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# Comparison of Echocardiography and 64-Multislice Spiral Computed Tomography for the Diagnosis of Pediatric Congenital Heart Disease

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Background:** The goals of this study were: to compare echocardiogram and 64-multislice spiral computed tomography (64-MSCT) in diagnosing pediatric congenital heart disease; to determine the significance of ECHO for diagnosing congenital heart disease; and to identify the appropriate diagnosis for congenital heart disease through combined use of 64-MSCT and ECHO.


**Material/Methods:** Thirty patients underwent both ECHO and 64-MSCT diagnoses before their surgeries. Imaging from ECHO and 64-MSCT were analyzed by 4 specialists. The diagnostic accuracy and kappa value of ECHO and 64-MSCT were evaluated based on the operation results. The accuracy of the 2 methods was evaluated using the McNemar  $\chi^2$  test.

**Results:** We confirmed 138 malformations in 30 children by surgery. The diagnostic accuracy of ECHO and 64-MSCT was 98.40% and 96.20%, respectively, with a significant difference between the 2 results ( $\chi^2=6.404$ ,  $P=0.011$ ). We compared prognosis accuracy and uniformity on 3 types of congenital heart disease (cardiac malformation, heart-large vascular connecting malformation, and large vascular malformation): 56 cardiac malformations were confirmed by surgery, in which the diagnostic accuracy of ECHO and 64-MSCT was 99.50% and 94.80%, respectively. ( $\chi^2=8.578$ ,  $P=0.034$ ); 31 heart-large vascular connecting malformations were confirmed by surgery, in which the diagnostic accuracy of ECHO and 64-MSCT was 99.00% and 95.42% ( $\chi^2=6.779$ ,  $P=0.009$ ); and 51 vascular malformations were confirmed, in which the diagnostic accuracy of ECHO and 64-MSCT was 96.30% and 98.30% ( $\chi^2=1.806$ ,  $P=0.179$ ).

**Conclusions:** ECHO is more effective than 64-MSCT in preoperative diagnosis of congenital heart disease, especially for children.

**MeSH Keywords:** **Heart Defects, Congenital • Pediatrics • Tomography, Spiral Computed**

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## Background

Congenital heart disease (CHD) is the most frequent type of congenital birth deficiency disease, with an incidence of 8% among newborns [1]. CHD is caused by many factors, including intrauterine infection, environmental pollution, and inheritable factors [2]. It was reported that the primary cause of mortality from birth defects was related to the structure or function of the heart lesion [3]. The incidence of CHD was reported to be common among older mothers [4]. However, the pathogenesis of the CHD is extremely complex and the association between maternal age and CHD has not been confirmed yet. Acute CHD is hypothesized to be associated with genetics and environmental factors, and the life expectancy of patients has always been short because of the absence of surgical and medical therapies [5]. Fast and accurate diagnosis and timely intervention and therapy of CHD can remarkably improve cardiac function [6], ameliorating the poor prognosis and problems such as neurodevelopment delay [7]. In recent years, prenatal diagnosis of CHD has greatly improved the survival rates of children via decreasing the risk of complications [5,8]. As a consequence, timely and accurate preoperative diagnosis is crucial for both prevention and treatment of CHD. Accordingly, ECHO and 64-MSCT have been widely used in diagnosing CHD [9].

ECHO is the criterion standard and first-line diagnostic technique in diagnosing patients with CHD [10]. For example, fetal echocardiography plays an important role in classifying the CHDs in utero, allowing patients to be classified as having major, minor, or no CHD based on the echocardiographic results. Although echocardiography is mostly applied among high-risk pregnant women, it still is not currently a routine prenatal screening tool [11]. Fetal echocardiography is only based on limited indications, which can result in some CHDs going undetected, thereby increasing risk of early neonatal mortality. MSCT provides detailed, minimally invasive diagnosis and data on coronary artery anatomy in infants, children, and adults with CHD [12–14]. The ongoing advances of MSCT in diagnostic modality include evaluation of aortic disease, pericardial disease, cardiovascular function, and coronary artery plaque imaging. Furthermore, 64-MSCT can be equipped with cardiac defibrillators, pacemakers, and other helpful implants in patients in which ECHO examination may be contraindicated [15]. Use of 64-MSCT improves the limitations of catheter angiography since the acquisition of natural volumetric analysis allows visualization of 3-dimensional spatial images such as the anomalous coronary coursing among the great arteries [16]. However, one of the potential disadvantages of 64-MSCT is the nephrotoxic ionizing radiation [17]. As diagnostic approaches, ECHO and 64-MSCT both have advantages and limitations. Several studies have compared the performance of ECHO and 64-MSCT in coronary artery disease (CAD)

patients as the target population, showing that left ventricular (LV) systolic function assessed by 64-MDST is very comparable to 2-month 2-dimensional (2D) echocardiography (TTE), and LV function is a powerful indicator of CAD [18]. Among CHD subjects, 64-detector CT is also documented to detect unexpected cases [19]. However, few studies have meticulously compared 64-MDST and ECHO in terms of cardiac malformation, malformation in the connecting area between heart and large vascular, and large vascular malformation. Therefore, this study investigated whether ECHO and 64-MSCT have a synergetic effect in CHD diagnosis and evaluated the accuracy of ECHO and 64-MSCT.

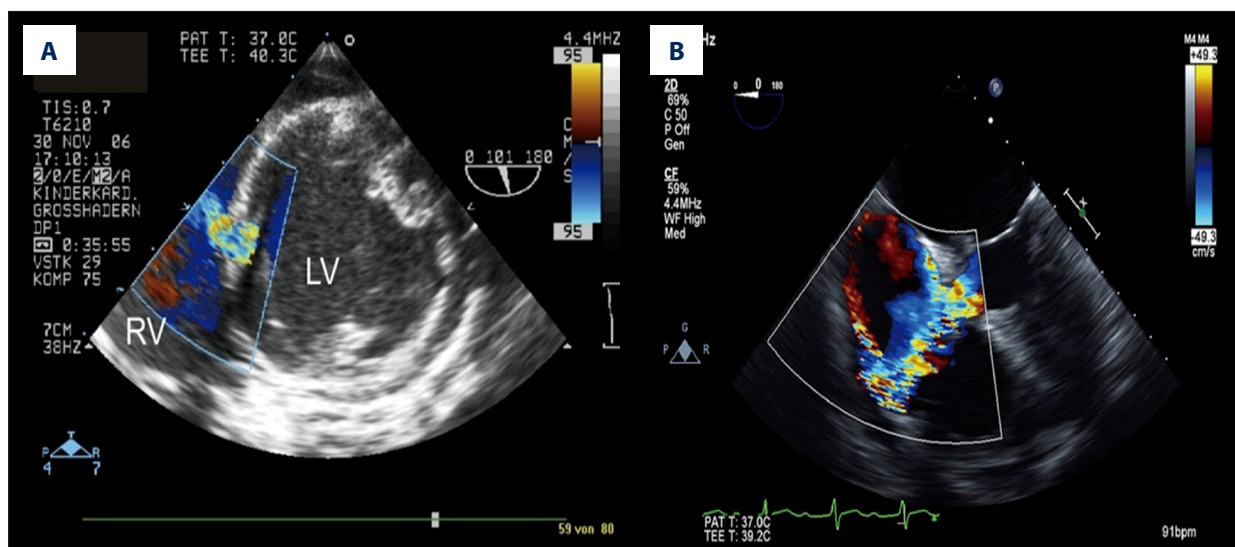
## Material and Methods

### Patients

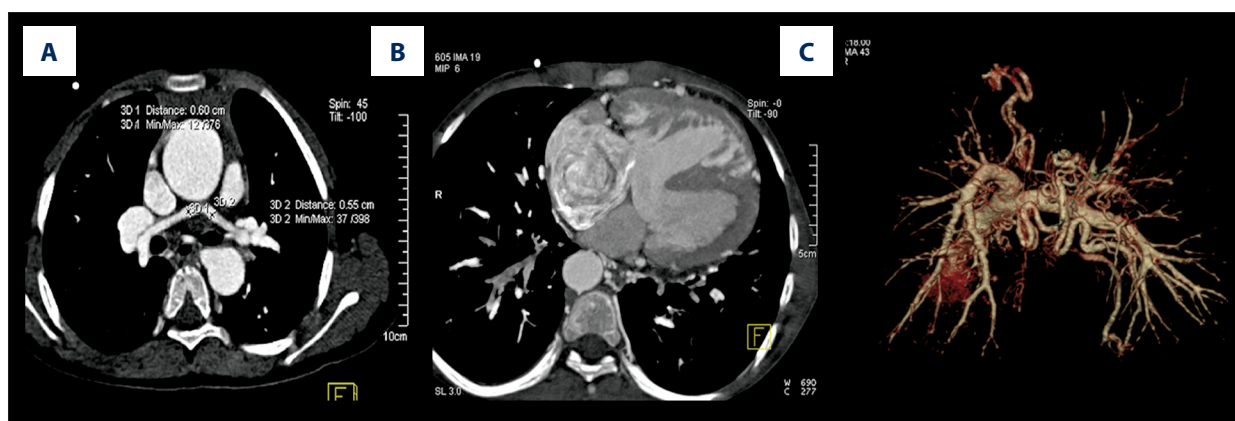
We enrolled 30 children with CHD confirmed by surgery. All of these patients underwent both ECHO and 64-MSCT before the operation. Subjects were excluded if: (1) they were aged more than 5 years old; or (2) they weighed more than 30 kilograms; (3) they suffered from renal disease (more than 150 mmol/L of serum creatinine); (4) they had non-sinus rhythm; or (5) they were allergic to iodinated contrast media [20,21]. The CHD was divided into 3 types – cardiac malformation, heart-large vascular connecting malformation, and large vascular malformation – based on Van Praagh segmental analysis [22]. Cardiac malformation includes atrial septal defect, ventricular septal defect, single atrium, single ventricle, right ventricular outflow tract stenosis, mitral deformity, and tricuspid valve subdisplacement malformation. Malformation in the connecting area between heart and large vascular consists of overriding aorta, complete transposition of the great arteries, aortic valve deformity, pulmonary valve malformation, and double outlet of ventricle. Large vascular malformation comprises aortic root dilatation, aortic coarctation, interruption of aortic arch, and dilation of pulmonary artery.

### ECHO

ECHO was performed using the Diamond Select iE33 Ultrasound system (Philips Medical Systems, Netherlands) [23]. Cardiac functions were measured using multiple imaging modalities, such as biplanar 2D echo, 2D color flow Doppler imaging, and conventional B-mode 2D echo [23]. The procedures of the cardiac acoustic window were strictly followed. ECHO often started with subcostal an acoustic window or subcostal acoustic window, and the major cardiovascular structures were assessed according to Van Praagh segmental analysis [24,25].



**Figure 1.** (A). Mid-muscle ventricular septal defect. Blood flow from the left ventricular outflow tract to the right atrium (LV – left ventricle; RV – right ventricle). (B) Tetralogy of fallot. Blood flow from the left ventricular outflow tract to the right atrium (LV – left ventricle; RV – right ventricle).



**Figure 2.** (A). Pulmonary trunk and pulmonary stenosis. (B) Right ventricular hypertrophy and ventricular septal defect. (C) Pulmonary arteriovenous fistulas and many pulmonary side branches arising from the aorta.

## 64-MSCT

Patients were given oral chloral hydrate solution with a dosage of 50 mg/kg. The 64-MSCT examination was performed by SOMATOM Perspective (Siemens, Germany) [26] with tube voltage of 80-100Kv, tube current of 80-100 mAs (varied during acquisition and according to the weight of the children), pitch of 1.2, and 0.6 mm collimation. A contrast medium dosage was 1.2–2.0 mL/kg (Omnipaque 350 mg/mL) followed by the same volume of saline chaser with an injection rate of 1–1.5 mL/s [27]. Bolus tracking was applied to determine acquisition delay (the ROI was the aortic sinus, trigger-threshold 80 HU). For all patients, the effective thickness was 1 mm and the reconstructive interval was 0.6 mm. For image reconstruction, Kernel B25f was chosen [28]. All the data were transferred to Syngo Multi-Modality Workplace (Siemens,

Germany). We used multi-planar reconstruction (MPR), volume render (VR), and maximum intensity projection (MIP) to process images [29,30].

## Image identification

The ECHO and 64-MSCT images were analyzed by 4 experienced cardiologists with at least 8-year clinical practices. The typical ECHO image for CHD is shown in Figure 1, which consists of mid-muscular ventricular septal defect and tetralogy of Fallot. A typical 64-MSCT image is shown in Figure 2, in which the pulmonary trunk, a periphery pulmonary stenosis, VSD and right ventricular hypertrophy, pulmonary arteriovenous fistulas, and many pulmonary side branches arising from aorta can be seen.

**Table 1.** The baseline characteristics of the study subjects.

Items	All patients		
	Size	Median	Range
Age (years old)	30	5.5	1–13
Sex (male/female)	16/14	—	—
Weight (kg)	30	19.2	6.2–46.1
Height (cm)	30	122	46–177
Heart rate (beats per minute)	30	118	90–152
Blood pressure (mmHg)	30	73	60–86

**Table 2.** The comparison of diagnosis precision between ECHO and 64-MSCT.

Diagnosis	Operation result		$\chi^2$	P value
	+	–		
ECHO	+	133	6.404	0.011
	–	8		
64-MSCT	+	128		
	–	18		

**Table 3.** Comparison details in the diagnosis of congenital heart disease between ECHO and 64-MSCT.

Method	Diagnosis efficiency	Specificity	Positive predictive value	Negative predictive value	AUC	Accuracy	Uniformity
ECHO	93.70%	99.50%	97.80%	98.57%	0.982	98.40%*	0.950*
64-MSCT	94.10%	98.50%	94.12%	96.75%	0.955	96.20%*	

AUC – area under receiver operating characteristic curve; \*  $\chi^2$  test; # Kappa value.

### Statistical analysis

The diagnostic accuracy and kappa value of ECHO and 64-MSCT diagnoses were evaluated based on the operation results. Power calculation was conducted with PASS11 software (NSCC Corporation, USA). GraphPad Prism 6.0 was used to do the statistical analysis. The measurement data are all presented as mean value  $\pm$  standard deviation ( $\bar{x} \pm SD$ ). Kruskal-Wallis test were carried out to compare differences in continuous data among groups. The discrete data were compared using the chi-square test. The accuracy of the 2 methods was evaluated using McNemar  $\chi^2$  test, while the uniformity was evaluated using kappa value. Receiver operating characteristic curve (ROC) analysis was conducted to compare diagnostic area under the ROC (AUC) values of the 2 methods. A  $P < 0.05$  was considered to be statistically significant.

### Results

#### Baseline characteristics of children with CHD

We recruited 30 children in our hospital during January 2014 and March 2015. The comparison was powered after evaluation with PASS11 software. We included 14 males and 16 females. The mean age of the cohort was 6.2 years old, ranging from 4 to 13 years old. The mean body weight was 21.9 kg, and the mean height was 114 cm with a range from 44 to 177 cm. The mean heart rate was 118 beats/min, with a range from 90 to 152 beats/min. The average blood pressure was 73 mmHg (Table 1). Baseline characteristics of this cohort are also shown in Supplementary Table 1.

#### Comparison in the congenital heart disease

As seen in Table 2, 30 patients were recruited. We confirmed 138 malformations by surgery. We detected 697 areas by

ECHO, in which 133 true positives, 553 true negatives, 3 false positives, and 8 false negatives. The diagnostic efficiency was 93.70%, and diagnostic specificity was 99.50%. The results of comparison between ECHO and 64-MSCT revealed that there was a significant difference in diagnostic accuracy between the 2 methods ( $\chi^2=9.538$ ,  $P=0.023$ ). As Table 3 shown, the positive predictive value was 97.80% and negative predictive value was 98.57%. The diagnostic accuracy was 98.40% for ECHO. The AUC value of ECHO was slightly larger than that of 64-MSCT (0.982 vs. 0.955). 64-MSCT detected 690 areas: 128 true positives, 536 true negatives, 8 false positives, and 18 false negatives (Table 2). The diagnostic efficiency, specificity, positive predictive value, and negative predictive values were 94.10%, 98.50%, 94.12%, and 96.75%, respectively, with an accuracy of 96.20%. The 2 methods are consistent with each other in congenital heart disease diagnosis ( $\kappa=0.950$ ).

### Comparison in the cardiac malformation

We confirmed by surgery 56 cardiac malformations. As seen in Table 4, we found that only 1 case with single atrium was underdiagnosed by ECHO, while a total of 7 malformations were underdiagnosed by 64-MSCT, including 1 ventricular septal defect, 2 atrial septal defects, 3 right ventricular outflow tract stenoses, and 1 tricuspid valve subdisplacement malformation. In addition, there were 4 misdiagnosed malformations by 64-MSCT, including 1 atrial septal defect, 2 right ventricular outflow tract stenosis and 1 tricuspid valve subdisplacement malformation. The diagnostic accuracy of ECHO and 64-MSCT were 99.50% and 94.80%, respectively ( $\chi^2=8.578$ ,  $P=0.034$ ) (Table 5). The 2 diagnoses showed high uniformity ( $\kappa=0.987$ ).

### Comparison in the heart-large vascular connecting malformation

We confirmed by surgery 31 heart-large vascular connecting malformations. As seen in Table 4, 1 aortic valve deformity was misdiagnosed, and 1 complete transposition of the great arteries and 1 pulmonary valve malformation of the great arteries were underdiagnosed by ECHO. 64-MSCT misdiagnosed 2 aorta saddles and 1 pulmonary valve malformation, and underdiagnosed 3 aorta saddles, 1 complete transposition of the great arteries, 1 anomaly of aortic valve, and 3 pulmonary valve malformations. The diagnostic accuracy of ECHO and 64-MSCT were 99.00% and 95.40%, respectively ( $\chi^2=6.779$ ,  $P=0.009$ ) (Table 6). The kappa coefficient was 0.955, which suggested that the 2 diagnoses were consistent with each other.

### Comparison in the large vascular malformation

We confirmed 51 large vascular malformations by surgery. As seen in Table 4, 1 interruption of the aortic arch and 1 anomalous inferior vena cava drainage were misdiagnosed. ECHO

underdiagnosed 1 pulmonic stenosis or atresia, 2 patent ducti arteriosus, 1 double superior vena cava, and 1 anomalous inferior vena cava drainage. 64-MSCT misdiagnosed 1 dilation of pulmonary artery, and underdiagnosed 2 pulmonic stenosis or atresia and 1 double superior vena cava. The diagnostic accuracy of ECHO and 64-MSCT were 96.30% and 98.30%, respectively. ECHO and 64-MSCT had no significant difference in diagnosing large vascular malformations ( $\chi^2=1.806$ ,  $P=0.179$ ) (Table 7). ECHO and 64-MSCT showed high uniformity ( $\kappa=0.903$ ).

## Discussion

Based on our results, the diagnostic accuracy of the lesions in the macrovascular structures is different between ECHO and 64-MSCT; ECHO provided higher diagnosis accuracy in the heart and the heart-macrovascular malformations. Thus, we recommend ECHO diagnosis in the case of heart and the heart-macrovascular malformation, whereas 64-MSCT is better for macrovascular malformations.

In our study, we examined 30 patients diagnosed with both ECHO and 64-MSCT. Compared with the criterion standard, we found that the diagnostic efficiency of ECHO and 64-MSCT is 93.70% and 94.10%, respectively; with specificity of 99.50% and 98.50%, respectively; and diagnostic accuracy of 98.40% and 96.20%, respectively. There was a high consistency between ECHO and 64-MSCT diagnoses. ECHO displays 2D images, depending on the experience of technicians to monitor and judge the structure and blood flow of the heart and macrovascular structures [31]. 64-MSCT is mainly used to observe the function of the cardiac ventricular wall and ventricle through electrocardiographically gated layer scanning, and its high scan speed, high resolution, and 3D images significantly facilitate the diagnosis of CHD [31].

In diagnosing the malformation in the heart, our results showed that the diagnosis accuracy of ECHO and 64-MSCT is 99.50% and 94.80% respectively with a significant difference ( $P=0.034$ ). 64-MSCT had 7 underdiagnoses and 4 misdiagnoses, since 64-MSCT could not distinguish small atrial septal that are smaller than 5mm in width. Besides, the static images that 64-MSCT displayed make it difficult to elucidate the structure of cardiac valves or evaluate the dynamic changes precisely. So falsities and misdiagnoses occur when the lesions are at the cardiac valves, in the meantime diagnosing with 64-MSCT [32].

64-MSCT had a higher rate of misdiagnoses in the heart-macrovascular malformation compared with ECHO. Some researchers deemed that 64-MSCT cannot clearly exhibit abnormalities in the heart and macrovascular, and it becomes more complicated when there are artifacts [33].

**Table 4.** Comparison between ECHO and 64-MSCT in the diagnosis of children with congenital heart disease.

Malformation type (surgery results as gold standard)	ECHO			64-MSCT			Malformation	
	Discovery	Mis-diagnosis	Under-diagnosis	Discovery	Mis-diagnosis	Under-diagnosis		
Cardiac malformation	Ventricular septal defect	21	0	0	20	0	1	21
	Atrial septal defect	12	0	0	11	1	2	12
	Single atrium	4	0	1	5	0	0	5
	Single ventricle	6	0	0	6	0	0	6
	Right ventricular outflow tract Stenosis	9	0	0	8	2	3	9
	Tricuspid valve subdisplacement malformation	1	0	0	1	1	1	1
	Mitral deformity	2	0	0	2	0	0	2
	<b>Total</b>	<b>55</b>	<b>0</b>	<b>1</b>	<b>37</b>	<b>4</b>	<b>7</b>	<b>56</b>
Heart-large vascular connecting malformation	Aorta saddle	12	0	0	11	2	3	12
	Complete transposition of the great arteries	3	0	1	3	0	1	4
	Aortic valve deformity	3	1	0	1	0	1	2
	Pulmonary valve malformation	8	0	1	7	1	3	9
	Double outlet of ventricle	4	0	0	4	0	0	4
	<b>Total</b>	<b>30</b>	<b>1</b>	<b>2</b>	<b>18</b>	<b>0</b>	<b>5</b>	<b>31</b>
Large vascular malformation	Aortic root dilatation	4	0	0	4	0	0	4
	Aortic coarctation	5	0	0	5	0	0	5
	Interruption of aortic arch	3	1	0	2	0	0	2
	Dilation of pulmonary artery	2	0	0	3	1	0	2
	Pulmonic stenosis or atresia	20	0	1	19	0	2	21
	Pulmonary artery-aortashare branches	3	0	0	3	0	0	3
	Anomalous pulmonary venous drainage	1	0	0	1	0	0	1
	Patent ductus arteriosus	1	0	2	3	0	0	3
	Double superior vena cava	6	0	1	6	0	1	7
	Anomalous inferior vena cava drainage	2	1	1	2	0	0	2
	Coronary artery dissection variations	1	0	0	1	0	0	1
	<b>Total</b>	<b>48</b>	<b>2</b>	<b>5</b>	<b>36</b>	<b>1</b>	<b>2</b>	<b>51</b>

There is no significant difference in diagnostic accuracy between ECHO and 64-MSCT in the case of macrovascular malformation ( $P=0.1790$ ). However, there were 5 errors made when diagnosing the abnormality in the macrovascular part using

ECHO. ECHO displays a 2D image, which relies on the experience of the technicians. Due to the acoustical window, it becomes more complex for the technicians to diagnose the abnormality in the macrovascular part by ECHO [34]. Although

**Table 5.** The diagnosis analyses of ECHO and 64-MSCT in the cardiac malformations.

	Diagnosis	Operation result		$\chi^2$	P value	Accuracy	Uniformity
		+	-				
ECHO	+	55	0	8.578	0.034	99.50%*	0.987#
	-	1	154				
64-MSCT	+	53	4				
	-	7	153				

\* McNemar  $\chi^2$  test; # Kappa value.

**Table 6.** The diagnosis analyses of ECHO and 64-MSCT in the heart-large vascular connecting malformations.

	Diagnosis	Operation result		$\chi^2$	P value	Accuracy	Uniformity
		+	-				
ECHO	+	30	1	6.779	0.009	99.00%*	0.955#
	-	2	267				
64-MSCT	+	26	3				
	-	8	203				

\* McNemar  $\chi^2$  test; # Kappa value.

**Table 7.** The diagnosis analyses of ECHO and 64-MSCT in the large vascular malformation.

	Diagnosis	Operation result		$\chi^2$	P value	Accuracy	Uniformity
		+	-				
ECHO	+	48	2	1.806	0.179	96.30%	0.903#
	-	5	132				
64-MSCT	+	49	1				
	-	3	187				

\* McNemar  $\chi^2$  test; # Kappa value.

64-MSCT displayed 3D images with high scan speed and high resolution, errors occur in the presence of artifacts when contrast media is used for the abnormal transit [35]. Generally, 64-MSCT may be a better choice than ECHO when diagnosing lesions in the macrovascular part.

One major limitation of this research is the small sample size, and more samples would make the accuracy and specificity of ECHO and 64-MSCT in diagnosing CHD more reliable. As for the operators, skilled technicians were hired to avoid errors and misdiagnoses as much as possible, which makes our results credible. The diagnoses done by professional pediatric cardiologists, which also makes our results convincing.

### Conclusions

In conclusion, errors and misdiagnoses occur when diagnosing the lesions in congenital heart disease with ECHO or 64-MSCT. Overall ECHO had a higher accuracy than 64-MSCT. In addition, ECHO has no radiation, which makes it a better choice for children, who are usually very sensitive it. Taking the diagnostic accuracy and application into consideration, we recommend ECHO when diagnosing, rechecking, and following up the lesion in diagnosis of the heart and the heart-macrovascular malformations, while 64-MSCT is recommended in the diagnosis of macrovascular malformation. Our research could serve as the theoretical basis for making a better choice in use of imaging methods when diagnosing CHD.

## Supplementary Table

**Supplementary Table 1.** Baseline characteristics of cohort.

No.	Age (years)	Sex	Weight (kg)	Height (cm)	Heart rate (beats/min)	Blood pressure (mmHg)
1	13	F	46.1	177	90	75
2	10	M	32.5	138	100	82
3	3	M	12.5	94	138	68
4	4	M	15.9	101	134	75
5	2	F	11.5	90	143	73
6	5	F	18.6	107	126	60
7	7	M	21.8	121	111	70
8	2	M	11.8	87	141	68
9	8	F	25.3	126	106	73
10	6	F	19.6	115	117	76
11	9	M	28.4	132	102	81
12	11	F	35.3	143	96	76
13	12	M	41.5	152	92	73
14	3	F	14.1	91	136	72
15	4	F	16.6	103	132	73
16	6	M	20.5	115	115	72
17	4	F	17.2	101	130	86
18	5	F	17.6	108	124	71
19	1	M	6.2	46	152	75
20	5	F	16.7	107	122	76
21	7	M	22.3	122	109	71
22	10	M	33.1	135	98	75
23	2	M	10.9	80	139	69
24	8	F	26.1	128	104	76
25	6	F	18.8	114	113	77
26	11	M	36.9	144	94	68
27	5	F	20.1	110	119	72
28	4	M	15.3	104	128	69
29	5	M	18.3	109	121	70
30	7	M	24.1	125	107	66

F – female; M – male.



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