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Original article

Echocardiographic screening for congenital heart disease in 8819 children: A report from local community events for children's healthcare

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ABSTRACT

Background: We had the opportunity to perform echocardiographic screening of children at local community events for children's healthcare sponsored by the prefectural government. The aim of this study was to assess the utility of echocardiographic screening by measuring the prevalence of congenital heart disease (CHD) and abnormal findings in children without history of diagnosed CHD.
Methods: Subjects consisted of 8819 infants and preschool children (1 month to 6 years) who underwent echocardiographic examination at public events from 2001 to 2013. Children with known CHD were excluded.
Results: We performed echocardiographic screening on 752 (range: 464–993) children at each event. At a total of 12 events, subjects consisted of 3175 infants less than one year (36%), 2292 one-year-olds (26%), 1058 two-year-olds (12%), 794 three-year-olds (9%), and other children up to age six years. We identified echocardiographic abnormalities in 137 children (15.5/1000 subjects), and 89 children (10.1/1000 subjects) were diagnosed with CHD. The prevalence of an echocardiographic abnormality did not change over the 12-year period (Kendall's tau = −0.272, $p = 0.19$).
Conclusions: CHD which could not be identified by prenatal echocardiography and neonatal auscultation could be detected in a substantial number of young children by echocardiographic screening. Echocardiographic screening may be useful for early diagnosis of CHD. However, our study is based on cross-sectional data without follow-up. Larger prospective studies are needed to verify the utility of echocardiographic screening with follow-up data in this cohort.

Introduction

Congenital heart disease (CHD) forms the largest group of congenital malformations [1]. Many prevalence studies of CHD showed a wide range of incidences, from about 4 to 50 per 1000 subjects [2–8]. Reasons for the wide range of CHD prevalence included differing diagnostic tools used in each study, population, region, age, and observation period. Most previous studies assessed the prevalence of CHD in a hospital.

In Japan, prenatal echocardiography has been performed for early prenatal diagnosis of major CHD. After that, cardiac screening of neonates and infants is usually performed by auscultation. Medical check-ups in young children are required at 3–4 months, 18 months, and 3 years after birth in Japan, and the compliance rate for undergoing the health examinations is 92–95% (reports from Ministry of Health, Labour and Welfare, Japan). Even with the high rate of these physical examinations, CHD can be diagnosed initially in school age children or adulthood, sometimes in an advanced stage. Prenatal echocardiographic images can be technically difficult to obtain because of the small and narrow window. Screening echocardiography may provide additional information in children who could not be identified by prenatal echocardiography and neonatal auscultation.

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We had the opportunity to perform echocardiographic screening for infants and preschool children in annual community events sponsored by the Tokushima prefectural government. The aim of this study was to assess the utility of echocardiographic screening by measuring the prevalence of CHD in children without history of diagnosed CHD.

Methods

Study population

A cohort screening study was conducted from the data collected in community healthcare events for children named "Ogyatto 21 Tokushima" between 2001 and 2013, which was organized by the Hagukumi Tokushima Foundation, partially sponsored by the Tokushima prefectural government (Fig. 1). This community event began in May 2001 aiming to improve the health and well being of infants and preschool children (≤6 years). The event occurred 2 days in every year except 2009, when there was a novel influenza epidemic. The health event was free for everyone to attend. A section of echocardiographic examination was held in conjunction with this event. Children previously diagnosed with any CHD, according to the medical interview, were excluded. In this cohort, the data obtained from the records included age, gender, and clinical diagnosis. This prefecture has a population of about 0.78 million people, and the average number of neonates born in 2012 was 7.4 per 1000.

Echocardiographic assessment

The echocardiographic examinations were performed with either the Toshiba Aplio (Toshiba Medical Systems Inc., Tochigi, Japan) or the GE Vivid 7 or E9 (General Electric Medical Systems, Milwaukee, WI, USA) with a 7-MHz transducer. The examination protocol included two-dimensional and color Doppler imaging from the parasternal, suprasternal, subxiphoid, apical, and, when necessary, modified views. CHD is defined as a structural abnormality of the heart or intra-thoracic great vessels with functional significance or which has the potential to be significant [9]. We defined other abnormalities as a valve regurgitation, valve prolapse, coronary sinus dilatation, arrhythmia, left ventricular (LV) hypertrophy, LV dilatation, and septal aneurysm. Atrial septal defect (ASD) is assumed when the left atrial (LA) to right atrial (RA) shunt flow is recognized, with a defect size more than 3 mm. Patent ductus arteriosus (PDA) and ventricular septal defect (VSD) are assumed when there is left to right shunt flow in the pulmonary artery and right ventricle. Significant valve stenosis was defined as the peak systolic velocity more than 2.5 m/s, and significant valve regurgitation was defined as more than mild grade in mitral and tricuspid regurgitation, equal to or more than mild grade in aortic regurgitation. Each echocardiographic examination was performed by experienced sonographers certified as Japanese Registered Medical Sonographers. After the echocardiographic examination, a pediatric cardiologist reviewed the images and confirmed the diagnosis, and a short medical interview was done on site. Sedation was not required for any case. The mean time required for the echocardiographic examination was 2 min.

Statistical analysis

Data are presented as mean ± SD. The prevalence of CHD was based on the number of CHD cases divided by the total number of children who came to the events. The Chi-square test was used to compare differences between the rates, and the Student's *t*-test was used to compare differences between the means. To eliminate the impact of non-normal distribution, we correlated the prevalence of echocardiographic abnormality, the age distribution, and time using the Kendall tau rank correlation coefficient. A *p*-value of <0.05 was

Fig. 1. Snapshots from the community event "Ogyatto 21 Tokushima" for children's healthcare in Tokushima Prefecture. (A) Overview of the community event. The number of visitors was around 9000. (B) Echocardiographic examination was performed by experienced licensed sonographers certified as Japanese Registered Diagnostic Cardiovascular Sonographers. (C) A pediatric cardiologist reviewed the images and confirmed the diagnosis. A short medical interview was done on the site.

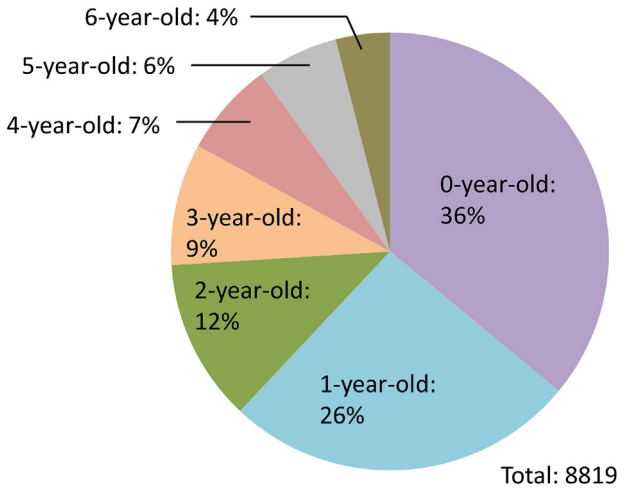

Fig. 2. Age distribution of the screening cohort. Subjects consisted of 3175 infants aged less than one year (36%), 2292 one-year-olds (26%), 1058 two-year-olds (12%), 794 three-year-olds (9%), and other children up to age 6 years (17%).

considered to be significant. Statistical analysis was performed using SPSS statistical package version 20.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 8819 children with no history of diagnosed CHD had a screening echocardiography between 2001 and 2013, with the exception of 2009. There was no overlap of participants in each yearly event due to the prior notification that this echocardiogram should be done only for children without CHD history. We have also excluded children who previously underwent screening echocardiography by an interview. Of a total of 12 events, subjects consisted of 3175 infants less than one year (36%), 2292 one-year-olds (26%), 1058 two-year-olds (12%), 794 three-year-olds (9%), and other children up to age 6 years (17%) (Fig. 2). The age range was between 0 and 6 years with a median age of 1.6 years.

In all subjects at 12 events, we performed echocardiographic screening on 752 (range: 464–993) children at each event. We identified an echocardiographic abnormality in 137 children (15.53 per 1000 subjects). The prevalence of echocardiographic abnormality did not significantly change over the 12-year period (Kendall's tau = −0.272, $p = 0.19$, Fig. 3). Table 1 shows the age distribution in each year in the most recent 5 years. There is no trend in the changes of age distribution.

Eighty-nine children (10.1/1000 subjects) were diagnosed with CHD, which included 31 ASD (22.5%, 3.52 per 1000 subjects), 21 PDA (15.2%, 2.38 per 1000 subjects), 8 VSD (5.8%, 0.91 per 1000 subjects), 8 pulmonary artery stenosis (5.8%, 0.91 per 1000 subjects), and 7 pulmonary valve stenosis (5.1% and 0.79 per 1000 subjects) (Table 2). The prevalence of CHD in children less than one year was higher than in 1- to 6-year-olds ($p < 0.001$, Fig. 4). An example of a serious case was a one-month-old boy with Bland-White-Garland syndrome which was detected by significant mitral regurgitation and severe left ventricular dysfunction. It was the most serious case in this study, and he was admitted to a hospital the next day for treatment. In addition, clinical follow-up was available in 19 patients (61%) with ASD and 6 patients (29%) with PDA at Tokushima Municipal Hospital. At the time of follow up, 6 patients with ASD and 3 patients with PDA were transferred

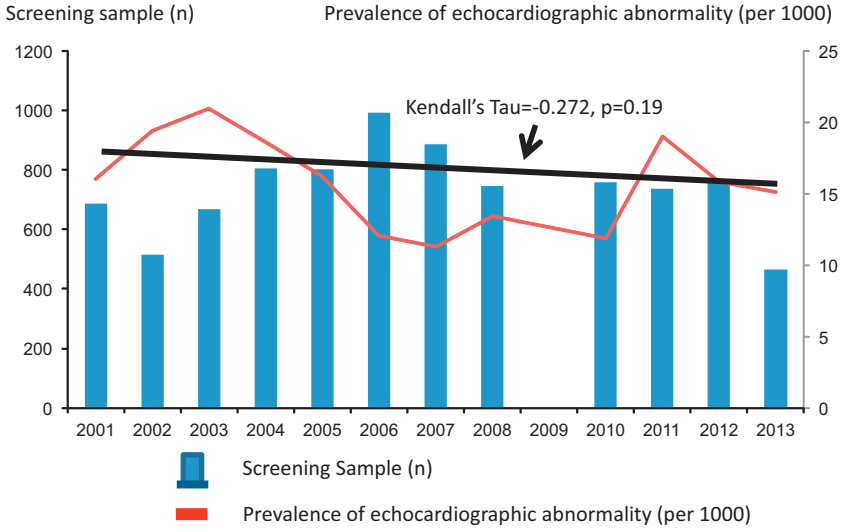

Fig. 3. The number of screening samples and prevalence of echocardiographic abnormalities in each year. There was no trend between the prevalence and time ($p = 0.19$).

Table 1
Age distribution in the most recent 5 years.

Year	<1 y.o. (%)	1 y.o. (%)	2 y.o. (%)	3 y.o. (%)	4 y.o. (%)	5 y.o. (%)	6 y.o. (%)
2008	41.2	20.8	11.4	6.4	7.0	7.1	6.1
2010	36.4	20.2	13.2	9.6	7.4	7.9	5.3
2011	37.8	23.8	12.8	7.1	7.5	5.8	5.2
2012	34.2	23.2	12.9	9.5	6.6	6.6	7.0
2013	37.9	24.8	13.1	8.0	6.9	5.2	4.1
p-value for the trend	0.46	0.22	0.46	0.81	0.46	0.09	0.22

y.o., year(s) old.

Table 2
Number of children with congenital heart disease or other abnormalities.

	n	%	Prevalence/1000	Hoffman & Kaplan* Prevalence IQR
Congenital heart disease				
Atrial septal defect	31	22.5	3.52	0.37–1.06
Patent ductus arteriosus	21	15.2	2.38	0.4–0.8
Ventricular septal defect	8	5.8	0.91	1.76–4.48
Pulmonary stenosis	8	5.8	0.91	0.76–1.47
Pulmonary valve stenosis	7	5.1	0.79	0.36–0.84
Aortic bicuspid valve	5	3.6	0.57	5.34–13.8
Quadricuspid valve	2	1.4	0.23	–
Bland-White-Garland syndrome	1	0.7	0.11	–
Coronary-pulmonary artery fistulae	2	1.4	0.23	–
AVSD	1	0.7	0.11	0.24–0.40
Left ventricular-right atrial communication	1	0.7	0.11	–
Supravalvular aortic stenosis	1	0.7	0.11	0.16–0.39
Cor triatriatum	1	0.7	0.11	–
Sub total	89	67.2	10.10	
Other abnormality				
Mitral prolapse	5	3.6	0.57	–
Mitral regurgitation	3	2.1	0.34	
Aortic regurgitation	9	6.6	1.02	–
Tricuspid regurgitation	6	4.3	0.68	–
Coronary sinus dilatation	7	6.6	1.02	
Arrhythmia (VPC)	5	3.6	0.57	–
LV hypertrophy	4	2.9	0.45	–
Atrium septal aneurysm	4	2.6	0.45	–
Ventricular septal aneurysm	3	2.1	0.34	–
Dextrocardia (inverted normal)	1	0.7	0.11	
LV dilatation	1	0.7	0.11	–
Sub total	48	32.8	5.44	
Total	137	100	15.54	

IQR, interquartile range; LV, left ventricular; AVSD, atrioventricular septal defects; VPC, ventricular premature contraction.
* Adapted from Hoffman and Kaplan [3].

to the surgical section. Therefore, screening echocardiography had a role in detecting serious CHD compared with only a physical examination due to the short time required for this echocardiographic examination (the mean time was 2 min).

Discussion

This is the first report evaluating the prevalence of CHD using echocardiographic screening in a large number of children without history of diagnosed CHD in Japan. Our main findings are as follows. 1) Several echocardiographic abnormalities were detected in 137 children, and there was no significant time-trend in the prevalence of echocardiographic abnormality from 2001 to 2013. 2) Eighty-nine children (10.1/1000 subjects) were diagnosed with CHD. The most common CHD abnormality was ASD, which occurred in 3.5 per 1000 subjects, followed by PDA (2.4 per 1000) and VSD (1 per 1000). The prevalence of CHD in the less than one-year-old group was higher than that in the older groups.

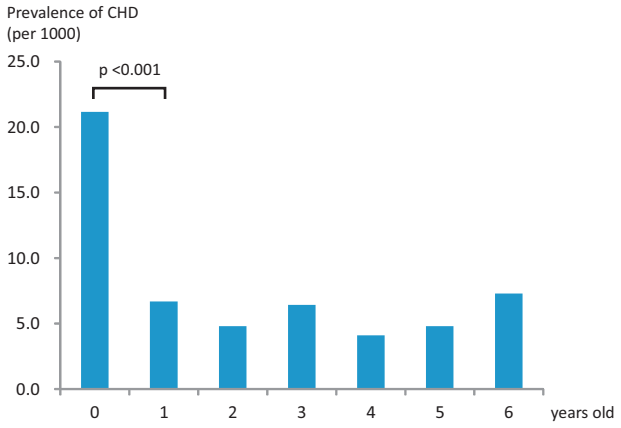

Fig. 4. Comparison of prevalence of congenital heart disease (CHD) between children less than one year and 1-year-olds. There is a significant difference between the two groups ($p < 0.001$).

Recently, prenatal echocardiography has allowed for early detection of CHD and may help to increase the number of incidental findings. However, prenatal echocardiography mainly helps to diagnose severe, major heart anatomical abnormalities, such as tetralogy of Fallot. Therefore, even when prenatal echocardiography is widely used, screening echocardiography in this population has the potential to identify echocardiographic abnormalities in infants and preschool children. From these echocardiographic abnormal cases, we found 68% CHD. Even if we exclude the minor echocardiographic abnormalities, the number of CHD remains large (10.1/1000 subjects).

In our cohort without history of diagnosed CHD, the most common subtype of CHD was ASD, which occurred in 3.5 per 1000 subjects. In addition, we also showed the prevalence of PDA to be 2.4 per 1000 subjects. We were able to detect silent PDA in this screening, which is a tiny arterial duct and is undetected by auscultation [10]. On the other hand, the prevalence of VSD in children without history of diagnosed CHD was 0.91 per 1000 children and relatively small compared with ASD and PDA. One possible explanation is that our cohort was a specific population who could not be identified by prenatal echocardiography and neonatal auscultation. VSD causes a pathognomonic pansystolic murmur. Auscultation is generally considered to be sufficient for detecting a significant VSD.

The prevalence of CHD in the less than one-year-old group was higher than in the older groups. One simple explanation is that we avoid overlap examinations in our cohort. The other possible explanation could be that the some ASD will naturally close before pre-school, and the number may be overestimated [11]. However, in several studies, the wide ranges (4–70%) of spontaneous closure

of ASD were reported [12,13]. In addition, Tortoriello et al. reported that small ASD (defect 3–4 mm) enlarged to 24 mm after 6 years [14]. If the defects remained open, they sometimes may become problematic. In available follow-up data, some patients with ASD or PDA were transferred to the surgical section. Historical cohorts suggest long-term right heart failure, functional decline, arrhythmia, and early death [15]. Our screening may help to detect these subjects who need follow-up echocardiographic examination. We believe that it can serve as an impetus for a properly designed follow-up study.

In addition, we found a serious case of Bland-White-Garland syndrome in this screening. In this case, poor weight gain had been noted, but there was no murmur in the one-month regular screening physical examination. Bland-White-Garland syndrome is a rare congenital coronary artery anomaly and is considered one of the most serious of anomalies. Thus, in spite of the high rate of screening physical examinations in Japan, there is a possibility of missing some diagnoses of severe heart disease. Therefore, echocardiographic screening may help to detect these severe heart defects. Despite expert prenatal echocardiography and auscultation examination, CHD can be found in school age children or adulthood, sometimes in an advanced stage. In children with no history of diagnosed CHD, there is a relatively high prevalence of echocardiographic abnormality (15.7/1000 subjects) and CHD (10.1/1000 subjects) by screening echocardiography.

Our main limitation was that we were unable to obtain detailed characteristics and follow-up data in this cohort. There is no follow-up system in this event. We believe that a follow-up system will be provided in future. This was a community-based transverse study that only included children without history of diagnosed CHD who were taken to this event by their parent. There is a possibility that many of the children had parents with high health awareness. There may be potential selection and referral biases. Despite an otherwise standardized protocol, minor variations in image quality were observed by reporting sonographers and pediatric cardiologists. We may underestimate the prevalence of CHD because of the limited time and views of echocardiography. Some defects (VSD and ASD) we noticed in our study may close naturally in the future and diagnosing them as CHD would be unnecessary at that time; however, we believe it is important to detect such defects that have some possibility to persist and have significant implications when they are older. We did not perform a cost-benefit analysis because of the limited data. Sonographers and physicians joined this event as volunteers, and the echocardiographic machines were freely provided by the vendors. Finally, participants at these events did not include all children in Tokushima city (ex. 2006: participants/all children = 993/2321, 42.8%). We believe larger studies with follow-up data are warranted.

Conclusions

CHD which was not recognized by prenatal echocardiography and neonatal auscultation could be identified in substantial numbers by echocardiographic screening. Echocardiographic screening in infants and preschool children in the community may be useful for early diagnosis of CHD. Because our study is based on a retrospective group without follow-up data, we believe prospective studies with follow-up data are warranted to confirm this result.

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Disclosures

The authors declare that there is no conflict of interest.

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References

[1] Mitchell SC, Korones SB, Berendes HW. Congenital heart disease in 56,109 births. Incidence and natural history. Circulation 1971;43:323–32.
[2] Meberg A, Otterstad JE, Froland G, Lindberg H, Sorland SJ. Outcome of congenital heart defects – a population-based study. Acta Paediatr 2000;89:1344–51.
[3] Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol 2002;39:1890–900.
[4] Wu MH, Chen HC, Lu CW, Wang JK, Huang SC, Huang SK. Prevalence of congenital heart disease at live birth in Taiwan. J Pediatr 2010;156:782–5.
[5] Trigas V, Nagdyman N, Pildner von Steinburg S, Oechslin E, Vogt M, Berger F, Schneider KT, Ewert P, Hess J, Kaemmerer H. Pregnancy-related obstetric and cardiologic problems in women after atrial switch operation for transposition of the great arteries. Circ J 2014;78:443–9.
[6] Mizuno A, Niwa K, Matsuo K, Kawada M, Miyazaki A, Mori Y, Nakanishi N, Ohuchi H, Watanabe M, Yao A, Inai K. Survey of reoperation indications in tetralogy of fallot in Japan. Circ J 2013;77:2942–7.
[7] Ohuchi H, Tanabe Y, Kamiya C, Noritake K, Yasuda K, Miyazaki A, Ikeda T, Yamada O. Cardiopulmonary variables during exercise predict pregnancy outcome in women with congenital heart disease. Circ J 2013;77:470–6.
[8] Akagi T. Catheter intervention for adult patients with congenital heart disease. J Cardiol 2012;60:151–9.
[9] Driscoll D, Allen HD, Atkins DL, Brenner J, Dunnigan A, Franklin W, Gutgesell HP, Herndon P, Shaddy RE, Taubert KA, Zahka K, Garson A, Skorton DJ, Danielson GK. Guidelines for evaluation and management of common congenital cardiac problems in infants, children, and adolescents. A statement for healthcare professionals from the Committee on Congenital Cardiac Defects of the Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 1994;90:2180–8.
[10] McGrath RL, McGuinness GA, Way GL, Wolfe RR, Nora JJ, Simmons MA. The silent ductus arteriosus. J Pediatr 1978;93:110–3.
[11] Saito T, Ohta K, Nakayama Y, Hashida Y, Maeda A, Maruhashi K, Yachie A. Natural history of medium-sized atrial septal defect in pediatric cases. J Cardiol 2012;60:248–51.
[12] Garne E. Atrial and ventricular septal defects – epidemiology and spontaneous closure. J Matern Fetal Neonatal Med 2006;19:271–6.
[13] McMahon CJ, Feltes TF, Fraley JK, Bricker JT, Grifka RG, Tortoriello TA, Blake R, Bezold LI. Natural history of growth of secundum atrial septal defects and implications for transcatheter closure. Heart 2002;87:256–9.
[14] Tortoriello TA, McMahon C, Kovalchin JP, Bricker JT, Grifka RG. Growth of an atrial septal defect: missing the window for transcatheter closure. Pediatr Cardiol 2002;23:542–4.
[15] Campbell M. Natural history of atrial septal defect. Br Heart J 1970;32:820–6.