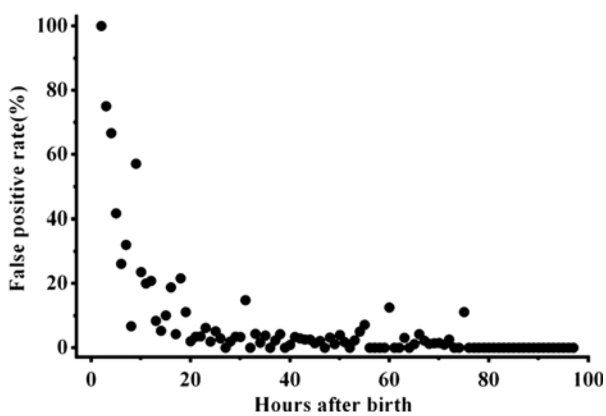

Figure 1. The relationship between the false positive rate and auscultation time in major CHD with murmurs of grade ≥2.

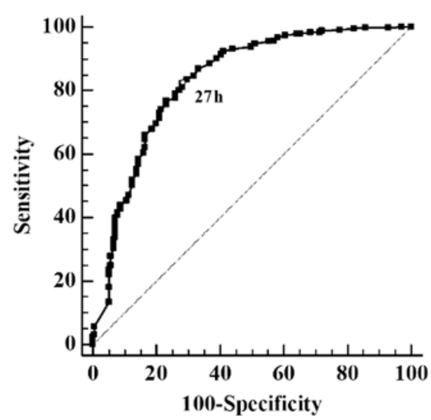

Figure 2. The ROC curve predicting a time when the probability of false positives in major CHD is significantly reduced for murmurs of grade ≥2.

Cardiac murmurs were identified in 6.6% (445/6750) of newborns, of which 49.7% (221/445) were grade 1, 36.6% (163/445) were grade 2, and 13.7% (61/445) were grade ≥3. For all CHD, 44.4% (80/180) had varying degrees of murmurs, 39.1% (70/180) were grade ≥2 and 28.3% (51/180) were grade ≥3. For major CHD, 89.6% (43/48) had varying degrees of murmurs, all of which were grade ≥2. The diagnostic accuracy of murmurs of different grades for detecting major CHD are shown in Table 2.

Murmurs of grade ≥2 had higher diagnostic accuracy in detecting major CHD than grade ≥1 and ≥3. This is despite the difference being statistically insignificant to murmurs of grade ≥3 (AUC 0.932 versus 0.917, Z = 0.800, P = 0.424), but significantly greater than murmurs of grade ≥1 (AUC 0.932 versus 0.916, Z = 13.258, P<0.0001). The overall FPR of murmurs of grade ≥2 in screening for major CHD was 2.7% (180/6702), and was significantly negatively related to auscultation time (in 1-hour increments) (Spearman R = −0.78, P<0.0001) (Fig 1). The ROC curve (Fig 2) identified the best time period for predicting true negatives (i.e. the probability of a false positive being significantly reduced) was ≥27h (AUC = 0.832, sensitivity 82.27%, specificity 71.94%). Screening in this time period can decrease the FPR to 0.9% (51/5390), indicating murmurs of grade ≥2 at ≥27 hours of life may be used as a standard in detecting major CHD by auscultation.

With major CHD as a screening target, there were 181 false positive cases (Table 3), of which, 24 (13.3%) were non-major CHD. Though 132 (72.9%) were not categorised as CHD, they were cardiac conditions that required regular follow-up. Only 25 (15.6%) were simple PFO cases. In the five false negative cases, three cases of complex CHD could be detected by POX; one simple and one complex CHD case were missed by POX.

Discussion

Due to the challenges in recognising neonatal murmurs and the lack of standard guidelines, even at tertiary hospitals, heart auscultations may produce a number of false positive results which can cause unnecessary parental anxiety and a waste of healthcare resources. Conversely, many doctors in remote areas may be lacking in the understanding of murmurs. This, compounded with the absence of a comprehensive follow-up system for neonates, can result in many children with simple CHD not presenting until there are symptoms of cardiac insufficiency.[10,18] There has been no previous report on the accuracy of cardiac auscultation by general paediatricians in the Chinese maternity hospital setting. This study shows that general paediatricians have a high detection

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Table 3. False positive and false negative cases of major CHD with murmur of grade ≥2

Echocardiography findings	Cases	Notes
False positive cases		
PDA	95	3 cases were non-major CHD (no spontaneous closure after 3 months)
Interatrial communications	30	10 cases were non-major CHD (diameter >5 mm after 3 months)
PFO	25	Met PFO morphology criteria
VSD	9	2 cases were perimenbranous, 7 cases were muscular
Tricuspid regurgitation	9	Moderate to severe
Increased pulmonary artery flow rate	8	2 cases were non-major CHD (anatomical stenosis in pulmonary valve with flow rate >3 m/s during follow-up)
Increased aortic valve flow rate	3	No obvious anatomical stenosis, flow rate 1.8–2.2 m/s
Mitral regurgitation	2	Moderate
False negative cases		
Complete atrioventricular septal defect	2	1 case was detected with POX screening, 1 case was missed with POX+auscultation
VSD (doubly committed subarterial)	1	Missed by POX+ausculation
Double outlet right ventricle	1	Detected with POX screening
Single ventricle (double inlet left ventricle)	1	Detected with POX screening

rate and acceptable false positive rate for major CHD through cardiac auscultation.

Correlation between cardiac murmurs in the days after birth and their relationship with CHD is rather complex, and results from different studies vary greatly. For example, prevalence of neonatal murmurs ranged from 0.9 to 77.3%, rates of CHD in neonates with murmurs ranging from 32.6 to 84%, and the detection rate of CHD being between 40 and 83%.[12–17,19–22] Our study has the following characteristics: (1) This prospective study has a uniform set of murmur criteria and diagnostic criteria for CHD. (2) All newborns are diagnosed using echocardiography within 1 hour of auscultation, with the number of echocardiographic studies done 15 times greater than previous retrospective studies.[20] (3) Judging only the grade of murmur is more realistic for general paediatricians to carry out. We found that when the median auscultation age was 43 hours, the incidence of all murmurs at grades ≥1, ≥2, and ≥3 was 6.6%, 3.3%, and 0.9%, respectively. 44.4% of all CHD and 89.58% of major CHD had murmurs of varying degrees. Excluding minor CHDs (e.g. small VSD, ASD, and PDA) that spontaneously closed during the 2-year follow-up period, 81.48% (66/81) of CHDs had murmurs of varying degrees.

As the auscultation of neonates is affected by the presence of PDAs, relatively fast heart and respiratory rates, and increased peripheral blood flow, pathological murmurs are more difficult to discern as compared to those in older children and adults. The skills held by paediatricians at maternity hospitals in different countries and regions also vary. It is a challenge to require each doctor to determine whether murmurs are significant through its location, timing, and characteristics in most maternity hospitals that have 20–40 deliveries per day, while paediatricians are relatively scarce.[23] Our study found that murmurs of grade ≥2 can be used as a criterion for major CHD with a sensitivity of 89.58%. For asymptomatic newborns, confirmation of murmurs is recommended after 27h of life, which can reduce the FPR of major CHD to 0.9%. Moreover, with major CHD as the screening target,84.4% of "false positives" found with murmurs of grade ≥2 were not completely normal, and included mild CHD, valvular regurgitation, and increased flow rates. It is necessary to identify these infants through auscultation and carry out regular follow-up with echocardiography. We also found that although only 16.7% (8/48) of major CHD were detected by POX, which was because most CHD were large septal defects without hypoxemia, POX can detect 60% (3/5) of false negatives produced by cardiac auscultation alone (Table 3). These missed cyanotic CHD may need earlier intervention. POX plus cardiac auscultation can increase the detection rate of major CHD to 95.8% (46/48).

This study also has some limitations. First, although performing echocardiography for 6750 continuous births is a huge workload, the overall incidence of cyanotic CHD is not particularly high (10 cases in our study), this study can only demonstrate that auscultation has a relatively high sensitivity for major CHD (because most major CHD are still classified as simple large septal defects). For some critical CHDs, such as pulmonary atresia, truncus arteriosus, single ventricle, and critical coarctation of aorta, the value of auscultation may be lower. Secondly, because of the prospective nature of this study, the reason behind the high sensitivity level of detecting murmurs is somewhat attributable to our emphasis on cardiac auscultation. However, data on the accuracy of detecting murmurs by untrained general paediatricians from Chinese maternity hospitals were absent. Third, since the study population was asymptomatic newborns in the maternity hospital setting (generally 1-3 days after birth), it was infeasible to compare the accuracy of cardiac auscultation by paediatric cardiologists in this population.

Conclusion

Cardiac auscultation is as important as POX in detecting major neonatal CHD. The presence of murmurs of grade ≥2 at ≥27 h of life for detecting major CHD by auscultation by general paediatricians has high sensitivity with an acceptable false positive rate.

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Conflict of Interest. None.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in

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2008, and was approved by the Ethics Committee of the Children's Hospital of Fudan University.

References

1. Hu XJ, Ma XJ, Zhao QM, et al. Pulse oximetry and auscultation for congenital heart disease detection. Pediatrics 2017; 140: e20171154.
2. Zhao QM, Ma XJ, Ge XL, et al. Pulse oximetry with clinical assessment to screen for congenital heart disease in neonates in China: a prospective study. Lancet 2014; 384: 747–754.
3. Ewer AK, Middleton LJ, Furmston AT, et al. Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study. Lancet 2011; 378: 785–794.
4. de-Wahl Granelli A, Wennergren M, Sandberg K, et al. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39, 821 newborns. BMJ 2009; 338: a3037.
5. de-Wahl Granelli A, Meberg A, Ojala T, Steensberg J, Oskarsson G, Mellander M. Nordic pulse oximetry screening–implementation status and proposal for uniform guidelines. Acta Paediatr 2014; 103: 1136–1142.
6. Singh A, Ewer AK. Pulse oximetry screening for critical congenital heart defects: a UK national survey. Lancet 2013; 381: 535.
7. Saxena A. Pediatric cardiac care in India: current status and the way forward. Future Cardiol 2018; 14: 1–4.
8. Reichert HA, Rath TE. Cardiac surgery in developing countries. J Extra Corpor Technol 2017; 49: 98–106.
9. Iyer PU, Moreno GE, Fernando Caneo L, Faiz T, Shekerdemian LS, Lyer KS. Management of late presentation congenital heart disease. Cardiol Young 2017; 27: S31–S39.
10. Ho TC, Ouyang H, Lu Y, Young AH, Chintala K, Detrano RC. Postprocedural outcomes of rural children undergoing correction of congenital heart lesions in Yunnan Province, China. Pediatr Cardiol 2011; 32: 811–814.
11. Saxena A. Congenital cardiac surgery in the less privileged regions of the world. Expert Rev Cardiovasc Ther 2009; 7: 1621–1629.
12. Shenvi A, Kapur J, Rasiah SV. Management of asymptomatic cardiac murmurs in term neonates. Pediatr Cardiol 2013; 34: 1438–1446.
13. Mackie AS, Jutras LC, Dancea AB, Rohicek CV, Platt R, Beland MJ. Can cardiologists distinguish innocent from pathologic murmurs in neonates? J Pediatr 2009; 154: 50–4 e1.
14. Karatza AA, Fouzas S, Tzifas S, Mermiga A, Dimitriou G, Mantagos S. Accuracy of cardiac auscultation in asymptomatic neonates with heart murmurs: comparison between pediatric trainees and neonatologists. Pediatr Cardiol 2011;32: 473–477.
15. Gokmen Z, Tunaoglu FS, Kula S, Ergenekon E, Ozkiraz S, Olgunturk R. Comparison of initial evaluation of neonatal heart murmurs by pediatrician and pediatric cardiologist. J Matern Fetal Neonatal Med 2009; 22: 1086–1091.
16. Azhar AS, Habib HS. Accuracy of the initial evaluation of heart murmurs in neonates: do we need an echocardiogram? Pediatr Cardiol 2006; 27: 234–237.
17. Brunetti ND, Rosania S, D'Antuono C, et al. Diagnostic accuracy of heart murmur in newborns with suspected congenital heart disease. J Cardiovasc Med 2015; 16: 556–561.
18. Hu Z, Yuan X, Rao K, Zheng Z, Hu S. National trend in congenital heart disease mortality in China during 2003 to 2010: a population-based study. J Thorac Cardiovasc Surg 2014; 148: 596–602 e1.
19. Ainsworth S, Wyllie JP, Wren C. Prevalence and clinical significance of cardiac murmurs in neonates. Arch Dis Child Fetal Neonatal Ed 1999; 80: F43–F45.
20. Du ZD, Roguin N, Barak M. Clinical and echocardiographic evaluation of neonates with heart murmurs. Acta Paediatr 1997; 86: 752–756.
21. Singh A, Desai T, Miller P, Rasiah SV. Benefits of predischarge echocardiography service for postnatal heart murmurs. Acta Paediatr 2012; 101: e333–e336.
22. O'Reilly KM, Hall FM, Richens T, Cunningham C, Simpson JH. An audit of the management of heart murmurs on the postnatal wards. Scott Med J 2013; 58: e11–e14.
23. Xu W, Zhang SC. Chinese pediatricians face a crisis: should they stay or leave? Pediatrics 2014; 134: 1045–1047.

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